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Evidence of reversible addition of carbon-centered radicals to aromatic nuclei

Henschel, Rouget Frederick, Ph.D.

City University of New York, 1990

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A

Evidence of Reversible Addition of Carbon-centered Radicals to Aromatic Nuclei

by

Rouget Frederick Henschel

A dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

1990

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This manuscript has been read and accepted for the Graduate Faculty in Chemistry in satisfaction for the dissertation requirement for the degree of Doctor of Philosophy.

4/26/90
Date

Leonard H. Schwartz
Chairman of Examining Committee

4/26/90
Date

Executive Officer

Professor Fitzgerald Bramwell

Professor Michael Weiner

Professor Samuel Wilen

Supervisory Committee

The City University of New York

Abstract

Evidence of Reversible Addition of Carbon-centered
Radicals to Aromatic Nuclei
by
Rouget F. Henschel

Advisor: Professor Leonard H. Schwartz

Radical systems catalyze the racemization of optically active methyl 2,2'-dicarboxy-9,9'-bianthryl (**11**). The racemization is inhibited by hydrogen donors. The optical activity of **11** is due to restricted rotation around the carbon-carbon bond linking the two aromatic rings. It is suggested that the racemization is catalyzed by the reversible formation of a sigma-complex addition intermediate which has a lower rotational barrier compared to the aromatic substrate. The Arrhenius parameters for the thermal racemization of **11** in bromobenzene have been determined.

Radical-catalyzed racemization of **11** has been observed previously, however the identity of the radical or radicals responsible was uncertain because solvent radicals were also formed. Racemization of **11** in the presence of dibenzylmercury, a thermal source of benzyl radicals, was investigated in two inert solvents, bromobenzene and *tert*-butylbenzene. Racemization of **11** was accompanied by very little product formation. Both solvents were shown to be inert to benzyl radical. It is concluded that racemization of **11** is exclusively due to reversible addition of benzyl radical.

Diisopropylmercury and diethylmercury were used as thermal sources of isopropyl and ethyl radicals, respectively. The half-lives of diethylmercury

(at 200 °C) and diisopropylmercury (at 170 °C) were established in bromobenzene. The kinetic order was determined for the racemization of **11** by diethylmercury and diisopropylmercury in bromobenzene. Azoisopropane and azoethane were used as alternative sources of isopropyl and ethyl radicals. Both catalyzed the racemization of **11** when heated in bromobenzene.

Attempts to catalyze the racemization of dimethyl 6,6'-dinitrobiphenyl-2,2'-dicarboxylate (**3**), dineopentyl 6,6'-dinitrobiphenyl-2,2'-dicarboxylate (**4**), and dimethyl 4,4',6,6'-tetranitrodiphenate (**5**) in the presence of nucleophiles were unsuccessful.

This thesis is dedicated to the students and faculty of CCNY, past, present and future.

Peace.

Acknowledgements

I would like to thank the members of my thesis committee: Professor Fitzgerald Bramwell, Professor Samuel Wilen, Professor Michael Weiner, and my thesis advisor Professor Leonard Schwartz.

Thanks are due to the following for assistance and encouragement during these long years:
Professor Gil Riley, Hugo Schimatz, Mike LaVerde, Stan Davis Porus Aria, Inez Sewell, Pete Campione, Steve Cohen, Ramsay Pal, Dan Medbury, Professor Daniel Akins, Cordie Stokes, Professor Neil McKelvie and many others.

I must also acknowledge Professor Birke and Professor Lombardi for convincing me to enter the PhD program in Chemistry.

Finally, I thank the Northeast Resource Center for Science & Engineering at City College of New York for a research fellowship, the Chemistry Department of York College for a teaching fellowship, and the Rockefeller University Mass Spectrometry Resource for performing mass spectra of samples.

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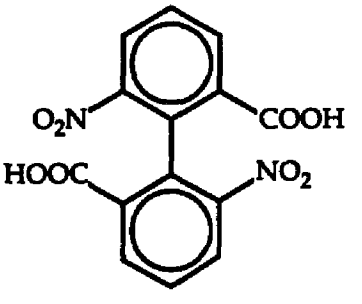
Chapter 1:
Introduction

A. Atropisomeric Biaryls

Atropisomeric compounds are an unusual class of chiral compounds whose chirality is due to restricted rotation about a carbon-carbon single bond. The term atropisomeric is normally restricted to those cases where the isomers can actually be isolated.[1a,b] One consequence of the restricted rotation is that atropisomeric compounds can be chiral but contain no chiral centers. In contrast to optically active compounds containing a chiral carbon, racemization of an atropisomeric compound occurs by the bending and stretching of bonds to overcome a rotational barrier and not by the rupture and reformation of bonds. The first compound of this type to be resolved was 6,6'-dinitrobiphenyl-2,2'-dicarboxylic acid (1).[2]



1

Free rotation around the phenyl-phenyl bond is restricted by the steric interactions of the ortho substituents. Many atropisomeric biaryls of this type

have been prepared and resolved.[3] Figure 1 shows the numbering system used to describe the ring carbons in biphenyls, binaphthyls, and bianthryls.

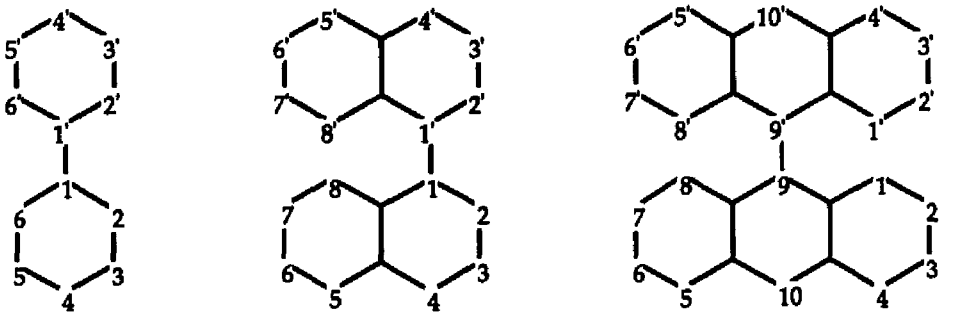


Figure 1. Ring carbon numbering in biaryls.

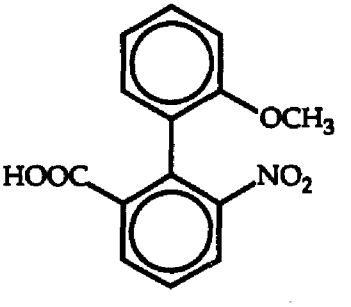
The nature of the restricted rotation about the aryl-aryl bond in atropisomeric biaryls has been the target of extensive investigation. The measure of optical stability which is the easiest to determine experimentally is the rotational half-life at a particular temperature. The Arrhenius parameters for the racemization process, which are the activation energy (E_a) and the pre-exponential factor A (see equation 1), can also be determined by following the loss of optical activity at several temperatures.

$$k = A \exp(-E_a/RT) \qquad (1)$$

The Arrhenius parameters and half-lives of a large number of atropisomeric biaryls have been reported in the literature.[4] The simplest model for the racemization process involves a completely planar transition

state in which both sets of blocking groups interact at the same time. This would be the case if the aromatic ring carbons are all rigidly held in one plane in the transition state.

Although the initial focus was purely on the size of the functional groups which impede free rotation,[5] it soon became apparent that consideration of the size of the interacting groups alone could not adequately explain the relative optical stability of some biaryls. For example a substituent X in the 3' position of 2'-methoxy-6-nitrobiphenyl-2-carboxylic acid (2) increases the optical half-life more than when in any other position.[6] This was attributed to a buttressing effect[7] which reduces an important stabilizing bond angle distortion in the transition state. The 3' substituent X in **2a** prevents the substituent in the 2' position from moving away from the blocking group it encounters in the transition state.



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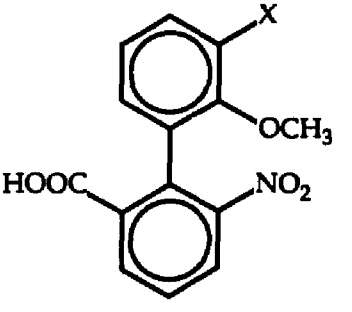
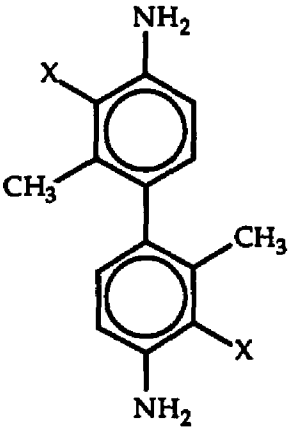
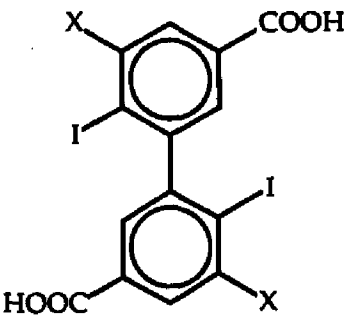


2a

Similarly, biphenyl **3a** could be successfully resolved, while biphenyl **3b** could not,[8] and the activation energy for the racemization of **4a** is 6.4 kcal/mol more than that of **4b**.[9]





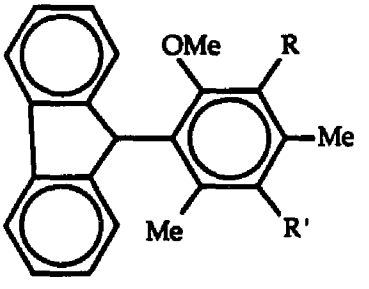
3a (X = CH_3)

b (X = H)

4a (X = I)

b (X = H)

In a recent example, Oki and co-workers found a buttressing effect in fluorene **5**. The rotational barrier increases along the series **5a** < **5b** < **5c**.[10]



5a (R = R' = H)

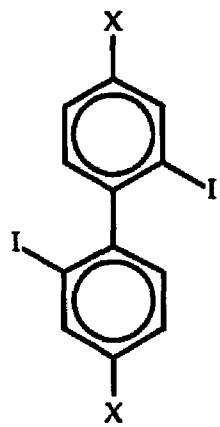
b (R = Br, R' = H)

c (R = R' = Br)

A "reverse" buttressing effect was observed in a pair of triptycene derivatives. A large peri-substituent reduced the rotational barrier whereas the opposite was expected because of the butressing effect.[11] It was suggested that the bulky peri-substituent causes a ground state bond-angle distortion in

the blocking substituent which results in sequential rather than concerted interaction of the blocking groups during the rotational process.

In another study,[12] the effect of substituents at the 4 and 4' positions in 2,2'-dihalogenobiphenyls (**6**) was attributed to out-of-plane bending of the phenyl-phenyl bond relative to each phenyl ring. Specifically, it was suggested that amine groups in the 4 and 4' positions reduce the rotational barrier by conjugation with the aromatic rings. This results in contributing structures such as **6a**, in which the rings have negative charges at the 1 and 1' carbons. These carbon atoms tend towards sp^3 hybridization, and the distorted geometry results in a reduced steric barrier in the transition state.



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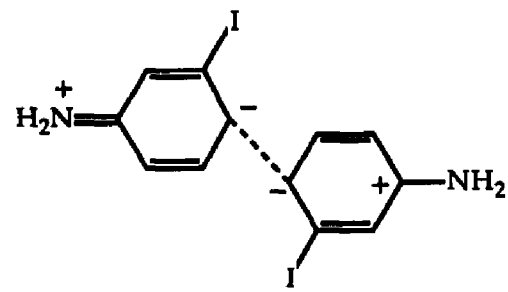


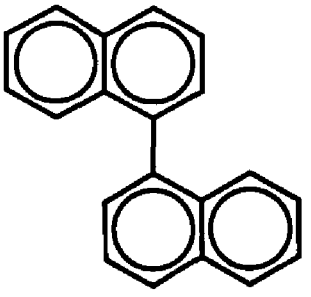
6a

Similar results were found with derivatives of **3** substituted at the 4 and 4' positions.[13] Electron-withdrawing groups increase, while electron-donating groups reduce the rotational barrier relative to the unsubstituted compound.

X-ray crystallographic studies of ortho-halobenzoic acids[14] have shown that the substituents are displaced away from each other as well as above and below the plane of the phenyl rings. It has been argued that the same type of distortion must exist in the halogenobiphenyls. This distorted geometry

allows the major steric interactions in the rotational transition state to occur one at a time rather than simultaneously, which results in a reduction in the activation energy.

Some results have suggested that ground-state strain plays a significant role in determining configurational stability. For example, an increased rate of racemization of 1,1'-binaphthyl (7) has been observed in liquid crystals.[15] This has been attributed to a flattening of the binaphthyl framework in this medium, which raises the ground-state energy.



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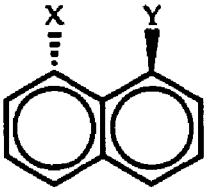
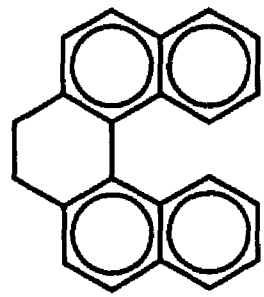


8

Ground-state strain has also been suggested to account for the unexpectedly small effect of added substituents at the 8 and 8' positions on the configurational stability of 1,1'-binaphthyls.[16] A large effect was anticipated because the presence of substituents in these positions were expected to create a large steric barrier to racemization. Evidence was cited which showed that the 1 and 8 substituents on a naphthyl ring such as 8 can displace each other above and below the plane of the aromatic ring. The blocking groups pass each other sequentially rather than simultaneously, which reduces the activation energy.[16]

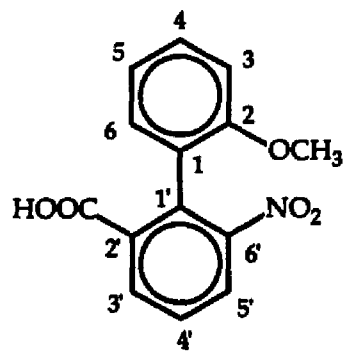
Various systems have been found to catalyze the racemization of optically active biaryls. Colter reported that 7 and 9,10-dihydro-3,4,5,6-dibenzophenanthrene (9) racemize more rapidly in the presence of electron acceptors

with which they form charge-transfer complexes.[17] It was argued that since the strength of the complex increases when the biaryl is planar, the transition state energy is lower than in the uncomplexed biaryl.



9

Ito found that the radical ion of binaphthyl **7** racemizes more easily than the neutral substrate.[18] The reason for this was not discussed. Heterogeneous catalysis of racemization of **7** in the presence of activated and unactivated carbon blacks,[19] Raney nickel,[20] and platinum[21] has also been observed. Although it was initially suggested that the catalysis might be due to adsorption onto the catalyst surface, the results with Raney nickel and platinum pointed towards a rapid reversible electron transfer as the cause of the enhanced racemization rate. The suggestion was made[18,19] that Colter's observations reported above with **7** and **9** may be due to the formation of a radical ion in the charge-transfer complex.



10

Electrophilic attack by hydrogen ions on C(1') of biphenyl **10** has been suggested to be responsible for the effect of the orientation of a substituent on the rate of racemization.[22] A substituent was expected to only exert an influence on the optical stability from the meta position (meta to the aryl-aryl bond) where it could exert a butressing effect on the group in the ortho position (OCH_3). With **10** it was found that substituents in the 4' and 5' positions have an unexpected effect. The effect is the same as what would be expected for electrophilic substitution at the C(1') carbon. For example when the substituent is NO_2 (a deactivating group) the rate of racemization is reduced to a greater extent from the 4' position (para to C(1')) than from the 5' position (meta to C(1')). When the substituent is OCH_3 (an activating group) the racemization rate is enhanced to a greater degree when the methoxy group is in the 4' position than when it is in the 5' position.

B. <u>The Radical-catalyzed Racemization of 2,2'-Dicarbomethoxy-9,9'-bianthryl</u>

2,2'-Dicarbomethoxy-9,9'-bianthryl (**11**) has a high rotational barrier because the hydrogens in the 1 and 8 positions lie directly in the path of the 1' and 8' hydrogens as the anthryl rings are rotated around the C(9)-C(9') bond. There are thus two benzo-benzo interactions in the planar transition state **11a**.

Figure 2 shows the racemization pathway for the bianthryl. During the racemization process, the bianthryl must pass through a planar transition state (**11a**) in which there are two benzo-benzo interactions, i.e. both steric interactions occur at the same time.

The rotational barrier was estimated to be at least 42 kcal/mol by Koukotas,[23] which indicates high optical stability. In the present work, more accurate values for the Arrhenius parameters have been established.

Koukotas reported that **11** racemizes when heated in the presence of oxygen. No racemization was observed in the absence of oxygen under the same conditions. It was suggested that oxygen, or a radical derived from reaction of oxygen with the solvent, adds reversibly to one of the anthryl rings. This results in a distortion of the geometry of the ring which is attacked, lowering the rotational barrier.

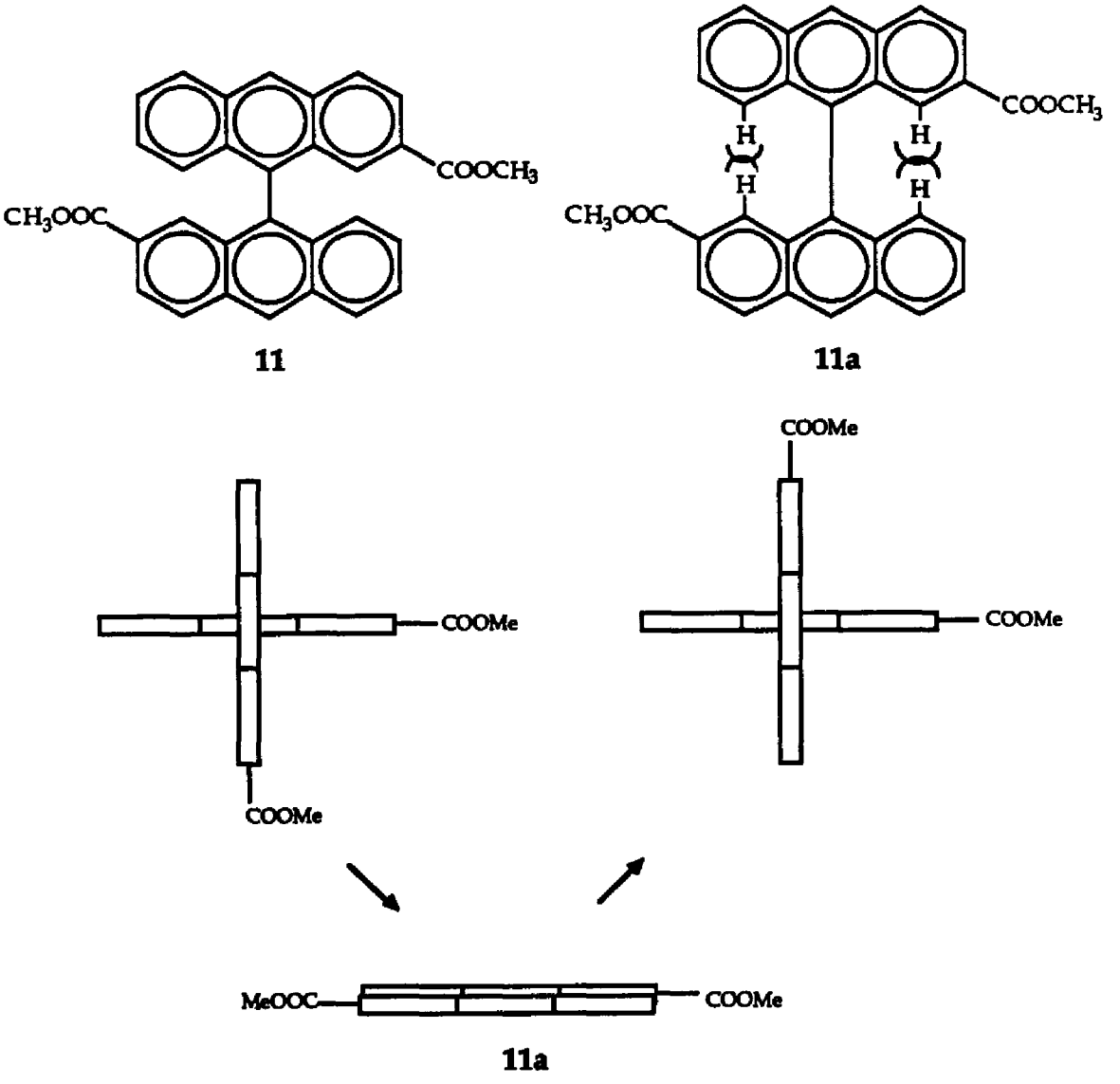


Figure 2. Simultaneous interaction of blocking groups in the racemization of bianthryl **11**.

Further investigation by Chen[24] showed that the racemization of **11** in the presence of oxygen was caused by solvent radicals produced by the abstraction of hydrogen by oxygen. Products were found which corresponded to substitution of a ring hydrogen by a solvent radical. Similar results were obtained when **11** was heated in the presence of diphenyl disulfide, dibenzylmercury, or *tert*-butyl peroxide with either 1,2-bis-(methoxyethoxy) ethane (triglyme) or dimethyl suberate as solvent. Diphenyl disulfide is a thermal source of phenylthiyl radicals, dibenzylmercury is a source of benzyl radicals, and *tert*-butyl peroxide is a source of *tert*-butoxy radicals as shown in equations **2–4**, respectively.[25]

$$\mathrm{PhSSPh} \rightleftharpoons 2\,\mathrm{PhS}\bullet \qquad (2)$$

$$\mathrm{Hg(CH_2Ph)_2} \rightarrow \mathrm{Hg} + 2\,\mathrm{PhCH_2}\bullet \qquad (3)$$

$$t\text{-BuO–O}t\text{-Bu} \rightarrow 2\,t\text{-BuO}\bullet \qquad (4)$$

Oxygen was excluded in these systems by degassing the solutions before heating. In all cases **11** was racemized, and products corresponding to substitution by solvent radicals were isolated. Products of substitution by other than solvent radicals were only isolated when dibenzylmercury was used as the radical source. In this case benzyl-substituted products were isolated. No racemization was observed in the absence of the radical source. Chen postulated that the enhanced rate of racemization was due to the reversible formation of a radical addition intermediate which could racemize more easily than the substrate. Addition of a radical at any position on one of the anthryl rings would facilitate rotation around the C(9)-C(9') bond. The addition produces a tetrahedral carbon, which would distort the ring from planarity. A loss of planarity in any one of the three six-membered rings of either anthryl unit would allow the blocking groups, i.e. the hydrogen atoms

at the 2 ,2' and 8 ,8' positions to pass each other sequentially rather than simultaneously (see Figures 3 and 4).

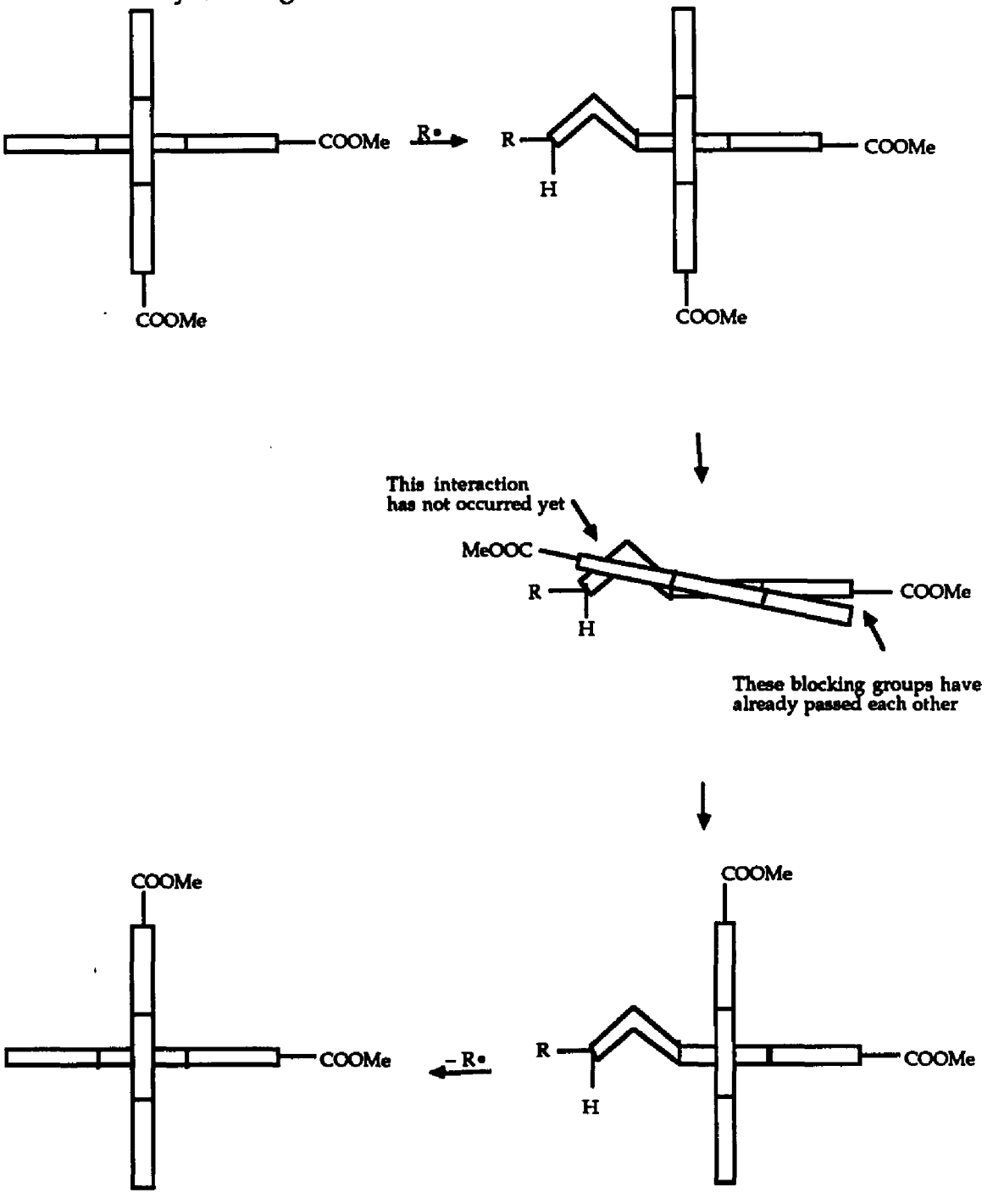


Figure 3. Sequential interaction of blocking groups in the racemization of a cyclohexadienyl intermediate from addition at an end ring of bianthryl **11**.

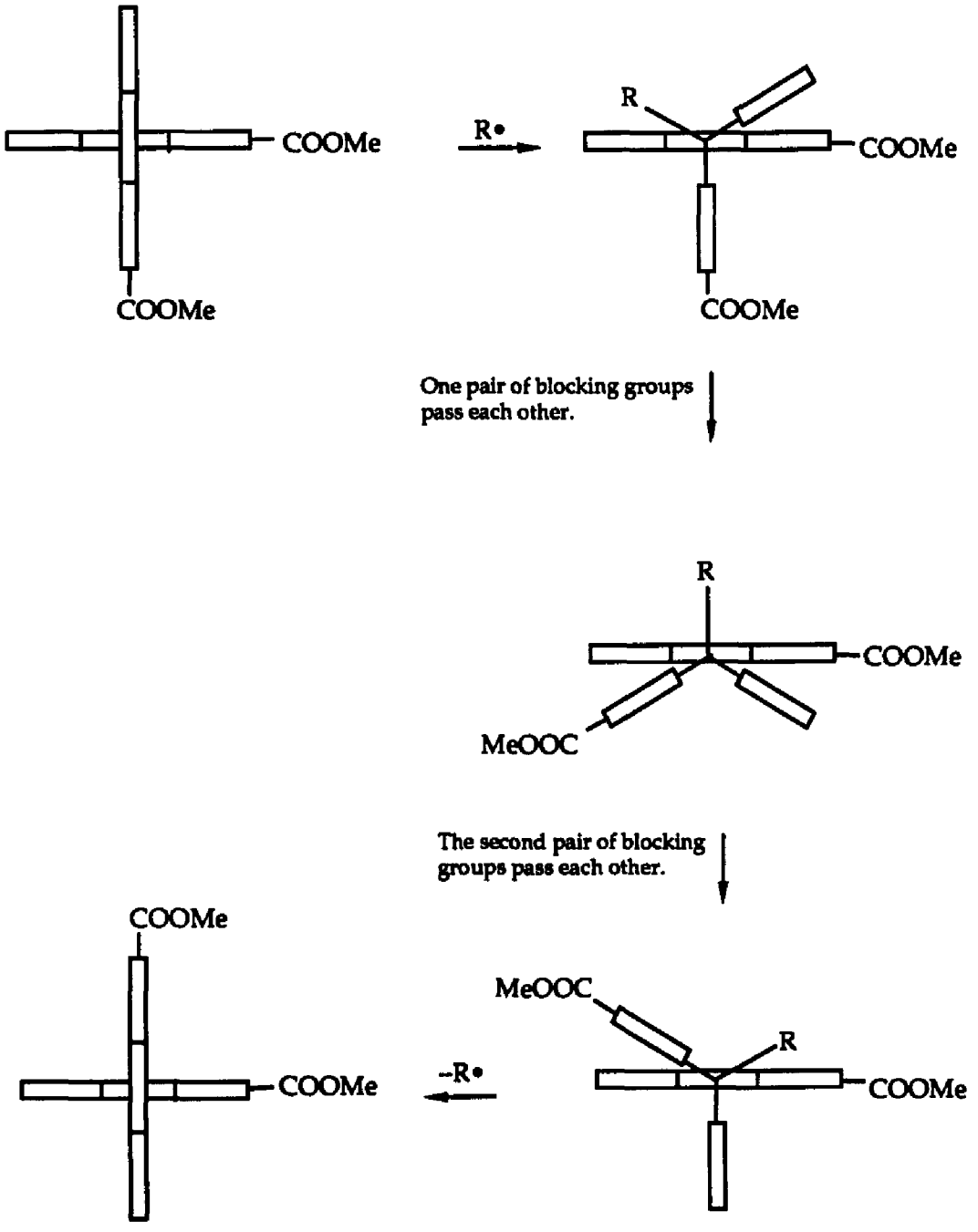


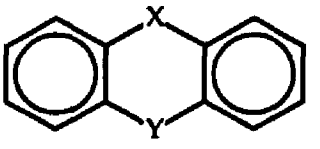
Figure 4. Sequential interaction of blocking groups in the racemization of a cyclohexadienyl intermediate from addition at C(9) in bianthryl **11**.

The relative reactivities of the ring carbons of anthracene (**12**, X= Y = CH) towards phenyl radical are 50 : 4 : 1 for the C(9), C(1), and C(2) atoms, respectively.[26] In bianthryl **11** the C(9) carbon is at the ring juncture, and approach to C(9) by a radical is hindered by the attached anthryl ring. Attack at C(10) may thus be favored for steric reasons. However, addition of a radical at C(9) would be expected to reduce the rotational barrier considerably. The central C–C bond would lengthen as the hybridization of the attacked carbon changes from sp^2 to sp^3. The steric interactions would be reduced in the transition state because the distance between the blocking groups is increased. Addition at C(10) would yield a cyclohexadienyl radical which could exist in a boat conformation. This would produce a structure similar to that from addition at C(9), but with less sp^3 character at C(9). The reduction in the rotational barrier might be less pronounced than from attack at C(9), but the two-step process shown in Figure 4 would still apply.

Consequently the ring which is attacked in **11** will probably not remain planar. Compounds with carbon frameworks similar to **11** were shown to exist in non-planar geometries. For example, evidence shows that compounds such as **12a-d** are not planar. Each phenyl ring is in the same plane as the atoms X and Y, but the planes are folded at an angle α, as shown in **12x**, which can vary in size.[27] The X-ray crystal structure of 9,10-dihydroanthracene (**12a**) was found to have a similar structure with a folding angle of 145°.[28]

Boat-shaped conformations were assumed for mono- and di-anions produced in the metal-ammonia reduction of 9,10-dialkyl-9,10-dihydroanthracenes (**13**)[29] as well as for 9-alkyl-10-lithio-9,10-dihydroanthracenes (**14**).[30,31] A boat-shaped intermediate, along with the

assumption that bulkier alkyl groups prefer the quasi-axial position,[32] was used to explain the stereochemistry of the reaction products.



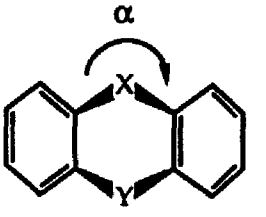
12a (X = Y = CH_2)

b (X = Y = S)

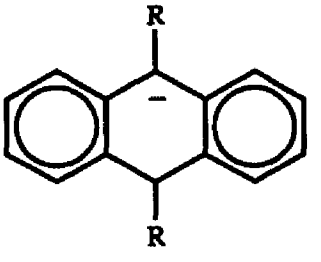
c (X = Y = O)

d (X = O, Y = Se)

e (X = O, Y = Te)



12x



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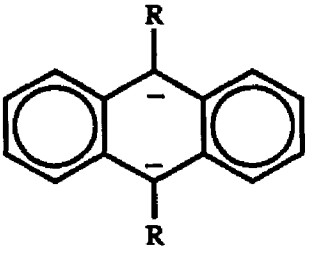
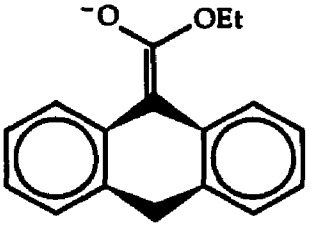


14

Recent results indicate that the degree of planarity can vary. An MNDO calculation of monoanions of 9-alkyl substituted 9,10-dihydroanthracenes yielded nearly planar flattened boat structures.[33] The C(10)-anions were found to be more puckered than the C(9)-anions which showed very little non-planarity.

A recent study of the stereochemistry of the products of metal-ammonia reduction of cyclohexadienyl ring systems containing carbonyl substituents indicated the structures were non-planar for phenyl, naphthyl, and anthryl derivatives. A coalescence temperature experiment with the

anion of ethyl 9,10-dihydroanthroate indicated a non-planar structure (**15**) with considerable enolate character and rapid boat-boat inversion.[34]



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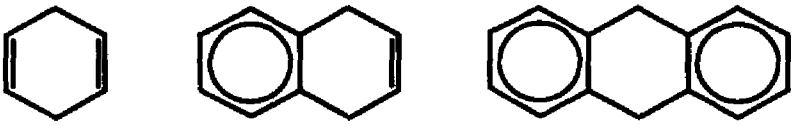
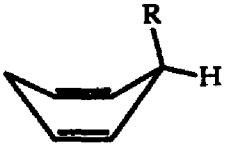
The geometry of the 1,4-cyclohexadiene ring system, which includes 1,4-dihydrobenzene (**16**), 1,4-dihydronaphthalene (**17**), and **12a**, has been reviewed.[35]



16 **17** **18**

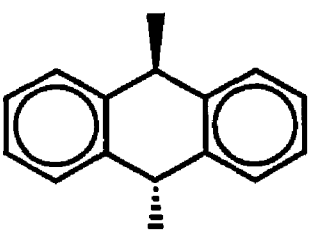
Molecular mechanics (MMI, MM2, and MMPI) and molecular orbital (MINDO/3, MNDO, and 3-21G) calculations gave similar results: the energy minima indicate planar structures.[36] A distortion of 20° from planarity along the folding plane involves an energy gain of ≤ 1 kcal/mol which decreases along the series **16** > **17** > **18**. The energy surface is particularly flat for **18**, and the authors suggest that the non-planar X-ray structure previously observed (see reference 28) may not represent the optimum solution or gas-phase structure. Molecular mechanics calculations using MMI and MMPI of 1-alkyl substituted derivatives of **16**, **17**, and **18** gave somewhat steeper energy wells, and an energy minimum with a non-planar structure. For example it was concluded that structure **19** (R = methyl, ethyl, isopropyl, and *tert*-butyl) contains the alkyl group in the pseudo-axial position.[37]



19

An *ab initio* calculation with optimized geometry found 1,4-cyclohexadiene to be planar.[38] This result was in agreement with an earlier *ab initio* calculation which involved a comparison of fixed geometries and found the planar structure to be the most stable.[39]

An NMR study of dimethylated dihydroanthracenes found that *trans*-9,10-dimethyl-9,10-dihydroanthracene (**20**) and 9,9'-dimethyl-10,10'-dihydroanthracene (**21**) exist in a boat conformation in the solid state based on the presence of distinct methyl peaks for the pseudo-axial and pseudo-equatorial methyl groups. In the liquid state these two compounds only showed single methyl peaks, even when the temperature was reduced to –70 °C.[40] The authors concluded that this was due to a flattened boat geometry with rapid boat-boat inversion. They noted that there is considerable variation in the extent of non-planarity among the members of the series, and added that the 9,10-dihydroanthracene ring system appears to be quite flexible. In contrast, a molecular mechanics calculation using MM2 and MMPI yielded a non-planar structure only for the *cis*-9,10-dimethyl compound (**22**).[41] The other dimethylated dihydroanthracenes yielded planar energy minima. Distortions from the most stable geometry involved small energy gains, supporting the assertion that these ring systems are flexible.



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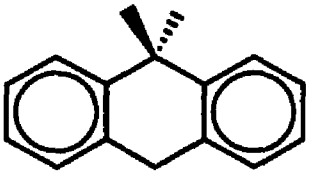

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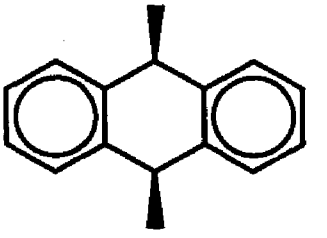

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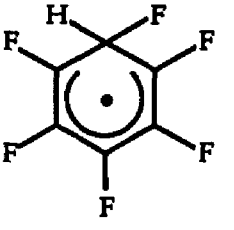

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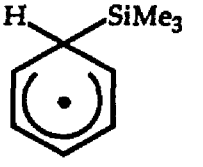
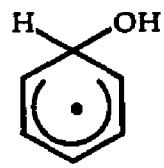


25

The methylene hydrogens of radical **23** were found to have a hyperfine splitting constant (hfs) of 48 Gauss. None of the other hydrogens in **23** were found to have an hfs over 15 Gauss. The large hyperfine splitting of the methylene protons in radical **23** was attributed to hyperconjugation with the singly occupied π-molecular orbital (SOMO) in the ring, and a planar structure was proposed.[42] A planar structure maximizes overlap from both methylene sigma bonds. For the corresponding fluorinated radical (**24**), the hfs was found to be much smaller (19 Gauss).[43] A planar structure was inferred. It was suggested that in radical **24** the electron-withdrawing effect of fluorine reduces the effective hyperconjugation between the π-system SOMO and the C-H sigma bond.

However Kira and co-workers[44] found that H-1 of the trimethylsilyl radical **25** has an hfs in the range 35-40 in spite of the fact that trimethylsilyl groups are electron-donating and are therefore expected to enhance hyperconjugation. They suggested that the radical is distorted from planarity

with the trimethylsilyl group in the pseudo-axial position. This leads to enhanced hyperconjugation of the C-Si sigma bond with the ring SOMO. While the pseudo-axial C-Si bond adopts an orientation which is more favorable for overlap, the opposite is true for the pseudo-equatorial C-H bond. This unfavorable orientation of the C-H bond offsets the effect of the electron-donating trimethylsilyl substituent.



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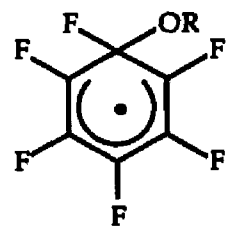

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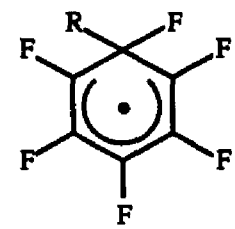
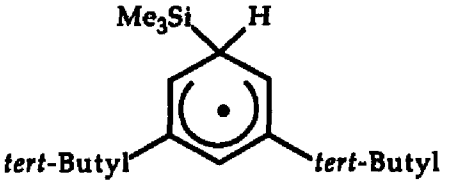


28

The belief that inductive effects do influence hfs constants is confirmed by the observation that the hfs of H-1 in radical **26** is 10 units smaller than in radical **23**,[45] and that the hfs of F-1 in radicals of type **27** are >20 Gauss smaller than in radicals of type **28** (R = alkyl for both).[46] In radicals **26** and **27** the electron-withdrawing oxy-substituent reduces the available electron density for hyperconjugation with the ring SOMO, thus reducing the hfs.

The planarity of cyclohexadienyl radicals cannot be predicted *a priori* without considering the effect of hyperconjugation or steric strain. For example, radical **29** has an H-1 hfs of 34.6, whereas radical **30** has an H-1 hfs of only 6.00.[47] Another example is the decrease in the F-1 hfs in the series **31a, b, c, d** (F-1 hfs 126, 110, 103, 78, respectively).[48] On the other hand for radical **32a** the H-1 hfs is 47.5, and for **32b** the hfs is 43.6.[49] Apparently the geometry of this radical is not as sensitive to the steric bulk of the C-1 substituent as radical **31**.



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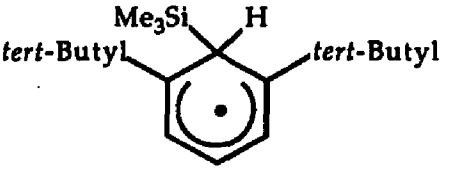

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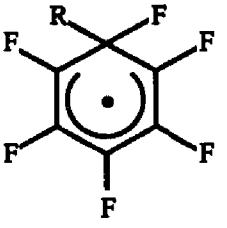
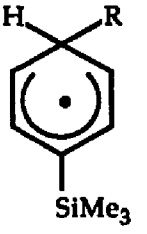


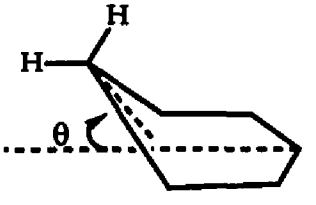
31 **a** (R = H)
b (R = methyl)
c (R = isopropyl)
b (R = *tert*-butyl)



32 **a** (R = H)
b (R = *tert*-butyl)

An INDO calculation[50] found that the out-of-plane distortions at room temperature of radical **23** involving angle θ in **33** range over 20°, which represents considerably more flexibility than an aromatic ring. A similar situation is expected for the cyclohexadienyl intermediate resulting from addition of a radical to bianthryl **11**. Loss of rigidity facilitates bond distortions in the intermediate, which should allow the blocking groups to pass each other more easily in the transition state to racemization.

23



33

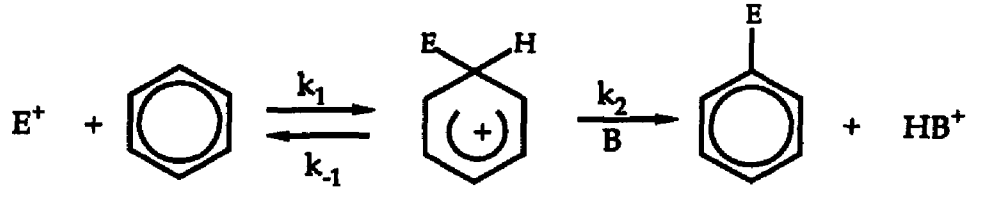
As the ring which is attacked becomes more flexible, strain in the transition state should be reduced. Any loss of rigidity in the aromatic ring

systems or any deviation from coplanarity of the ring juncture carbon and the benzo hydrogens will reduce the rotational barrier.

An interesting possibility was put forth by Chen[24] that the racemization of an optically active biaryl could serve as a probe of reversible addition. The great advantage to this method is that no products need be formed. Even in the absence of any products, which might suggest that the radical does not attack the aromatic ring, loss of optical activity in recovered substrate would indicate that the radical added reversibly.

C. Reversible Addition in Aromatic Substitution

Aromatic substitution mechanisms that involve an addition intermediate in the first step can be classified as electrophilic, nucleophilic, or radical depending on the nature of the attacking species. The addition intermediate produced contains a positive charge, a negative charge, or an unpaired electron, respectively (see Figures 5-7).



34

Figure 5. General mechanism of electrophilic aromatic substitution (E = electrophile, B = base).

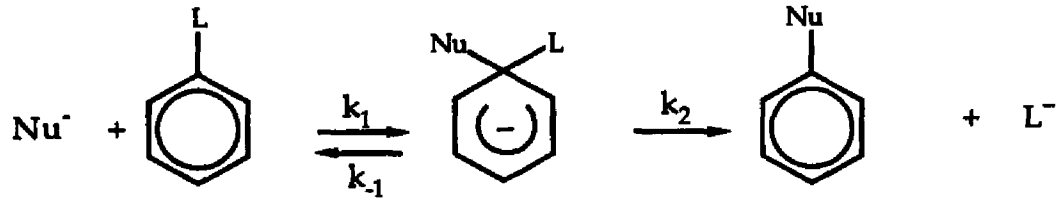


Figure 6. General mechanism of nucleophilic aromatic substitution (L = leaving group).

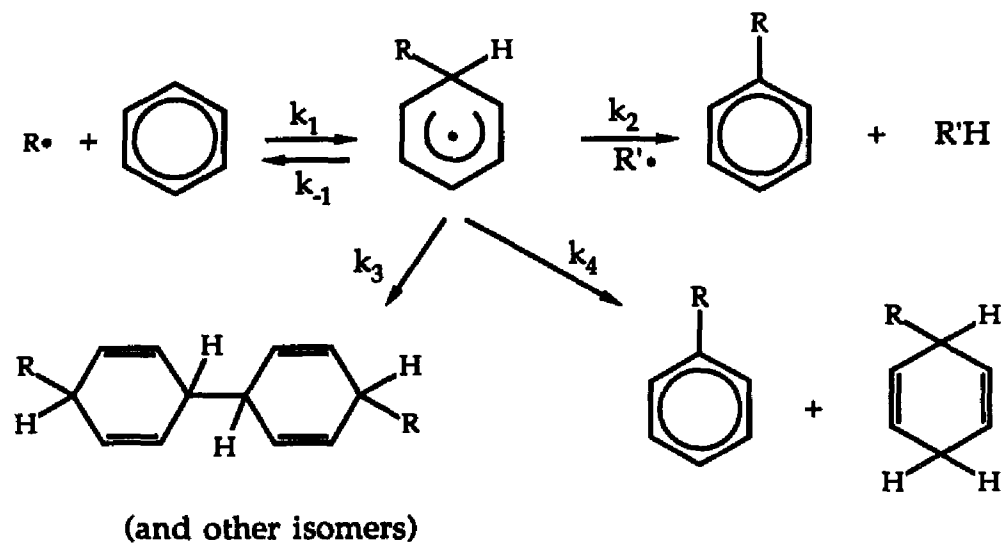
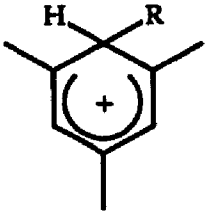


Figure 7. General mechanism of homolytic aromatic substitution.

In some cases electrophilic addition intermediates (**34**) have been observed by NMR spectroscopy, and even isolated. For example intermediates **35** (R = methyl, ethyl, *i*-propyl, *n*-propyl, and formyl) in the Friedel-Crafts alklylation and acylation of 1,3,5-trimethylbenzene have been isolated as tetrafluoroborate salts.[51] Other isolated intermediates of this type were also reported in the same paper. The heptamethylbenzonium ion **36** was observed by NMR and UV spectroscopy during the Friedel-Crafts methylation of

hexamethylbenzene.[52] Recently, intermediates **37 (a-c)** were isolated as perchlorate and bromide salts and analyzed by X-ray crystallography.[53]



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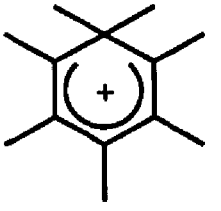

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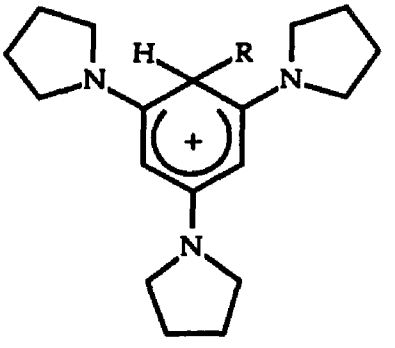


37 a (R = H)

b (R = CH_3)

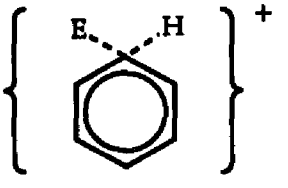
c (R = CHO)

The cyclohexadienyl radical **23** was first observed by esr spectroscopy in 1963.[54] Since then many cyclohexadienyl radicals have been detected by esr as well as UV spectroscopy.[55]

23

A key point of interest in an aromatic substitution reaction is whether or not the addition step is reversible. In other words, is a reversible equilibrium established between the reagents and the addition intermediate, followed by a rate-determining product formation step ($k_{-1} \gg k_2$)? Or is the addition intermediate formed irreversibly in the rate-determining step, followed by rapid product formation ($k_2 \gg k_{-1}$)?

Electrophilic aromatic substitution reactions have been extensively studied using kinetic isotope effects.[56] Isotope effect studies were initially conducted to determine whether the mechanism was a one-step process involving an aromatic transition state **38**, or a two-step process with an addition intermediate as shown in Figure 5.



38

Once it became generally accepted that the mechanism involved an intermediate, the focus shifted to determining the reversibility of the first step.[57] A primary isotope effect is interpreted as a sign of C–H(D) bond-breaking in the rate-determining step. Since only the second step involves this type of bond-breakage, an isotope effect implies that the second step is rate-determining. The first step would therefore be relatively fast and involve a reversible formation of the addition intermediate. The absence of an isotope effect would imply that the first step is rate-determining and therefore irreversible. A small isotope effect may be difficult to interpret. It was suggested that only isotope effects larger than 2.0 should be assumed to imply

that carbon-hydrogen bond-breakage takes place in the rate-determining step.[58]

The homolytic aromatic substitution mechanism is more complicated, as can be seen from comparing Figure 7 with Figure 5. Just as with electrophilic systems, isotope effects which are not large may be ambiguous. For example observed isotope effects with values ranging from 1.3 to 1.6 were attributed to reversible addition[59] on the one hand, and to a second-order effect[60] on the other.

Another major problem encountered with radical systems is the possibility of a misleading isotope effect arising from alternative pathways to the product. This can occur if the isotope effect is determined simply as the ratio of labeled to unlabeled product formed. An example of this was described by Eliel[61] who concluded that a large isotope effect observed in the phenylation of benzene was the result of competing side reactions such as step 3 in Figure 7. This interpretation was substantiated by the observation that the isotopic composition of recovered starting material was unchanged.

Trapping agents have been used to investigate the reversibility of the addition step. Conclusions were drawn based on the effect of the trapping agent on the product distribution. Cyclohexadienyl radicals are rapidly oxidized by oxygen. In the presence of oxygen, such a radical would not have the opportunity to revert back to reactants. This might result in a change in the product distribution. For example, the presence of oxygen in the reaction between benzoyl peroxide and benzene (see Figure 8) increases the relative amount of phenyl benzoate formed compared to biphenyl.[62]

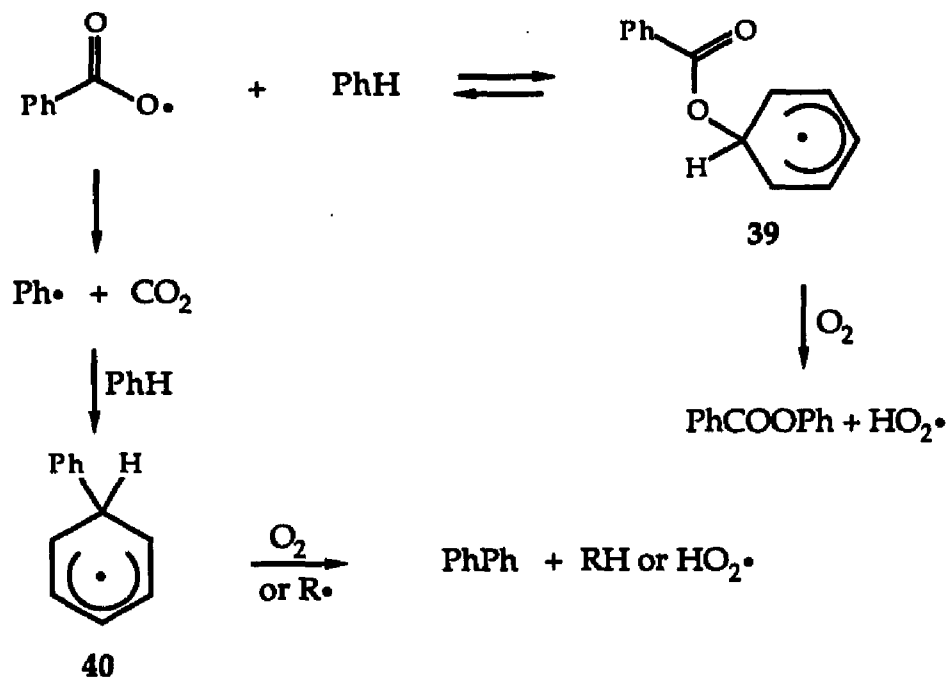


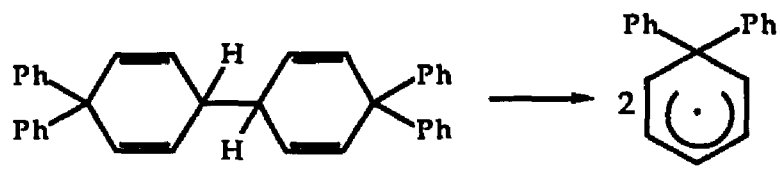
Figure 8. Reaction of benzoyl radical with benzene.

This suggests that intermediate **39** is formed more reversibly than intermediate **40**. Oxygen traps **39** by oxidizing it to phenyl benzoate. When less oxygen is present, and **39** is able to revert back to reactants, the benzoyl radical has time to decompose to phenyl radical and the major product becomes biphenyl. The presence of a trapping agent may also affect the reaction mechanism or the attacking radical. This possibility is difficult to rule out completely, casting possible doubt on conclusions obtained by the use of this method.

In another study it was concluded that formation of the addition intermediate may be reversible when the site of attachment is *ortho* to a substituent.[63] Apparently the steric strain raises the energy of the

intermediate, reducing the activation energy to reversion. The conclusion that the addition step was reversible was based on the effect of adding copper (II) salts on the product distribution in the phenylation of *o*-dichlorobenzene and on the partial rate factor for the phenylation of *p*-dichlorobenzene. Copper (II) salts rapidly oxidize cyclohexadienyl radicals, trapping them before they can revert back to reactants.[64]

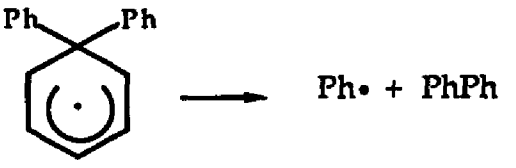
An alternative method which has been used to determine reversibility involves the generation of the cyclohexadienyl intermediate by heating the corresponding dimer and seeing if it undergoes decomposition, i.e., the reverse of the homolytic addition step to benzene. An example is shown in Figure 9.



41 42

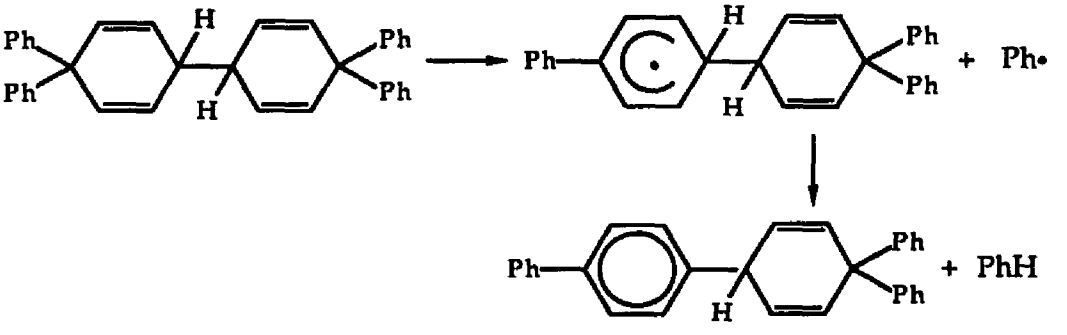
Figure 9. Formation of a cyclohexadienyl radical from a dimer.

Dimer **41** was decomposed at 230 °C.[65] The major products were benzene, biphenyl, and compound **43**. Based on these results, the mechanism shown in equations 5 and 6 was proposed. The phenyl radical is produced by equation 5, which corresponds to the reversal of the addition step in the phenylation of biphenyl. When the decomposition was carried out in chlorobenzene, chlorobiphenyls were among the products formed (see equation 7). This reinforces the conclusion that phenyl radicals were formed from intermediate **42**.



(5)

42



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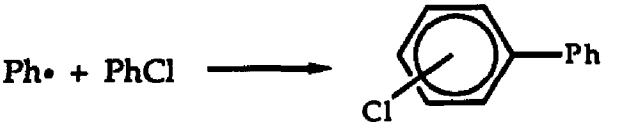
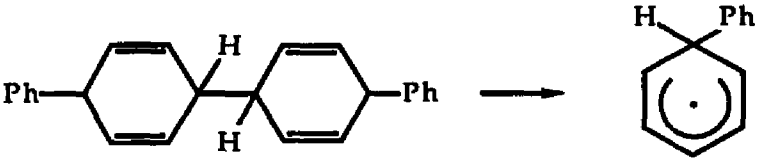


(7)

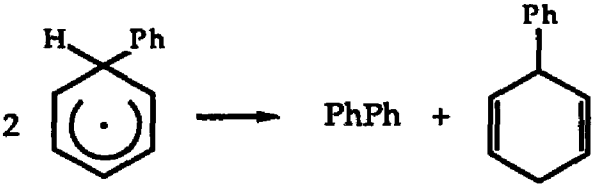
Radical **42** is not very likely to form as a phenylation intermediate from biphenyl because it represents attack at the most hindered position of biphenyl. Thus, the system does not appear to be a good model for the investigation of the reversibility of the addition of phenyl radical to an aromatic system.

When the dimer **44** was decomposed at 170 °C in chlorobenzene, only biphenyl and dihydrobiphenyl were formed. This implies that disproportionation of the cyclohexadienyl radical **45** (equation 9) is faster than loss of phenyl radical (equation 10). Evidence was presented that at 210 °C

some phenyl radical formation took place: about 10% of the C_{12} products isolated were chlorobiphenyl isomers (see equation 11). The authors concluded that the ready loss of phenyl radical from **42** was due to steric strain. The less hindered radical **45** loses phenyl radical much more slowly. The results do suggest that phenylation of benzene may become reversible as the temperature is increased.



44 **45** (8)



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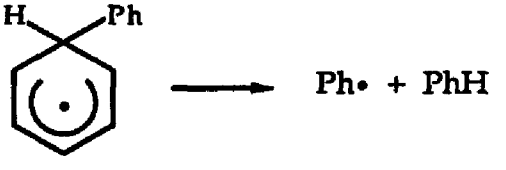

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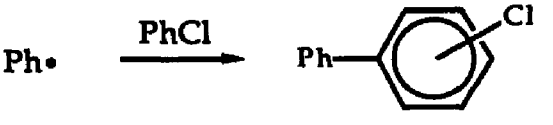
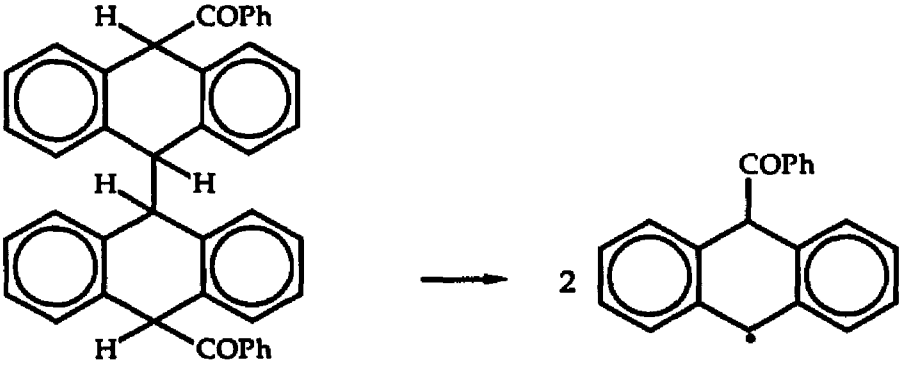


(11)

When dimer **46** was thermally decomposed (see equation 12), anthracene and benzaldehyde were among the products isolated. Since they arise from decomposition of cyclohexadienyl radical **47**, in a process which

corresponds to the reverse of the addition of benzoyl radical to anthracene, it was concluded that benzoyl radical adds reversibly.[66] It should be noted that the decomposition of the dimer was conducted at a considerably higher temperature than the benzoylation reaction itself.



(12)

46 **47**

Several problems are associated with this method of determining reversibility. The number of systems that can be investigated using this method is limited by the availability of the appropriate dimers. In addition, the cycohexadienyl radical is usually generated at higher temperatures than that at which the substitution reaction is carried out. The intermediate may be formed reversibly at higher temperatures but irreversibly at lower temperatures. The extent of reversibility should not remain constant as the temperature is varied.

The methods of studying reversibility outlined above all have problems associated with their use. We suggest that loss of optical activity in an atropisomeric biaryl can serve as an alternative probe for studying the reversibility of radical addition to an aromatic nucleus. This approach has the advantage of greater simplicity in both execution and interpretation, and therefore provides a useful alternative to the other methods.

Chapter 2:

Determination of the Arrhenius Parameters for the Thermal Racemization of Optically Active 2,2'-Dicarbomethoxy-9,9'-bianthryl.

The atropisomeric biaryl 2,2'-dicarbomethoxy-9,9'-bianthryl (11) has very high optical stability. The interactions of the pairs of hydrogens at the 1,1' and 8,8' positions in the transition state create a sizeable barrier to rotation around the aryl-aryl bond. No thermal racemization of this compound has been previously observed. Koukotas[67] estimated a minimum activation energy (E_a) of 42 kcal/mol in dimethyl phthalate. This estimate was based on the absence of racemization after six hours heating at 200°C.

It was found that thermal racemization can be observed at 225 °C, and experiments were therefore undertaken to obtain accurate values for both Arrhenius parameters (A and E_a). Five points in duplicate were taken at each of three temperatures (235°, 245° and 255°C). The experiment was repeated to confirm the results. Figures 10 and 11 show plots of ln R vs. time for each experiment where $R = \alpha_o/\alpha$. The rate constant (k_{rac}) at each temperature is equal to the slope of the straight line, as shown in equation 13.[68]

$$\ln(\alpha_o/\alpha) = k_{rac}\, t \qquad (13)$$

An Arrhenius plot of ln k_{rac} vs. 1/T allows the pre-exponential factor and the activation energy to be calculated from Equation 15, which is derived from the Arrhenius equation shown in Equation 14.

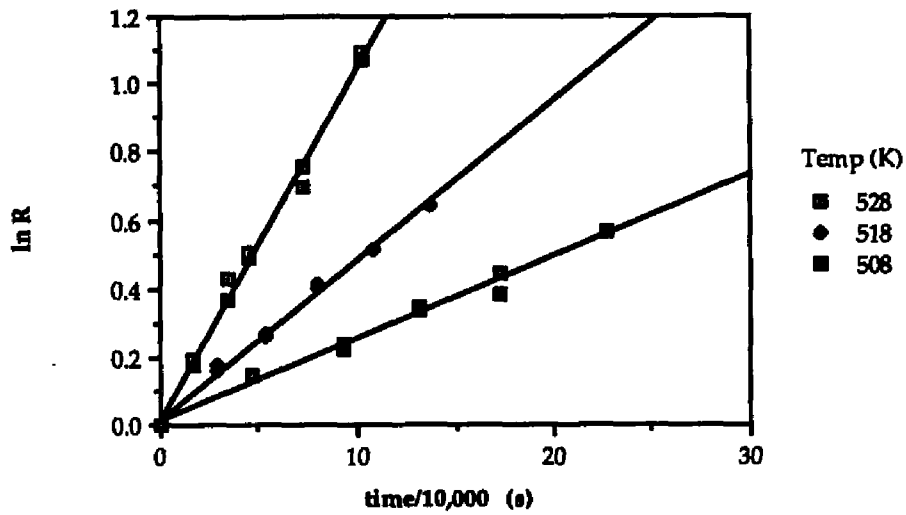


Figure 10. Plot of $\ln(\alpha_0/\alpha)$ vs time for the thermal racemization of optically active **11** in bromobenzene (run #1).

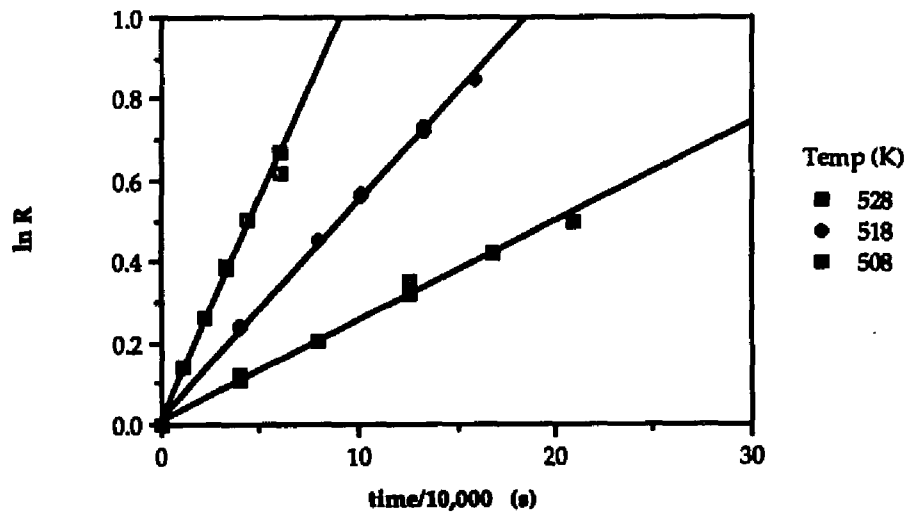


Figure 11. Plot of $\ln(\alpha_0/\alpha)$ vs time for the thermal racemization of optically active **11** in bromobenzene (run #2).

$$k_{rac} = A \exp(-E_a/RT) \quad (14)$$

$$\ln k_{rac} = \ln A - \frac{E_a}{RT} \quad (15)$$

Since the optical rotation (α) at time = 0 equals the initial rotation (α_o) by definition, the thermal racemization data has fixed intercept zero, i.e. at t = 0, $\ln(\alpha_o/\alpha) = 0$. The best fit slope for a line with fixed intercept zero was calculated from Equation (16)[69] where $y = \ln(\alpha_o/\alpha)$ and x = time.

$$\text{slope} = \frac{\sum yx}{\sum x^2} \quad (16)$$

Tables I and II show the values for k_{rac} obtained using this equation along with the values for 1/T and $\ln k_{rac}$ used for the Arrhenius plots shown in Figures 12 and 13. The values of the Arrhenius parameters obtained from the first experiment were $\log_{10} A = 10.91$ and $E_a = 38.5$ kcal/mol, and from the second experiment $\log_{10} A = 11.3$ and $E_a = 39.4$ kcal/mol. Based on both experiments $\log_{10} A = 11.1 \pm 0.2$ and $E_a = 39.0 \pm 0.5$ kcal/mol.

Table I. Rate constants at three temperatures for the thermal racemization of **11** (run #1).

°C	K	1/T	$\ln k_{rac}$	k_{rac}(slope)
255	528	0.001894	-11.461	1.05×10^{-5}
245	518	0.001931	-12.236	4.85×10^{-6}
235	508	0.001969	-12.906	2.48×10^{-6}

Table II. Rate constants at three temperatures for the thermal racemization of **11** (run #2).

°C	K	1/T	ln k_{rac}	k_{rac}(slope)
255	528	0.001894	-11.406	1.11×10^{-5}
245	518	0.001931	-12.117	5.47×10^{-6}
235	508	0.001969	-12.892	2.52×10^{-6}

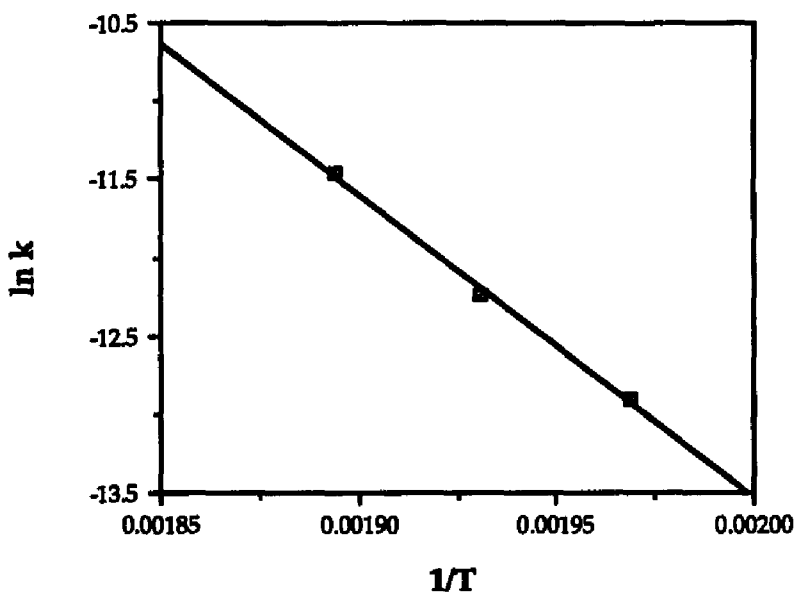


Figure 12. Arrhenius plot of the thermal racemization of **11** in bromobenzene (data from Table I).

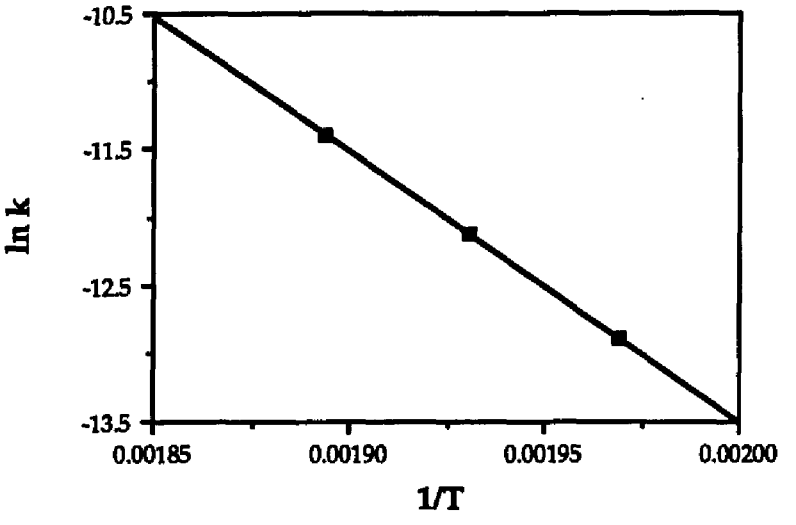
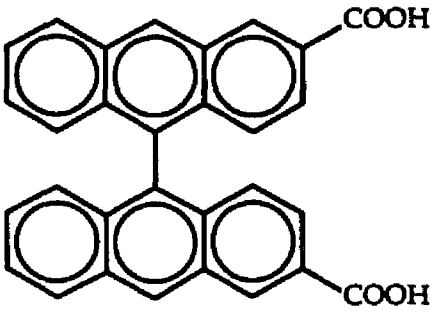


Figure 13. Arrhenius plot of the thermal racemization of **11** in bromobenzene (data from Table II).

The activation energy found is slightly lower than Koukotas' minimum value of 42 kcal/mol which was established using a value of 10^{-12} for the pre-exponential factor A. The latter value had been chosen based on pre-exponential factors reported for 1,1'-binaphthyls. Of all the compounds whose Arrhenius parameters are known, binaphthyls are the most structurally similar to **11**. No Arrhenius parameters have been reported for optically active 9,9'-bianthryls to date. The only other known optically active 9,9'-bianthryl is 3,3'-dicarboxy-9,9'-bianthryl (**34**). The only information reported about its optical stability is that no thermal racemization was observed after refluxing for 4 h in xylene (139 °C).[70] It might be interesting to determine the Arrhenius parameters of the dimethyl ester of this compound to allow a comparison with **11**, and to find out whether the location of the carbomethoxy group has any effect on the rotational barrier. Another

interesting experiment would be to determine whether the dimethyl ester of **48** would racemize in the presence of the radicals which racemize **11**.



48

The activation energy to thermal racemization of bianthryl **11** is considerably higher than that of any other biaryl previously reported. Activation energies of this magnitude for rotational barriers have only been observed with a relatively few compounds.[71]

Chapter 3:

The Racemization of Optically Active 2,2'-Dicarbomethoxy-9,9'-bianthryl by Benzyl Radicals Derived from Dibenzylmercury.

Dibenzylmercury has been used extensively as a thermal source of benzyl radicals.[72] The decomposition occurs in a stepwise manner[73] as shown in equation 17 and 18. The second step is fast because of the low bond dissociation energy of the mercury-carbon bond in $\bullet HgCH_2Ph$,[74] and therefore only a very low concentration of this radical is expected to exist. No evidence of a reaction involving $\bullet HgCH_2Ph$ was found in the literature. In some cases the simple net reaction shown in equation 19 has been assumed instead .[75]

$$Hg(CH_2Ph)_2 \rightarrow PhCH_2\bullet + \bullet HgCH_2Ph \quad (17)$$

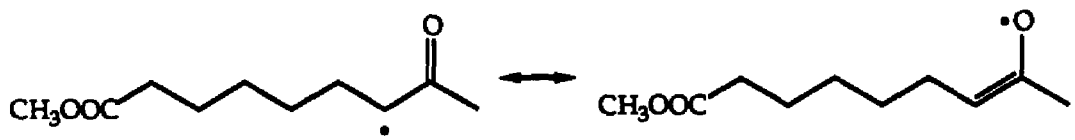
$$\bullet HgCH_2Ph \rightarrow Hg + PhCH_2\bullet \quad (18)$$

$$Hg(CH_2Ph)_2 \rightarrow Hg + 2PhCH_2\bullet \quad (19)$$

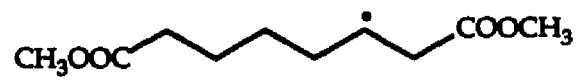
Bianthryl **11** racemizes when heated with dibenzylmercury using dimethyl suberate (DMS) as solvent.[76] Minor amounts of products derived from DMS radicals as well as benzyl radical were formed. Apparently benzyl radicals reacted with the solvent, abstracting a hydrogen atom to produce DMS radicals (see equation 20). Therefore it is not clear whether or not it was the reversible addition of the benzyl radical which caused the racemization. Addition intermediates formed between the benzyl radical and **11** may have reverted to the educts without any racemization taking place. The racemization observed could have occurred exclusively in the intermediates formed by addition of DMS radicals to **11**.

$$PhCH_2\bullet + DMS \rightarrow PhCH_3 + DMS\bullet \qquad (20)$$

Bromobenzene and *tert*-butylbenzene should be much more inert towards benzyl radical than DMS. Neither solvent has easily abstractable hydrogens. Bromobenzene only contains aryl hydrogens and *tert*-butylbenzene contains aryl and methyl hydrogens. It's unlikely that a benzyl radical could easily abstract phenyl or methyl hydrogens. *tert*-Butylbenzene was found to be inert to dibenzylmercury at 140–170 °C.[77] DMS, on the other hand, can lose a hydrogen alpha to the carbomethoxy group to form a resonance-stabilized radical as shown in equation 21, or can form a secondary radical such as **49**.



(21)



49

When dibenzylmercury was decomposed at 190 °C in *tert*-butylbenzene, quantitative amounts of bibenzyl (the dimer of the benzyl radical) and metallic mercury were obtained. No products of reaction between the solvent and benzyl radical could be isolated. The solvent is therefore inert, and any racemization observed can be ascribed to the benzyl radical.

The same result was found with bromobenzene. The observation that bianthryl **11** racemizes when heated in the presence of dibenzylmercury in these two inert solvents, bromobenzene and *tert*-butylbenzene, is interpreted to mean that the benzyl radical is the radical that attacks the anthryl ring.

Table III. Percent racemization vs time in *tert*-butylbenzene at 190 °C.

time	% racemization
15 min	38.9
1 h	43.1, 42.8
2 h	42.1, 42.
14 h	42.6

Table IV. Percent racemization vs time in bromobenzene at 190 °C.

time	% racemization
15 min	37.3, 37.3
30 min	41.3, 40.8, 40.8
1 h	40.4
2 h	41.2

The percent racemization [$(1 - \alpha/\alpha_o) \times 100\%$] reached a maximum of 43% after 1 h and 41% after 30 min with *tert*-butylbenzene and bromobenzene, respectively (see Tables III and IV). The molar ratio of dibenzylmercury to **11** used in *tert*-butylbenzene was 4.4 : 1. The molar ratio of dibenzylmercury to **11** in bromobenzene was 4.8 : 1.

Very little formation of substitution products occurred under these conditions in either solvent. Quantitative yields of **11** were recovered. The sigma complex intermediate must revert back to starting material at a much faster rate than it reacts to form products. In the absence of dibenzylmercury no racemization was observed with either solvent under the same conditions.

This is clearly an example of a situation where the absence of reaction products would normally lead to the conclusion that there is no reaction between the radical and the aromatic substrate. The loss of optical activity of the biaryl indicates that a reaction did indeed take place. Racemization of the optically active aromatic substrate serves as evidence that fast, reversible addition of the radical took place but without any product formation.

At 150 °C, racemization occurred more slowly in both solvents. The racemization of **11** reached a maximum of 58% after 3 h when heated to 150 °C with dibenzylmercury in *tert*-butylbenzene. A maximum of 67% racemization was reached in bromobenzene after 6 h. Figures 14 and 15 show the results at 150 °C for *tert*-butylbenzene and bromobenzene, respectively. In the absence of dibenzylmercury no racemization was observed at 150 °C with either solvent. At 135 °C the racemization leveled off at 70% after 8-10 h in *tert*-butylbenzene and at 80% after 24 hours in bromobenzene. The results at 135 °C are shown in Figures 16 and 17 for *tert*-butylbenzene and bromobenzene, respectively.

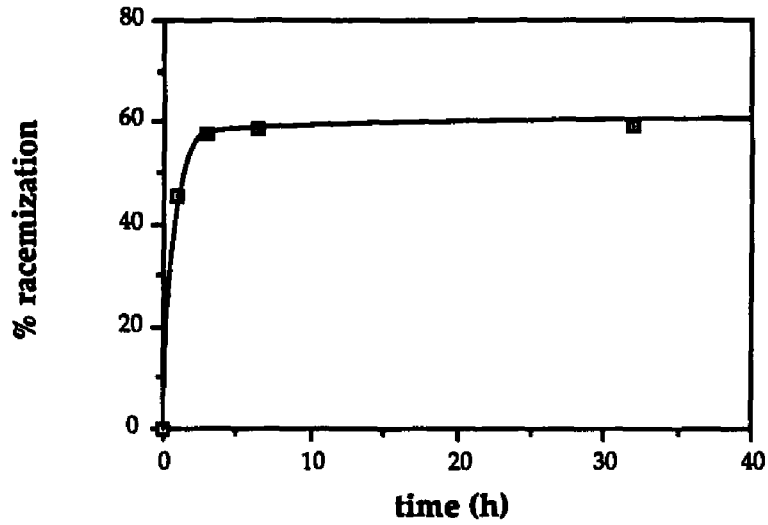


Figure 14. Racemization of **11** by dibenzylmercury in *t*-BuPh at 150 °C.

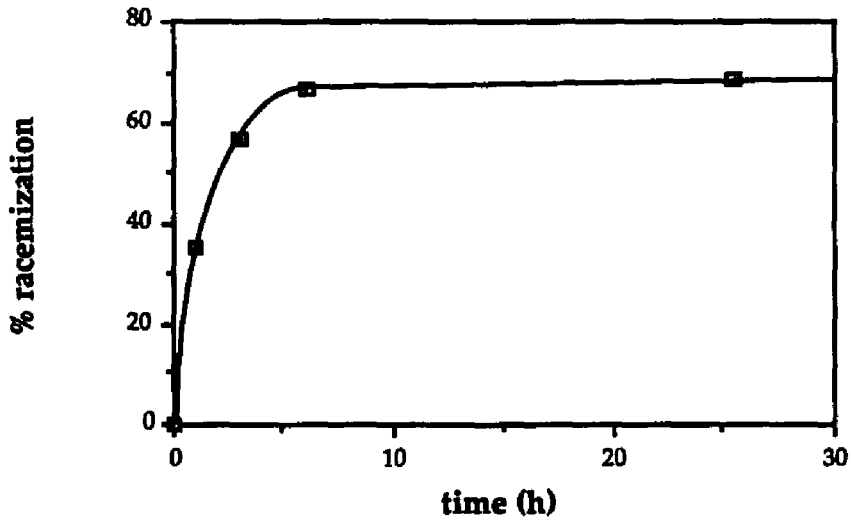


Figure 15. Racemization of **11** by dibenzylmercury in PhBr at 150 °C.

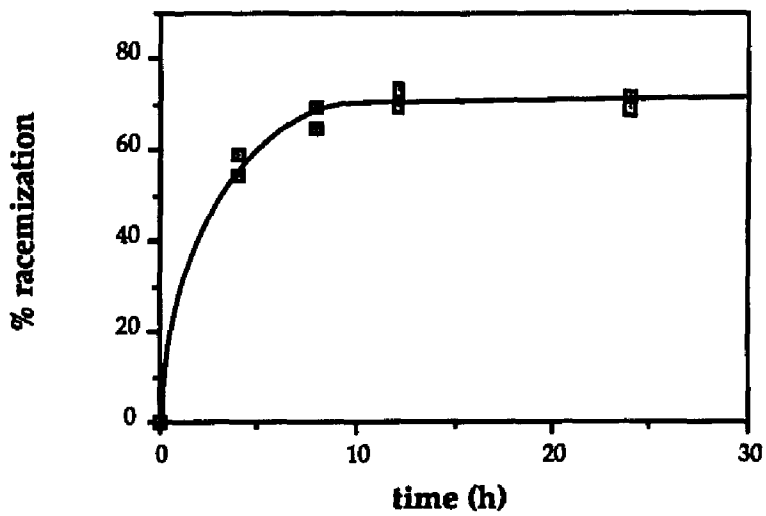


Figure 16. Racemization of **11** by dibenzylmercury in *t*-BuPh at 135 °C.

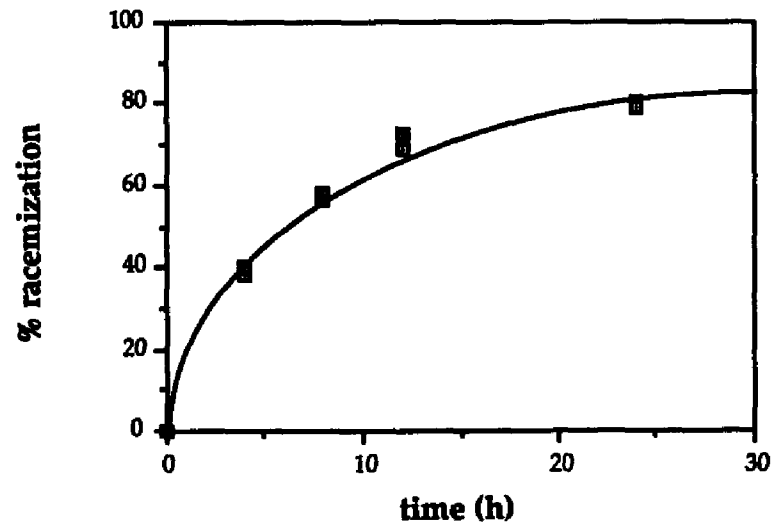
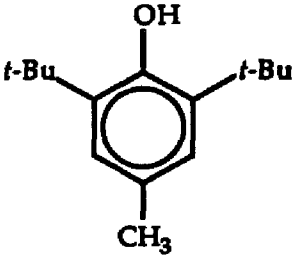


Figure 17. Racemization of **11** by dibenzylmercury in PhBr at 135 °C.

The extent of the racemization period increased as the temperature was lowered. This is consistent with racemization caused by reversible addition of benzyl radical to the anthryl ring. The half-life of dibenzylmercury is increased by the reduction in temperature, which results in benzyl radicals being generated over a longer period of time. The extent of racemization also increased as the temperature was lowered. Radical dimerization is second order in benzyl radical, whereas the addition of benzyl radical to the diester is first order in benzyl radical. If the concentration of benzyl radicals is increased by raising the temperature, the rate of benzyl radical dimerization would increase faster than the rate of attack by benzyl radical on the aromatic ring.

Inhibitors were utilized in order to confirm that a radical mechanism was responsible for the observed racemization of **11**. The results are shown in Table V. The reference solution was heated in the same oil bath for the same length of time. It contained no inhibitor but was identical in all other respects. The inhibitor solutions were prepared by adding the inhibitor to a solution of **11** and the mercury compound in bromobenzene. The reference solution was just a portion of the solution to which no inhibitor had been added.



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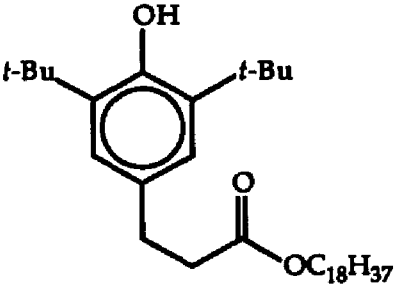


51

Butylated hydroxytoluene (BHT, **50**) and Irganox 1076 (**51**) were not effective in inhibiting racemization. Massive amounts of each inhibitor only partially inhibited racemization (see Table V). When bianthryl **11** was heated to 190 °C for 1 h in *tert*-butylbenzene with a 20 : 1 molar ratio of BHT to

dibenzylmercury, **11** racemized to the extent of 27.4%. Irganox 1076, which is structurally analogous to BHT, was used under the same conditions in a 10 : 1 molar ratio to dibenzylmercury. Biaryl **11** showed 32.4% racemization. An identical solution without inhibitor racemized to the extent of 45.7%. Similar results were obtained in bromobenzene. With 20 : 1 BHT/dibenzylmercury 26.4% racemization of **11** was observed. With 10 : 1 Irganox 1076/dibenzylmercury 31.0% racemization was found. An identical solution without inhibitor showed 38.1% racemization. BHT and related hindered phenols are not effective antioxidants in the range 150 - 200 °C.[78] BHT and Irganox 1076 are also not effective inhibitors in our system.

Table V. BHT and Irganox 1076 as inhibitors of racemization of **11** in *tert*-butylbenzene and bromobenzene at 190 °C.

	percent racemization	
inhibitor	*tert*-butylbenzene	bromobenzene
none	45.9 (1 h)	38.2 (1 h)
	45.4 (2 h)	38.0 (2 h)
BHT	26.3 (1 h)	26.4 (1 h)
	28.5 (2 h)	26.4 (2 h)
Irganox 1076	32.2 (1 h)	31.0 (1 h)
	32.5 (1 h)	31.3 (1 h)

Thiophenol is an effective inhibitor of alkyl radical reactions because it is a good hydrogen donor. Thiophenol rapidly transfers a hydrogen atom to benzyl radical (see equation 22).[79] The resulting phenylthiyl radical can dimerize to form diphenyl disulfide, with which it is in equilibrium at elevated temperatures (equation 23).[80] As expected, thiophenol effectively inhibited the racemization of bianthryl **11** by dibenzylmercury. The presence of thiophenol in a 2 : 1 molar ratio to dibenzylmercury reduced the extent of

racemization by about 90% in both solvents (see Table VI). No inhibition was observed when thiophenol was present in a 0.5 : 1 molar ratio. Since two benzyl radicals are formed from every molecule of dibenzylmercury, at least a 2 : 1 ratio of inhibitor would be necessary to completely consume all benzyl radicals formed. Mercuric thiophenolate, which exists in equilibrium with mercury and phenylthiyl radical (Equation 24),[81] formed as white crystals. These were filtered before measuring the optical rotation of the solutions.

$$PhSH + PhCH_2\bullet \rightarrow PhS\bullet + PhCH_3 \quad (22)$$

$$PhS\bullet \rightleftharpoons PhSSPh \quad (23)$$

$$2\,PhS\bullet + Hg \rightleftharpoons Hg(SPh)_2 \quad (24)$$

Table VI. Thiophenol as inhibitor of racemization of **11** in *tert*-butylbenzene and bromobenzene at 190 °C.

molar ratio	percent racemization	
$PhSH/HgR_2$	*tert*-butylbenzene	bromobenzene
no inhibitor	42.1, 42.4	38.8, 39.0
0.5 : 1	44.3, 45.5	41.6, 44.1
2 : 1	3.9, 3.3	4.6, 4.4

Phenylthiyl radical does not racemize bianthryl in either solvent under the conditions of the inhibition experiment. When **11** was heated to 190 °C with a 5 : 1 molar ratio of diphenyl disulfide in *tert*-butylbenzene or bromobenzene, no racemization was observed after 66 h. Diphenyl disulfide is a thermal source of phenylthiyl radical.[81a]

The results of this chapter support the hypothesis that the racemization of bianthryl **11** is due to the reversible addition of benzyl radical. The racemization is clearly a radical process. Catalysis is brought about by a radical precursor, and inhibition occurs in the presence of a radical trap. Inert solvents were used, eliminating the possibility that a solvent radical could be generated.

Chapter 4:

The Racemization of Optically Active 2,2'-Dicarbomethoxy-9,9'-bianthryl by Isopropyl Radicals Derived from Diisopropylmercury.

Diisopropylmercury decomposes when heated to yield isopropyl radicals and mercury. It has been concluded that the thermal decomposition of diisopropylmercury involves concerted rupture of both C–Hg bonds[82] as shown in equation 25. The two-step mechanism shown in equations 26 and 27 is also possible.

$$Hg\textit{i}\text{-}Pr_2 \rightarrow Hg + 2\,\textit{i}\text{-}Pr\bullet \quad (25)$$

$$Hg\textit{i}\text{-}Pr_2 \rightarrow \bullet Hg\textit{i}\text{-}Pr + \textit{i}\text{-}Pr\bullet \quad (26)$$

$$\bullet Hg\textit{i}\text{-}Pr \rightarrow Hg + \textit{i}\text{-}Pr\bullet \quad (27)$$

It appears that alkylmercury radicals such as •Hg*i*-Pr, if formed, fragment very rapidly before they can react with any other species in solution. For example, in the reaction of di-*n*-butylmercury with carbon tetrachloride, one of the products formed was *n*-BuHgCl. It was suggested[83] that this compound was formed as the result of chlorine abstraction by *n*-BuHg• from CCl_4 (see equation 28). A kinetic isotope effect study showed that this was not the case, and it was suggested that RHgCl actually forms by chlorinolysis of the dialkylmercury (equation 29).[84]

$$\textit{n}\text{-}BuHg\bullet + CCl_4 \rightarrow \textit{n}\text{-}BuHgCl + \bullet CCl_3 \quad (28)$$

$$Cl\bullet + Hg\textit{n}\text{-}Bu_2 \rightarrow \textit{n}\text{-}BuHgCl + \textit{n}\text{-}Bu\bullet \quad (29)$$

Diisopropylmercury can therefore serve as a thermal source of isopropyl radicals to investigate the possibility of catalyzing the racemization of **11** by reversible addition.

When a bromobenzene solution of diisopropylmercury and **11** in a 5.9 : 1 molar ratio was heated at 190 °C for one hour, a complex product mixture was obtained from which none of the original **11** could be recovered. Analytical TLC indicated that at least four components were present with R_f values very close to that of bianthryl **11**. Attempts to separate the components or at least recover starting material to determine whether any racemization had transpired were unsuccessful. It was thus not possible to determine whether any racemization of **11** had taken place or whether any unreacted starting material was present in the mixture.

A lower molar ratio of diisopropylmercury to **11** (0.29 : 1) was used under the same conditions to ensure that the starting material would not be consumed entirely. Since two isopropyl radicals are produced from each diisopropylmercury molecule (see equation 25) no more than roughly 60% of **11** could be transformed to product using this molar ratio. After 2.5 h, 91% of the starting material was recovered. The sample was 94% racemized. A trace amount (<3% by mass) of a mixture of unidentified material was also isolated. Proton NMR spectra suggested that this material could be derived from reaction of **11** and isopropyl radicals, however further identification was not established.

The extensive racemization of **11** requires that an isopropyl radical be capable of racemizing more than one molecule of **11**. Each molecule of diisopropylmercury can yield a maximum of two free isopropyl radicals. If each radical were able to attack just one molecule of **11** before being terminated, no more than 60% racemization would be possible. This assumes

that no cage recombination takes place. Cage recombination of isopropyl radicals would reduce the total number of free isopropyl radicals available for reaction and would therefore also reduce the extent of racemization.

In order to investigate the racemization process further, the reaction was run at lower temperatures. Reducing the temperature lengthens the half-life of diisopropylmercury and should therefore prolong the duration of the racemization process as long as the rotation around the aryl-aryl bond in the sigma-complex intermediate is still rapid relative to the reversal of the addition step. This was indeed observed when the racemization was conducted at 170, 160, and 150 °C (see Figure 18). The racemization process continued for progressively longer periods of time as the temperature was decreased.

Similar results were obtained when *tert*-butylbenzene was used as solvent instead of bromobenzene. Extensive product formation took place with excess diisopropylmercury at 190 °C, but extensive racemization with very little product formation was observed when **11** was used in excess. The racemization tapered off after about 1 h at 190 °C in *tert*-butylbenzene. As the temperature was reduced the racemization continued for a longer length of time (see Figure 19). The similarity of the results in both solvents points against the possibility that the racemization is mediated by a radical derived from either solvent.

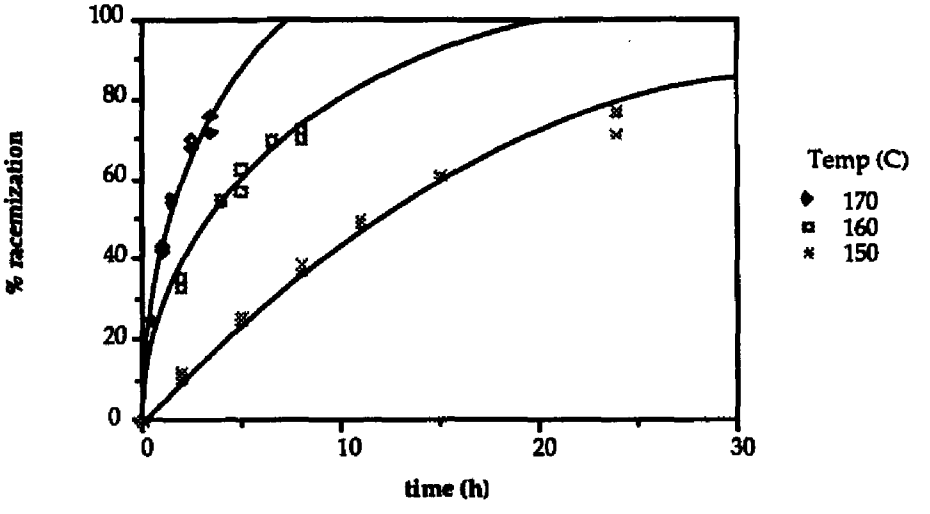


Figure 18. Racemization of **11** by diisopropylmercury at 170, 160, and 150 °C in bromobenzene (1 : 4 molar ratio diisopropylmercury/**11**).

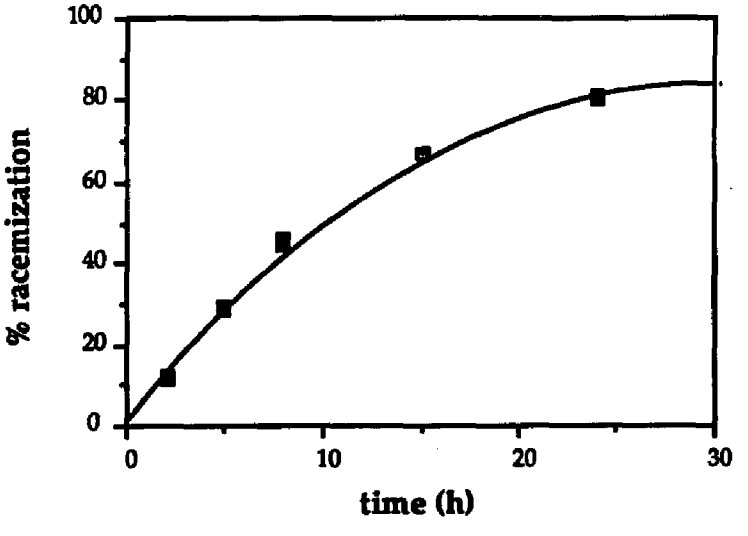


Figure 19. Racemization of 11 by diisopropylmercury at 150 °C in *tert*-butylbenzene (1 : 4 molar ratio diisopropylmercury/ **11**).

A series of experiments was carried out at 170 °C to establish the order of the racemization with respect to diisopropylmercury and with respect to **11**. The concentration of **11** was held constant as the concentration of diisopropylmercury was varied for one series of runs and the concentration of diisopropylmercury was held constant as the concentration of **11** was varied for another series of runs. Each series was repeated. The results were plotted using the CricketGraph program (Cricket Software, Inc.). The data is plotted as rotation vs time (see Figures 20-23) since the optical rotation is proportional to concentration of active material. The rate of racemization in units of degrees over time is equal to the slope of the tangent to the line at a particular point. A third order polynomial fit was applied to each set of data. The slope at time zero is just the x coefficient of the polynomial equation. All other terms drop out after taking the first derivative and setting $x = 0$. The initial rates obtained by this method using the plots in Figures 20-23 are shown in Tables VII-X.

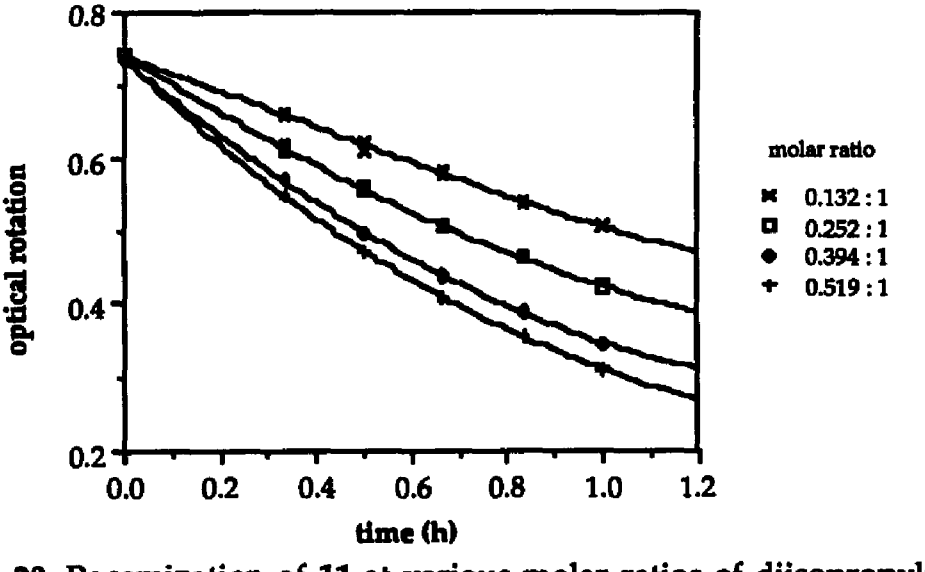


Figure 20. Racemization of **11** at various molar ratios of diisopropylmercury : **11** at 170 °C (run #1). Constant concentration of **11**.

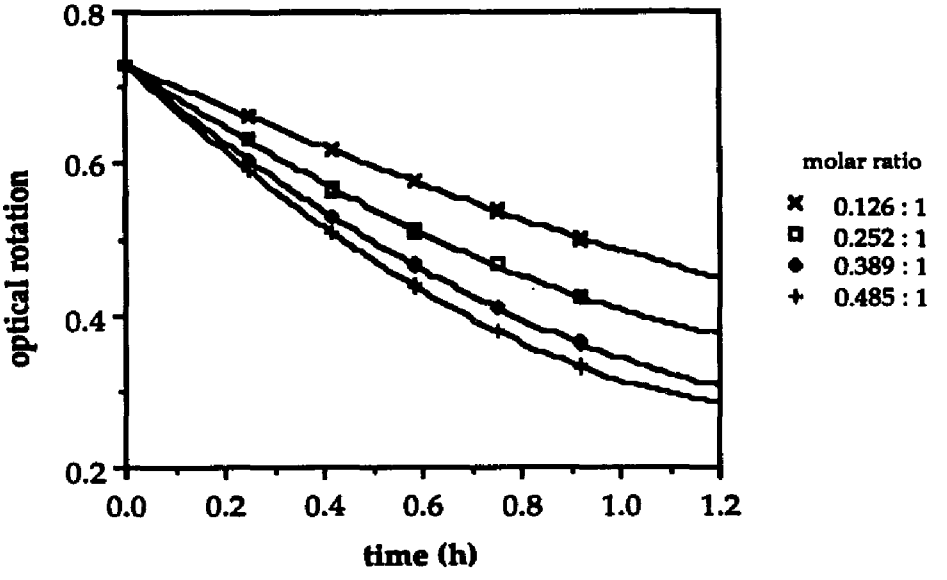


Figure 21. Racemization of **11** at various molar ratios of diisopropylmercury : **11** at 170 °C (run #2). Constant concentration of **11**.

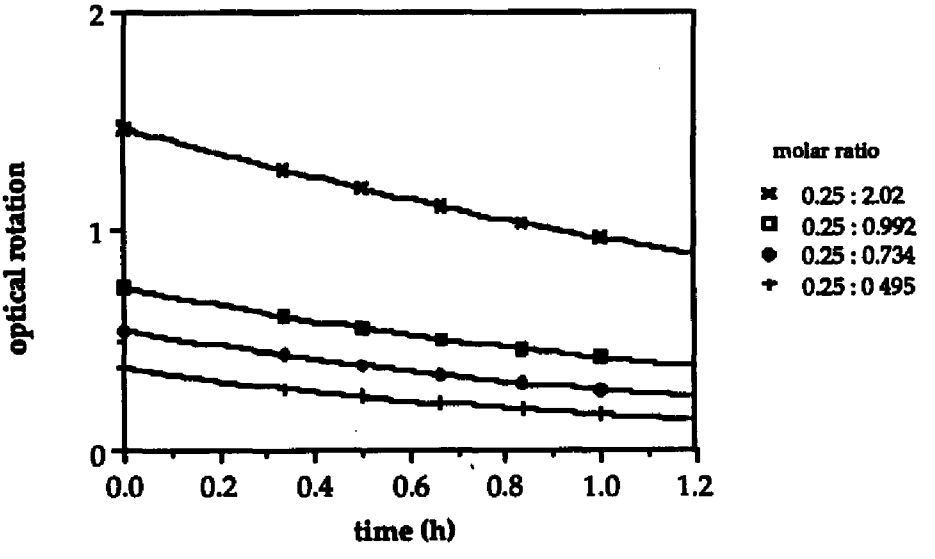


Figure 22. Racemization of **11** by diisopropylmercury at various molar ratios of diisopropylmercury : **11** at 170 °C (run #1). Constant concentration of diisopropylmercury.

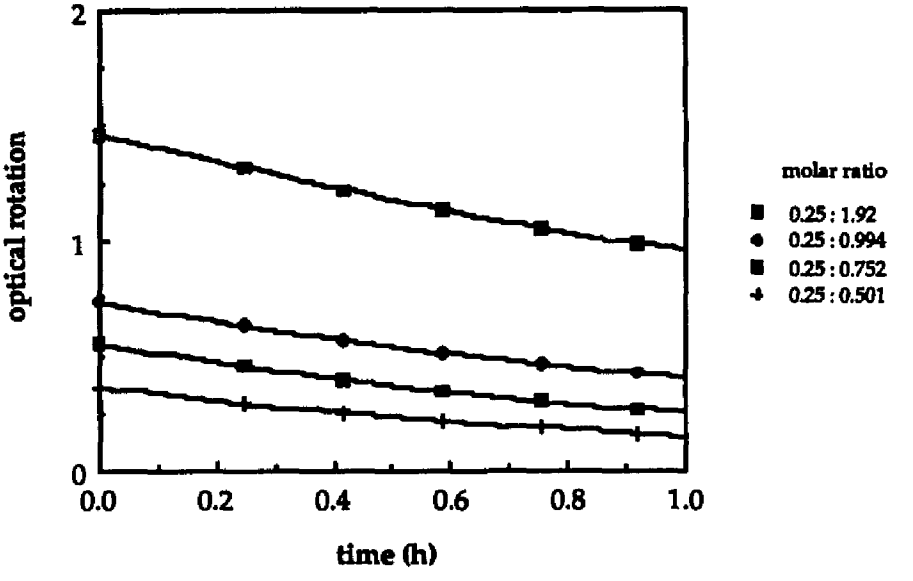


Figure 23. Racemization of **11** by diisopropylmercury at various molar ratios of diisopropylmercury : **11** at 170 °C (run #2). Constant concentration of diisopropylmercury.

Table VII. Variation of the initial rate of racemization of **11** with change in the concentration of diisopropylmercury at constant concentration of **11** (run #1).

molar ratio HgR_2 / **11**	rate at t = 0
0.132 : 1	-0.226
0.252 : 1	-0.412
0.394 : 1	-0.542
0.519 : 1	-0.643

Table VIII. Variation of the initial rate of racemization of **11** with change in the concentration of diisopropylmercury at constant concentration of **11** (run #2).

molar ratio HgR_2 /**11**	rate at t = 0
0.126 : 1	-0.277
0.252 : 1	-0.422
0.389 : 1	-0.541
0.485 : 1	-0.598

Table IX. Variation of the initial rate of racemization of **11** with change in the concentration of **11** at constant concentration of diisopropylmercury (run #1).

molar ratio HgR_2 /**11**	rate at t = 0
0.25 : 2.02	-0.595
0.25 : 0.992	-0.412
0.25 : 0.734	-0.349
0.25 : 0.495	-0.312

Table X. Variation of the initial rate of racemization of **11** with change in the concentration of **11** at constant concentration of diisopropylmercury (run #2).

molar ratio HgR_2 /**11**	rate at t = 0
0.25 : 1.92	-0.553
0.25 : 0.994	-0.422
0.25 : 0.752	-0.405
0.25 : 0.501	-0.338

A rate constant was obtained for every possible combination of concentrations using equation (30) derived as follows:

$$conc_1 = [Z]$$

$$conc_2 = y[Z]$$

where y is the ratio of $conc_2$ to $conc_1$, and Z is the reagent whose concentration is being varied

$$rate_2 = k\{y[Z]\}^x$$

where x is the order with respect to Z.

$$rate_1 = k[Z]^x$$

$$\frac{rate_2}{rate_1} = \frac{k\{y[Z]\}^x}{k[Z]^x}$$

Since k and $[Z]^x$ cancel out, this leaves:

$$\frac{rate_2}{rate_1} = y^x$$

or

$$\ln \frac{rate_2}{rate_1} = x \ln(y) \qquad (30)$$

A plot of ln(y) vs $\ln(rate_2/rate_1)$ will have a slope x equal to the order with respect to the reagent whose concentration is varied. The plots and slopes are shown in Figures 24-27 (generated using the CricketGraph program).

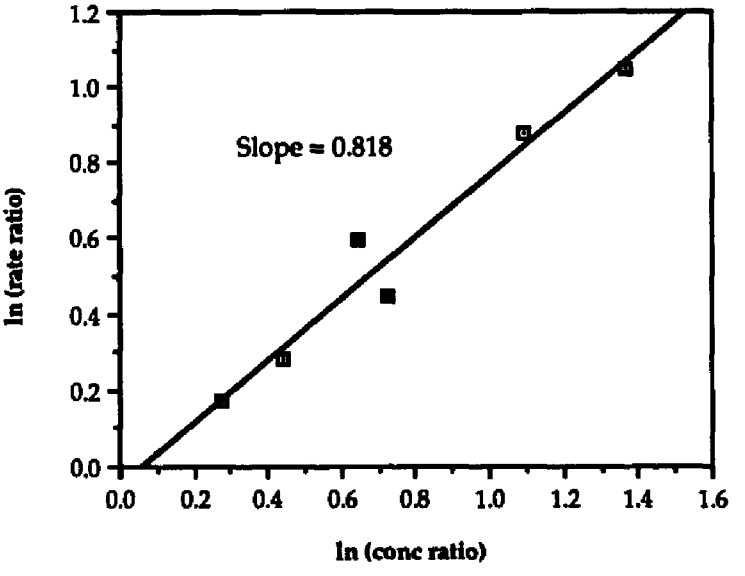


Figure 24. Plot of ln ($rate_2/rate_1$) vs ln ($conc_2/conc_1$) to determine the order in diisopropylmercury for the racemization of **11** at 170 °C (run #1).

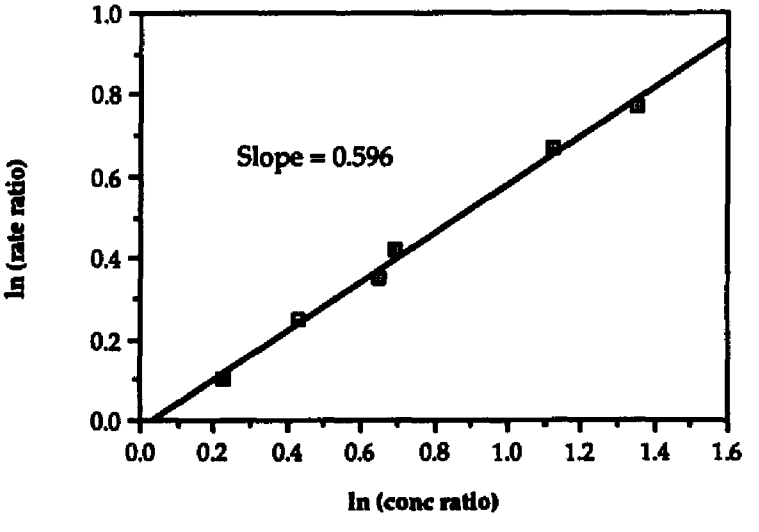


Figure 25. Plot of ln ($rate_2/rate_1$) vs ln ($conc_2/conc_1$) to determine the order in diisopropylmercury for the racemization of **11** at 170 °C (run #2).

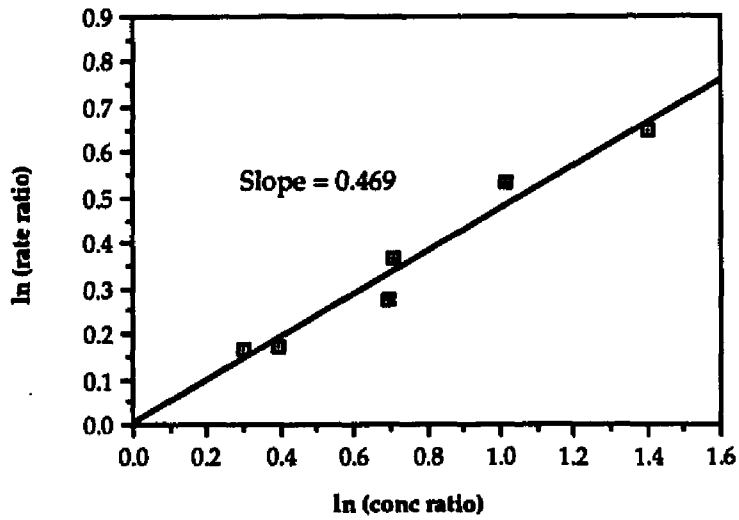


Figure 26. Plot of ln ($rate_2/rate_1$) vs ln ($conc_2/conc_1$) to determine the order in **11** for the racemization by diisopropylmercury at 170 °C (run #1).

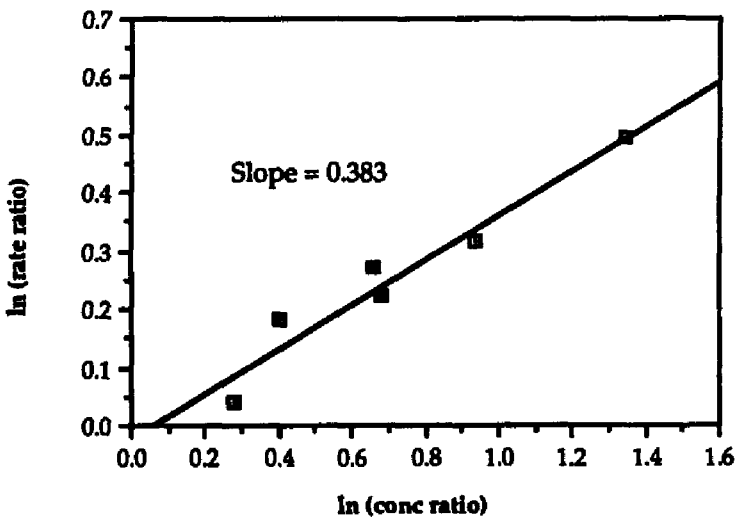


Figure 27. Plot of ln ($rate_2/rate_1$) vs ln ($conc_2/conc_1$) to determine the order in **11** for the racemization by diisopropylmercury at 170 °C (run #2).

The average of the orders found for diisopropylmercury from the slopes of the plots in Figures **24** and **25** is 0.71. The plots in Figures **26** and **27** yielded an average slope of 0.43. This suggests that the racemization has an order of 0.43 with respect to **11** and 0.71 with respect to diisopropylmercury.

It is not clear what could account for the observation of approximately one half order with respect to **11**. The rate of racemization certainly depends on the concentration of the addition intermediate (see Figure 28, step 4). Since the formation of the sigma-complex intermediate (step 3) is first order with respect to **11**, one would expect the racemization to also be first order with respect to this reagent.

It is not obvious what order might be expected for diisopropylmercury. If the racemization is proceeding via reversible addition of isopropyl radical to the biaryl, then the rate of formation of the addition intermediate (and therefore the rate of racemization) will depend on the concentration of this radical as well as on the concentration of bianthryl **11**. The radical is being generated at a steadily decreasing rate by first order thermal decomposition of diisopropylmercury. If a steady state concentration of diisopropyl radicals ensues and the steady state concentration is proportional to the initial concentration of diisopropylmercury, the racemization may show first order kinetics in this reagent. An order of less than one with respect to the dialkylmercury compound may be an outcome of the steady-state kinetics. As the concentration of the alkyl radical increases, the rate of the termination step increases more than the rate of attack on **11** because the former is second order in isopropyl radical while the latter is only first order in this radical. Because of the complex nature of this radical system it is difficult to explain the observed orders based on the information that is available.

Initiation

1. $HgR_2 \rightarrow HgR\bullet + R\bullet$

2. $HgR\bullet \rightarrow Hg + R\bullet$

Racemization

3. $R\bullet$ + (+)-ArH $\rightarrow$ (+)-RArH$\bullet$

4. (+)-RArH$\bullet \rightarrow$ (±)-RArH$\bullet$

5. (+)-RArH$\bullet \rightarrow R\bullet$ + (+)-ArH

6. (±)-RArH$\bullet \rightarrow R\bullet$ + (±)-ArH

Termination

7. $2R\bullet \rightarrow R_2$

8. $2R\bullet \rightarrow R' + R''$

9. $2RArH\bullet \rightarrow (RArH)_2$

10. RArH$\bullet$ + $R\bullet \rightarrow$ RArHR

11. Aromatization of dimers formed in steps 9 and 10.

Figure 28. Proposed mechanism of racemization of **11** by dialkylmercurials

The half-life of the radical source under the conditions of the racemization experiments would provide some insight into how the rates of radical formation and racemization compare. The very low concentration of diisopropylmercury used in the racemization experiments makes it difficult to make a statement about the extent of its decomposition. No mercury was visible at the bottom of the tubes after the racemization.

Attempts to determine the half-life for the decomposition of diisopropylmercury by gravimetric or volumetric analysis of mercury required about sixty times the concentration used in the racemization experiments and did not give consistent results. A method involving HPLC analysis of the solution gave reproducible results at a concentration roughly fifteen times that used in the racemization experiments. A selective wavelength UV detector allowed the solvent to be used as internal standard at a wavelength at which the solvent is much less UV active than diisopropylmercury. A combination of eluent, flow rate, and column was found which completely separated the diisopropylmercury and bromobenzene peaks. Electronic integration gave the area % of the peaks. The ratio (R) of the peak area % of diisopropylmercury to the peak area % of bromobenzene was used as a measure of the concentration.

Solutions of known concentrations were analyzed by this method to verify the accuracy of the method. Two independent experiments gave the same result: a plot of relative concentration vs the area % ratio gives a straight line (see Figures 29 and 30). Before heating the tubes containing diisopropylmercury, a tube was broken open for analysis. The HPLC area percent ratio of the solution was unchanged. The degassing and sealing process therefore has no effect on the concentration of diisopropylmercury. A plot of $\ln(R/R_0)$ vs time at 170°C where R_0 = initial peak area % ratio and

R = observed peak area % ratio is a straight line through the origin (see Figure 31). This is consistent with first order thermal decomposition as represented by equation 31. The experiment was repeated, and the same result was obtained (see Figure 32). The half-lives can be calculated from the slope using equation 32 and were found to be 0.64 h and 0.68 h (average = 0.66 h). The graphs and slopes were generated using the CricketGraph program.

$$\ln (R/R_o) = -kt \tag{31}$$

$$t_{1/2} = \frac{0.693}{k} \tag{32}$$

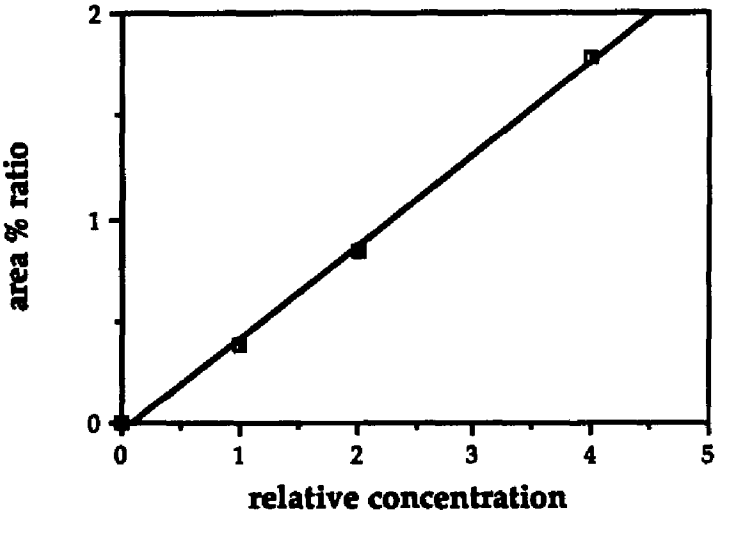


Figure 29. Area percent ratio (diisopropylmercury/bromobenzene) vs. relative concentration (run #1).

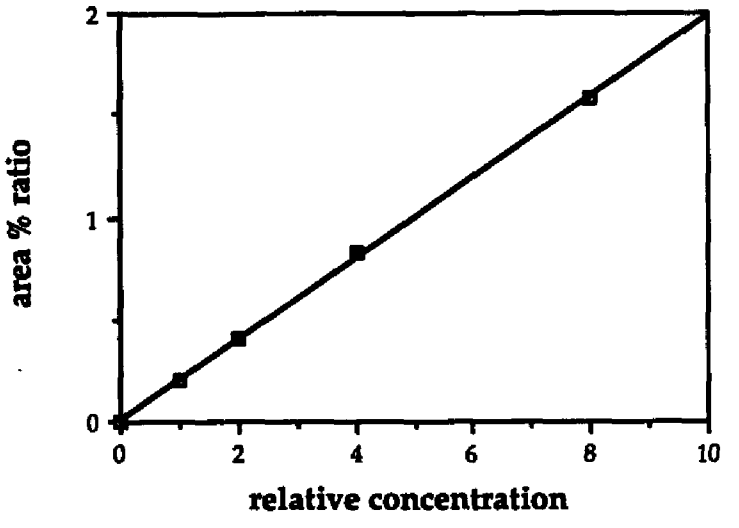


Figure 30. Area percent ratio (diisopropylmercury/bromobenzene) vs. relative concentration (run #2).

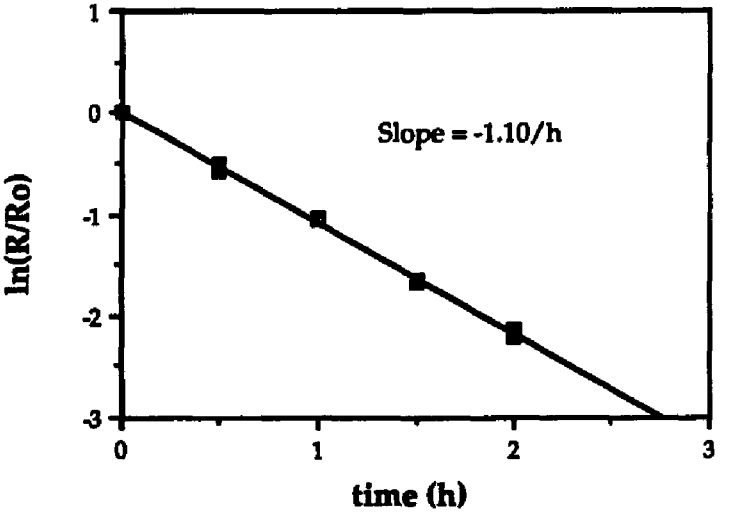


Figure 31. Thermal decomposition of diisopropylmercury at 170 °C (run #1).

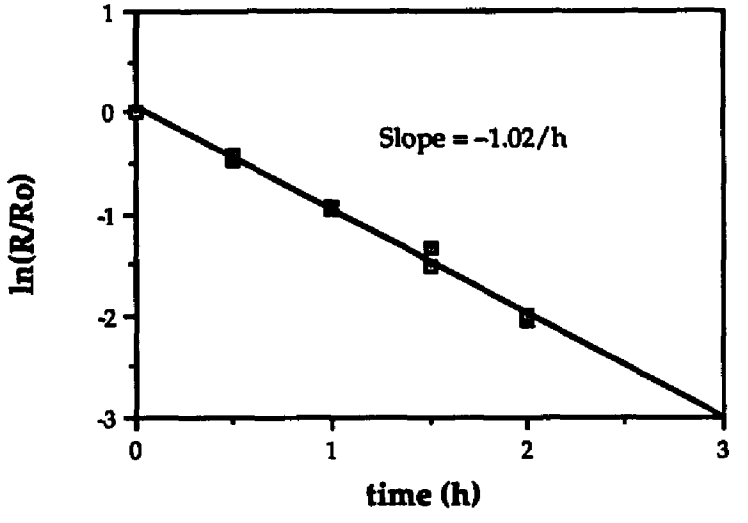


Figure 32. Thermal decomposition of diisopropylmercury at 170 °C (run #2).

This is the very close to the gas phase half-life of diisopropylmercury calculated from Arrhenius parameters obtained in the literature.[85] This result is consistent with the racemization results obtained at 170 °C (see Figure 18), where racemization tapers off after less than 4 h or less than 6 half-lives. It is interesting to compare the relative amount of isopropyl radicals formed to the extent of racemization. With a 0.25 : 1 ratio of diisopropylmercury to **11**, after 1.0 h 43% racemization was observed. This reaction time corresponds to 1.5 half-lives, so we could expect that approximately 65% of the diisopropylmercury decomposed. If we assume that no cage-recombination occurs,[86] since two radicals form from each molecule of diisopropylmercury, the ratio of isopropyl radicals formed relative to **11** would be 2 x 0.65 x (0.25 : 1) or 0.33 : 1. This means that 33 radicals were formed for every 100 molecules of **11** and changed the configuration of 21.5 of those bianthryl molecules.

Table XI shows the effect of various inhibitors on the racemization reaction. The results are similar to those obtained with dibenzylmercury (see Table V, p. 43). The least effective inhibitors are BHT and Irganox 1076. Thiophenol and dicyclohexylphosphine[87] (DCPH) are good hydrogen donors,[88] and as expected are much better inhibitors. DCPH can donate a hydrogen atom to the isopropyl radical (see equations 33 and 34) just as thiophenol does. An absolute rate expression has actually been determined for the rapid transfer of hydrogen from thiophenol to isopropyl radical.[89] Although DCPH is more effective than BHT or Irganox 1076 in inhibiting the racemization, it is less effective than thiophenol (see Table XI). This is consistent with less rapid hydrogen atom transfer to alkyl radicals from DCPH than from thiophenol which has been reported in the literature.[90] Air and oxygen inhibit racemization by diisopropylmercury, possibly due to the formation of unreactive peroxides.

$$(C_6H_{11})_2PH + (CH_3)_2CH\bullet \rightarrow (C_6H_{11})_2P\bullet + (CH_3)_2CH_2 \qquad (33)$$

$$C_6H_5SH + (CH_3)_2CH\bullet \rightarrow C_6H_5S\bullet + (CH_3)_2CH_2 \qquad (34)$$

Table XI. Effect of inhibitors on the racemization of **11** by diisopropylmercury in bromobenzene at 170 °C.

inhibitor	molar ratio inhibitor/HgR_2	% inhibition
Thiophenol	15 : 1	100
	24 : 1	100
Air[a]	1 atm	93.9
Oxygen[a]	1 atm	92.9
DCPH	14.4 : 1	64.8
	23 : 1	75.4
	155 : 1	84.8
BHT	48.2 : 1	32.3
Irganox 1076	50.7 : 1	17.8

[a]The space above the reaction solution in the sealed tubes was at least 1 mL. The number of moles this corresponds to at -78 °C is: 1 mL gas x (273/195) x (1 mol)/22,400 mL = 7×10^{-5} mol gas. Therefore the tubes sealed under oxygen contained 7×10^{-5} mol oxygen. Since air is 20% oxygen, the tubes sealed under air contained at least 1.4×10^{-5} mol of oxygen. Each solution contained 3.3×10^{-6} mol of diisopropylmercury. The experiments with air and oxygen therefore represented a 4 : 1 ratio and a 21 : 1 ratio of oxygen to diisopropylmercury, respectively.

Reversible addition of isopropyl radical to **11** is the most likely explanation for the catalyzed racemization in the presence of diisopropylmercury. The inertness of the solvent could not be easily verified by simply recovering the products of the decomposition, as was done with dibenzylmercury. Smaller amounts of termination products will form because less diisopropylmercury was used, and the termination products which are expected to form (by equations 35 and 36 for dimerization and disproportionation, respectively) are volatile and therefore difficult to isolate.

$$2\,(CH_3)_2CH\bullet \rightarrow (CH_3)_2CHCH(CH_3)_2 \qquad (35)$$

$$2\,(CH_3)_2CH\bullet \rightarrow CH_3CH{=}CH_2 + CH_3CH_2CH_3 \qquad (36)$$

It is unlikely that isopropyl radical could abstract hydrogen from either solvent, since only phenyl and methyl hydrogens are present in *tert*-butylbenzene and only phenyl hydrogens exist in bromobenzene.

Chapter 5:

The Racemization of Optically Active 2,2'-Dicarbomethoxy-9,9'-bianthryl by Ethyl Radicals Derived from Diethylmercury.

Diethylmercury decomposes when heated in a manner similar to dibenzylmercury and diisopropylmercury to give mercury and two ethyl radicals. Based on the magnitude of the Arrhenius parameters it was concluded that the decomposition occurs in the gas phase in a two-step process[91] involving sequential formation of two ethyl radicals as shown in equations 37 and 38. The first step is rate-determining. Based on the low bond dissociation energy of the carbon-mercury bond in $\bullet HgCH_2CH_3$, the second step is expected to be very rapid.[92] For this reason the concentration of the ethylmercury radical should be much lower than that of ethyl radical. As was concluded for the other dialkylmercurates, the alkylmercury radical is expected to be in too low concentration to compete with the alkyl radical for a reagent.

$$Hg(CH_2CH_3)_2 \rightarrow \bullet HgCH_2CH_3 + CH_3CH_2\bullet \quad (37)$$

$$\bullet HgCH_2CH_3 \rightarrow Hg + CH_3CH_2\bullet \quad (38)$$

Diethylmercury is much more thermally stable than either of the two previously discussed dialkylmercury compounds. The gas phase half-life of diethylmercury is much larger ($t_{1/2}$ = 75 h at 200 °C[93] compared to half-lives of several minutes for dibenzyl- and diisopropylmercury). The half-life of diethylmercury in bromobenzene is 260 h at 200 °C while that of diisopropylmercury is 0.66 h at 170 °C, and dibenzylmercury decomposes completely at 190 °C in <0.5 h.[94] This is understandable since ethyl radical is

considerably more reactive than benzyl or isopropyl radical,[95] and therefore diethylmercury should be more stable than the corresponding dialkylmercurates. For this reason it was expected that larger amounts of diethylmercury at higher temperatures would be necessary to bring about decomposition at effective rates. This was found to be the case. Whereas an excess of bianthryl **11** relative to diisopropylmercury was used to avoid extensive product formation at 170 °C, a large excess of diethylmercury was necessary at 200 °C to bring about comparable racemization.

Extensive racemization of **11** was observed when a bromobenzene solution containing diethylmercury in a 10 : 1 molar ratio was heated to 200 °C over a period of 9 h (see Figure 33). Over 94% of **11** was recovered, and only very small amounts of unidentified products were isolated. Very little diethylmercury actually decomposed since no mercury was visible after the reaction. The system was run at 180 °C using a 20 : 1 molar ratio of diethylmercury to **11**, and extensive racemization was observed over a longer period of time (see Figure 33).

No mercury was visible at the bottom of the racemization tubes with either diisopropylmercury or diethylmercury, but for different reasons. Mercury was not visible in the racemization experiments with diisopropylmercury because less than 1 mg would have been formed in the event of complete decomposition. Much higher concentrations of diethylmercury to **11** were used, but the ethyl compound is so much more stable that only a very small fraction of it is actually decomposed during the racemization experiment. Based on the thermal half-life of diethylmercury in bromobenzene (*vide infra*), less than 1% decomposes, which leads to the formation of less than 1 mg of mercury. The same method of HPLC analysis used for diisopropylmercury (see page 59) was used to determine the half-life

of diethylmercury. The eluent, flow rate, and wavelength were adjusted to optimize the analysis. As in the experiments with diisopropylmercury, the diethylmercury and bromobenzene peaks were completely separated. The concentration of diethylmercury used was about twice that used in the racemization experiments. The results of analyses of solutions of known concentration are shown in Figures 34 and 35. Both experiments gave straight lines through the origin. Figures 36 and 37 show a plot of $\ln(R/R_0)$ for each of two thermal decomposition experiments (see p. 59 for a description of R and R_0). The half-life of diethylmercury at 200 °C calculated from the slopes was 253 h and 267 h (average = 260 h).

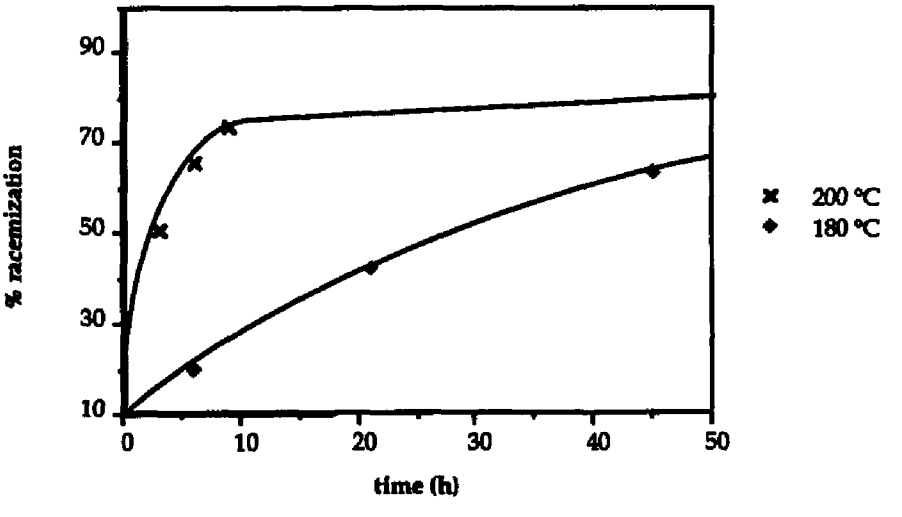


Figure 33. Racemization of **11** at 200 °C with a 10 : 1 molar ratio and at 180 °C with a 20 : 1 molar ratio of diethylmercury : **11**.

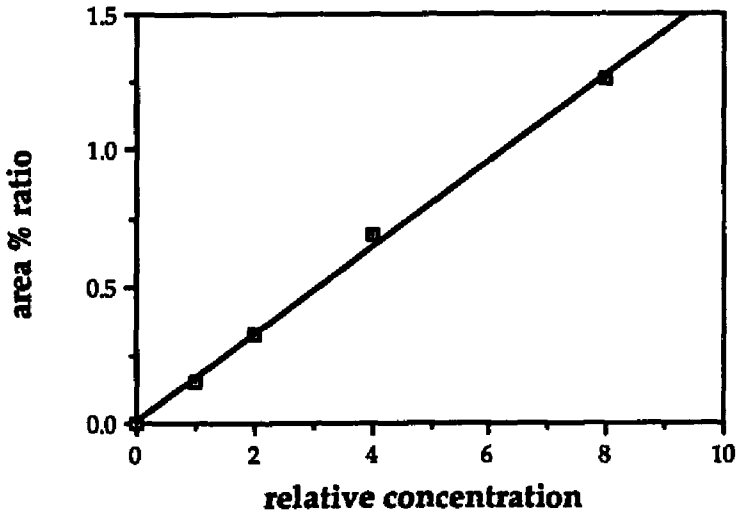


Figure 34. Area percent ratio (diethylmercury/bromobenzene) vs. relative concentration (run #1).

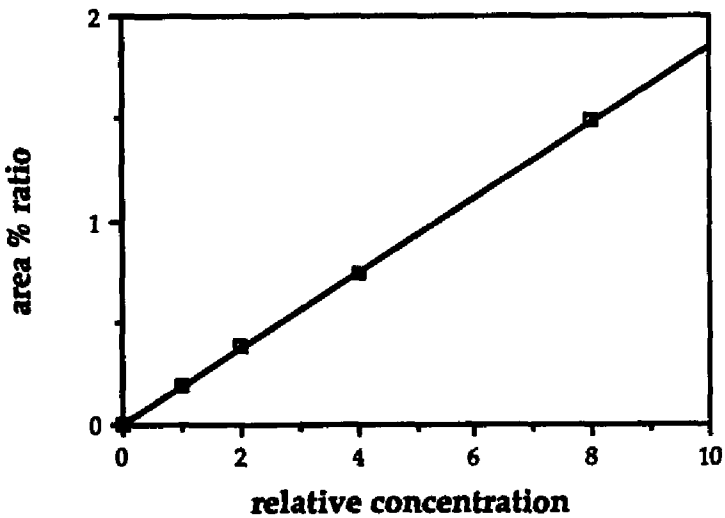


Figure 35. Area percent ratio (diethylmercury/bromobenzene) vs. relative concentration (run #2).

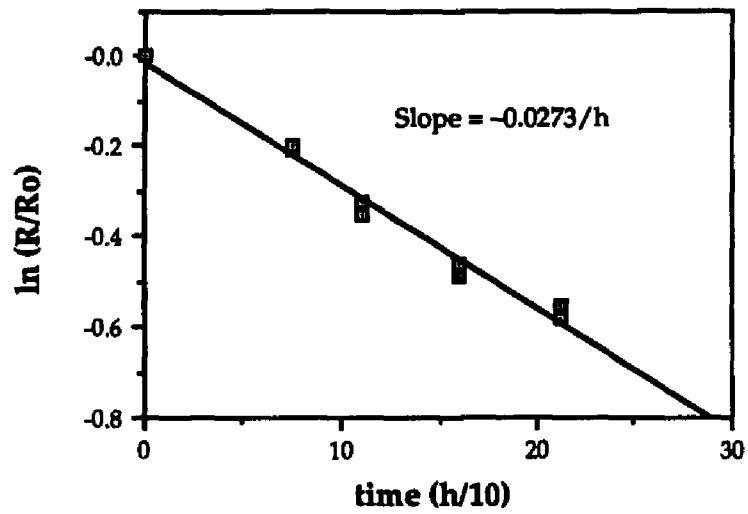


Figure 36. Thermal decomposition of diethylmercury at 200 °C (run #1).

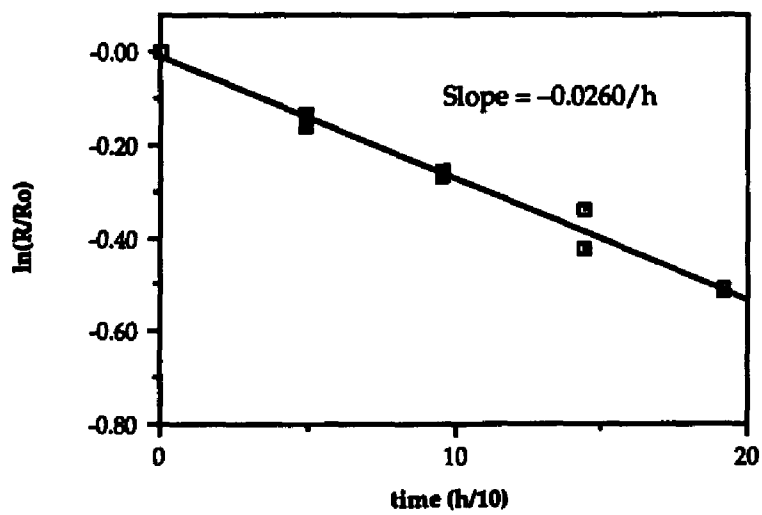


Figure 37. Thermal decomposition of diethylmercury at 200 °C (run #2).

Table XII. Effect of inhibitors on the racemization of **11** by diethylmercury in bromobenzene at 200 °C.

inhibitor	molar ratio inhibitor/HgR_2	% inhibition
Thiophenol	1.9 : 1	74.4
	11 : 1	100
Air, oxygen	(accelerated racemization at 1 atm)	
DCPH	1.8 : 1	68.2
	9.7 : 1	100
BHT	9.3 : 1	36.0
Irganox 1076	6.7 : 1	0.0

The same general method was used to investigate the effect of various radical inhibitors on the racemization of **11** by diethylmercury as was used for diisopropylmercury. The results were similar (see Table XII). Butylated hydroxytoluene (BHT) and Irganox 1076 are less effective inhibitors than dicyclohexylphosphine (DCPH) and thiophenol.

Diethylmercury is less selective than diisopropylmercury towards inhibition by DCPH and thiophenol, most likely because ethyl radical is more reactive than diisopropyl radical. It is interesting that while air and oxygen inhibit racemization by diisopropylmercury, they accelerate racemization by diethylmercury. This type of phenomenon has been observed previously. For example the presence of oxygen enhanced a polymerization reaction initiated by some dialkylmercurials but inhibited the polymerization reaction when initiated by others.[96]

The order of the racemization of **11** by diethylmercury at 200 °C with respect to both reagents was established by the same method as was used for the racemization of **11** by diisopropylmercury. The concentration of **11** was held constant as the concentration of diethylmercury was varied for one series of runs and the concentration of diethylmercury was held constant as the concentration of **11** was varied for another series of runs. Each series was repeated. The results were plotted using the CricketGraph program (see Figures 38–41).

The initial rates are shown in Tables XIII–XVI. The same method was used to determine the order of the racemization with respect to **11** and diethylmercury as was described earlier for diisopropylmercury, and the corresponding plots are shown in Figures 42-45. The average order found for diethylmercury was 0.46, and for **11** the average order found was 0.56. The racemization is therefore approximately one half order in both **11** and diethylmercury.

The orders are comparable to those found for the racemization of **11** in the presence of diisopropylmercury, that is fractional and near one half. This may indicate similarity in the mechanisms involved. It is not clear what could result in an order of less than one in **11**.

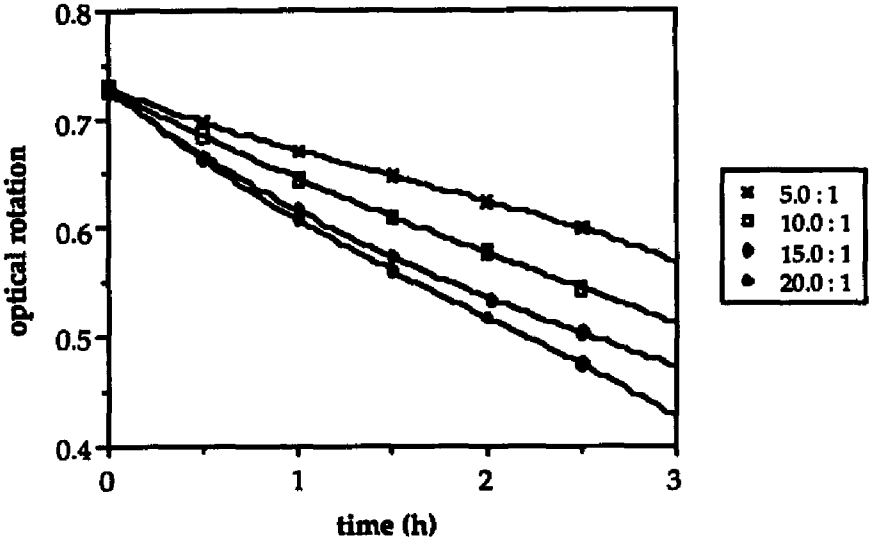


Figure 38. Racemization of **11** by diethylmercury at various molar ratios of diethylmercury : **11** at 200 °C (run #1). Constant concentration of **11**.

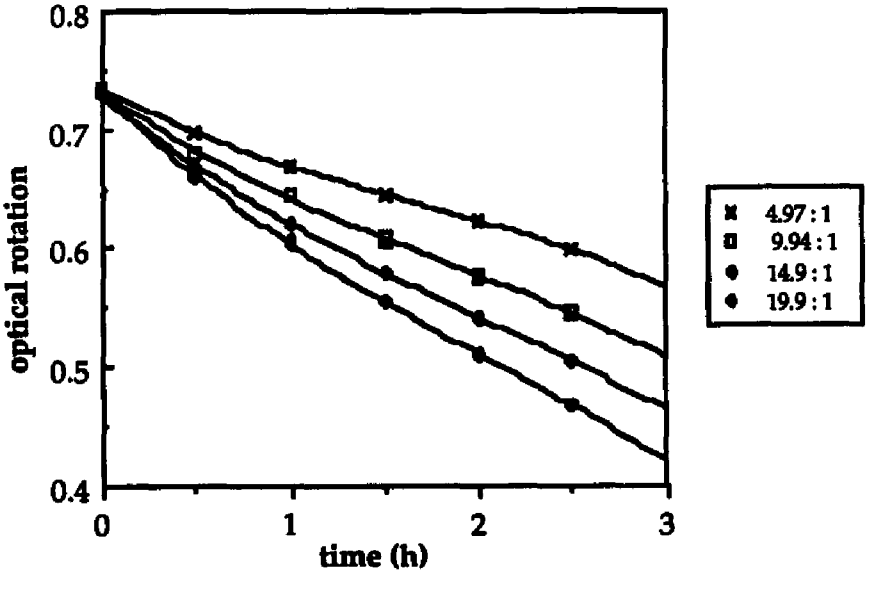


Figure 39. Racemization of **11** by diethylmercury at various molar ratios of diethylmercury : **11** at 200 °C (run #2). Constant concentration of **11**.

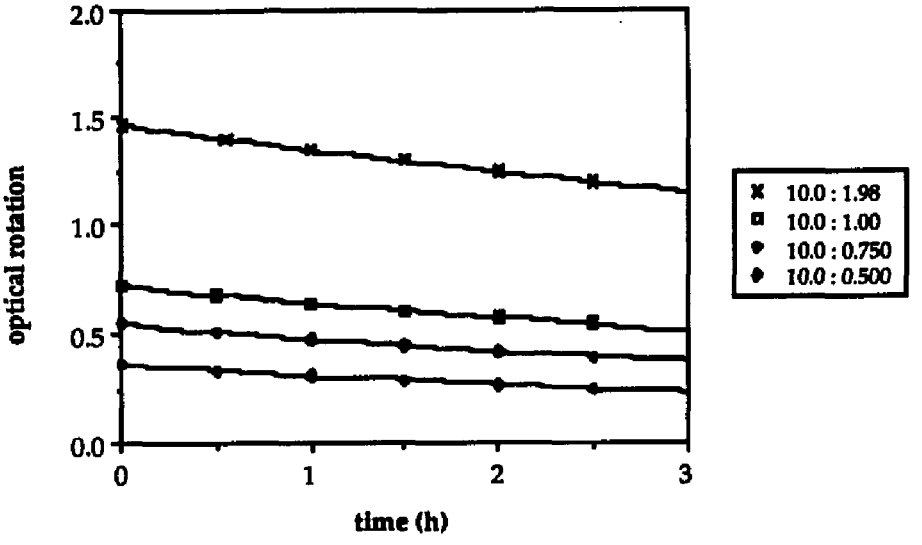


Figure 40. Racemization of **11** by diethylmercury at various molar ratios of **11** : diethylmercury at 200 °C (run #1). Constant concentration of diethylmercury.

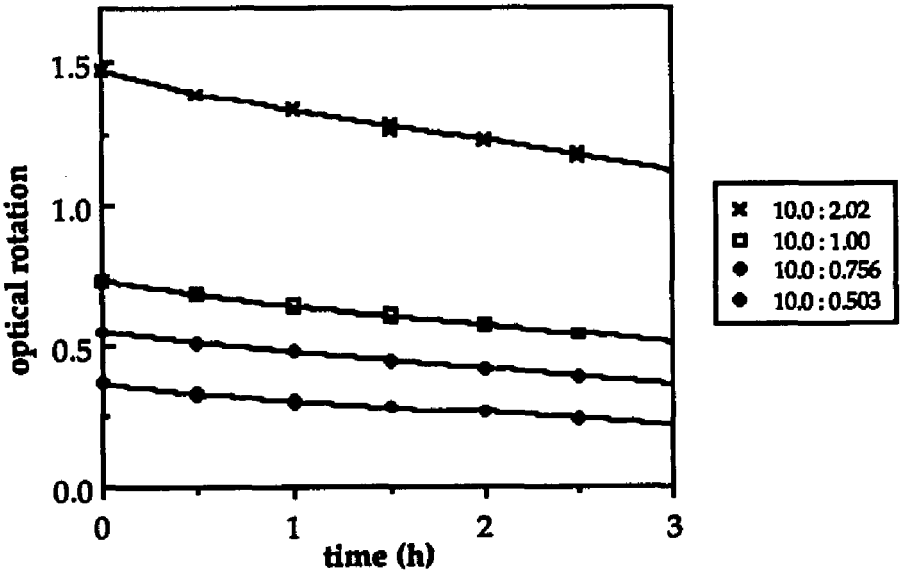


Figure 41. Racemization of **11** by diethylmercury at various molar ratios of **11** : diethylmercury at 200 °C (run #2). Constant concentration of diethylmercury.

Table XIII. Variation of the initial rate of racemization of **11** with change in the concentration of diethylmercury at constant concentration of **11** (run #1).

molar ratio HgR_2 / **11**	rate at t = 0
5.00 : 1	-0.0726
10.0 : 1	-0.0920
15.0 : 1	-0.134
20.0 : 1	-0.153

Table XIV. Variation of the initial rate of racemization of **11** with change in the concentration of diethylmercury at constant concentration of **11** (run #2).

molar ratio HgR_2 / **11**	rate at t = 0
4.97 : 1	-0.0842
9.94 : 1	-0.113
14.9 : 1	-0.132
19.9 : 1	-0.155

Table XV. Variation of the initial rate of racemization of **11** with change in the concentration of **11** at constant concentration of diethylmercury (run #1).

molar ratio HgR_2 / **11**	rate at t = 0
10.0 : 1.98	-0.132
10.0 : 1.00	-0.0920
10.0 : 0.750	-0.0851
10.0 : 0.500	-0.0712

Table XVI. Variation of the initial rate of racemization of **11** with change in the concentration of **11** at constant concentration of diethylmercury (run #2).

molar ratio HgR_2 /**11**	rate at t = 0
10.0 : 2.02	-0.184
10.0 : 1.00	-0.113
10.0 : 0.756	-0.0896
10.0 : 0.503	-0.0833

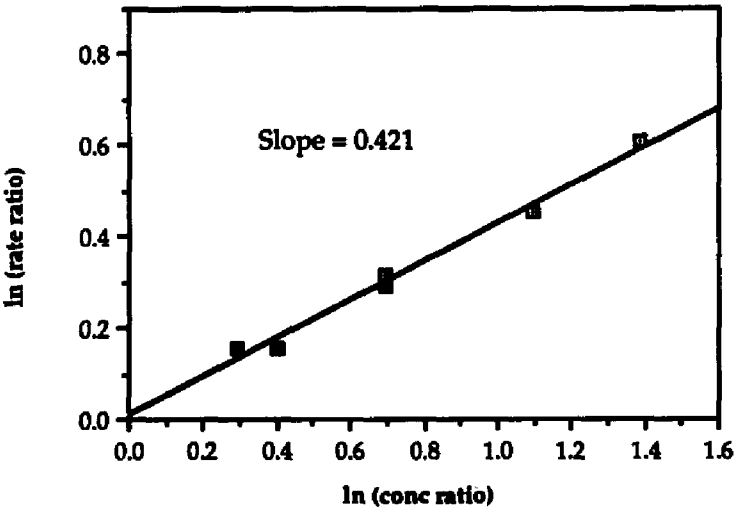


Figure 42. Plot of ln ($rate_2/rate_1$) vs ln ($conc_2/conc_1$) to determine the order in diethylmercury for the racemization of **11** at 200 °C (run #1).

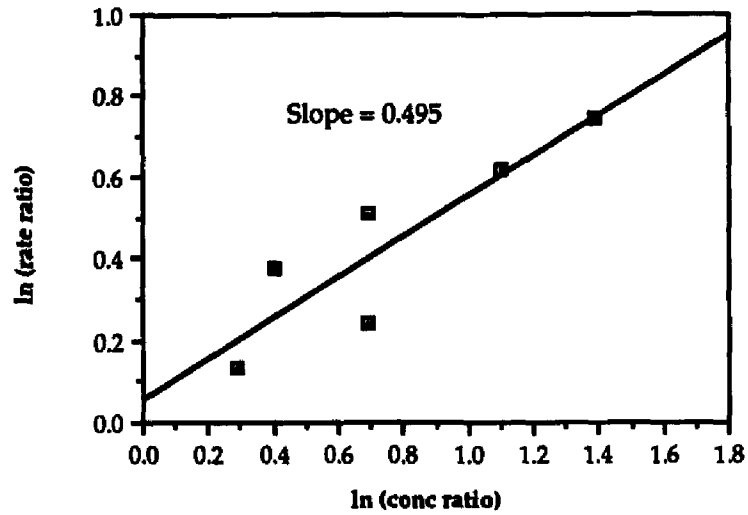


Figure 43. Plot of ln ($rate_2/rate_1$) vs ln ($conc_2/conc_1$) to determine the order in diethylmercury for the racemization of **11** at 200 °C (run #2).

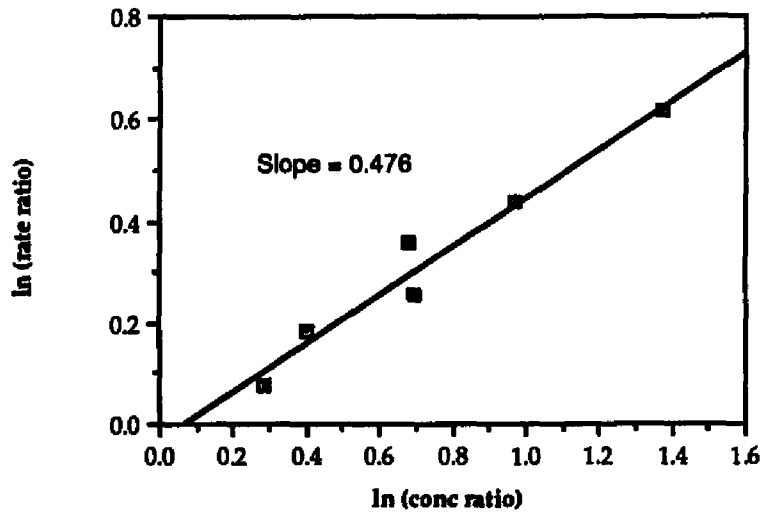


Figure 44. Plot of ln ($rate_2/rate_1$) vs ln ($conc_2/conc_1$) to determine the order in **11** for the racemization by diethylmercury at 200 °C (run #1).

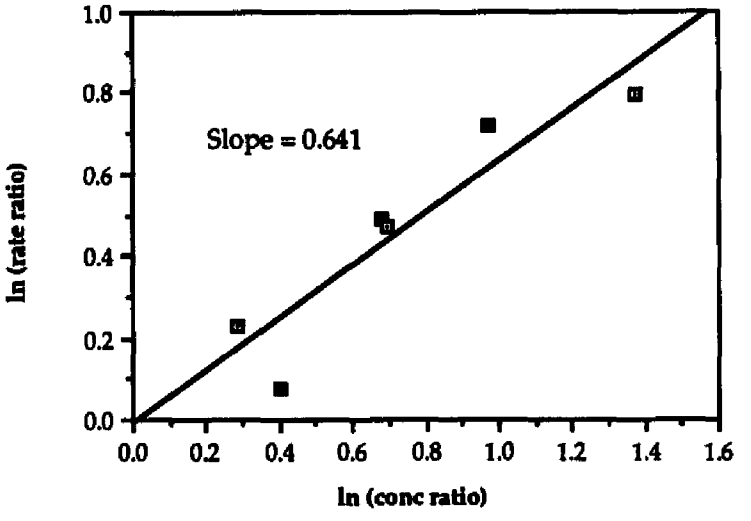


Figure 45. Plot of ln ($rate_2/rate_1$) vs ln ($conc_2/conc_1$) to determine the order in **11** for the racemization by diethylmercury at 200 °C (run #2).

It is conceivable that the racemization process occurs by reversible formation of a charge-transfer complex rather than by reversible addition of a radical. Charge-transfer complexes involving dialkylmercurials as electron donors have been observed.[97] Their formation was attributed to their relatively low ionization potential (7–10 eV).[98] As mentioned earlier (see page 7) the formation of the radical anion of 1,1'-binaphthyl catalyzes the racemization of this compound. The same could be true for **11**. If this were the case one wouldn't expect such a large difference in reactivity between diethyl- and diisopropylmercury because they have essentially identical ionization potentials (8.45 and 8.03 eV, respectively).[99] The very large difference in reactivity observed between the two compounds is more consistent with racemization catalyzed by the alkyl radicals generated by thermal decomposition.

If no cage-recombination takes place, two free ethyl radicals are formed from each molecule of diethylmercury. Since the half-life of diethylmercury is 260 h at 200 °C, only 0.7% will have decomposed after 2.5 h. For the experiment which used a 5 to 1 molar ratio (diethylmercury/**11**) the maximum possible ratio of free ethyl radical to **11** generated over the span of the reaction is 0.07 to 1 (1.4% of 5 to 1).

After 2.5 h, 17.8% racemization was observed. There are a maximum of 7 ethyl radicals produced for every 100 bianthryl molecules. Nine bianthryl molecules out of 100 changed configuration (17.8% racemization), so each ethyl radical must be responsible for changing the configuration of 1.3 bianthryl molecules. This means that on average each ethyl radical adds reversibly to at least 1.3 bianthryl molecules during its lifetime.

Very little diethylmercury decomposed during the racemization experiments, because the reaction time was relatively short compared to the half-life of diethylmercury. It was therefore not possible to establish the inertness of bromobenzene by simply isolating the products of the decomposition of diethylmercury.

Chapter 6:

The Racemization of Optically Active 2,2'-Dicarbomethoxy-9,9'-bianthryl by Radicals Generated by Thermal Decomposition of Azoalkanes.

Azoalkanes decompose on heating to yield alkyl radicals and nitrogen,[100] as shown in equation 39. Azoisopropane and azoethane can therefore serve as alternative sources to the dialkylmercurials for isopropyl and ethyl radicals, respectively (see equations 40 and 41).

$$R—N=N—R \rightarrow 2\,R\bullet + N_2 \quad (39)$$

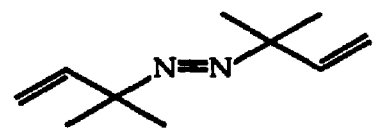
$$i\text{-}Pr—N=N—i\text{-}Pr \rightarrow 2\,i\text{-}Pr\bullet + N_2 \quad (40)$$

$$Et—N=N—Et \rightarrow 2\,Et\bullet + N_2 \quad (41)$$

Azoisopropane is much more thermally stable in the gas phase than diisopropylmercury. In the gas phase at 170° (the temperature of diisopropylmercury kinetic runs), the half-life of diisopropylmercury is about 0.5 hour,[101] compared to 14 days for azoisopropane.[102] Note that the half-life of diisopropylmercury in bromobenzene was found to be roughly the same as in the gas phase; however, the same may not be true for azoisopropane. The gas phase half-life of azoisopropane at 200 °C is 20 hours.[103] This half-life is considerably longer than the half-life of diisopropylmercury at 170 °C. If azoisopropane decomposes at a similar rate in bromobenzene, higher temperatures and a larger mole ratio would be necessary to generate a significant amount of isopropyl radical.

When a bromobenzene solution with a 20 : 1 ratio of azoisopropane/bianthryl **11** was heated at 200 °C for 41 h, **11** was recovered

with 47% racemization. Traces of unidentified products were found, and 65% of starting material was recovered. The highest ratio run with diisopropylmercury at 170° was 0.5 : 1 (to avoid product formation), and the runs typically lasted less than ten hours. Apparently azoisopropane is considerably more stable than diisopropylmercury in bromobenzene. Another possibility is that extensive cage-recombination limits the number of isopropyl radicals that are available to racemize the bianthryl. Engel and co-workers found 40-42% cage recombination for the thermolysis of azo compound **52**.[104]



52

The presence of thiophenol inhibits the racemization of **11** by azoisopropane. A 2.5 : 1 ratio of thiophenol to azoalkane reduced the observed percent racemization from 51% to 13%. A 20 : 1 ratio caused a reduction to 4.5%, which is near the limit of experimental error.

The fact that racemization of **11** is catalyzed by another source of isopropyl radicals besides diisopropylmercury adds strength to the conclusion that the process takes place by the reversible formation of an addition intermediate between **11** and an isopropyl radical.

Racemization of **11** was also observed in the presence of azoethane. Azoethane is only slightly more thermally stable than diethylmercury in the gas phase. The gas phase half-life of azoethane at 200° is 450 hours,[105] while the gas-phase half-life of diethylmercury is 75 hours at the same

temperature.[106] The solution half-life of diethylmercury in bromobenzene was found to be 250 hours at 200°, as reported earlier in this work.

Only 40% of **11** was recovered, which was 36% racemized when a 20 : 1 mixture of azoethane/**11** was heated to 200°C for 48 h. When the molar ratio was reduced to 10 : 1, the amount of **11** recovered increased and the percent racemization decreased. The recovery was about 60% and the racemization was 35%.

Since the ethyl radical is less stable than the isopropyl radical, an addition intermediate formed between an ethyl radical and **11** will be less likely to revert to educts compared to the corresponding addition intermediate with an isopropyl radical. A greater percentage of the ethyl intermediates are expected to go on to form products compared to the intermediates from the isopropyl radical.

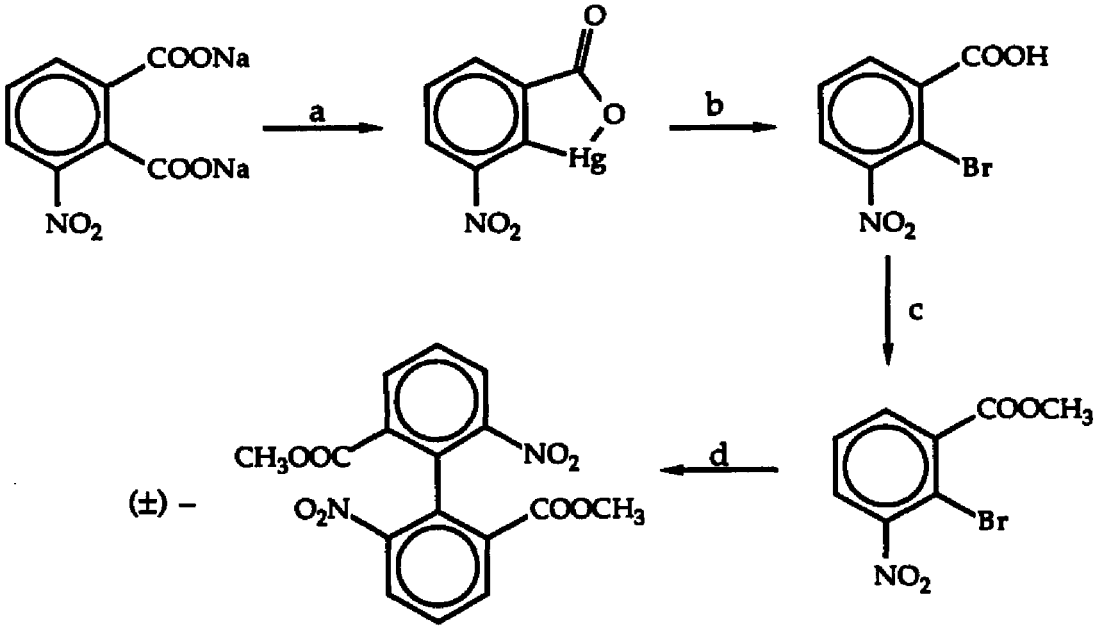
Surprisingly, thiophenol proved to have a limited effect on the racemization. The percent inhibition was the same (65%) whether a 2.0, 3.8, or 7.5 : 1 ratio of inhibitor/azoethane was used. The effect of the inhibitor appears to be insensitive to the amount of thiophenol for the range used. In contrast, complete inhibition of racemization was observed with a 10 : 1 ratio of inhibitor/azoethane using diethylmercury as the source of ethyl radicals. The major difference between the conditions employed for the two sources of ethyl radicals is the length of the reaction time, which was several hours for diethylmercury and several days for azoethane.

Chapter 7:

Attempted Racemization of Esters of 6,6'-Dinitrobiphenyl-2,2'-dicarboxylic Acid.

Optically active dimethyl 6,6'-dinitrobiphenyl-2,2'-dicarboxylate (53) was subjected to several nucleophilic systems in an attempt to induce racemization via reversible formation of a σ-complex.

The preparation of (±)-53 is shown in Figure 46. Optically active diester 53 was obtained using the method of A. W. Ingersoll (see reference 133 and Figure 47).



53

Figure 46. Preparation of racemic diester 53.
(a) $Hg(OCOCH_3)_2$/acetic acid; (b) NaBr/Br_2; (c) CH_2N_2; (d) Cu.

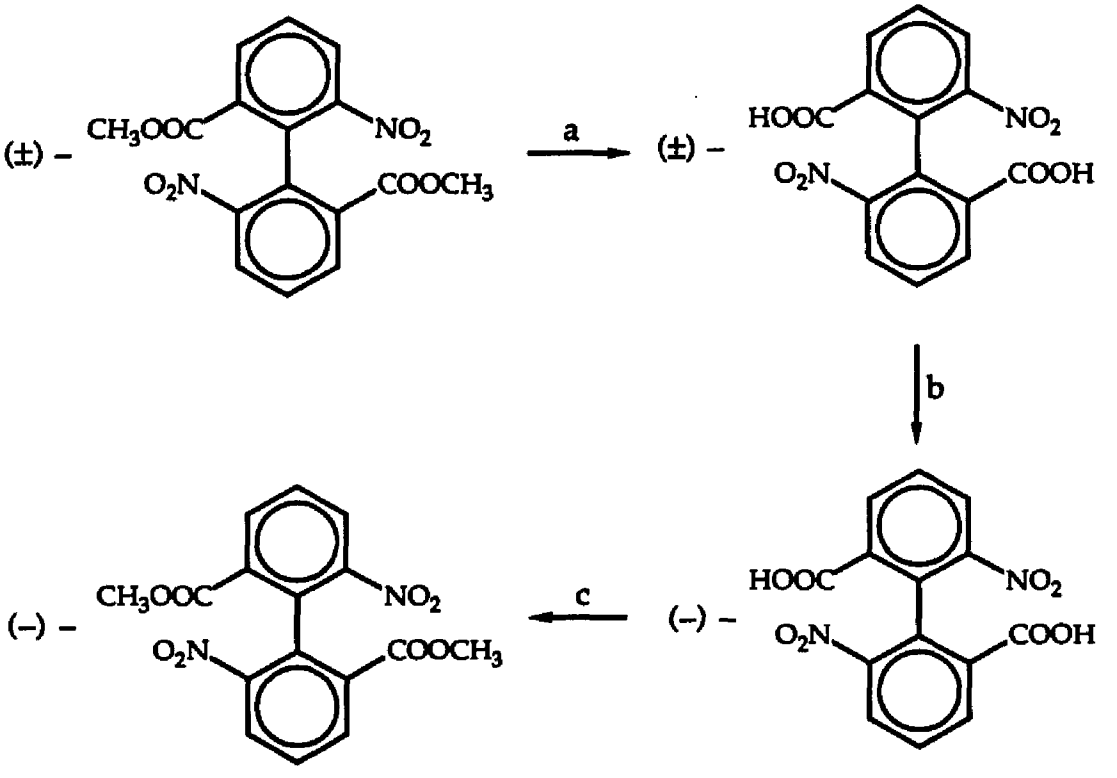


Figure 47. Resolution of (±)-53.
(a) NaOH/ethanol(aq.); (b) α-phenylethylamine; (c) CH_2N_2.

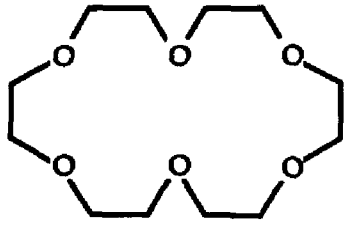
Many σ-complexes have been reported with oxygen nucleophiles, mainly with hydroxide, methoxide and ethoxide ions.[107] Hydroxide and ethoxide were not used with **53** because hydrolysis and ester exchange could destroy starting material.

Potassium methoxide ($KOCH_3$) in methanol was the first system tried. After refluxing 21 hours at 65 °C, starting material was recovered (>95%) along with what appears to be the monoacid resulting from hydrolysis of one of the two ester groups. After 42 hours, recovery of starting material dropped to 27%. The low recovery is not completely attributable to hydrolysis since the isolated monoacid of diester **53** accounted for only 6 % of starting material

and no diacid was recovered. Recovered diester 53 showed a small loss of optical activity (original: 114°; recovered samples: 109°, 106°, 98°). Because of the presence of impurities the reason for the reduced rotation could not be ascertained. It could be due to racemization, or it could be due to an impurity of lower or zero optical rotation.

Raising the temperature should increase the likelihood of attack on the aromatic ring as well as facilitate the rotation around the central carbon-carbon bond of the intermediate σ-complex which leads to racemization. The experiment was therefore carried out at 150 °C in sealed tubes. Complete hydrolysis of the ester groups was observed after only 4.5 hours. 6,6'-Dinitrobiphenyl-2,2'-dicarboxylic acid accounting for 70% of starting diester 53 was isolated after the reaction. No starting material or monoacid was isolated. The isolated diacid was esterified to yield unracemized starting material. Destruction of the starting material is very fast at this temperature, and once formed, the acid apparently does not racemize.

The crown ethers 18-crown-6 (54) and dicyclohexyl-18-crown-6 (55) increase the reactivity of nucleophilic potassium salts by solvating the potassium ion.[108]



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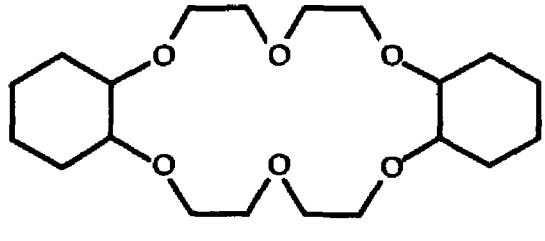

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These crown ethers have the optimum ring size for complexing the potassium ion. They have high stability constants for their complexes with

potassium ion.[109] It was hoped that by increasing the strength of the nucleophile by adding a crown ether, attack on the ring could be made more competitive. The system $KOCH_3$/18-crown-6/methanol did not cause any racemization of **53**. Starting material was recovered unracemized after refluxing 50 hours. The extent of loss of starting diester was comparable to that found in the absence of crown ether.

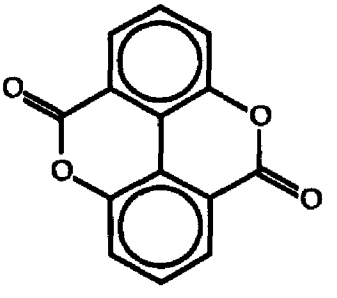
The reactivity of nucleophiles is greater in aprotic solvents than in protic solvents because they are no longer solvated by hydrogen bonds.[110] In an attempt to increase the reactivity of the system, the solvent was changed from methanol to the polar aprotic solvent acetonitrile. The combination of $KOCH_3$/18-crown-6/acetonitrile has been used to substitute methoxide for chloride in the chromium tricarbonyl complexes of unactivated chlorobenzenes. No reaction was observed to occur with such compounds using sodium methoxide/methanol or $KOCH_3$/acetonitrile (without crown ether).[111] This system appears to be much too reactive for diester **53**. After refluxing 12 hours in acetonitrile (83 °C) with $KOCH_3$/18-crown-6, neither starting material nor mono- or diacid were recovered in pure form, only an unidentified mixture of products.

Potassium fluoride is a powerful nucleophile in aprotic solvents,[112] but has very low solubility in most organic solvents.[113] The crown ether 18-crown-6 increases the solubility of KF by solvating the potassium ion. The system KF/18-crown-6/acetonitrile was investigated. Sixty eight percent of **53** was recovered unracemized after refluxing for 23 hours. This same system was tried at 125 °C in sealed tubes. After 48 hours 80% starting material was recovered unracemized.

An attempt was made to racemize biphenyl **53** with KF by using the system KF/N,N-dimethylformamide (DMF). A nitro group, in relatively

unactivated nitrobenzenes, can be displaced by fluoride using KF in a high boiling dipolar aprotic solvent such as DMF.[114] The solubility of KF is greater in DMF than in acetonitrile.[115] The boiling point of DMF is also much higher than that of acetonitrile (153 vs. 83 °C). Use of DMF allows a higher concentration of KF and a higher reflux temperature. Unfortunately, no starting material could be recovered after refluxing for 12 hours. A small amount of an unidentified product mixture was recovered.

KI/DMF was tried in order to expose the diester **53** to another halide ion in a polar aprotic solvent. After refluxing for 12 hours, no starting material could be recovered. A dilactone, 4,9-dioxapyrene-5,10-dione (**56**), was isolated. This was apparently formed through internal displacement of the nitro groups by the carboxylate groups of 6,6'-dinitrobiphenyl-2,2'-dicarboxylic acid (see Figure 48) which was formed from diester **53**.



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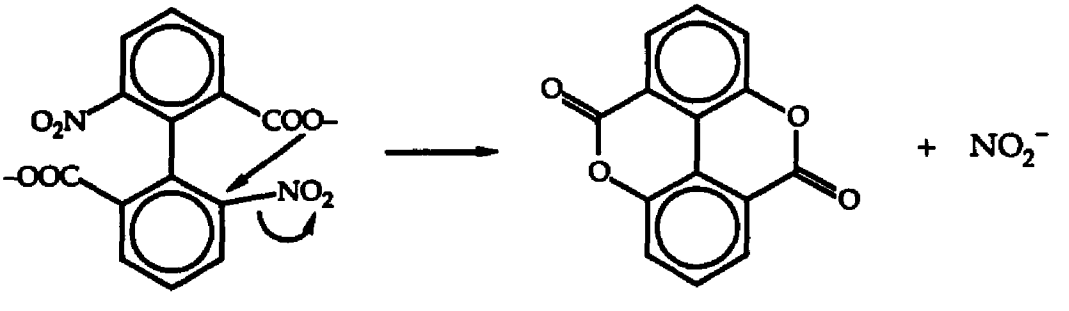


Figure 48. Internal displacement of a nitro group.

This dilactone is known to form when 6,6'-dinitrobiphenyl-2,2'-dicarboxylic acid is heated.[116] The recovered sample was found to be identical to a sample of the dilactone prepared from 6,6'-dinitrobiphenyl-2,2'-dicarboxylic acid. The temperature of the system was lowered to 100 °C to try and recover starting material. After 12 hours, 71% of impure starting material was recovered with a small loss (10%) in optical activity. The sample was not purified further, and therefore no conclusion can be drawn beyond that little or no racemization of **53** took place.

None of the systems investigated catalyzed the racemization of diester **53**. Generally, milder conditions led to recovery of unracemized starting material, while harsher conditions led to extensive reaction without any detectable racemization. Hydrolysis of the ester groups was a persistent problem in spite of the extreme care taken to exclude water from the systems. Solvents were rigorously dried and stored over molecular sieves, all glassware was oven-dried before use and all transfers were made via syringe. This suggests that the hydrolysis was not due to the presence of water but rather came about through S_N2 displacement of the carboxylate ion by the nucleophile at the methyl carbon of the ester as shown in Figure 49.

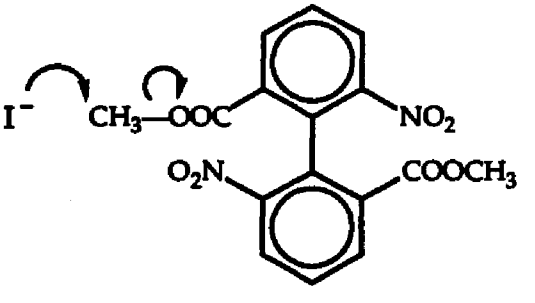
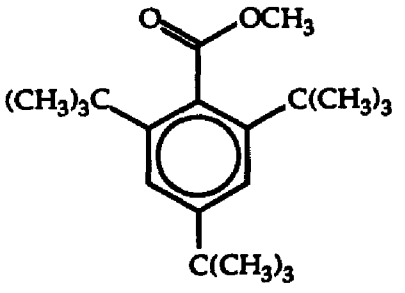


Figure 49. S_N2 displacement of a carboxylate ion.

The operation of this type of mechanism has been previously observed, e.g., methyl 2,4,6-tri-*t*-butylbenzoate (**57**) and methyl 2-methyl-4,6-di-*t*-butylbenzoate (**58**), two highly hindered esters, both undergo alkaline hydrolysis by the $B_{Al}2$ mechanism (bimolecular, with alkyl/oxygen fission).[117]



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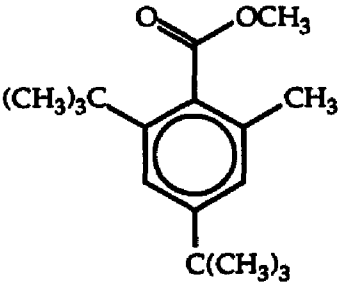

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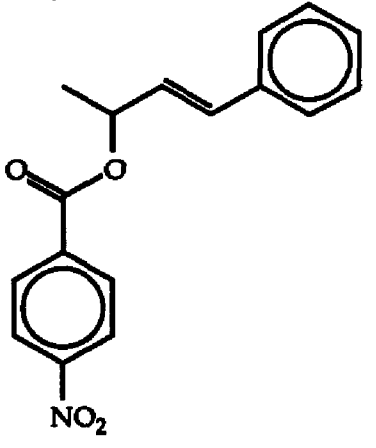
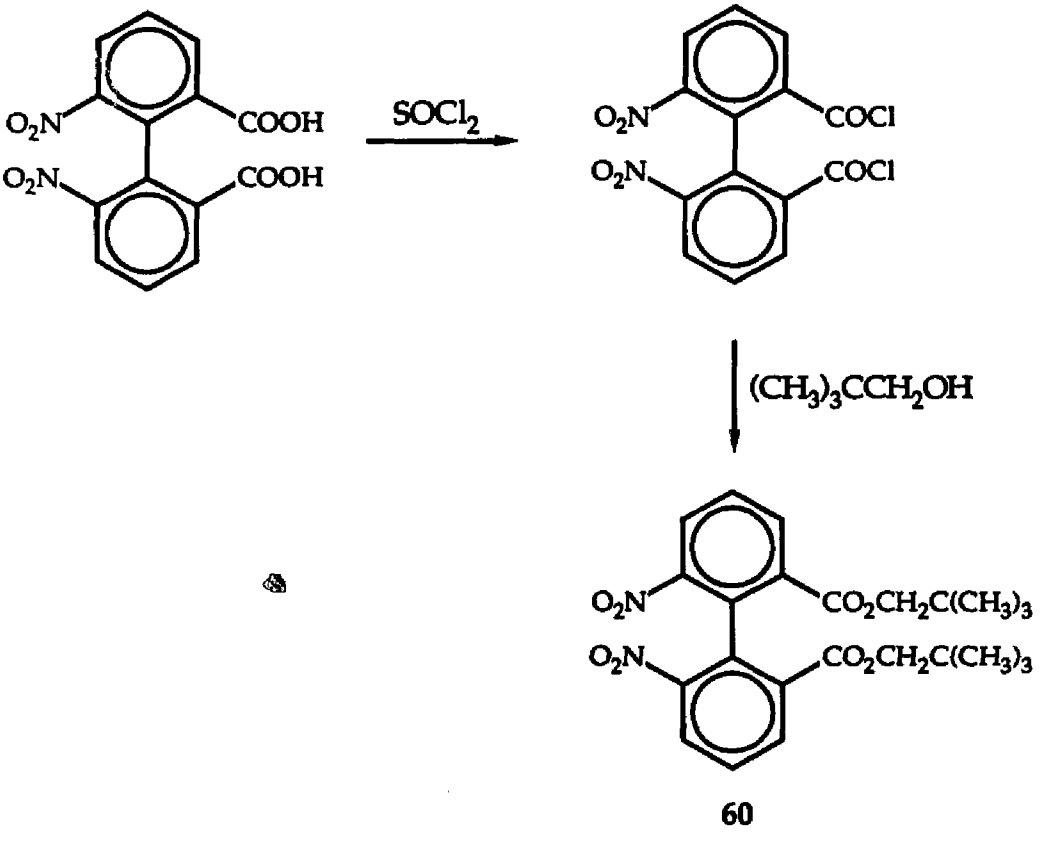
Another example is the hydrolysis of α-methyl-γ-phenylallyl *p*-nitrobenzoate (**59**) by sodium methoxide/methanol, claimed to involve $B_{Al}2$ hydrolysis of the intermediate methyl ester.[118]



59

This possibility could be eliminated by using the dineopentyl ester of 6,6'-dinitrobiphenyl-2,2'-dicarboxylic acid rather than the dimethyl ester. It is

known that S_N2 displacements are more difficult to carry out at neopentyl sites because of the steric hindrance of the alpha tert-butyl group.[119] Dineopentyl 6,6'-dinitrobiphenyl-2,2'-dicarboxylate, was prepared by reacting the acid chloride with 2,2-dimethylpropanol (see Figure 50).



60

Figure 50. Preparation of neopentyl diester **60**.

As expected, when optically active **60** was exposed to KI in refluxing DMF almost 90% of starting material was recovered. This supports the contention that cleavage of methyl 6,6'-dinitrodiphenate occurred through S_N2 displacement by the nucleophile at the methyl group. No racemization was observed.

Similarly, after being exposed to KF in refluxing DMF for 12 hours, neopentyl diester **60** was recovered, although in lower yield (65%). The recovered starting material was not racemized. When heated with KI/DMF neopentyl diester **60** was recovered unracemized, under conditions where diester **53** was completely destroyed. The same result was obtained with KF/DMF.

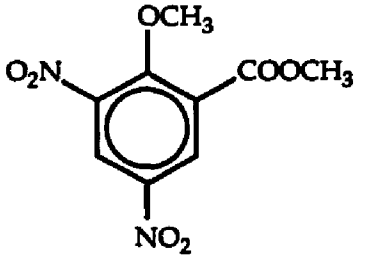
Several other systems were used in an attempt to racemize neopentyl diester **60**. Sodium thiophenolate (NaSPh) is known to be a reactive nucleophile towards aromatic rings. This nucleophile in methanol reapidly displaces one of the nitro groups of 1,2,4-trinitrobenzene,[120] and therefore might reversibly add to a less activated aromatic such as neopentyl diester **60** without leading to product formation. No racemization was observed in recovered starting material (88%) after exposure to NaSPh in refluxing methanol for 14 hours.

No conclusive evidence of racemization of the methyl and neopentyl esters of 6,6'-dinitrobiphenyl-2,2'-dicarboxylic acid was observed in any of the systems investigated. Recovery of unracemized starting material can occur for two reasons. Possibly there was no addition to the phenyl ring. It is also possible that reversible addition occurred, but without racemization. Reversible formation of the addition intermediate could take place without racemization if the lifetime of the complex is too short for rotation around the central carbon-carbon bond of the σ-complex or if insufficient energy is available for rotation. The esters of 6,6'-dinitrobiphenyl-2,2'-dicarboxylic acid do not appear to work as probes of the reversible addition of anions such as methoxide, iodide, and fluoride to a phenyl ring.

Chapter 8:

Attempted Racemization of Dimethyl 4,4',6,6'-tetranitrobiphenyl-2,2'-dicarboxylate.

Highly activated benzenes with two or more strongly electron withdrawing groups reversibly form σ-complexes with methoxide ion. Equilibrium constants have been determined for complex formation in many cases. For example, the equilibrium constants for formation of the σ-complexes between methoxide ion and 2-methoxycarbonyl-4,6-dinitroanisole (**61**) and between methoxide ion and 4-methoxycarbonyl-2,6-dinitroanisole (**62**) in methanol have been determined spectrophotometrically.[121]



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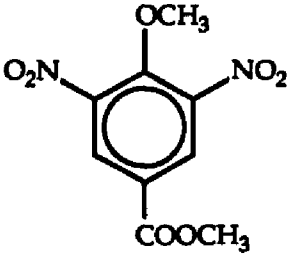

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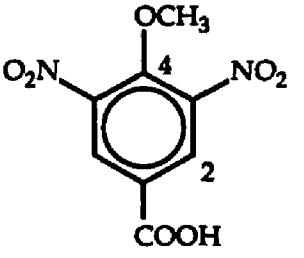
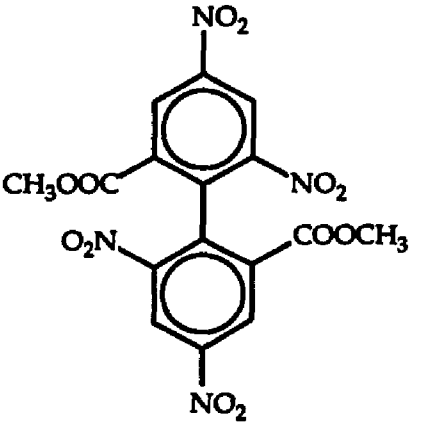


63

Spectrophotometry was also used to follow the reversible formation of an intermediate σ-complex in the reaction of 4-methoxy-3,5-dinitrobenzoic acid (**63**) with methoxide ion. After 1/3 s the visible absorption spectrum was assigned to the complex formed by attack at the 2 position. After 5 s a new spectrum was observed which was assigned to the complex formed by attack at the 4 position,[122] which indicated that the first complex observed was formed reversibly.



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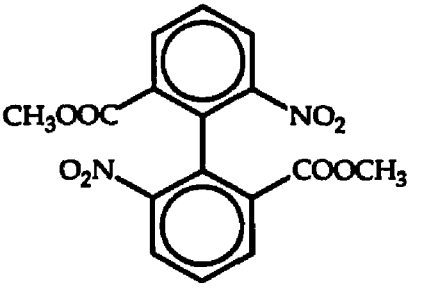


53

Dimethyl 4,4',6,6'-tetranitrobiphenyl-2,2'-dicarboxylate (**64**) is more activated towards nucleophiles than is dimethyl 6,6'-dinitrobiphenyl-2,2'-dicarboxylate (**53**) because it has two nitro groups on each ring instead of one. Dimethyl 4,4',6,6'-tetranitrobiphenyl-2,2'-dicarboxylate is therefore more likely to form an addition intermediate with a nucleophile than methyl 6,6'-dinitrodiphenate. A σ-complex formed with tetranitrodiester **64** should also have a longer lifetime than the corresponding complex with dinitrodiester **53**. Since racemization of the biphenyl should be catalyzed by the formation of the σ-complex addition intermediate, diester **64** should be more likely to be racemized by nucleophiles than diester **53**.

Diester **64** was prepared according to the method of G. H. Christie[123] except that the Ullmann coupling reaction to yield racemic diester **64** was modified by the use of nitrobenzene as solvent (see Figure 51). The resolution procedure for diester **64** described by Christie gave very low yields and was also modified (see Figure 52).

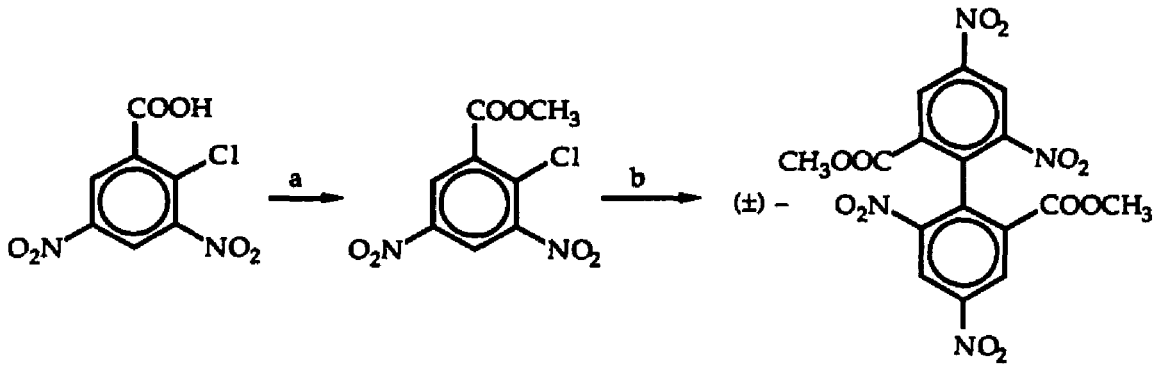


Figure 51. Preparation of diester **64**.
(a) CH_2N_2; (b) $Cu/PhNO_2$, 211°.

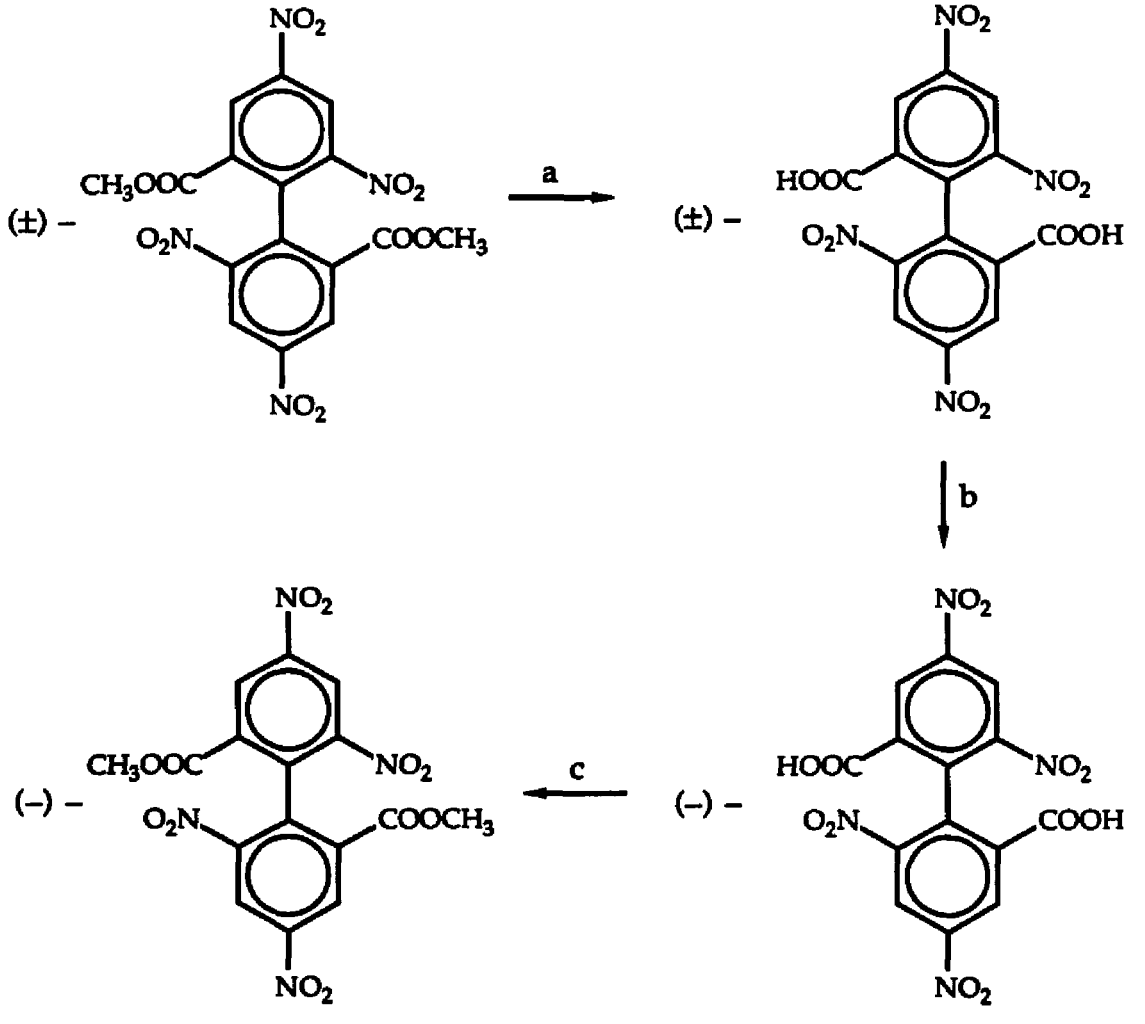
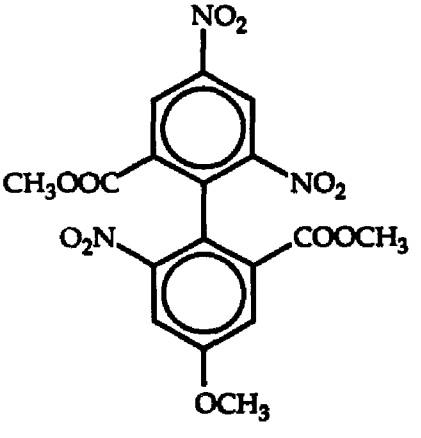
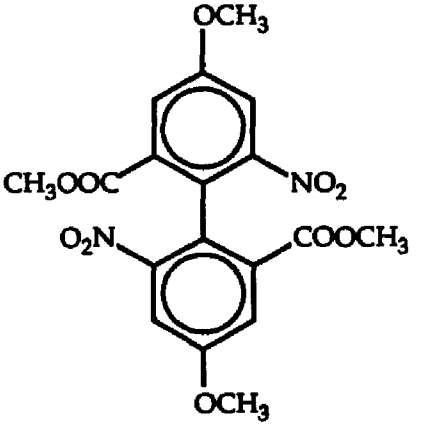


Figure 52. Resolution of diester **64**.
(a) H_2SO_4/acetic acid; (b) Brucine/*n*-propanol; (c) CH_2N_2.

Because of its low solubility in methanol, diester **64** could not be exposed to methoxide/methanol at room temperature. Treatment with potassium methoxide in refluxing methanol resulted in complete destruction of starting material. Two products were isolated, dimethyl 4-methoxy-4,6,6'-trinitrobiphenyl-2,2'-dicarboxylate (**65**) and dimethyl 4,4'-dimethoxy-6,6'-dinitrobiphenyl-2,2'-dicarboxylate (**66**), corresponding to displacement of one and two nitro groups by methoxide ion, respectively. Products of hydrolysis were also recovered. Methoxy substitution was indicated by their ^{1}H-NMR spectra. Less product formation should occur at room temperature, but the solubility of diester **64** is too low, as stated earlier.



65



66

The system KF/18-crown-6/acetonitrile gave similar results. After refluxing for 20 hours, no dimethyl 4,4',6,6'-tetranitrobiphenyl-2,2'-dicarboxylate was recovered. Analytical thin layer chromatography (TLC) indicated that at least three products were formed. Their R_f values were very similar, and they could not be separated after repeated preparative TLC.

Diester **64** appears to be too reactive to serve as substrate for racemization studies. The presence of the second nitro group on each phenyl ring leads to product formation rather than racemization. Attempts to racemize **64** under conditions where dinitrodiester **53** was recovered unracemized only led to extensive product formation.

No conclusive evidence regarding the catalysis of racemization of the aromatic substrates has been obtained with any of the nucleophilic systems tried.

Conclusion: This thesis uses a novel method to demonstrate that benzyl, isopropyl, and ethyl radicals add reversibly to bianthryl **11**. The optical activity of **11** is used as a probe of reversibility of addition of these radicals to the aromatic ring system. After the optically active biaryl is heated in the presence of dibenzylmercury, diisopropylmercury, or diethylmercury, under conditions which generate the corresponding alkyl radicals, racemization of **11** is observed, which indicates that reversible addition occurred.

The absence of product formation in significant amounts might otherwise have led to the conclusion that no addition to the aromatic rings of **11** took place at all; however, in our system the loss of optical activity allows us to conclude that the radical added in a reversible manner.

Racemization of **11** is also observed when the alkyl radicals are generated by thermal decomposition of azoalkanes, which confirms the role of the alkyl radicals in the racemization process.

New compounds prepared:

- Dineopentyl 6,6'-dinitrobiphenyl-2,2'-dicarboxylate (**60**)
- Dimethyl 4-methoxy-4,6,6'-trinitrobiphenyl-2,2'-dicarboxylate (**65**)
- Dimethyl 4,4'-dimethoxy-6,6'-dinitrobiphenyl-2,2'-dicarboxylate (**66**)

Experimental

General. Sealed tube reactions were set up as follows. The reaction solutions were transferred to 3 x 10 cm heavy-wall glass tubes. Each tube had a 10/30 outer joint at the end of a 10-cm neck. The contents of the tubes were degassed on a vacuum manifold by the freeze/pump/thaw method. The tubes were frozen in a Dewar filled with dry ice/acetone or liquid nitrogen and evacuated. After closing the stopcock to each tube, the contents were thawed. The tubes were then frozen and refilled with gaseous nitrogen. The nitrogen (ultra high purity grade, Union Carbide–Linde Division, Danbury, Connecticut 06817) line contained a drying tube and an oxygen scrubber. This consisted of one cycle. After three such cycles the tubes were frozen, filled with nitrogen to 100 torr (unless otherwise specified), and sealed. Sealed tubes were heated in a thermoregulated Haake NBS Constant Temperature Circulator filled with silicone oil (Dow Corning, 210 H fluid).

Reagent grade bromobenzene was purified by extraction with concentrated H_2SO_4 (4x), 10% NaOH (2x), and with water until neutral to litmus. The bromobenzene was sequentially dried over $CaSO_4$ and Na_2SO_4, decanted, and distilled at reduced pressure. Reagent grade *tert*-butylbenzene was purified by the same method. Dibenzylmercury (Alfa Products, Danvers, Massachusets 01923) was used without purification. Diisopropylmercury and diethylmercury (Pfaltz and Bauer, Waterbury, Connecticut 06708) were filtered just prior to use. Thiophenol (Gold label, Aldrich Chemical Co., Milwaukee, Wisconsin 53233), dicyclohexylphosphine (Aldrich Chemical Co.), and Irganox 1076 (Ciba-Geigy, Ardsley, NY 10502) were used without purification. All solvents used with nucleophilic systems were stored over 3Å molecular sieves (Aldrich Chemical Co., Milwaukee, Wisconsin 53233). The

molecular sieves were activated by heating at 300 °C in an oven for 2 h. Absolute methanol was prepared by distilling reagent grade methanol from Mg/I_2. Reagent grade acetonitrile was dried over 3Å molecular sieves, decanted, and distilled from CaH_2. Reagent grade DMF was fractionally distilled at reduced pressure (4–5 torr). The first 20% of the distillate was discarded.

KF (ultrapure, Alfa Products, Danvers, Massachusetts 01923) was dried before use by heating at 160 °C for 48 h or by heating at 350 °C for 2 h. KI (Amend Drug and Chemical Co., Irvington, New Jersey 07111) was dried by heating at 185 °C for 2 h at 1 torr. Ethereal diazomethane was generated from DIAZALD™ (Aldrich Chemical Co.) by the method described in Aldrich Technical Bulletin No. AL-113.

Melting points were measured on a Thomas Hoover Unimelt apparatus (mp < 300°) or on a Mel-Temp apparatus (mp > 300°) and are uncorrected. Optical rotations were measured on a Perkin-Elmer 141 polarimeter in a 1.0-dm microcell with a water jacket. The cell temperature was maintained at 25.0 ± 0.1 °C in all rotation measurements by a Forma-Scientific circulating bath. Percent racemization was often based on the optical rotation of reaction solutions. In various cases the accuracy of this method was verified by isolating racemized starting material. Care was taken during chromatography to recover the entire band of optically active starting material to avoid fractionation. ^1H NMR spectra were recorded on Varian EM-360, Bruker NR/200, or Bruker NR/300 spectrometers. Infrared spectra were recorded on a Perkin-Elmer 247 grating spectrophotometer. Mass spectra were taken at the Rockefeller University Mass Spectrometric Biotechnology Resource, 1230 York Ave, New York, NY 10021.

I. Radical Systems

1. Purification of (±)-2,2'-Dicyano-9,9'-bianthryl. Crude 2,2'-dicyano-9,9'-bianthryl[124] (10.0 g) was treated with 200 mL of boiling $CHCl_3$ for 45 min and filtered. The filtrates were evaporated. The residue was dissolved in a solution of 120 mL $CHCl_3$ and 10 mL ethanol. The resulting solution was divided in half. Each half was purified by column chromatography on a 2.4 x 60 cm column of silica gel (200 g of Davisil 60, Aldrich Chemical Co., Milwaukee, Wisconsin 53233) eluted with 50% $CHCl_3$/benzene. The pure material from both columns was combined to yield 2.04 g: mp 334–346 °C (lit 342–344 °C[125]). Impure cyanobianthryl from both columns was combined to yield 1.94 g, which was purified by repeating the column chromatography in the same way to yield 1.27 g: mp 346-349 °C (lit. 342–344 °C[24]). Analytical TLC (silica gel, eluent: 50% $CHCl_3$/benzene) of both samples showed only one spot at R_f 0.44 (same as an authentic sample[24]).

2. Preparation of (±)-2,2'-Dicarboxy-9,9'-bianthryl. In a 1-L round-bottom flask were combined 4.62 g (0.114 mol) of 2,2'-dicyano-9,9'-bianthryl, 500 mL of ethanol, 100 mL of water, 50 g of solid NaOH, and a magnetic stirrer. The mixture was heated to reflux with vigorous stirring for 15 h. A solution was obtained after 2 h. The solution was cooled in an ice bath and acidified with 100 mL of concentrated HCl. Fine yellow crystals were collected on a Büchner funnel and washed with 3 x 20 mL of water and 1 x 20 mL of ethanol. The crystals were oven-dried for 30 min at 120 °C and dried in vacuo (3 mm, 135 °C, 14 h) to yield 4.66 g (92%): mp 404 °C (decomp.) (lit. 417–420 °C[24]). Analytical TLC (silica gel, eluent: 5% HOAc/$CHCl_3$) showed one spot at R_f 0.24 (same as an authentic sample[24]).

3. Resolution of (±)-2,2'-Dicarboxy-9,9'-bianthryl. Quinidine sulfate (10.1 g, Aldrich Chemical Co., Milwaukee, Wisconsin 53233) was treated with 100 mL of water and 100 mL of 15% NH_4OH. The mixture was stirred magnetically for 20 minutes and transferred to a separatory funnel. The free base was extracted with 200 mL of $CHCl_3$. The organic layer was washed with 100 mL of water, dried over $MgSO_4$, filtered, and evaporated. The residue was dried in vacuo (0.5 torr, 60 °C, 40 min) to yield 8.85 g of quinidine hydrate: mp 170–171 °C (lit. 171.5 °C[126]). A heterogeneous mixture of 4.66 g (10.5 mmol) of (±)-2,2'-dicarboxy-9,9'-bianthryl and 500 mL of acetone was stirred in a liquid-liquid extraction apparatus. The side-arm of the flask led to a 3-neck round-bottom flask equipped with a mechanical stirrer containing a solution of 8.45 g (22.9 mmol) of quinidine hydrate in 650 mL of acetone. After all of the diacid was transferred (30 h) the extraction was stopped. Yellow crystals formed in the 3-neck flask and were collected on a Büchner funnel, washed with 6 x 25 mL of acetone, and dried in vacuo (0.2 torr, 65 °C, 1 h) to yield 4.87 g of the quinidine/(–)-acid salt: $[\alpha]_D$+13.9 (c 0.290, methanol). The combined filtrates were concentrated to 100 mL, and a spongy solid was filtered out. The solution was evaporated to dryness to yield 7.31 g of the quinidine/(+)-acid salt. The quinidine/(+)-acid salt was heated to boiling in a solution of 60 mL of ethanol and 60 mL of 10% HCl. After allowing the mixture to cool to room temperature, the free acid was collected on a Büchner funnel and washed with 50 mL of the aqueous acidic ethanol solution and with 25 mL of ethanol. The crystals were heated in vacuo (0.4 torr, 80 °C, 2 h) to yield 1.94 g of (+)-2,2'-dicarboxy-9,9'-bianthryl: $[\alpha]_D$+86.4 (c 1.02, acetone) (lit. $[\alpha]_D$+101,[24] acetone). The quinidine/(–)-acid salt was hydrolyzed in the same way to yield 1.82 g of (–)-2,2'-dicarboxy-9,9'-bianthryl: $[\alpha]_D$–106 (c 1.00, acetone) (lit. $[\alpha]_D$–115,[24] acetone).

Analytical TLC (silica gel, 5% HOAc/$CHCl_3$) of both samples showed one spot at R_f 0.36 (same as an authentic sample[24]).

4. Preparation of (–)-2,2'-Dicarbomethoxy-9,9'-bianthryl (11). (–)-2,2'-Dicarboxy-9,9'-bianthryl ($[\alpha]_D$–106, c 1.00, acetone) (1.82 g, 4.16 mmol) was dissolved in 80 mL of tetrahydrofuran. The solution was cooled in an ice/water bath. Ethereal diazomethane at 0 °C was added via Pasteur pipet as the solution was stirred magnetically. Excess diazomethane was destroyed by adding several drops of glacial acetic acid. The solution was evaporated to dryness, and the residue was heated in vacuo (0.2 torr, 65 °C, 1 h) to yield 2.02 g. The crude product was purified by column chromatography on a 2.2 x 24 cm column (50 g of Davisil 60 silica gel, Aldrich Chemical Co., Milwaukee, Wisconsin 53233) eluted with 50% $CHCl_3$/benzene to yield 1.65 g (85%): $[\alpha]_D$–153, $[\alpha]_{546}$–219 (c 1.22, $CHCl_3$) (lit. $[\alpha]_D$–159,[24] $CHCl_3$).

5. Thermal Racemization of 11. An experiment was performed to find the best conditions for determining the Arrhenius parameters of the thermal racemization of bianthryl **11**. A solution was prepared by combining 6.0 mL of a bromobenzene solution of **11** (6.16 mg/mL) with 6.0 mL of bromobenzene. Six tubes were filled with 2 mL each of the resulting solution (α_o–0.734, 546 nm), degassed (freeze/pump/thaw), and sealed under 100 torr of nitrogen.The tubes were heated at three different temperatures. The optical rotation of each solution was measured after heating. Table XVII gives results based on solution rotations.

Table XVII. Thermal racemization of bianthryl **11**.

Temperature	time	α_{546}	% racemization
235.1 ± 0.1 °C	16 h	–0.623	15.1
	24 h	–0.576	21.5
245.5 ± 0.1 °C	14 h	–0.543	26.0
	24 h	–0.458	37.6
256.0 ± 0.1 °C	12 h	–0.429	41.6
	18 h	–0.348	52.6

The contents of the tubes run at 256° were combined and distilled at reduced pressure. The residue was heated in vacuo (0.2 torr, 56 °C, 3 h) to drive off residual bromobenzene. This yielded 10.8 mg (88%). The optical rotation of this sample was reduced by 46%, essentially the same as the average of the solution rotations. The ^{1}H NMR spectrum showed no signs of any impurities.

The same three temperatures (235, 245, and 255 °C) were used for thermal racemization experiments using ten tubes at each temperature. The tubes were set up by the same method described above. The series of experiments was repeated. The results are shown in Tables XVIII and XIX. The solution in a tube which was heated without degassing changed from pale yellow to deep brown, and the optical rotation of the solution could not be measured.

Table XVII.1 Racemization of bianthryl **11** by dibenzylmercury in bromobenzene at 190 °C.

time	α_D	% racemization
15 min	–0.326, –0.326	37.3
30 min	–0.308, –0.305	41.1
1.0 h	–0.310	40.4
2.0 h	–0.306	41.2

Table XVIII. Thermal racemization of bianthryl **11**(run #1).

235°C		245°C		255°C	
time (h)	$\ln(\alpha_o/\alpha)$	time (h)	$\ln(\alpha_o/\alpha)$	time (h)	$\ln(\alpha_o/\alpha)$
0.0	0.0	0.0	0.0	0.0	0.0
4.5	0.178	8.0	0.174	13.0	0.143
4.5	0.190	8.0	0.159	13.0	0.148
9.5	0.368	15.0	0.270	26.0	0.221
9.5	0.427	15.0	0.259	26.0	0.235
12.5	0.492	22.0	0.408	36.5	0.342
12.5	0.504	22.0	0.410	36.5	0.340
20.0	0.693	30.0	0.513	48.0	0.381
20.0	0.755	30.0	0.513	48.0	0.443
28.5	1.09	38.0	0.640	63.0	0.564
28.5	1.07				

Table XIX. Thermal racemization of bianthryl **11** (run #2).

235°C		245°C		255°C	
time (h)	$\ln(\alpha_o/\alpha)$	time (h)	$\ln(\alpha_o/\alpha)$	time (h)	$\ln(\alpha_o/\alpha)$
0.0	0.0	0.0	0.0	0.0	0.0
3.00	0.142	11.0	0.240	11.0	0.109
3.00	0.137	11.0	0.234	11.0	0.121
6.00	0.264	22.0	0.455	22.0	0.206
6.00	0.262	22.0	0.453	22.0	0.201
9.00	0.388	28.0	0.564	35.0	0.353
9.00	0.382	28.0	0.560	35.0	0.317
12.00	0.501	37.0	0.717	47.0	0.423
12.00	0.503	37.0	0.730	58.0	0.499
16.55	0.618	44.0	0.844		
16.55	0.668	44.0	0.850		

6. Racemization of (–)-11 by Dibenzylmercury in Bromobenzene at 190 °C.

A. A solution was prepared by dissolving 217 mg (0.461 mmol) of (–)-11 ($[\alpha]_D$–148 (c 1.63, $CHCl_3$) in 70.0 mL of bromobenzene (α_o–0.520, 589 nm). Six tubes were filled with 5.0 mL each of this solution to serve as blanks. Dibenzylmercury (482 mg, 1.26 mmol) was dissolved in the remaining 40 mL of the solution. Eight tubes were filled with 5.0 mL each of the resulting solution (α_o–0.520, 589 nm). Two of the blank tubes and two of the tubes containing dibenzylmercury were sealed without degassing. All other tubes were degassed (freeze-pump-thaw) and sealed under 350 torr of nitrogen. The tubes were heated at 190.2 ± 0.2 °C in a silicone oil bath. See Table XVII.1, p. 102 for results. Blank solutions were not racemized (7.0 h: α_D –0.519).

B. A solution was prepared by dissolving 184 mg (0.390 mmol) of (+)-11 ($[\alpha]_D$+141, c 1.59, $CHCl_3$) and 740 mg (1.93 mmol) of dibenzylmercury in 57 mL of bromobenzene. The resulting solution (α_o+0.510, 589 nm) was transferred to a 100-mL round-bottom flask, degassed (freeze-pump-thaw), and sealed under 300 torr of nitrogen. The sealed flask was heated in a silicone oil bath set at 190.3 ± 0.2 °C for 1 h. The supernatant liquid was transferred to a distilling flask. The residual mercury was washed several times with 1 mL portions of methylene chloride to yield 361 mg (93%). The washings were combined with the contents of the distilling flask, and distilled at reduced pressure. The residue was subjected to column chromatography using 25 g silica gel (Davisil 60, Aldrich Chemical Co., Milwaukee, Wisconsin 53233) in a 2 x 18 cm column. The column was developed with 50% hexanes/benzene. Bibenzyl (303 mg, 86%) was obtained by eluting with 100 mL of this solvent mixture. Impure bianthryl 11 (194 mg) was eluted using benzene and 50% chloroform/benzene. The impure 11 was purified by preparative TLC using a 2000 micron silica gel plate (Analtech, Newark, Delaware 19711) eluted twice

with 50% chloroform/benzene. This yielded 177 mg (96%) of bianthryl **11**: $[\alpha]_D$+72.7 (c 1.65, chloroform), 48% racemized. The identity of recovered samples was established by ^{1}H NMR.

7. Decomposition of Dibenzylmercury in Bromobenzene at 190 °C. Dibenzylmercury (720 mg, 1.88 mmol) was dissolved in 60 mL of bromobenzene and was transferred to a 100-mL flask with a narrow neck leading to a 10/30 inner joint. The flask was degassed (freeze-pump-thaw) and sealed under 350 torr of nitrogen. The flask was heated at 190.2 ± 0.2 °C in a silicone oil bath for 3.25 h. The bromobenzene solution was drawn out of the flask with a Pasteur pipet leaving behind a ball of mercury. The mercury was washed several times with small portions of methylene chloride. Residual methylene chloride was removed under aspirator suction to yield 341 mg (90%) of mercury. The combined methylene chloride washings and bromobenzene solution were distilled at reduced pressure. The residue was heated in vacuo (0.2 torr, 50 °C, 2 h) to yield 326 mg (95%) of bibenzyl (confirmed by ^{1}H NMR).

8. Racemization of (–)-11 by Dibenzylmercury in Bromobenzene at 150 °C. (–)-**11** (58.8 mg, 0.125 mmol) was dissolved in 18 mL of bromobenzene. Two tubes were filled with 3 mL each of this solution (α_o–0.562, 589 nm) to serve as blanks. Dibenzylmercury (147 mg, 0.384 mmol) was dissolved in the remaining solution. Four tubes were filled with 3 mL each of this solution (α_o–0.557, 589 nm). All six tubes were degassed (freeze-pump-thaw), sealed under 350 torr of nitrogen and heated at 150.3 ± 0.1 °C in a silicone oil bath. Solution rotations are shown in Table XX. No racemization was observed in the solutions without dibenzylmercury (3.0 h: α_D –0.567; 25.5 h: α_D –0.560).

Table XX. Racemization of **11** with dibenzylmercury at 150 °C in bromobenzene.

time (h)	α_D	% racemization
1.0	–0.362	35.0
3.0	–0.243	56.4
6.0	–0.187	66.5
25.5	–0.175	68.6

9. Effect of Concentration of Dibenzylmercury on the Racemization of (–)-11 in Bromobenzene at 190 °C. A solution (molar ratio dibenzylmercury/bianthryl **11** = 9.9 : 1) was prepared by dissolving 18.7 mg (0.0397 mmol) of (–)-**11** and 150 mg (0.391 mmol) of dibenzylmercury in 6.0 mL of bromobenzene (α_o–0.51, 589 nm). Two tubes were filled with 3.0 mL each of this solution. Another solution (molar ratio dibenzylmercury/bianthryl **11** = 5.3 : 1) was prepared by dissolving 17.6 mg (0.0374 mmol) of (–)-**11** and 75.5 mg (0.197 mmol) of dibenzylmercury in 6.0 mL of bromobenzene (α_o–0.483, 589 nm). Two tubes were filled with 3 mL each of this solution. The final solution (molar ratio dibenzylmercury/bianthryl **11** = 1.1 : 1) was prepared by dissolving 18.5 mg (0.0393 mmol) of (–)-**11** and 16.3 mg (0.0426 mmol) of dibenzylmercury in 6.0 mL of bromobenzene (α_o–0.494, 589 nm). Two tubes were filled with 3 mL each of this solution. All six tubes were degassed (freeze-pump-thaw), sealed under 350 torr of nitrogen, and heated at 190.3 ± 0.1 °C in a silicone oil bath for 1.0 h. The optical rotation of each solution was measured after heating (see Table XXI). Analytical TLC of the solutions (silica gel plates, 25% hexane/$CHCl_3$) showed one spot at R_f 0.24 (same as starting bianthryl **11**). The

solution of molar ratio 5.3 : 1 showed a very faint second spot at R_f 0.30. This spot was more clearly visible in the analytical TLC of the solution of molar ratio 9.9 : 1.

Table XXI. Effect of the concentration of dibenzylmercury on the percent racemization of **11** in bromobenzene.

molar ratio dibenzylmercury : **11**	α_D	% racemization
9.9 : 1	–0.258	49.1
	–0.255	49.7
5.3 : 1	–0.288	40.4
	–0.302	37.5
1.1 : 1	–0.394	20.2
	–0.395	20.0

10. Racemization of (–)-11 by Dibenzylmercury in Bromobenzene at 135 °C. (-)-**11** (73.5 mg, 0.156 mmol) and 385 mg (1.00 mmol) of dibenzylmercury were dissolved in 24 mL of bromobenzene (α_o-0.470, 589 nm). Eight tubes were filled with 3 mL each of this solution, degassed (freeze-pump-thaw) , sealed under 350 torr of nitrogen, and heated at 135.0 ± 0.1 °C in a silicone oil bath. Two tubes were removed after 4 h, 8 h, 12 h, and 24 h. Solution rotations are shown in Table XXII. Mercury was visible at the bottom of all the tubes. The mercury at the bottom of the 24 h tubes was recovered by drawing off the bromobenzene solution with a Pasteur pipet, washing the mercury with methylene chloride, and driving off residual solvent under aspirator suction. This yielded 22.3 mg (89%) and 21.7 mg (86%). Analytical TLC (silica gel plate,

25% hexane/$CHCl_3$) was similar for all the tubes: the major spot at R_f 0.32 (same as starting bianthryl **11**) and very small spots at R_f 0.40 and 0.46.

Table XXII. Racemization of bianthryl **11** with dibenzylmercury at 135 °C in bromobenzene.

time (h)	α_D	% racemization
4.0	–0.289	38.5
	–0.282	40.0
8.0	–0.202	57.0
	–0.198	57.9
12.0	–0.130	72.3
	–0.145	69.1
24.0	–0.094	80
	–0.099	79

11. Effect of Butylated Hydroxytoluene (BHT) on the Racemization of (–)-11 by Dibenzylmercury in Bromobenzene at 190 °C. A solution was prepared by dissolving 37.2 mg (0.0791 mmol) of (–)-**11** and 147 mg (0.384 mmol) of dibenzylmercury in 12.0 mL of bromobenzene. Two tubes were filled with 3 mL each of this solution.(α_o–0.482, 589 nm). Butylated hydroxytoluene (217 mg, 0.982 mmol) was dissolved in the remaining solution (α_o–0.463, 589 nm). The molar ratio of BHT to dibenzylmercury was 5 : 1. The four tubes were degassed (freeze-pump-thaw) and sealed under 350 torr of nitrogen. The sealed tubes were heated at 190.5 ± 0.1 °C in a silicone oil bath. The solutions without BHT had identical optical rotations after heating (α_D+0.296, 38.6% racemized). The solutions containing BHT also had identical optical rotations after heating (α_D+0.296, 36.1% racemized).

12. Effect of Irganox 1076 and BHT on the Racemization of (–)-11 by Dibenzylmercury in Bromobenzene at 190 °C. A solution was prepared by dissolving 54.4 mg (0.166 mmol) of (–)-11 and 219 mg (0.573 mmol) of dibenzylmercury in 18.0 mL of bromobenzene. Two tubes were filled with 3 mL each of this solution (α_o+0.471, 589 nm) to serve as blanks. BHT (868 mg, 3.94 mmol) was dissolved in 6.0 mL of the original solution, and two tubes were filled with 3 mL each of the resulting solution (α_o+0.394, 589 nm). The molar ratio of BHT to dibenzylmercury was 20 : 1. Irganox 1076 (1.00 g, 1.89 mmol) was dissolved in 6.0 mL of the original solution, and two tubes were filled with 3 mL each of the resulting solution (α_o+0.371, 589 nm). The molar ratio of Irganox 1076 to dibenzylmercury was 10 : 1. The six tubes were degassed (freeze-pump-thaw) and sealed under 350 torr of nitrogen. The sealed tubes were heated at 190.5 ± 0.1 °C in a silicone oil bath. The results are shown in Table XXIII.

Table XXIII. Effect of inhibitors on the racemization of 11 by dibenzylmercury in bromobenzene at 190 °C.

inhibitor	α_D	% racemization
none (1 h)	+0.291	38.2
none (2 h)	+0.292	38.0
BHT (1 h)	+0.290	26.4
(2 h)	+0.290	26.4
Irganox 1076		
(1 h)	+0.256	31.0
(2 h)	+0.255	31.3

13. Racemization of (+)-11 by diphenyl disulfide. Diphenyl disulfide (40.5 mg, 0.186 mmol) and (+)-11 (18.3 mg, 0.0389 mmol) were dissolved in 6.0 mL of bromobenzene (α_o+0.464, 589 nm). Two tubes were filled with 3 mL each of this solution and degassed (freeze-pump-thaw) and sealed under 350 torr of nitrogen. The sealed tubes were heated at 190.5 ± 0.1 °C in a silicone oil bath.

The solutions darkened slightly. A tube was removed after 24 h and after 66 h. The optical rotation was unchanged in both tubes.

14. Effect of Thiophenol on the Racemization of (+)-11 by Dibenzylmercury in Bromobenzene at 190 °C. (+)-11 (55.2 mg, 0.117 mmol) and dibenzylmercury (224 mg, 0.586 mmol) were dissolved in 18.0 mL of bromobenzene. Two tubes were filled with 3 mL each of this solution (α_o+0.479, 589 nm). Thiophenol (11 mg, 0.096 mmol) was dissolved in 6.0 mL of the original solution and two tubes were filled with 3 mL each of the resulting solution (α_o+0.478, 589 nm). The molar ratio of thiophenol/dibenzylmercury was 0.49 : 1. Thiophenol (43.7 mg, 0.397 mmol) was dissolved in 6.0 mL of the original solution and two tubes were filled with 3 mL each of the resulting solution (α_o+0.478, 589 nm). The molar ratio of thiophenol/dibenzylmercury was 2.03 : 1. The six tubes were degassed (freeze-pump-thaw), sealed under 350 torr of nitrogen, and heated to 190.1 ± 0.1 °C in a silicone oil bath. Solution rotations are shown in Table XXIV. A fine white powder formed in the tubes containing thiophenol. The solid was filtered out of one of the tubes with thiophenol of molar ratio 2.03 : 1, washed with small portions of chloroform, and heated in vacuo to yield 5 mg of mercuric thiophenolate: mp 149.5–150 °C (lit.[127] 150–152 °C); ^{1}H NMR (200 MHz, DMSO-d_6) δ7.1–7.4 (m). Solution rotations were obtained by either drawing off the supernatant liquid using a Pasteur pipet or by filtering out the mercuric thiophenolate.

15. Preparation of Mercuric Thiophenolate. A solution of 172 mg (1.57 mmol) of thiophenol in 5 mL of absolute ethanol was combined with a solution of 222 mg (0.819 mmol) of mercuric chloride (technical grade) in 5 ml of absolute ethanol. A massive white precipitate immediately formed. Absolute ethanol

(10 mL) was added. The solid was broken up, collected in a Büchner funnel, and washed with 4 x 5 mL of absolute ethanol. Recrystallizing once from absolute ethanol yielded 136 mg of white crystals: mp 148–149 °C (lit.[127] 150–152 °C); ^{1}H NMR (200 MHz, DMSO-d_6) δ7.1–7.6 (m).

Table XXIV. Thiophenol as inhibitor of racemization of **11** with dibenzylmercury in bromobenzene.

Molar ratio PhSH/dibenzylmercury	α_D	% racemization
none (1 h)	+0.293	38.8
none (2 h)	+0.292	39.0
0.49 : 1 (1 h)	+0.279	41.6
(2 h)	+0.267	44.1
2.03 : 1 (1 h)	+0.453	4.6
(2 h)	+0.454	4.4

Table XXIV.1 Racemization of bianthryl **11** by dibenzylmercury in *tert*-butylbenzene at 190 °C.

time	α_D	% racemization (avg)
15 min	–0.264	38.9
1.0 h	–0.246, –0.247	43.0
2.0 h	–0.247, –0.250	42.5
14 h	–0.248	42.6

16. Racemization of (–)-11 by Dibenzylmercury in *tert*-Butylbenzene at 190 °C.

A. A solution was prepared by dissolving 280 mg (0.595 mmol) of (–)-**11** ($[\alpha]_D$–148, c 1.63, $CHCl_3$) in 80 mL of *tert*-butylbenzene. Three tubes were filled with 8 mL each of this solution to serve as blanks (α_o–0.430, 589 nm). Dibenzylmercury (703 mg, 1.84 mmol) was dissolved in 40 mL of the remaining solution. Seven tubes were filled with 5 mL each of the resulting solution (α_o–0.432, 589 nm). The tubes were degassed (freeze-pump-thaw) and sealed under 350 torr of nitrogen. The tubes were heated at 189.2 ± 0.2 °C in a silicone oil bath (See Table XXIV.1, p. 111 for results). Blank solutions were not racemized (2.0 h: α_D –0.427).

B. A solution was prepared by dissolving 180 mg (0.382 mmol) of (+)-**11** and 735 mg (1.92 mmol) of dibenzylmercury in 60 mL of *tert*-butylbenzene. The resulting solution (α_o–0.510, 589 nm) was transferred to a 100-mL round-bottom flask, degassed (freeze-pump-thaw), and sealed under 400 torr of nitrogen. The sealed flask was heated in a silicone oil bath set at 190.3 ± 0.2 °C for 1 h. The supernatant liquid (α_o–0.181, 589 nm, 46% racemized) was filtered through a Hirsch funnel, and the mercury was washed several times with 1 mL portions of methylene chloride to yield 392 mg (86%). The filtrates and washings were combined and distilled at reduced pressure. The residue was subjected to column chromatography using 23 g silica gel (Davisil 60, Aldrich Chemical Col, Milwaukee, Wisconsin 53233) in a 2 x 17 cm column. The column was eluted with 50% hexanes/benzene. Bibenzyl (306 mg, 87%) was obtained by eluting with 100 mL of this solvent mixture. Impure bianthryl **11** (194 mg) was eluted using neat benzene, 50%, and 80% chloroform/benzene. The impure **11** was purified by preparative TLC using a 2000 micron silica gel plate (Analtech, Newark, Delaware 19711) eluted twice with 50% chloroform/benzene. An additional preparative TLC procedure was necessary in order to completely separate **11** from trace impurity. This yielded less than 3 mg of an unidentified product and 166 mg (92%) of bianthryl **11**: $[\alpha]_D$+73.6 (c 0.89, chloroform), 47.7% racemized. The identity of the recovered bibenzyl and bianthryl **11** was established by ^{1}H NMR.

17. Decomposition of Dibenzylmercury in *tert*-Butylbenzene at 190 °C. Dibenzylmercury (750 mg, 1.96 mmol) was dissolved in 60 mL of *tert*-butylbenzene and transferred to a 100-mL flask with a narrow neck leading to a 10/30 inner joint. The flask was degassed (freeze-pump-thaw) and sealed under 350 torr of nitrogen. The flask was heated at 190.5 ± 0.2 °C in a silicone

oil bath for 3 h. The *tert*-butylbenzene solution was drawn out of the flask with a Pasteur pipet leaving behind a ball of mercury. The mercury was washed several times with small portions of methylene chloride. Residual methylene chloride was removed under aspirator suction to yield 375 mg (95%) of mercury. The combined methylene chloride washings and *tert*-butylbenzene solution were distilled at reduced pressure. The residue was heated in vacuo (0.2 torr, 50 °C, 2 h) to yield 335 mg (94%) of bibenzyl (confirmed by ^{1}H NMR).

18. Racemization of (–)-11 by Dibenzylmercury in *t*-Butylbenzene at 150 °C. (-)-11 (56.4 mg, 0.120 mmol) was dissolved in 18 mL of *tert*-butylbenzene. Two tubes were filled with 3 mL each of this solution (α_o–0.379, 589 nm). Dibenzylmercury (155 mg, 0.405 mmol) was dissolved in the remaining solution. Four tubes were filled with 3 mL each of this solution (α_o–0.383, 589 nm). All six tubes were degassed (freeze-pump-thaw) and sealed under 350 torr of nitrogen and heated at 150.2 ± 0.1 °C in a silicone oil bath. Solution rotations are shown in Table XXV. Racemization was not observed in the solutions without dibenzylmercury (3.0 h: α_D–0.377, 32 h: α_D–0.378).

Table XXV. Racemization of **11** with dibenzylmercury at 150 °C in *tert*-butylbenzene.

time (h)	α_D	% racemization
1.0	–0.208	45.6
3.0	–0.162	57.7
6.3	–0.159	58.5
32.0	–0.156	59.3

19. Effect of Concentration of Dibenzylmercury on the Racemization of (–)-11 in *tert*-Butylbenzene at 190 °C. A solution was prepared by dissolving 18.8 mg (0.0400 mmol) of (–)-11 and 114 mg (0.298 mmol) of dibenzylmercury in 6.0

mL of *tert*-butylbenzene (α_o–0.333, 589 nm). Two tubes were filled with 3 mL each of this solution (molar ratio dibenzylmercury/bianthryl **11** = 7.5 : 1). Another solution was prepared by dissolving 18.8 mg (0.0400 mmol) of (–)-**11** and 74.8 mg (0.195 mmol) of dibenzylmercury in 6.0 mL of *tert*-butylbenzene (α_o–0.357, 589 nm). Two tubes were filled with 3 mL each of this solution (molar ratio dibenzylmercury/bianthryl **11** = 4.9 : 1). The final solution was prepared by dissolving 18.1 mg (0.0385 mmol) of (–)-**11** and 16.6 mg (0.0434 mmol) of dibenzylmercury in 6.0 mL of *tert*-butylbenzene (α_o–0.333, 589 nm). Two tubes were filled with 3 mL each of this solution (molar ratio dibenzylmercury/bianthryl **11** = 1.1 : 1). All six tubes were degassed (freeze-pump-thaw), sealed under 350 torr of nitrogen, and heated at 190.3 ± 0.1 °C in a silicone oil bath for 1.0 h. The optical rotation of each solution was measured after heating (see Table XXVI). Analytical TLC of the solutions (silica gel plates, 25% hexane/$CHCl_3$) showed one spot at R_f 0.24 (same as starting bianthryl **11**). The solution of molar ratio 4.9 : 1 showed a very faint second spot at R_f 0.29. This spot was more clearly visible in the analytical TLC of the solution of molar ratio 7.5 : 1.

Table XXVI. Effect of concentration of dibenzylmercury on the racemization of **11** in *tert*-butylbenzene at 190 °C.

molar ratio dibenzylmercury : **11**	α_D	% racemization
7.5 : 1	+0.179	46.2
	+0.176	47.1
4.9 : 1	–0.209	41.5
	–0.210	41.2
1.1 : 1	–0.244	26.7
	–0.244	26.7

Table XXVII. Racemization of **11** with dibenzylmercury at 135 °C in *tert*-butylbenzene at 190 °C.

time (h)	α_D	% racemization
4.0	+0.141	59.0
	+0.156	54.7
8.0	+0.106	69.2
	+0.122	64.5
12.0	+0.095	72.4
	+0.107	68.9
24.0	+0.102	70.3
	+0.109	68.3

20. Racemization of (+)-11 by Dibenzylmercury in *tert*-Butylbenzene at 135 °C. (+)-**11** (73.1 mg, 0.155 mmol) and 381 mg (0.994 mmol) dibenzylmercury were dissolved in 24.0 mL of *tert*-butylbenzene (α_o–0.344, 589 nm). Eight tubes were filled with 3 mL each of this solution, degassed (freeze-pump-thaw), sealed under 350 torr of nitrogen, and heated at 135.0 ± 0.1 °C in a silicone oil bath. Two tubes were removed after 4 h, 8 h, 12 h, and 24 h. Optical rotations are shown in Table XXVII. Mercury was visible at the bottom of all the tubes. The mercury at the bottom of the 24 h tubes was recovered by drawing off the *tert*-butylbenzene solution with a Pasteur pipet, washing the mercury with methylene chloride, and driving off residual solvent under aspirator suction. This yielded 21.4 mg (88%) and 24.5 mg (98%). Analytical TLC (silica gel plate,

25% hexane/$CHCl_3$) was similar for all the tubes: the major spot at R_f 0.32 (same as starting bianthryl **11**) and very small spots at R_f 0.40 and 0.46.

21. Effect of Irganox 1076 and BHT on the Racemization of (+)-11 by Dibenzylmercury in *tert*-Butylbenzene at 190 °C. A solution was prepared by dissolving 56.7 mg (0.121 mmol) of (+)-**11** and 229 mg (0.597 mmol) of dibenzylmercury in 18.0 mL of *tert*-butylbenzene. Two tubes were filled with 3 mL each of this solution (α_o+0.295, 589 nm) to serve as blanks. BHT (874 mg, 3.97 mmol) was dissolved in 6.0 mL of the original solution, and two tubes were filled with 3 mL each of the resulting solution (α_o+0.316, 589 nm). The molar ratio of BHT to dibenzylmercury was 20 : 1. Irganox 1076 (0.998 g, 1.88 mmol) was dissolved in 6.0 mL of the original solution, and two tubes were filled with 3 mL each of the resulting solution (α_o+295, 589 nm). The molar ratio of Irganox 1076 to dibenzylmercury was 10 : 1. The six tubes were degassed (freeze-pump-thaw) and sealed under 350 torr of nitrogen. The sealed tubes were heated at 190.3 ± 0.1 °C in a silicone oil bath. Table XXVIII shows the solution rotations.

Table XXVIII. Effect of inhibitors on the racemization of **11** by dibenzylmercury in *tert*-butylbenzene at 190 °C.

inhibitor	α_D	% racemization
none (1 h)	+0.193	45.9
none (2 h)	+0.194	45.4
BHT (1 h)	+0.233	26.3
(2 h)	+0.226	28.5
Irganox 1076		
(1 h)	+0.200	32.2
(2 h)	+0.199	32.5

22. Racemization of (+)-11 by diphenyl disulfide in *tert*-Butylbenzene at 190 °C. Diphenyl disulfide (85.8 mg, 0.393 mmol) and (+)-11 (36.0 mg, 0.0765 mmol) were dissolved in 12.0 mL of *tert*-butylbenzene (α_o+0.331, 589 nm). Four tubes were filled with 3.0 mL each of this solution, degassed (freeze-pump-thaw), and sealed under 350 torr of nitrogen. The sealed tubes were heated at 190.2 ± 0.2 °C in a silicone oil bath. Tubes were removed after 24, 48, 72, and 90 h. The optical rotation was unchanged in all tubes.

23. Effect of Thiophenol on the Racemization of (+)-11 by Dibenzylmercury in *tert*-Butylbenzene at 190 °C. (+)-11 (55.1 mg, 0.117 mmol) and dibenzylmercury (218 mg, 0.570 mmol) were dissolved in 18.0 mL of *tert*-butylbenzene. Two tubes were filled with 3.0 mL each of this solution (α_o+0.337, 589 nm). Thiophenol (11.8 mg, 0.107 mmol) was dissolved in 6.0 mL of the original solution, and two tubes were filled with 3.0 mL each of the resulting solution (α_o+0.336, 589 nm). The molar ratio of thiophenol/dibenzylmercury was 0.56 : 1. Thiophenol (43.8 mg, 0.397 mmol) was dissolved in 6.0 mL of the original solution, and two tubes were filled with 3.0 mL each of the resulting solution (α_o+0.336, 589 nm). The molar ratio of thiophenol/dibenzylmercury was 2.1 : 1. The six tubes were degassed (freeze-pump-thaw), sealed under 350 torr of nitrogen, and heated to 190.1 ± 0.1 °C in a silicone oil bath. Mercuric thiophenolate was either filtered out of the solutions before measuring the optical rotation, or the supernatant liquid was drawn off using a Pasteur pipet. Solution rotations are shown in Table XXIX.

Table XXIX. Thiophenol as inhibitor of the racemization of 11 with dibenzylmercury in *tert*-butylbenzene at 190 °C.

molar ratio PhSH/HgR_2		α_D	% racemization
—	(1 h)	+0.195	42.1
	(2 h)	+0.194	42.4
0.49 : 1	(1 h)	+0.187	44.3
	(2 h)	+0.183	45.5
2.03 : 1	(1 h)	+0.323	3.9
	(2 h)	+0.325	3.3

24. Reaction of Diisopropylmercury with (+)-2,2'-Dicarbomethoxy-9,9'-bianthryl (11) in Bromobenzene at 190 °C.

A. Diisopropylmercury (111 mg, 0.386 mmol) and 37.9 mg (0.0841 mmol) of (+)-11 were dissolved in 12.0 mL of bromobenzene, and four tubes were filled with 3 mL each of the resulting solution (α_o+0.499, 589 nm). The molar ratio of diisopropylmercury to (+)-11 was 4.6 : 1. The tubes were degassed (freeze-pump-thaw), sealed under 300 torr of nitrogen, and heated at 190 ± 0.1 °C in a silicone oil bath. A tube was removed after 1 h, a second tube was removed after 2 h, and the remaining two tubes were removed after 3 h. The solutions in all four tubes had the same optical rotation (+0.016, 97% racemized). The solutions in the tubes were drawn out using a Pasteur pipet, leaving behind a ball of mercury in each tube. The mercury was washed twice with CH_2Cl_2. The CH_2Cl_2 washings were added to the combined bromobenzene solutions and distilled at reduced pressure to yield 58 mg of a solid residue: ^{1}H NMR (60 MHz, $CDCl_3$) δ0.8–1.6 (m), δ3.4–3.9 (m), δ6.7–8.6 (m). Analytical TLC (silica gel plate, eluent: 50% $CHCl_3$/benzene) showed an elongated spot at R_f 0.30–0.70. A known sample of 11 had R_f value 0.38.

B. A solution of 177 mg (0.376 mmol) of (+)-11 ($[\alpha]_D$ +141, c 1.59, $CHCl_3$) and 639 mg (2.23 mmol) of diisopropylmercury in 60.0 mL of bromobenzene was prepared in a 100-mL flask with a narrow neck and a 10/30 inner joint. The molar ratio of diisopropylmercury to (+)-11 was 5.9 : 1. The solution was degassed (freeze-pump-thaw), sealed under 350 torr of nitrogen, and heated at 190.4 ± 0.2 °C for 1 h in a silicone oil bath. The solution was drawn out and the mercury was washed as described above. The residue was heated in vacuo (0.15 torr, 55 °C, 1.75 h) to drive off residual solvent to yield 371 mg of a solid residue: $[\alpha]_D$ +2.7 (c 1.60, $CHCl_3$), 98% racemized. Analytical TLC (silica gel plate, eluent: 50% $CHCl_3$/benzene) showed four spots at R_f 0.24, 0.35, 0.52, 0.72.

Bianthryl **11** had R_f value 0.31. Column chromatography on a 1.8 x 14.5 cm column using 25 g Davisil 60 silica gel (Aldrich Chemical Co., Milwaukee, Wisconsin 53233) eluted with solvents of increasing polarity was unsuccessful in isolating any components of the mixture in pure form.

25. Racemization of (+)-11 in the Presence of Diisopropylmercury in Bromobenzene at 190 °C. Diisopropylmercury (23.7 mg, 0.0826 mmol), 138 mg (0.292 mmol) of **11** ($[\alpha]_D$+141, 1.59, $CHCl_3$), and 45 mL of bromobenzene were combined in a 100 mL flask with a narrow neck and a 10/30 inner joint. The molar ratio of diisopropylmercury to **11** was 0.29 : 1. The solution (α_D+0.498, 589 nm) was degassed (freeze-pump-thaw) and the flask was sealed under 350 torr of nitrogen. The sealed flask was heated at 190 ± 0.2 °C for 2.5 h in a silicone oil bath. The solution (α_D+0.036, 589, 93% racemized) was drawn out of the bulb using a Pasteur pipet and distilled at reduced pressure (2.5 torr, 28 °C). The residue was dissolved in 35 mL of methylene chloride and filtered to remove a small amount of mercury. The filtrates were evaporated, and **11** was isolated from the residue by preparative TLC using a 2000 micron silica gel plate (Analtech, Newark, Delaware 19711) eluted 6x with 50% hexane/$CHCl_3$. Three bands (R_f 0.75, 0.63, and 0.55–0.13) appeared after 6 elutions. The band at R_f 0.55–0.13 was extracted with THF to recover 126 mg (91.3%) of **11**, $[\alpha]_D$+8.8 (c 0.75, $CHCl_3$) 93.7% racemized. The band at R_f 0.63 yielded 2.9 mg: ^{1}H NMR (200 MHz, $CDCl_3$) δ0.9–2.5 (m), δ3.5–4.3 (m), δ6.6–8.7 (m). The band at R_f 0.75 yielded 1.5 mg: ^{1}H NMR (200 MHz, $CDCl_3$) δ0.8–1.3 (m), δ2.3–2.5 (m), δ3.5 (d), δ3.7 (s), δ6.9–7.8 (m); MS (EI^+) MI 556 (see Appendix for discussion).

26. Racemization of 11 in the Presence of Diisopropylmercury in Bromobenzene at 170 °C. A solution was prepared by combining 4.0 mL of a 0.0129 mmol/mL solution of (+)-**11** ($[\alpha]_D$ +134, c 1.20, $CHCl_3$) with 4.0 mL of bromobenzene and 7.5 mg (0.026 mmol) of diisopropylmercury. The molar ratio of diisopropylmercury to **11** was 0.50 : 1. The solution (α_D+0.670, 546 nm) was transferred to a reaction tube, degassed (freeze-pump-thaw), and sealed under 100 torr of nitrogen. The sealed tube was heated at 170 ± 0.1 °C for 2 h in a silicone oil bath. The solution (α_D+0.100, 79% racemized) was distilled at reduced pressure (3 torr, 30 °C) to yield 26 mg of residue. Diester **11** was isolated by repeated preparative TLC using a 1000 micron silica gel plate with preadsorbent (Analtech, Newark, Delaware 19711) eluted 5x with 50% hexane/$CHCl_3$. This yielded 21.2 mg (79%) of **11**, $[\alpha]_D$+29.2 (c 0.900, $CHCl_3$) 78.2% racemized. The identity of the sample was confirmed by ^1H NMR.

27. Thiophenol and Dicyclohexylphosphine (DCP) as Inhibitors of Racemization of 11 by Diisopropylmercury. A solution was prepared by combining 6.5 mg (0.0227 mmol) of diisopropylmercury, 6.0 mL of bromobenzene, and 6.0 mL of a 0.0131 mmol/mL stock solution of **11** in bromobenzene (solution A, α_{546}–0.741). Two tubes were filled with 2.0 mL each of this solution (molar ratio 0.25 : 1 diisopropylmercury/**11**) to serve as references. Thiophenol (20.2 mg, 0.183 mmol) was dissolved in 4.0 mL of the solution and two tubes were filled with 2.0 mL each of the resulting solution (molar ratio 24 : 1 thiophenol/diisopropylmercury). Dicyclohexylphosphine (21.6 mg, 0.109 mmol) was dissolved in the remaining 4.0 mL of the original diisopropylmercury solution, and two tubes were filled with 2.0 mL each of the resulting solution (molar ratio 14.4 : 1 DCP/diisopropylmercury). The same method was used with 12.6 mg (0.114 mmol) of thiophenol and 34.3 mg

(0.173 mmol) of DCP to obtain solutions of molar ratio 15.1 : 1 thiophenol/diisopropylmercury and 22.9 : 1 DCP/diisopropylmercury (solution B, α_{546}–0.736). All tubes were degassed (freeze-pump-thaw), sealed under 100 torr of nitrogen, and heated for 1 h in a silicone oil bath set at 170.0 ± 0.1 °C. The results are shown in Table XXX.

Table XXX. Thiophenol and DCP as inhibitors of the racemization of **11** by diisopropylmercury at 170 °C.

inhibitor	molar ratio inhibitor/HgR_2	a_{546}
none (solution A)		–0.393, –0.392
DCP (soln. A)	14 : 1	–0.615, –0.612
thiophenol (soln. A)	24 : 1	–0.730, –0.739
none (solution B)		–0.390, –0.388
DCP (soln. B)	23 : 1	–0.660, –0.654
thiophenol (soln. B)	15 : 1	–0.742, –0.742

28. Butylated Hydroxytoluene (BHT), Irganox 1076, and DCP as Inhibitors of Racemization of 11 by Diisopropylmercury. A solution was prepared by combining 2.0 mL of a 0.0130 mmol/mL stock solution of diisopropylmercury in bromobenzene, 8.0 mL of a 0.0131 mmol/mL stock solution of **11**, and 6.0 mL of bromobenzene. Two tubes were filled with 2 mL each of this solution to serve as references. BHT (34.7 mg, 0.157 mmol) was dissolved in 4.0 mL of the solution (molar ratio BHT/diisopropylmercury 48 : 1), and two tubes were filled with 2 mL each of the resulting solution. Irganox 1076 (87.7 mg, .165 mmol) was dissolved in 4.0 mL of the original solution (molar ratio Irganox 1076/diisopropylmercury 51 : 1), and two tubes were filled with 2 mL each of

the resulting solution. DCP (99.9 mg, 0.504 mmol) was dissolved in 4.0 mL of the original solution (molar ratio DCP/diisopropylmercury 155 : 1), and two tubes were filled with 2 mL each of the resulting solution. All eight tubes (α_{546} –0.734) were degassed (freeze-pump-thaw), sealed under 100 torr of nitrogen, and heated for 1 h in a silicone oil bath set at 170.0 ± 0.1 °C. The results are shown in Table XXXI.

Table XXXI. BHT, Irganox 1076, and DCP as inhibitors of the racemization of **11** by diisopropylmercury at 170 °C.

inhibitor	molar ratio inhibitor/HgR_2	α_{546}
none	—	–0.430, –0.429
BHT	48.2 : 1	–0.524, –0.531
Irganox 1076	50.7 : 1	–0.489, –0.478
DCP	155 : 1	–0.687, –0.689

29. Effect of Optical Purity on the Racemization of (–)-11 in the Presence of Diisopropylmercury in Bromobenzene at 170 °C. Bromobenzene solutions of diisopropylmercury (solution A, 6.7 x 10^{-3} mmol/mL), (±)-**11** (solution B, 0.0266 mmol/mL), and (–)-**11** (solution C, 0.0131 mmol/mL) were prepared. Two solutions of the same concentration of diester **11**, but of different optical purity were prepared. The first solution was prepared by combining 2.0 mL of solution C, 1.0 mL of solution A, and 1.0 mL of bromobenzene (α_o–0.736, 546 nm). Two tubes were filled with 2 mL each of the resulting solution. The second solution was prepared by combining 1.0 mL of solution C, 0.5 mL of solution B, 1.0 mL of solution A, and 1.5 mL of bromobenzene (α_o–0.377, 546 nm). Two tubes were filled with 2 mL each of the resulting solution. All four tubes were degassed (freeze-pump-thaw), sealed under 100 torr of nitrogen,

and heated for 1 h in a silicone oil bath set at 170.0 ± 0.1 °C. The results are shown in Table XXXII.

Table XXXII. Effect of optical purity of **11** on the racemization of **11** by diisopropylmercury.

α_o	% racemization
–0.736	44.0, 44.2
–0.377	43.5, 44.0

30. Racemization of (+)-11 in the Presence of Diisopropylmercury in Bromobenzene at 150 °C. A solution was prepared by dissolving 108 mg (0.228 mmol) of (+)-**11** and 15.2 mg (0.0530 mmol) of diisopropylmercury in 35.0 mL of bromobenzene. The molar ratio diisopropylmercury/**11** was 0.23 : 1. Twelve tubes were filled with 3 mL each of this solution (α_o+0.467, 589 nm), degassed (freeze-pump-thaw), and sealed under 350 torr of nitrogen. The sealed tubes were heated to 150.2 ± 0.1 °C in a silicone oil bath. Pairs of tubes were removed periodically and the optical rotation of the contents were measured (see Table XXIII).

Table XXIII. Racemization of **11** with diisopropylmercury at 150 °C in PhBr.

time (h)	α_D	% racemization
2.0	+0.412	11.8
2.0	+0.419	10.3
5.0	+0.347	25.7
5.0	+0.352	24.6
8.0	+0.289	38.1
8.0	+0.297	36.4
11.0	+0.240	48.6
11.0	+0.236	49.5
15.0	+0.185	60.4
15.0	+0.184	60.6
24.0	+0.135	71.1
24.0	+0.110	76.4

31. Racemization of (+)-11 in the Presence of Diisopropylmercury in Bromobenzene at 160 °C. A solution was prepared by combining 9.1 mg (0.032 mmol) of diisopropylmercury with 10.0 mL of a bromobenzene stock solution of **11** (0.0129 mmol/mL) and 10.0 mL of bromobenzene. The molar ratio diisopropylmercury/**11** was 0.25 : 1. Ten tubes were filled with 2 mL each of the resulting solution (α_o+0.666, 546 nm). The tubes were degassed (freeze-pump-thaw) and sealed under 100 torr of nitrogen. The sealed tubes were heated to 160.0 ± 0.1 °C in a silicone oil bath. Pairs of tubes were removed periodically and the optical rotation of the contents were measured (see Table XXXIV).

Table XXXIV. Racemization of **11** with diisopropylmercury at 160 °C in PhBr.

time (h)	α_{546}	% racemization
2.0	+0.434	34.8
2.0	+0.446	33.0
4.0	+0.302	54.7
4.0	+0.300	55.0
5.0	+0.251	62.3
5.0	+0.289	56.6
6.5	+0.204	69.4
6.5	+0.202	69.7
8.0	+0.185	72.2
8.0	+0.197	70.0

32. Racemization of (+)-11 in the Presence of Diisopropylmercury in Bromobenzene at 170 °C. A solution was prepared by combining 9.1 mg (0.032 mmol) of diisopropylmercury with 10.0 mL of a bromobenzene stock solution of **11** (0.0129 mmol/mL) and 10.0 mL of bromobenzene. The molar ratio diisopropylmercury/**11** was 0.25 : 1. Ten tubes were filled with 2 mL each of

the resulting solution (α_o+0.664, 546 nm). The tubes were degassed (freeze-pump-thaw) and sealed under 100 torr of nitrogen. The sealed tubes were heated to 170.0 ± 0.1 °C in a silicone oil bath. Pairs of tubes were removed periodically and the optical rotation of the contents were measured (see Table XXXV).

Table XXXV. Racemization of **11** with diisopropylmercury at 170 °C in PhBr.

time (h)	α_{546}	% racemization
0.50	+0.502	24.3
0.50	+0.503	24.1
1.0	+0.387	41.6
1.0	+0.381	42.5
1.5	+0.299	54.9
1.5	+0.307	53.5
2.5	+0.202	69.5
2.5	+0.217	67.3
3.5	+0.193	70.9
3.5	+0.163	75.4

33. Effect of Air and Oxygen on the Racemization of (+)-11 in the Presence of Diisopropylmercury in Bromobenzene at 170 °C. A solution was prepared by combining 12.5 mg (0.0436 mmol) of diisopropylmercury with 14.0 mL of a bromobenzene stock solution of (+)-**11** (0.0131 mmol/mL) and 14.0 mL of bromobenzene. The molar ratio diisopropylmercury/**11** was 0.24 : 1. Six tubes were filled with 2 mL each of the resulting solution (α_o+0.673, 546 nm). Two reference tubes were degassed (freeze-pump-thaw) and sealed under 100 torr of nitrogen. Two tubes were sealed under 1 atm of air without degassing. Two tubes were flushed with oxygen and sealed under 1 atm of oxygen. A blank

solution without diisopropylmercury was prepared by combining 1 mL of the (+)-**11** stock solution with 1 mL of bromobenzene. The solution (α_o+0.647, 546 nm) was degassed (freeze-pump-thaw) and sealed. All the tubes were heated to 170.1 ± 0.1 °C in a silicone oil bath for 100 min. The solutions in the tubes which were degassed and sealed under nitrogen were racemized by 55.6% and 52.5%. The tubes sealed under air were racemized by 2.7% and 3.6%. The tubes sealed under oxygen were racemized by 3.7% and 4.2%.

34. Effect of Mercury on the Racemization of (+)-11 in Bromobenzene at 170 °C. A solution was prepared by combining 2.0 mL of a bromobenzene stock solution of (+)-**11** (0.0131 mmol/mL) and 2.0 mL of bromobenzene. Two tubes were filled with 2 mL each of the resulting solution (α_o+0.650, 546 nm). Mercury (149 mg, 0.743 mmol) was added to one of the tubes. Both tubes were degassed (freeze-pump-thaw), sealed under 100 torr of nitrogen, and heated to 170.1 ± 0.1 °C in a silicone oil bath for 1 h. The optical rotation of the solutions in both tubes was unchanged.

35. Variation of the Concentration of Diisopropylmercury and 11 at 170 °C. Two general methods were used to prepare solutions for this series of experiments. In the first method, samples of diisopropylmercury were dissolved in various volumes of a bromobenzene stock solution of **11** and neat bromobenzene to achieve the desired concentrations. In the second method, a diisopropylmercury stock solution was prepared, and various combinations of volumes of this solution, the bromobenzene stock solution of **11**, and bromobenzene were combined to achieve the desired concentrations. Volumetric pipets were used for all transfers of solutions. For each concentration 20.0 mL of solution was prepared and 10 tubes were filled

with 2 mL each. Initial rotations were measured at 546 nm, and the tubes were degassed (freeze-pump-thaw) and sealed under 100 torr of nitrogen. The sealed tubes were heated at 170.0 ± 0.1 °C. Pairs of tubes were removed periodically and the solution rotations at 546 nm were compared to the initial rotation. The results are shown in Tables XXXVI–XXXIX.

Table XXXVI. Variation of concentration of diisopropylmercury at constant concentration of **11** (run #1).

	Solution rotations at 546 nm (molar ratio HgR_2 : **11**)			
time (h)	0.519 : 1	0.394 : 1	0.252 : 1	0.132 : 1
0.00	0.737	0.734	0.742	0.739
0.00	0.737	0.734	0.742	0.739
0.333	0.551	0.573	0.617	0.663
0.333	0.550	0.571	0.612	0.658
0.500	0.473	0.498	0.560	0.623
0.500	0.473	0.497	0.558	0.613
0.667	0.412	0.442	0.507	0.582
0.667	0.408	0.440	0.507	0.581
0.833	0.358	0.391	0.466	0.543
0.833	0.357	0.389	0.463	0.539
1.00	0.314	0.349	0.429	0.508
1.00	0.310	0.346	0.422	–

Table XXXVII. Variation of concentration of diisopropylmercury at constant concentration of **11** (run #2).

	Solution rotations at 546 nm (molar ratio HgR_2 : **11**)			
time (h)	0.126 : 1	0.252 : 1	0.389 : 1	0.485 : 1
0.000	0.729	0.729	0.730	0.729
0.000	0.729	0.729	0.730	0.729
0.250	0.663	0.631	–	0.589
0.250	0.660	0.630	0.603	0.590
0.417	0.617	0.565	0.530	0.508
0.417	0.616	0.567	0.530	0.507
0.583	0.577	0.509	0.467	0.436
0.583	0.576	0.510	0.463	0.439
0.750	0.538	0.466	0.409	0.380
0.750	0.536	0.468	0.408	0.377
0.917	0.503	0.421	0.361	0.331
0.917	0.499	0.423	0.364	0.333

Table XXXVIII. Variation of concentration of **11** at constant concentration of diisopropylmercury (run #1).

	Solution rotations at 546 nm (molar ratio HgR_2 : **11**)			
time (h)	0.25 : 2.02	0.25 : 0.992	0.25 : 0.734	0.25 : 0.495
0.00	1.468	0.742	0.548	0.377
0.00	1.468	0.742	0.548	0.377
0.333	1.279	0.617	0.444	0.285
0.333	1.273	0.612	0.436	0.284
0.500	1.196	0.560	0.389	0.249
0.500	1.193	0.558	0.387	0.248
0.667	1.110	0.507	0.347	0.217
0.667	1.110	0.507	0.347	0.211
0.833	1.034	0.466	0.311	0.189
0.833	1.032	0.463	0.308	0.188
1.00	0.969	0.429	0.280	0.166
1.00	0.967	0.422	0.275	0.165

Table XXXIX. Variation of concentration of **11** at constant concentration of diisopropylmercury (run #2).

	Solution rotations at 546 nm (molar ratio HgR_2 : **11**)			
time (h)	0.25 : 1.92	0.25 : 0.994	0.25 : 0.752	0.25 : 0.501
0.000	1.457	0.729	0.551	0.367
0.000	1.457	0.729	0.551	0.367
0.250	1.315	0.630	0.455	0.297
0.250	1.320	0.631	0.456	0.295
0.417	1.218	0.565	0.395	0.255
0.417	1.222	0.567	0.397	0.251
0.583	1.132	0.510	0.346	0.217
0.583	1.129	0.509	0.346	0.215
0.750	1.056	0.466	0.303	0.199
0.750	1.054	0.468	0.303	0.191
0.917	0.983	0.423	0.267	0.161
0.917	0.986	0.421	0.268	0.160

36. Reaction of Diisopropylmercury with (+)-11 in *tert*-Butylbenzene at 190 °C.

A. Diisopropylmercury (111 mg, 0.386 mmol) and 37.9 mg (0.0841 mmol) of (+)-**11** were dissolved in 12.0 mL of *tert*-butylbenzene, and two tubes were filled with 3 mL each of the resulting solution (α_o+0.348, 589 nm). The tubes were degassed (freeze-pump-thaw), sealed under 300 torr of nitrogen, and heated at 190 ± 0.1 °C. A tube was removed after 1 h, a second tube was removed after 2 h. Extensive racemization of the solutions was observed (1 h: 96%, 2 h: 95%). Analytical TLC (silica gel plate, eluent: 50% $CHCl_3$/benzene) showed four spots, barely resolved at R_f 0.1, 0.40, 0.52, 0.64. **11** had R_f value 0.37.

B. A solution was prepared by dissolving 38.0 mg (0.0808 mmol) of **11** and 6.1 (0.021 mmol) mg of diisopropylmercury in 12 mL of *tert*-butylbenzene.

Four tubes were filled with 3.0 mL each of the resulting solution (α_o+0.356, 589 nm). The tubes were degassed (freeze-pump-thaw), sealed under 300 torr of nitrogen, and heated at 190 ± 0.1 °C. The contents of the tubes (average: 95% racemized) were combined and distilled under reduced pressure (7.5 torr/49 °C). The residue was dried further in vacuo to yield 36.2 mg (95.3%) of **11**: $[\alpha]_D$ +6.6 (c 0.35, $CHCl_3$), 98% racemized. The identity of the sample was established by ^1H NMR and analytical TLC, which showed only trace impurity.

37. Racemization of (+)-11 in the Presence of Diisopropylmercury in *tert*-Butylbenzene at 150 °C. A solution was prepared by dissolving 108 mg (0.229 mmol) of (+)-**11** and 17.4 mg (0.0607 mmol) of diisopropylmercury in 36 mL of *tert*-butylbenzene. Twelve tubes were filled with 3 mL each of this solution (α_o+0.325, 589 nm), degassed (freeze-pump-thaw), and sealed under 350 torr of nitrogen. The sealed tubes were heated to 150.2 ± 0.1 °C. The optical rotation of the contents were measured and are shown in Table XL.

Table XL. Racemization of **11** in the presence of diisopropylmercury in *tert*-butylbenzene at 150 °C.

time (h)	α_D	% racemization
2.0	+0.286	12.0
2.0	+0.288	11.4
5.0	+0.229	29.5
5.0	+0.231	28.9
8.0	+0.176	45.8
8.0	+0.181	44.3
15.0	+0.107	67.1
15.0	+0.107	67.1
24.0	+0.062	80.9
24.0	+0.064	80.3

38. Racemization of (+)-11 in the Presence of Diethylmercury in Bromobenzene at 200 °C. A solution was prepared by dissolving 75.3 mg (0.160 mmol) of (+)-**11** ($[\alpha]_D$ +134, c 1.20, $CHCl_3$) and 396 mg (1.53 mmol) of diethylmercury in 18.0 mL of bromobenzene (α_o+0.663, 589 nm). The molar ratio of diethylmercury to (+)-**11** was 9.6 : 1. Six tubes were filled with 3 mL each of this solution, degassed (freeze-pump-thaw), and sealed under 20 torr of nitrogen. The sealed tubes were heated to 200.3 ± 0.2 °C in a silicone oil bath. A pair of tubes was removed after 3, 6, and 9 h, and the rotations of the solutions were measured. Each pair of tubes was combined and worked up in the following manner. The solution was distilled at reduced pressure (5 torr, 40 °C). Preparative TLC was performed on the residue using a 1000 micron silica gel plate (20 x 20 cm with preadsorbent, Analtech, Newark, Delaware 19711). After two elutions with 50% $CHCl_3$/hexane) the starting diester appeared as a band at R_f 0.07, and was recovered using THF. Table XLI shows the percent racemization after each time period based on solution rotations and the percent racemization of recovered **11**. The total recovery of **11** was 94.4 %. The identity of recovered **11** was confirmed by ^1H NMR.

Table XLI. Racemization of **11** by diethylmercury at 200 °C.

time	% racemization solution rotations	% racemization recovered **11**	recovery
3 h	48.1, 46.3	50.8	24.3 mg
6 h	64.0, 66.1	65.8	23.7 mg
9 h	73.8, 76.0	73.5	23.1 mg

39. Racemization of (+)-11 in the Presence of Diethylmercury in Bromobenzene at 181 °C. A solution was prepared by combining 405 mg (1.56 mmol) of diethylmercury, 6.0 mL of a 0.0129 mmol/mL bromobenzene stock solution of (+)-**11**, and 6 mL of bromobenzene (α_o+0.664, 546 nm). The molar ratio of diethylmercury to (+)-**11** was 20 : 1. Six tubes were filled with 2 mL each of the solution, degassed (freeze-pump-thaw), and sealed under 100 torr of nitrogen. A blank solution was prepared by combining 1.0 mL each of the bianthryl stock solution and bromobenzene. The solution was transferred to a tube, degassed, and sealed as described above. The sealed tubes were heated to 181.0 ± 0.1 °C in a silicone oil bath. The results are shown in Table XLII. No racemization was observed in the blank solution after 45 h.

Table XLII. Racemization of **11** by diethylmercury at 180 °C.

time	% racemization
6 h	19.6, 19.4
21 h	41.9, 42.6
45 h	63.0, 63.3

40. Thiophenol, Butylated Hydroxytoluene (BHT), Irganox 1076, and Dicyclohexylphosphine (DCP) as Inhibitors of Racemization of 11 by Diethylmercury.

I. Inhibitor/diethylmercury ratio 10 : 1

A solution was prepared by combining 349 mg (1.35 mmol) of diethylmercury with 10.0 mL of bromobenzene and 10.0 mL of a 0.131 mmol/mL bromobenzene stock solution of (+)-**11**. The molar ratio of diethylmercury to **11** was 10 : 1. Thiophenol (331 mg, 3.00 mmol) was

dissolved in 4.0 mL of the solution, and two tubes were filled with 2 mL each of the resulting solution. The same method was used to prepare tubes of solutions of the other inhibitors using 550 mg (2.50 mmol) of BHT, 966 mg, (1.82 mmol) of Irganox 1076, and 517 mg (2.61 mmol) of DCP. The tubes were degassed, sealed under 100 torr of nitrogen, and heated to 200.2 ± 0.1 °C for 5 h. Table XLIII contains the results with each inhibitor. The thiophenol tubes contained a white solid which was filtered out before measuring the optical rotation of the solution.

Table XLIII. Effect of inhibitors on the racemization of **11** by diethylmercury at 200 °C.

inhibitor	molar ratio (inhibitor/HgR_2)	% racemization
None	—	42.3, 43.1
PhSH	11 : 1	0.0, 0.0
DCP	9.7 : 1	0.0, 0.0
BHT	9.3 : 1	27.3, 27.4
Irganox 1076	6.7 : 1	48.0, 47.3

II. Inhibitor/diethylmercury ratio 2 : 1

A solution was prepared by combining 4.0 mL of a 0.260 mmol/mL bromobenzene stock solution of diethylmercury, 8.0 mL of a 0.0131 mmol/mL bromobenzene stock solution of (–)-**11** and 4.0 mL of bromobenzene. Four tubes were filled with 2 mL each of this solution to serve as blanks (α_o–0.736, 546 nm). Thiophenol (59.8 mg, 0.543 mmol) and DCP (113 mg, 0.567 mmol) were each dissolved in 4 mL of the remaining solution. Each inhibitor solution was divided equally among two tubes. Two of the blank tubes were

sealed under 740 torr of air without degassing. The remaining tubes were degassed (freeze-pump-thaw) and sealed under 100 torr of nitrogen. All of the tubes were heated to 200.2 ± 0.1 °C in a silicone oil bath for 5.0 h. The thiophenol tubes contained a white solid which was filtered out before measuring the optical rotation of the solution. One of the tubes sealed under air (80.3% racemized) darkened considerably. Table XLIV shows the results of this experiment.

Table XLIV. Effect of inhibitors on the racemization of **11** by diethylmercury at 200 °C.

inhibitor	molar ratio (inhibitor/HgR_2)	% racemization
None	—	55.6, 55.8
air	—	63.7, 80.3
PhSH	2.1 : 1	13.9, 14.3
DCP	2.2 : 1	18.1, 17.4

41. Effect of Air and Oxygen on the Racemization of (+)-11 in the Presence of Diethylmercury in Bromobenzene at 200 °C. A solution was prepared by combining 6.0 mL of (–)-11 ($[\alpha]_{546}$–219, c 1.22, $CHCl_3$) stock solution (0.0131 mmol/mL, , 3.0 mL of diethylmercury stock solution (0.260 mmol/mL), and 3.0 mL of bromobenzene. Six tubes were filled with 2 mL each of the solution (α_o–0.736, 546 nm). Two tubes were degassed (freeze-pump-thaw) and sealed under 100 torr of nitrogen. Two tubes were sealed under 750 torr of air, and the remaining two tubes were sealed under 750 torr of oxygen. All six tubes were heated to 200.3 ± 0.1 °C in a silicone bath for 5 h. Table XLV shows the results of this experiment. One of the tubes under an oxygen atmosphere

became too dark to measure the solution rotation. The contents of both tubes run under oxygen atmosphere were combined and **11** was recovered in the following manner. The solution was distilled under reduced pressure (5 torr/40 °C) and the residue was subjected to preparative TLC using a 1000 micron silica gel plate (20 x 20 cm with preadsorbent, Analtech, Newark, Delaware 19711). After two elutions with 50% $CHCl_3$/hexane, the diester **11** (at R_f 0.1) was clearly separated and was recovered by extracting with THF to yield 6.2 mg (50%): $[\alpha]_{546}$–42.3 (c 0.37, $CHCl_3$), 81% racemized. The contents of the tubes run under air were worked up in the same way to yield 9.4 mg (76%) of **11**: $[\alpha]_{546}$–62.4 (c 0.47, $CHCl_3$), 71% racemized. The identity of recovered samples was confirmed by ^1H NMR.

Table XLV. Effect of air and oxygen on the racemization of **11** by diethylmercury at 200 °C.

atmosphere	% racemization
nitrogen	42.9, 42.7
air	71.7, 70.2
oxygen	81.4

42. Effect of Optical Purity on the Racemization of (–)-11 in the Presence of Diethylmercury in Bromobenzene at 200 °C. Solution A was prepared by dissolving 25.2 mg (0.0536 mmol) of racemic **11** in bromobenzene and diluting to the mark in a 2 mL volumetric flask. Two solutions of identical total concentration of **11**, but of different optical purity were prepared as follows. Solution B was prepared by combining 2.0 mL of a stock solution of (–)-**11** (0.0131 mmol/mL bromobenzene) and 2.0 mL of diethylmercury stock solution (0.260 mmol/mL bromobenzene). Two tubes were filled with 2 mL

each of solution B (α_o–0.733, 546 nm). Solution C was prepared by combining 1.0 mL of the (–)-**11** stock solution, 0.50 mL of solution A (racemic **11**), 0.50 mL of bromobenzene, and 2.0 mL of the same diethylmercury stock solution used for solution B. Two tubes were filled with 2 mL each of solution C (α_o–0.371, 546 nm). All four tubes were degassed (freeze-pump-thaw), sealed under 100 torr, and heated to 200.2 ± 0.1 °C for 2.5 h in a silicone oil bath. The results are shown in Table XLVI.

Table XLVI. Effect of optical purity on the racemization of **11** with diethylmercury.

α_o	% racemization
–0.733	35.7, 35.7
–0.371	32.9, 33.7

43. Effect of Variation of the Concentration of Diethylmercury and 11 at 200 °C. Stock solutions of diethylmercury in bromobenzene (0.260 mmol/mL) and **11** in bromobenzene (0.0130 mmol/mL) were prepared in volumetric flasks. Pipets were used to combine various proportions of these solutions and bromobenzene to prepare a series of solutions in which the concentration of **11** was constant and the concentration of diethylmercury was varied, and another series of solutions in which the concentration of diethylmercury was constant and the concentration of **11** was varied. For each solution in a series 20 mL was prepared, and ten tubes were filled with 2 mL each. The tubes were degassed (freeze-pump-thaw), sealed under 100 torr N_2, and heated to 200.2 ± 0.2 °C in a silicone oil bath. Tubes were removed in pairs after each time interval. Each series was run twice. The results are shown in Tables XLVII -L.

Table XLVII. Variation of concentration of diethylmercury at constant concentration of **11** (run 1).

	Solution rotations at 546 nm (molar ratio HgR_2 : **11**)			
time (h)	5.00 : 1	10.0 : 1	15.0 : 1	20.0 : 1
0.000	0.730	0.727	0.728	0.731
0.500	0.698	0.688	0.665	0.661
0.500	0.698	0.682	0.664	0.661
1.00	0.671	0.645	0.617	0.609
1.00	0.670	0.643	0.617	0.607
1.50	0.650	0.610	0.574	0.561
1.50	0.647	0.610	0.573	0.560
2.00	0.625	–	0.579	0.517
2.00	0.624	–	0.575	0.517
2.03	–	0.533	–	–
2.03	–	0.532	–	–
2.50	0.600	0.547	0.505	0.476
2.50	0.599	0.542	0.503	0.474

Table XLVIII. Variation of concentration of diethylmercury at constant concentration of **11** (run 2).

	Solution rotations at 546 nm (molar ratio HgR_2 : **11**)			
time (h)	4.97 : 1	9.94 : 1	14.9 : 1	19.9 : 1
0.000	0.735	0.734	0.730	0.732
0.500	0.698	0.681	0.670	0.659
0.500	0.698	0.681	0.670	0.662
1.00	0.669	0.644	0.620	0.607
1.00	0.671	0.646	0.623	0.603
1.50	0.645	0.606	0.580	0.554
1.50	0.646	0.610	0.580	0.556
2.00	0.623	0.576	0.543	0.509
2.00	0.624	0.577	0.540	0.511
2.50	0.599	0.544	0.504	0.466
2.50	0.598	0.546	0.505	0.469

Table XLIX. Variation of concentration of **11** at constant concentration of diethylmercury (run 1).

	Solution rotations at 546 nm (molar ratio HgR_2 : **11**)			
time (h)	10 : 1.99	10 : 1.00	10 : 0.750	10 : 0.500
0.000	1.470	0.727	0.553	0.369
0.500	–	0.688	0.512	0.338
0.500	–	0.682	0.512	0.337
0.550	1.400	–	–	–
0.550	1.396	–	–	–
1.00	1.352	0.645	0.478	0.311
1.00	1.351	0.643	0.477	0.310
1.50	1.298	0.610	0.449	0.290
1.50	1.297	0.610	0.446	0.287
2.00	1.247	0.579	0.421	0.270
2.00	1.244	0.575	0.417	0.269
2.50	1.202	0.547	0.398	0.250
2.50	1.199	0.542	0.398	0.250

Table L. Variation of concentration of **11** at constant concentration of diethylmercury (run 2).

	Solution rotations at 546 nm (molar ratio HgR_2 : **11**)			
time (h)	10.0 : 2.02	10.0 : 1.00	10.0 : 0 75	10.0 : 0.500
0.00	1.477	0.734	0.553	0.371
0.500	1.392	0.681	0.510	0.336
0.500	1.392	0.681	0.510	0.333
1.00	1.335	0.644	0.482	0.307
1.00	1.339	0.646	0.478	0.309
1.50	1.268	0.606	0.448	0.285
1.50	1.280	0.610	0.449	0.284
2.00	1.232	0.576	0.420	0.265
2.00	1.232	0.577	0.422	0.266
2.50	1.183	0.544	0.394	0.243
2.50	1.176	0.546	0.396	0.244

44. Determination of the Half-life of Decomposition of Diisopropylmercury and Diethylmercury by HPLC Analysis. A Waters Associates Model 6000A Solvent Delivery System with a Rheodyne Model 7012 Loop Filler Port (20 μL loop) was connected to a Zorbax C8 column (Dupont Instruments). A Spectromonitor III variable wavelength detector was used along with a Spectra-Physics SP4270 integrator. Reaction solutions were analyzed after each heating period as follows. An analysis sample was prepared by dissolving 10 drops of the reaction solution in 5 mL of the eluent (either H_2O/MeOH or H_2O/MeCN). The resulting solution was loaded onto the injector loop. The area % of the diisopropylmercury peak reported by the integrator was divided by the area % of the bromobenzene peak. Since the concentration of the reaction solvent bromobenzene remains essentially unchanged during the course of the reaction, bromobenzene served as internal standard.

I. Diisopropylmercury

The optimum wavelength for diisopropylmercury was found to be 288 nm. The relative size of the bromobenzene peak was the least at this wavelength. The greatest peak separation was obtained using 15% H_2O/MeOH as eluent with flow rate 1.7 mL/min.

A. Analysis of Solutions of Known Concentration: A solution was prepared by dissolving 53.4 mg of diisopropylmercury in 5.0 mL of bromobenzene. Serial dilutions of the resulting solution with bromobenzene yielded two more solutions with relative concentration one half and one fourth that of the original solution. HPLC analysis of the solutions gave the results shown in Table LI.

The experiment was repeated. A solution was prepared by dissolving 116 mg (0.405 mmol) of diisopropylmercury in bromobenzene and diluting to

the mark in a 10 mL volumetric flask. Serial dilutions yielded three more solutions. HPLC analysis of the solutions gave the results shown in Table LII.

Table LI. HPLC analysis of solutions of known concentration of diisopropylmercury in PhBr (run #1).

Rel. concentration	area % ratio (see p. 140)
4.0	1.78
2.0	0.844
1.0	0.388

Table LII. HPLC analysis of solutions of known concentration of diisopropylmercury in PhBr (run #2).

Rel. concentration	area % ratio (see p. 140)
8.0	1.58
4.0	0.825
2.0	0.414
1.0	0.202

B. Determination of the Half-life of Diisopropylmercury at 170 °C: A solution was prepared by dissolving 221 mg (0.770 mmol) of diisopropylmercury in 20.0 mL of bromobenzene. Ten tubes were filled with 2 mL each of the resulting solution, degassed (freeze-pump-thaw), and sealed under 100 torr of nitrogen. One of the tubes was opened immediately after sealing and the contents analyzed by HPLC to determine if the degassing

procedure caused any change. The remaining tubes were heated to 170 ± 0.2 °C in a silicone oil bath. Tubes were removed in pairs at the specified time intervals. Mercury was visible at the bottom of the tubes after heating. No color change was observed in any of the tubes. The experiment was repeated. Both sets of data are shown in Table LIII. The experiments in the Table gave calculated half-lives of 0.64 h and 0.68 h (run #1 and #2, respectively).

Table LIII. Thermal decomposition of diisopropylmercury at 170 °C in PhBr.

	area % ratio (see p. 140)	
time (h)	Run #1	Run #2
0.0	1.89	1.47
0.0, after degassing	1.76	
0.5	1.03, 1.11	0.914, 0.954
1.0	0.645, 0.633	0.571, 560
1.5	0.345, 0.347	0.324, 0.286
2.0	0.199, 0.215	0.186, 0.200

II. Diethylmercury

The detector wavelength was set at 282 nm. The eluent was 25% H_2O/MeCN and the flow rate 1.2 mL/min. All other conditions were the same as those used for diisopropylmercury.

A. Analysis of Solutions of Known Concentration: A solution was prepared by dissolving 716 mg (2.77 mmol) of diethylmercury in bromobenzene and diluting to the mark in a 10 mL volumetric flask. Serial dilution of the resulting solution yielded three more solutions. The

experiment was repeated by the same method using 882 mg (3.41 mmol) of diisopropylmercury. The results of HPLC analysis are shown in Table LIV.

Table LIV. HPLC analysis of solutions of known concentration of diethylmercury in PhBr.

relative concentration	area % ratio (see p. 140) Run #1	Run #2
8	1.26	1.49
4	0.692	0.738
2	0.325	0.386
1	0.156	0.186

B. Determination of the Half-life of Diethylmercury at 200 °C: A solution was prepared by dissolving 1.94 g (7.49 mmol) of diethylmercury in bromobenzene and diluting to the mark in a 25 mL volumetric flask. Ten tubes were filled with 2 mL each, degassed (freeze-pump-thaw), and sealed under 100 torr of nitrogen. The sealed tubes were heated to 200.2 ± 0.4 °C in a silicone oil bath. Tubes were removed in pairs at the specified time intervals. The experiment was repeated. The results are shown in Tables LV and LVI. The half-lives calculated from the experiments in Tables LV and LVI were 253 h and 267 h, respectively.

Table LV. Decomposition of $HgEt_2$ at 200 °C (run 1).

time (h)	area % ratio
0.0	1.8
75.0	1.12, 1.14
111	1.00, 0.969
160	0.847, 0.873
212	0.771, 0.796

Table LVI. Decomposition of $HgEt_2$ at 200 °C (run 2).

time (h)	area % ratio
0.0	1.29
0.0, after degassing	1.27
49.0	1.12, 1.10
96.0	0.983, 0.995
144	0.850, 0.917
192	0.770, 0.772

45. Preparation of Isopropylideneazine. In a 1-L round-bottom flask were combined 100 g of (0.769 mol) of hydrazine sulfate and 117 mL of acetone. The flask was fitted with a reflux condenser. The mixture was magnetically stirred while 300 mL of 20% NaOH was slowly added through an addition funnel. The mixture became hot. The stirring was stopped after the addition was completed. Two layers formed. The flask was cooled in an ice bath, and 100 mL of NaCl was added. The layers were separated, and the aqueous layer was extracted with 3 x 100 mL of ether. The organic layers were combined, dried over $MgSO_4$, filtered, and evaporated. The liquid residue was distilled twice using a 1 x 20 cm Vigreaux column to yield 26.7 g (31%): bp 131 °C (lit.[129] 131 °C) ^{1}H-NMR (300 MHz, $CDCl_3$) δ1.84 (s, 6H), δ2.01 (s, 6H).

46. Preparation of Diisopropylhydrazine. A solution of 67.5 g (0.603 mol) of isopropylideneazine in 25 mL of ether was added dropwise through an addition funnel to a vigorously stirred slurry of 35.0 g of $LiAlH_4$ in 350 mL of anhydrous ether in a 1-L round-bottom flask fitted with a reflux condenser. The mixture refluxed slowly and was stirred overnight without external heating. An addition funnel was used to add 100 mL of 2N NaOH dropwise. The mixture was filtered on a Büchner funnel, and the white solid in the funnel was washed several times with 15 mL of ether. The combined filtrates were concentrated on a rotary evaporator and distilled. The fraction boiling at 110–135 °C was collected to yield 15.3 g (22.3%): d^{23} 0.785 (lit.[130] d^{26} 0.780), ^{1}H-NMR (300 MHz, $CDCl_3$) δ1.04 (d), δ2.94 (m).

47. Preparation of Azoisopropane. A solution of 15.3 g (0.134 mol) of diisopropylhydrazine and 60 mL of water was added dropwise through an addition funnel to a stirred suspension of 43.0 g of yellow HgO (Mallinkrodt

reagent) and 40 mL of water in a 250 mL round-bottom flask. The dark grey mixture was fractionally distilled using a 1 x 20 Vigreaux column to yield 6.76 g (45%): bp 89 °C (lit.[2] 88.5 °C) ^{1}H-NMR (300 MHz, $CDCl_3$) δ1.24 (d), δ3.54 (m).

48. Racemization of (–)-11 by Azoisopropane in Bromobenzene at 200 °C (small scale). A solution was prepared by combining 5.0 mL of a 0.131 mmol/mL stock solution of azoisopropane in bromobenzene with 5.0 mL of a 0.00652 mmol/mL stock solution of (–)-**11** ($[\alpha]_{546}$ –219, c 1.22, $CHCl_3$). The molar ratio of azoisopropane to **11** was 20.1 : 1. Six tubes were filled with 1.5 mL each of this solution (α_o–0.366, 546 nm). The tubes were degassed (freeze-pump-thaw) and sealed under 100 torr of nitrogen. The sealed tubes were heated in a silicone oil bath at 200.2 ± 0.2 °C. Solution rotations are shown in Table LVII.

Table LVII. Racemization of **11** by azoisopropane at 200 °C.

time	α	% racemization
4 h	–0.333	9.02
19 h	–0.288	21.3
	–0.285	22.1
30 h	–0.257	29.8
49 h	–0.233	36.3
	–0.227	38.0

The contents of the two 49 h tubes were combined and distilled at reduced pressure, and the residue was subjected to preparative TLC using a 1000 micron silica gel plate with preadsorbent (Analtech, Newark, Delaware 19711)

eluted six times with 50% hexane/chloroform. Two bands resulted at R_f 0.40 and 0.53. The band at Rf 0.40 yielded 3.0 mg of **11** which was 45% racemized: $[\alpha]_{546}$ –120 (c 0.30, $CHCl_3$). The identity of the sample was confirmed by NMR. The band at R_f 0.53 yielded <2 mg of an unidentified product.

49. Racemization of (–)-11 by Azoisopropane in Bromobenzene at 200 °C (large scale). A solution was prepared by combining 5.0 mL of a 0.264 mmol/mL stock solution of azoisopropane in bromobenzene with 5.0 mL of a 0.00652 mmol/mL stock solution of (–)-**11** ($[\alpha]_{546}$ –219, c 1.22, $CHCl_3$), and 10.0 mL of bromobenzene. The molar ratio of azoisopropane to (–)-**11** was 20 : 1. Five tubes were filled with 4 mL each of the resulting solution (α_o–0.363, 546 nm), degassed (freeze-pump-thaw), and sealed under 100 torr of nitrogen. The sealed tubes were heated in a silicone oil bath at 200.4 ± 0.2 °C for 49 h. The optical rotations of the solutions in the five tubes were measured: –0.214 (41.0% racemized), –0.198 (45.5%), –0.211 (41.9%), –0.214 (41.0%), –0.210 (41.9%). The contents of the tubes were combined and worked-up as described in the previous experiment to yield 19.6 mg (65%) of (–)-**11**: $[\alpha]_{546}$ –116 (c 0.30, $CHCl_3$). This represents 47.0% racemization. The identity of the sample was confirmed by NMR. The higher R_f band yielded 1 mg of unidentified product.

50. Thiophenol as Inhibitor of the Racemization of (–)-11 by Azoisopropane in Bromobenzene at 200 °C.

A. A solution was prepared by combining 5.0 mL of a 0.154 mmol/mL stock solution of azoisopropane in bromobenzene with 3.0 mL of a 0.0129 mmol/mL stock solution of (–)-**11** in bromobenzene. The molar ratio of azoisopropane to **11** was 20 : 1. Four tubes were filled with 2 mL each of the solution (α_o–0.364, 546 nm). Thiophenol (293 mg, 2.66 mmol) was dissolved

in the remaining 4 mL, and two tubes were filled with 2 mL each of the resulting solution (α_o–0.342, 546 nm). The molar ratio of thiophenol to azoisopropane was 6.9 : 1. The tubes were degassed (freeze-pump-thaw), and sealed under 100 torr of nitrogen. The sealed tubes were heated in a silicone oil bath at 200.2 ± 0.2 °C for 71 h. The solutions without inhibitor were racemized by 46.4 and 55.2%. The tubes containing thiophenol were racemized by 15.2 and 11.4%.

B. An azoisopropane/**11** solution (α_o–0.361, 546 nm) was prepared as described in A except that a 0.158 mmol/mL stock solution of azoisopropane in bromobenzene was used. Thiophenol (599 mg, 5.45 mmol) was dissolved in 4 mL of the azoisopropane/**11** solution yielding a solution with a 13.8 : 1. molar ratio of thiophenol to azoisopropane (α_o–0.342, 546 nm). The tubes were heated in a silicone oil bath at 200.3 ± 0.2 °C for 65 h. The solutions without inhibitor were racemized by 51.2% and 50.3%. The solutions containing thiophenol were racemized by 4.9% and 3.7%.

51. Preparation of Azoethane. A slurry of 20.0 g of diethylhydrazine dihydrochloride (Aldrich Chemical Co., Milwaukee, Wisconsin 53233) in 35 mL of water was stirred magnetically in a 250-mL round-bottom flask fitted with a reflux condenser and addition funnel. Dropwise addition of 50 mL of 40% KOH through the addition funnel gave a clear solution. The solution was distilled to dryness at 98–100 °C. The distillate was added dropwise through an addition funnel to a magnetically stirred slurry of 30.0 g of yellow HgO in 45 mL of water in a flask fitted with a reflux condenser. The slurry became dark gray. Simple distillation at 56 °C yielded crude product, which was dried over $CaCl_2$, filtered, and distilled to yield 6.19 g (57.9%): bp 58–60 °C (lit.[131] 58.0 °C), ^{1}H-NMR (300 MHz, $CDCl_3$) δ1.30 (t, 3H), δ3.80 (q, 2H).

52. Racemization of (–)-11 by Azoethane in Bromobenzene at 200 °C.

A. A solution was prepared by combining 3.0 mL of a 0.561 mmol/mL stock solution of azoethane in bromobenzene with 3.0 mL of a 0.0129 mmol/mL stock solution of (–)-**11** ($[\alpha]_{546}$ –219, c 1.22, $CHCl_3$) in bromobenzene and 6.0 mL of neat bromobenzene. The molar ratio of azoethane to **11** was 44 : 1. Six tubes were filled with 2 mL each of the resulting solution (α_o–0.363, 546 nm), degassed (freeze-pump-thaw), and sealed under 100 torr nitrogen. The sealed tubes were heated in a silicone oil bath at 200.3 ± 0.3 °C for 53.5 h. Solution rotations were –0.150, –0.146, –0.151, –0.165, –0.164, and –0.156. The average percent racemization was 57.2%. The solutions were combined and distilled at reduced pressure (5 torr, 50 °C). Preparative TLC of the residue using a silica gel plate (1000 micron with preadsorbent, Analtech, Newark, Delaware 19711) eluted once with 2 : 1 hexane/chloroform yielded three bands at R_f 0.0, 0.10, and 0.50. The band at R_f 0.50 yielded 4.5 mg (25%) of (–)-**11**: $[\alpha]_{546}$ –84 (c 0.30, $CHCl_3$). This represents 62% racemization. The identity of the sample was confirmed by NMR. The bands at R_f 0.0 and 0.10 yielded 2.3 mg and 1.3 mg of unidentified material, respectively.

B. A solution was prepared by combining 5.0 mL of a 0.261 mmol/mL stock solution of azoethane in bromobenzene with 5.0 mL of a 0.0129 mmol/mL stock solution of (–)-**11** in bromobenzene and 10.0 mL of bromobenzene. The molar ratio of azoethane to **11** was 20 : 1. Six tubes were filled with 2 mL each of the resulting solution (α_o–0.363, 546 nm). The tubes were degassed and sealed as described in A and heated in a silicone oil bath at 200.2 ± 0.3 °C for 48 h. Based on solution rotations the solutions were racemized by 42.1%, 41.0%, 38.6%, 39.7%, and 39.9%. The solutions were combined and worked up as described in A except that the preparative TLC plate was eluted twice with 50% hexane/chloroform. Two bands appeared at

R_f 0.20 and at the baseline. The band at R_f 0.20 yielded 12.1 mg (40%) of **11**: $[\alpha]_{546}$ –140 (c 0.605, $CHCl_3$). This represents 36% racemization. The identity of the sample was confirmed by NMR. The band at the baseline was recovered and prep TLC was repeated using neat chloroform as eluent (four elutions). Two major bands appeared at R_f 0.20 and at the baseline. Several faint bands were visible between these two bands and just above the band at R_f 0.20. The band at R_f 0.20 was recovered to yield 1.8 mg of unidentified product. The band at the baseline was recovered to yield 13.5 mg of unidentified product(s).

53. Thiophenol as Inhibitor of the Racemization of (–)-11 by Azoethane in Bromobenzene at 200 °C.

A. A solution was prepared by combining 5.0 mL of a 0.244 mmol/mL stock solution of azoethane in bromobenzene with 10.0 mL of a 0.0129 mmol/mL stock solution of (–)-**11** ($[\alpha]_{546}$ –219, $CHCl_3$) in bromobenzene and 25.0 mL of bromobenzene. The molar ratio of azoethane to **11** was 9.5 : 1. A bulb was filled with 20.0 mL of the solution (α_o–0.364, 546 nm). Thiophenol (284 mg, 2.58 mmol) was dissolved in the remaining 20 mL of the solution, and a bulb was filled with the resulting solution (α_o–0.356, 546 nm). The bulbs were degassed (freeze-pump-thaw), sealed under 100 torr of nitrogen, and heated in a silicone oil bath at 200.2 ± 0.2 °C for 48 h. Solution rotations indicated that the solution with thiophenol was 15.4% racemized, while the solution without thiophenol was 30.2% racemized. Both solutions were worked up as described in the previous experiment, except that prep TLC was performed only once, and the band at the baseline was not further purified. The solution without thiophenol yielded 15.8 mg of **11**: $[\alpha]_{546}$ –156 (c 0.790, $CHCl_3$). This represents 28.6% racemization. The baseline band yielded 13.7 mg of unidentified product. The solution with thiophenol yielded 15.7 mg of

11: $[\alpha]_{546}$ –183 (c 0.785, $CHCl_3$). This represents 16.2% racemization. The baseline band yielded 21.0 mg of unidentified material. The identity of the samples of **11** was confirmed by NMR.

B. A solution was prepared by combining 10.0 mL of a 0.267 mmol/mL stock solution of azoethane in bromobenzene with 20.0 mL of a 0.0128 mmol/mL stock solution of **11** ($[\alpha]_{546}$ –219, $CHCl_3$) in bromobenzene and 50.0 mL of neat bromobenzene. The molar ratio of azoethane to **11** was 10.5 : 1. Five tubes were filled with 4.0 mL each of this solution to serve as blanks (α_o–0.362, 546 nm). A solution was prepared by combining 150.3 mg (1.36 mmol) of thiophenol with 20.0 mL of the original solution. The molar ratio of thiophenol to azoethane was 2.0 : 1. Five tubes were filled with 4.0 mL each of the resulting solution (α_o–0.361, 546 nm). Another solution was prepared by combining 280 mg (2.55 mmol) of thiophenol with 20.0 mL of the original solution. The molar ratio of thiophenol to azoethane was 3.8 : 1. A bulb was filled with this solution (α_o–0.357, 546 nm). The final solution was prepared by combining 548 mg (4.98 mmol) of thiophenol with 20.0 mL of the original solution. The molar ratio of thiophenol to azoethane was 7.5 : 1. A bulb was filled with this solution (α_o–0.352, 546 nm). The tubes and the two bulbs were degassed (freeze-pump-thaw), sealed under 100 torr of nitrogen, and heated in a silicone oil bath at 200.3 ± 0.2 °C for 49 h. The solutions were worked up as described in part A to recover bianthryl **11** (see Table LVIII, recovery: 62%).

Table LVIII. PhSH as inhibitor of the racemization of **11** by azoethane.

molar ratio PhSH : **11**	α(soln.)	recovery	$[\alpha]_{546}$
reference (no PhSH)	–0.267	20.7 mg, 69%	–142
2.0 : 1	–0.329	17.1 mg, 57%	–192
3.8 : 1	–0.330	16.6 mg, 55%	–193
7.5 : 1	–0.325	18.9 mg, 63%	–192

II. Nucleophilic Systems

1. Preparation of Anhydro-2-hydromercuri-3-nitrobenzoic Acid.[132] To a solution of 20 g (0.50 mmol) of NaOH in 200 mL of water was added 52.8 g (0.250 mmol) of 3-nitrophthalic acid (99%, Aldrich Chem. Co., Milwaukee, Wisconsin 53233). The mixture was warmed slightly, and the acid dissolved. The solution was filtered through an oven-heated Büchner funnel directly into a 1-L round-bottom, long-neck flask. Another solution was prepared by dissolving 87.7 g (0.275 mmol) of mercuric acetate in 12.5 mL glacial acetic acid and 175 mL water. This solution was filtered directly into the reaction flask in the same manner. A white solid formed in the reaction flask after the addition of the second solution. A magnetic stirrer was added, and the flask was fitted with a condenser. The flask was immersed up to its neck in an oil bath set at 150 °C and heated with vigorous stirring for 4 days. Reaction progress was followed by leading a tube from the top of the condenser into a solution of barium chloride/NaOH. Formation of a white precipitate of barium carbonate indicated that the reaction is not over because carbon dioxide was still being evolved. The mixture was filtered hot through a Büchner funnel. The product was washed once with 40 mL of ethanol, and dried under aspirator suction in a round-bottom flask heated in a hot water bath (90 °C) for 1 h to yield 80.7 g (89%).

2. Preparation of 2-Bromo-3-nitrophthalic Acid. Crude anhydro-2-hydromercuri-3-nitrobenzoic acid (60.0 g, 0.165 mmol) and 10 g (0.25 mol) of NaOH were dissolved in 300 mL of boiling water. The solution was cooled and added to a 1-L 3-neck flask which was fitted with a mechanical stirrer in the middle neck, and a reflux condenser and an addition funnel in the outer

necks. The solution was heated to reflux in an oil bath and stirred vigorously. Concentrated HCl (17 mL) was added slowly through the addition funnel. A thick white precipitate formed. The bath was lowered and 6 mL of glacial acetic acid was added dropwise through the addition funnel. The flask was allowed to cool to room temperature. The addition funnel was replaced with a stopper. A solution of 20.6 g, (0.255 mol) of NaBr and 10 mL (0.18 mol) of bromine in 30 mL of water was rapidly added to the solution in the flask. The thick white precipitate dissolved. Vigorous stirring was maintained throughout the additions. The deep red solution was heated and allowed to reflux for 5 min. The heating bath was lowered, 4 g of solid NaOH was added, and a small amount of insoluble material was filtered out by gravity filtration. The filtrates were acidified to pH 1 by adding 30 mL of concentrated HCl. The resulting thick white precipitate was filtered through a Büchner funnel and washed with 3 x 30 mL of water. The crude product was crystallized from 30 mL of 40% ethanol to yield 25.3 g (62%): mp 185–188 °C (lit.[133] 185–187 °C).

3. Preparation of Methyl 3-nitro-2-bromobenzoate. Ethereal diazomethane was added in 1-mL portions to a stirred solution of 10.0 g (40.7 mmol) of 3-nitro-2-bromobenzoic acid in 100 mL of methanol until the addition no longer resulted in the evolution of bubbles. Excess diazomethane was destroyed by adding several drops of glacial acetic acid. The solvents were removed on a rotary evaporator and the residue was crystalized from 100 mL of 50% aqueous ethanol to yield 8.7 g of product: mp 78.5–79 °C (lit.[134] 81 °C). A second crop yielded 0.80 g: mp 77.5–78.5 °C. Total yield: 90%.

4. Preparation of (±)-Dimethyl 6,6'-Dinitrobiphenyl-2,2'-dicarboxylate (53). In a 50-mL flat bottom flask (45/50 outer joint) were combined 9.1 g (0.079 mol) of methyl 3-nitro-2-bromobenzoate and 5.0 g (0.080 g-atoms) of unactivated copper powder (99%, Aldrich Chem. Co., Milwaukee, Wisconsin 53233). The solid reagents were mixed thoroughly, and a mechanical stirrer extending to the bottom of the flask was fitted through the neck. The flask was heated with stirring for 25 h in an oil bath at 175°. An IR lamp was used to heat the region of the flask above the oil level to prevent material from solidifying and collecting in that area. The reaction progress was monitored by periodically dipping the tip of a microspatula in the hot mixture, swirling the microspatula in 1 mL of acetone in a centrifuge tube, centrifuging and decanting to remove Cu, evaporating to dryness, and taking an ^{1}H NMR spectrum of the residue in deutereoacetone. When the reaction was complete the mixture was brought to room temperature. The dark greenish-brown solid was ground to a powder with a mortar and pestle, and extracted overnight with 180 mL of ether in a Soxhlet extraction apparatus. The solution was evaporated on a rotary evaporator, and the residue was crystalized from 50 mL of ethanol to yield 4.0 g (63%) of pure **53** : mp 128.5–129 °C (lit. 129 °C,[134] 128–130 °C[135]); IR (KBr) (KBr) 3080, 2950, 1720, 1565, 1520, 1430, 1340, 1260, 1120, 980, 880, 820, 745, 710 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ3.65 (s, 6H), δ7.63–8.36 (m, 6H).

5. Preparation of (±)-6,6'-Dinitrobiphenyl-2,2'-dicarboxylic Acid (1). Sodium hydroxide (5.0 g, 0.13 mol), 11.2 g (31.2 mmol) of diester **53**, and 125 mL of 50% aqueous ethanol were combined in a 250-mL round-bottom flask. The diester dissolved on reflux. The progress of the reaction was monitored by analytical TLC (alumina plates, eluent: 25% HOAc/toluene). The solution was refluxed

for 3 h, and then concentrated to about 75 mL by removing the condenser while allowing the solution to continue boiling. The solution was brought to room temperature and acidified to pH 1 with concentrated HCl. The precipitated acid was collected on a Büchner funnel and washed several times with small portions of water. The crude diacid was crystallized from 150 mL glacial acetic acid to yield 7.34 g: mp 263.5–264 °C (lit.[135] 259–261 °C). The mother liquors were concentrated to yield a second crop of 2.15 g: mp 263.5–264 °C. Total yield: 88%.

6. Resolution of (±)-1. In a 150-mL beaker were combined 5.37 g (15.5 mmol) of (±)-**1**, 1.93 g (15.9 mmol) of d-(+)-methylbenzylamine (Aldrich Chem. Co., Milwaukee, Wisconsin 53233), and 45 mL of acetone at room temperature. After several hours the (+)-base/(+)-acid (dBdA) salt came out of solution. The salt was collected on a Büchner funnel and washed several times with 30 mL portions of boiling acetone. The dBdA salt was crystallized from 45 mL of ethanol to yield 2.44 g: mp 215.5–217 °C; $[\alpha]_D$+157 (c 3.23, methanol). The dBdA salt was hydrolyzed by dissolving in 35 mL of boiling water and adding 1 mL of concentrated HCl. The precipitated (+)-acid was collected on a Büchner funnel and dried by heating in vacuo to yield 1.59 g of (+)-**1**: mp 230.5–231 °C (lit.[135] 231–231.5 °C); $[\alpha]_D$+128 (c 4.50, methanol) (lit.[135] $[\alpha]_D$+127, methanol). The combined acetone extracts of the initial solution were evaporated on a rotary evaporator. The residue was hydrolyzed by dissolving in 60 mL of hot water and treating with 2 mL of concentrated HCl. Crude (–)-acid, which precipitated on cooling to room temperature, was collected on a Büchner funnel, washed twice with cold water and dried in vacuo to yield 2.37 g. This was dissolved in 25 mL of acetone and treated with 0.840 g (6.94 mmol) of l-(-)-methylbenzylamine. A precipitate of the (–)-base/(–)-acid (lBlA) salt soon

formed. The salt was collected on a Büchner funnel and washed several times with boiling acetone to yield 2.41 g: mp 210–213 °C; $[\alpha]_D$–152 (c 1.88, methanol). The lBlA salt was hydrolyzed by dissolving in 35 mL of water and adding 1 mL of concentrated HCl. The precipitated (–)-acid was collected on a Büchner funnel, washed twice with water, and dried by heating in vacuo to yield 1.49 g of (–)-**1**: mp 229.5–231 °C (lit.[135] 229 °C); $[\alpha]_D$–127 (c 3.85, methanol) (lit.[135] $[\alpha]_D$–126, methanol).

7. Preparation of (+)-Dimethyl 6,6'-dinitrobiphenyl-2,2'-dicarboxylate (53). A solution of 1.74 g (5.23 mmol) of (+)-**1** ($[\alpha]_D$+128, c 4.50, methanol) in 15 mL of methanol in a 100-mL round-bottom flask was stirred using a magnetic stirrer, while ethereal diazomethane was added in 1-mL portions until the addition no longer resulted in the evolution of bubbles. Excess diazomethane was destroyed by adding several drops of glacial acetic acid. The solution was evaporated, and the residue was dissolved in chloroform. The chloroform solution was extracted twice with 50 mL $NaHCO_3$, dried over $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography using 50 g of silica gel (230–400 mesh, E-M 60, E. Merck, Darmstadt, Germany) and eluting with chloroform. Fractions containing pure product were combined and evaporated. The residue was heated in vacuo (65 °C, 0.1 torr, 1.5 h) to yield 1.80 g (95%): mp 139–140 °C (lit.[136] 141-142°); $[\alpha]_D$+114 (c 3.30, ethyl acetate) (lit. $[\alpha]_D$+113,[136] +114,[137] ethyl acetate).

8. Reaction of (+)-53 with Potassium Methoxide/Methanol at Reflux. A piece of potassium metal (121 mg, 3.08 mg-atom) was cut under mineral oil, rinsed twice with hexane to remove mineral oil, and quickly transferred to a preweighed 50-mL 3-neck round-bottom flask fitted with a rubber septum and

two glass stoppers under an atmosphere of nitrogen. The flask was evacuated to remove the residual hexane using a syringe inserted through the rubber septum, flushed with nitrogen by repeatedly evacuating and refilling with nitrogen, and weighed under nitrogen. The weight of the potassium was determined by difference. A drying tube containing calcium sulfate was used in the nitrogen line to remove any traces of moisture. Anhydrous methanol (30 mL) was added with a syringe to yield a clear solution. Diester (+)-53 (208 mg, 0.567 mmol; $[\alpha]_D$+114, ethyl acetate) was quickly added to the flask along with several boiling chips. The rubber septum was replaced with a reflux condenser which had a rubber septum fitted at the top end. The set-up was flushed with nitrogen by repeatedly evacuating and refilling the flask using a syringe inserted through the rubber septum. The solution was heated to reflux under a nitrogen atmosphere. Aliquots of 10 mL were removed with a syringe after 4.5, 21, and 42 h. Each aliquot was cooled to 0 °C and acidified to pH 1 with concentrated HCl. After evaporating the solution to dryness, the residue was treated with methylene chloride and extracted with 25 mL of saturated sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and evaporated to recover starting material. The aqueous layer was acidified to pH 1 with concentrated HCl and extracted with methylene chloride to isolate acidic reaction products. The first aliquot yielded 66 mg (95%) of starting material: $[\alpha]_D$+109 (c 3.38, ethyl acetate). The aqueous layer yielded insufficient material for analysis (<2 mg). The second aliquot yielded 65 mg (94%) of starting material: $[\alpha]_D$+106 (c 3.25, ethyl acetate). The aqueous layer from the second aliquot yielded 10 mg of a solid which appeared to be methyl 6,6'-dinitrobiphenyl-2-carboxy-2'-carboxylate, the monoacid product of hydrolysis of one ester group of 53: ^{1}H NMR (60 MHz, CD_3COCD_3) δ3.6 (s, 3H), δ7.8–8.5 (m, 6H); IR (KBr) 3500–2500, 1720, 1680, 1600,

1570, 1520, 1450, 1430, 1350, 1270, 1210, 1130, 980, 900, 890, 840, 770, 750, 710, 700 cm^{-1}. The third aliquot yielded 18.5 mg (27%) of starting material: $[\alpha]_D$+98 (c 0.875, ethyl acetate) and 13.5 mg of the monoacid from the aqueous layer: ^1H NMR (60 MHz, CD_3COCD_3) δ3.6 (s, 3H), δ7.8–8.5 (m, 6H). The identity of recovered samples of **53** was confirmed by ^1H NMR. The ^1H NMR spectra of the recovered diester samples showed increasing amounts of impurities in the upfield region. The loss of optical activity may not be the result of racemization of the biphenyl, but rather may be due to the presence of optically inactive impurities. The samples could not be further purified.

9. Reaction of (+)-53 with Potassium Methoxide/Methanol at 150 °C. The reaction solution was prepared in the same way as the corresponding reaction at reflux (see p 156) with 154 mg (0.428 mmol; $[\alpha]_D$+115, ethyl acetate) of diester **53** (prepared from (+)-**1** of $[\alpha]_D$+128, c4.95, MeOH), 139 mg (3.56 mg-atom) of freshly cut potassium metal, and 30 mL of anhydrous methanol. After preparing the reaction solution, 10 mL of the solution was transferred to each of three ampules with a syringe. The ampules were degassed (freeze/pump/thaw) and sealed under 1 torr of nitrogen. The tubes were heated in a silicone oil bath set at 150 ± 1.5 °C. The workup consisted of acidifying the contents of the tube with 1 mL of 10% HCl in an ice-water bath, pouring the resulting solution into 50 mL of water and extracting with 6 x 50 mL of chloroform. The combined chloroform extracts were dried over magnesium sulfate, filtered, and evaporated. The residue was dried by heating in vacuo (typically 80 °C, 1 torr, 30 min). The first ampoule (4.5 h of heating) yielded 41.2 mg of impure diacid **1**, $[\alpha]_D$+110 (c 1.19, methanol). Analytical TLC (silica gel, eluent 10% acetic acid/chloroform) showed a major spot at R_f 0.50, and minor spots at R_f 0.28 and 0.72. A reference sample of **1** had

R_f 0.50. The second ampoule (24 h of heating) yielded 34.9 mg of impure diacid **1**. The third ampoule (45.5 h of heating) yielded 40.7 mg of impure **1**. Analytical TLC of the products from the second and third ampoules was essentially identical to that of the first, and indicated that no diester was present. Since the diester is much easier to purify than the diacid, the samples of impure diacid were esterified. Each sample was dissolved in 3 mL of acetone, and esterified by dropwise addition of ethereal diazomethane with a Pasteur pipet. Excess diazomethane was destroyed by adding several drops of glacial acetic acid. The solution was evaporated, and the crude **53** residue was purified by preparative TLC using a 1000 micron silica gel plate (20 x 20 cm with preadsorbent, Analtech, Newark, Delaware 19711) eluted with chloroform. Two clearly separated bands at R_f 0.10 and 0.40 resulted in each case. The band at R_f 0.40 was scraped off the plate and extracted with 3 x 5 mL of acetone. The filtrates were evaporated, and the residue was dried in vacuo (75 °C, 0.3 torr, 1 h) to yield pure diester (confirmed by ^{1}H NMR). Table LVIII shows the specific rotations of the recovered samples. The bands at R_f 0.1 from both plates were recovered in the same way and combined to yield 10 mg of an unidentified product: ^{1}H NMR (200 MHz, $CDCl_3$) δ8.1–9.0 (m), δ3.85 (d).

Table LVIII. Recovery of diester after heating to 150 °C with potassium methoxide/methanol.

time	recovery	$[a]_D$ (ethyl acetate)
4.5 h	34.6 mg	+112
24 h	22.9 mg	+122
46 h	24.0 mg	+112

10. Reaction of (+)-53 with $KOCH_3$/18-Crown-6/Methanol at Reflux. The method described on p 156 was used to weigh a clean piece of potassium metal (86.6 mg, 2.21 mg-atom) except that a calcium sulfate drying tube was used in the nitrogen line to the flask. Anhydrous methanol (3 mL) was added with a syringe to yield a clear solution of $KOCH_3$/methanol. A solution of 1.15 g (4.37 mmol) of 18-crown-6 (Aldrich Chem. Co., Milwaukee, Wisconsin 53233) in 4 mL of methanol and a solution of 215 mg (0.596 mmol) of (+)-53 ($[\alpha]_D$+115, ethyl acetate) in 5 mL of methanol were added to the flask with a syringe. Each addition was followed by rinsing the syringe with an equal volume of methanol which was added to the flask. The total volume of methanol used was 25 mL. The pale yellow solution was heated to reflux. Aliquots of 13 mL were removed after 25 and 52.5 h. The workup consisted of cooling the aliquot to 0° followed by the addition of 0.5 mL of concentrated HCl. The solution was evaporated on a rotary evaporator. Chloroform (25 mL) was added to the residue, and the solution was washed once with 50 mL water and three times with 25 mL of saturated sodium bicarbonate. The organic layer of the first aliquot (25 h) was dried over magnesium sulfate, filtered, and evaporated to yield 353 mg of a yellowish oil. Column chromatography (25 g of silica gel, 14 x 1.8 cm column, eluent: chloroform) yielded 48.1 mg of (+)-53: $[\alpha]_D$+107 (7% racemized) (c 2.41, ethyl acetate); ^1H NMR (60 MHz, $CDCl_3$) δ3.65 (s, 6H), δ7.6–8.4 (m, 6H). The aqueous layer of the sodium bicarbonate extraction of the first aliquot was acidified to pH 1 with concentrated HCl, extracted with 3 x 25 mL of chloroform, dried over magnesium sulfate, filtered, and evaporated to yield 22.6 mg of what appears to be the monoacid methyl 6,6'-dinitrobiphenyl-2-carboxy-2'-carboxylate: ^1H NMR (60 MHz, CD_3COCD_3) δ3.6 (s, 3H), δ7.8–8.5 (m, 6H). The second aliquot (52.5 h) was worked up in the same way to yield 62.7 mg of (+)-53: $[\alpha]_D$+113 (c

3.14, ethyl acetate); ^{1}H NMR (60 MHz, $CDCl_3$) δ3.65 (s, 6H), δ7.6–8.4 (m, 6H). The aqueous layer of the sodium bicarbonate extraction of the second aliquot was treated in the same way as that of the first aliquot to yield 22.6 mg of monoacid methyl 6,6'-dinitrobiphenyl-2-carboxy-2'-carboxylate: ^{1}H NMR (60 MHz, CD_3COCD_3) δ3.6 (s, 3H), δ7.8–8.5 (m, 6H).

11. Reaction of (±)-53 with $KOCH_3$/18-Crown-6/Acetonitrile at Reflux. The method described on p 156 was used to weigh a clean piece of potassium metal (30.0 mg, 0.767 mg-atom). Anhydrous methanol (1 mL) was added with a syringe and the resulting solution was evaporated on a rotary evaporator with a calcium sulfate drying tube between the aspirator and the flask. The oily residue was heated in vacuo (2.5 torr, 60 °C, 1 h) to yield 55.1 mg of white potassium methoxide. Dimethyl ester (±)-53 (110 mg, 0.305 mmol) and a magnetic stirrer were quickly added, and the flask was flushed with nitrogen. Anhydrous acetonitrile (10 mL) was added using a syringe. 18-Crown-6 (429 mg, 1.62 mmol) was dried in vacuo (62 °C, 8 torr) in a round-bottom flask fitted with a septum. The flask was filled with nitrogen. Anhydrous acetonitrile (15 mL) was added with a syringe and the resulting solution was transferred with a syringe to the flask containing the potassium methoxide/acetonitrile. Heating the contents to reflux gave a very deep, almost opaque red mixture. Apparently the potassium methoxide did not all dissolve. Reflux was continued for 12 h. After cooling to 5 °C, the contents of the flask were poured into 100 mL of cold water and acidified to pH 1 with concentrated HCl. The mixture turned brown. Acetonitrile was partially removed on a rotary evaporator, and the remaining aqueous solution was extracted with 3 x 50 mL of chloroform. The combined chloroform layers were dried over $MgSO_4$, filtered, and evaporated to yield 429 mg of a dark, oily

residue. This residue was dissolved in 50 mL of chloroform and extracted twice with 20% saturated Na_2CO_3. The organic layer was dried over $MgSO_4$, filtered, and evaporated. Crown ether was removed from the residue by column chromatography (25 g silica gel, 15 x 1.8 cm column, eluent: chloroform), to yield 18.6 mg of impure starting diester which contained at least one additional material: ^1H NMR (60 MHz, $CDCl_3$) δ7.5–8.4 (m, 4H), δ3.9 (broad, 3H), δ3.7 (s, 3H), δ3.5 (s, 1H); analytical TLC (5% HOAc/$CHCL_3$) produced spots at R_f 0.72 (same as the starting diester) and 0.52.

12. Reaction of (+)-53 with KF/18-Crown-6/MeCN at Reflux. 18-crown-6 (Aldrich Chemical Co., Milwaukee, Wisconsin 53233) was dried by heating at 40 °C in vacuo for 1 h. Diester (+)-**53** (57.8 mg, 0.161 mmol; $[\alpha]_D$+111, ethyl acetate) and 100 mg (1.72 mmol) of KF were combined in a 50-mL round-bottom flask along with a magnetic stirrer. The flask was fitted with a condenser. A syringe was inserted through a rubber septum at the top of the condenser and the flask was flushed with nitrogen by repeatedly evacuating and refilling the flask. A solution of 0.953 g (3.61 mmol) of 18-crown-6 in 20 mL of acetonitrile was added to the flask with a syringe. The KF only partially dissolved on heating to reflux. After refluxing 23 h, the flask was cooled to –5 °C, acidified to pH 1 with concentrated HCl, and the contents evaporated on the rotary evaporator. The residue was treated with 50 mL of chloroform, and the resulting mixture was extracted with 50 mL of saturated Na_2CO_3. The organic layer was dried over $MgSO_4$, filtered, and evaporated. Column chromatography (20 g of silica gel, 12.5 x 1.8 cm, eluent: chloroform) was used to separate crown ether from recovered diester. The fractions containing starting diester were combined and evaporated to yield 37.7 mg (65%) of unracemized (+)-**53**, $[\alpha]_D$+111 (c 1.97, ethyl acetate). The aqueous layer was

acidified to pH 1 with concentrated HCl and extracted twice with 50 mL of chloroform. The combined chloroform layers were evaporated, dried over $MgSO_4$, filtered, and evaporated to yield 79.0 mg of 18-crown-6 (confirmed by ^1H NMR).

13. Reaction of (+)-53 with KF/18-Crown-6/MeCN at 125 °C. 18-crown-6 (Aldrich Chemical Co., Milwaukee, Wisconsin 53233) was dried by heating at 40 °C in vacuo for 1 h. The crown ether (1.09 g, 4.14 mmol) and 120 mg (2.07 mmol) dried KF were combined in a 50-mL round-bottom flask which was fitted with a reflux condenser and a rubber septum. The flask was flushed with nitrogen using a syringe inserted through the rubber septum and 30 mL of anhydrous MeCN was added with a syringe. (+)-53 (157 mg, 0.436 mmol; $[\alpha]_D$+115, ethyl acetate) was added to the flask, which was again flushed with nitrogen. Everything dissolved except for a very small amount of material. A syringe was used to fill three tubes with 10 mL each of the solution, degassed (freeze/pump/thaw), and sealed at 1 torr of nitrogen. The sealed tubes were heated together in a silicone bath at 125 °C. Tubes were removed after 5, 24, and 48 h. Each tube was worked up in the same way. The tube was allowed to cool to room temperature, and the contents were poured into a separatory funnel containing 50 mL of 75% saturated NaCl. This was extracted once with chloroform. The chloroform layer was washed once with 50 mL of saturated NaCl, dried over $MgSO_4$, filtered, and evaporated. The residue was freed of crown ether by column chromatography (8 g of silica gel, 1.1 x 15 cm column, eluent: chloroform). The fractions containing starting diester were combined and evaporated, and the residue was heated in vacuo (typically 65 °C, 0.5 torr, 1 h). Optical rotations were measured in ethyl acetate. The results are shown

in Table LIX. The identity of each sample was confirmed by ^{1}H NMR. Total recovery of diester: 80%.

Table LIX. Recovery of diester (+)-53 after heating to 125 °C with KF/18-crown-6/MeCN.

Time	$[a]_D$	Recovery
5 h	+112	41.0 mg
24 h	+115	40.4 mg
48 h	+111	44.4 mg

14. Reaction of (±)-53 with KF\DMF at Reflux. KF (43.0 mg, 0.740 mmol), (±)-53 (100 mg, 0.279 mmol), and 30 mL of DMF were combined in a 50-mL round-bottom flask along with a magnetic stirrer. The flask was fitted with a reflux condenser and a rubber septum and flushed with nitrogen. All the KF dissolved on heating to reflux. The solution became bright yellow then deep brown. Reflux was continued for 46.5 h. The flask was allowed to cool to room temperature and poured into a separatory funnel containing 100 mL of chloroform. The solution was extracted with 5 x 100 mL of water, and the chloroform layer was dried over $MgSO_4$, filtered, and evaporated to yield 20.3 mg of residue: ^{1}H NMR (60 MHz, $CDCl_3$) δ3.9 (s), δ7.7–7.8 (m, weak); IR (KBr) 3300, 3100, 2950, 2900, 2850, 1720, 1690, 1660, 1440, 1420, 1310, 1290, 1200, 1180, 1140, 810, 760. The ^{1}H NMR spectrum indicated no starting diester was present. The aqueous layer was extracted once with 100 mL of EtOAc in an attempt to recover more material. The organic layer was dried over $MgSO_4$,

filtered, and evaporated. No starting diester was present in the residue (30 mg): ^{1}H NMR (60 MHz, $CDCl_3$) δ3.6 (s), δ3.9 (s), d4.0 (s), δ7.4–7.7 (m); IR (KBr) 3600-2900 (broad), 3100, 2950, 1720, 1600, 1530, 1440, 1360, 1300, 1280, 1200, 1170, 1140, 1010, 910, 820, 810, 760; analytical TLC (silica gel, ether) two spots, Rf 0.7 and 0.0 (starting material at Rf 0.6). Preparative TLC produced five bands, none of which yielded significant amounts of material. The aqueous extracts of the reaction solution were combined and evaporated. The brown residue was extracted with methanol, filtered, and evaporated to yield 52 mg of an off-white powder, IR (KBr) 1390 cm^{-1} (no other peaks). No starting diester was recovered.

15. Reaction of (+)-53 with KI/DMF at Reflux. KI (227 mg, 1.37 mmol), 91.2 mg (0.253 mmol) of (+)-**53** ($[\alpha]_D$+115, ethyl acetate), and a magnetic stirrer were combined in a 50-mL round-bottom flask. The flask was fitted with a reflux condenser and rubber septum and was flushed with nitrogen using a syringe inserted through the septum. DMF (25 mL) was added with a syringe through the septum. The resulting yellow solution darkened slightly on being heated to reflux. The solution was refluxed for 12 h. The final color of the solution was dark yellow. White needles crystallized out of the solution on cooling to room temperature. DMF was removed by vacuum distillation (35.5°, 4.3 torr). The residue was dissolved in 100 mL chloroform, and the solution was washed with 6 x 150 mL water to remove KI and residual DMF. The chloroform layer was dried over magnesium sulfate, filtered and evaporated. The residue only partially dissolved in 50 mL of acetone. The mixture was filtered on a Büchner funnel to yield bright yellow crystals of the dilactone 4,9-dioxapyrene-5,10-dione (7.1 mg): mp 368–370 °C (decomp.), lit.[138] 376° (sublim.); IR (KBr) 3100, 1740, 1610, 1440, 1330, 1290, 1230, 1095, 1070, 1000, 920,

820, 750 cm^{-1}, same as a sample prepared by a literature method; MS (OH^- /negative chemical ionization), calcd for $C_{14}H_6O_4$ 238.0266, found 238.0262. The filtrates were evaporated to yield 12.0 mg of residue. The IR spectrum of this residue contained peaks corresponding to 4,9-dioxapyrene-5,10-dione and dimethyl ester **53**. No attempt was made to recover starting material from this residue because of its low mass.

16. Preparation of 4,9-Dioxapyrene-5,10-dione (66). Reagent grade quinoline (bp 237 °C) was purified by simple distillation in vacuo (84 °C, 2.8 torr). The originally dark red, opaque liquid gave a clear, colorless distillate. Diacid **1** (101 mg, 0.291 mmol), 2 mL of quinoline, and several boiling chips were combined in a 5 mL round-bottom flask. The flask was fitted with a reflux condenser, and the yellow solution was heated to reflux. The solution turned dark brown. After 0.5 h the solution was allowed to cool to room temperature and was poured into 10 mL of 5N HCl. A dark gray solid (24 mg) was collected on a Büchner funnel It was transferred to a sublimation apparatus, dried in vacuo (0.5 torr, 2 h), and sublimed by heating in a 240 °C oil bath at reduced pressure (0.5 torr) to yield 5.5 mg of pale yellow crystals: mp 363–365 °C (decomp.), lit.[138] 376° (sublim.); IR (KBr) 1740, 1605, 1440, 1330, 1290, 1230, 1090, 1070, 1000, 920, 820, 750 cm^{-1}.

17. Reaction of (+)-53 with KI/DMF at 100 °C. The reaction solution was set up using 82.8 mg (0.230 mmol) of (+)-**53** ($[\alpha]_D$+115, ethyl acetate) and 238 mg (1.43 mmol) of KI by the same method as described for the corresponding experiment at reflux (see page 165). The reaction flask was heated in an oil bath set at 100 °C for 12 h. No precipitate formed when the flask was allowed to cool to room temperature. The contents were distilled at reduced pressure

(30 °C, 4.5 torr), and the residue was transferred to a separatory funnel with 100 mL of chloroform. The chloroform solution was extracted with 6 x 100 mL water. The dark yellow chloroform layer was dried over $MgSO_4$, filtered, and evaporated to yield 59.0 mg (71%) of (+)-**53**, $[\alpha]_D$+103 (c 2.71, ethyl acetate). Analytical TLC contained a spot at the origin and a spot which corresponded to **53**. The ^1H NMR spectrum showed the presence of traces of DMF and other impurities. The optical rotation of the recovered diester is 10% less than before the reaction. This reduction may be due to the presence of optically inactive impurities in the sample and not due to racemization of the diester.

18. Preparation of (–)-Dineopentyl 6,6'-Dinitrobiphenyl-2,2'-dicarboxylate (60). Thionyl chloride (purified grade, Fisher Scientific Co., Pittsburgh, Pennsylvania 15219) was purified by simple distillation. Reagent grade pyridine was refluxed over BaO for 1 h and distilled under nitrogen.The distillate was stored in a dark bottle over molecular seives. In a 10-mL round-bottom flask were combined 1.53 g (4.62 mmol) of (–)-**1** ($[\alpha]_D$–125, c 1.78, methanol), 5.0 mL of thionyl chloride, and a magnetic stirrer. The flask was fitted with a reflux condenser, and a drying tube filled with $CaSO_4$ was attached to the top of the condenser. The mixture was heated to reflux for 13 h. The acid dissolved after 3.5 h. The solution was allowed to cool to room temperature and the excess thionyl chloride was removed on a rotary evaporator. The yellow residue was dried in vacuo (50 °C, 0.2 torr, 2 h). Neopentanol (0.998 g, 11.3 mmol; 99%, Aldrich Chemical Co., Milwaukee, Wisconsin 53233) was added to the flask containing the crude acid chloride immediately after drying. The flask was fitted with a reflux condenser and rubber septum and the apparatus was flushed with nitrogen using a syringe inserted through the septum. Pyridine (10 mL) was added with a syringe

through a septum. The flask became hot. The mixture was heated in a 90 °C oil bath for 3.25 h. After cooling to room temperature, the mixture was evaporated on a rotary evaporator, and the residue was dried in vacuo (55 °C, 1 torr, 2 h). The crude ester was poured into a separatory funnel containing 100 mL each of benzene and 5% HCl. The layers were separated, and the benzene layer was washed with 4 x 100 mL of 5% HCl, 2 x 100 mL of 50% saturated $NaHCO_3$, dried over $MgSO_4$, filtered, and evaporated. The residue was heated in vacuo (0.2 torr, 70 °C, 1 hour) to yield 1.85 g of crude neopentyl diester. A 40 mg sample of the crude ester was crystallized from isopropanol to yield 31 mg: mp 126–126.5 °C. A second crystallization gave crystals of the same melting point. The remaining crude neopentyl diester was crystallized from 15 mL isopropanol to yield 1.61 g (total yield: 88%, based on diacid) of (-)-**60**: mp 125.5–126.5 °C; $[\alpha]_D$–79.9, $[\alpha]_{546}$–106 (c 1.47, ethyl acetate); IR (KBr) 2960, 2870, 1720, 1530, 1370, 1350, 1280, 1260, 1135, 980, 830, 770, 745, 700 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ8.33 (d, 4H), δ7.67 (t, 2H), δ3.77 (s, 4H), δ0.90 (s, 18 H); MS (OH^-/negative chemical ionization) calcd 472.1846, found 472.1775.

19. Reaction of (–)-60 with KI/DMF at Reflux. (–)-**60** (120 mg, 0.253 mmol; $[\alpha]_{546}$–106, ethyl acetate) and 209 mg (1.26 mmol) of KI were combined in a 50 mL round-bottom flask containing a magnetic stirrer. The flask was fitted with a condenser and flushed with nitrogen using a syringe inserted through a rubber septum at the top of the condenser. DMF (25 mL) was added with a syringe through the septum. The color of the solution changed from pale yellow to greenish-yellow on being heated to reflux . Reflux was continued for 12 h. DMF was removed by distillation at reduced pressure (35°, 4 torr). The residue was dissolved in 100 mL of benzene and extracted with 100 mL of 50% saturated sodium bicarbonate. The bicarbonate layer yielded no

precipitate when acidified to pH 1 with conc HCl. The benzene layer was washed with 5 x 100 mL saturated NaCl, dried over magnesium sulfate, filtered and evaporated. The residue was dried in vacuo (80°, 0.2 torr, 1 hour) to yield 104.2 mg (87%) of unracemized starting material: mp 125–126°; $[\alpha]_{546}$–107 (c 1.87, ethyl acetate). Analytical TLC (silica gel, eluent: benzene) showed only one spot at R_f 0.52 (same R_f as starting material).

20. Reaction of (–)-60 with KF/DMF for 12 h at Reflux. A 50-mL round-bottom flask containing 98.7 mg (1.70 mmol) of potassium fluoride was fitted with a reflux condenser and flushed with nitrogen using a syringe inserted through a rubber septum at the top of the condenser. (–)-60 (101 mg, 0.213 mmol; $[\alpha]_{546}$–106, ethyl acetate) was transferred to the flask with a syringe using 3 x 10 mL of anhydrous DMF. Most of the KF dissolved when the resulting mixture was heated to reflux. After 12 h the brown solution was distilled at reduced pressure (4 torr, 50° oil bath) to near dryness. The residue was transferred to a separatory funnel using 100 mL each of benzene and 50% saturated $NaHCO_3$. The benzene layer was washed with 5 x 100 mL of saturated NaCl, dried over $MgSO_4$, filtered, and evaporated. The residue (93 mg) was purified by preparative TLC using a 1000 micron silica gel plate (20 x 20 cm with preadsorbent, Analtech, Newark, Delaware 19711) eluted with benzene. The major band at Rf 0.5 was extracted in acetone, filtered, evaporated, and the residue dried in vacuo (50 °C, 0.3 torr, 1 hour) to yield 66.9 mg (67%) of unracemized (–)-60: $[\alpha]_{546}$–102 (c 1.80, ethyl acetate); mp 124.5–126 °C; ^{1}H NMR identical to that of a known sample.

21. Reaction of (–)-60 with KF/DMF (43 h) at Reflux. The reaction was set up the same way as described for the previous experiment using 101 mg (0.213

mmol) of (–)-**60** ($[\alpha]_{546}$–106, ethyl acetate) and 47.2 mg (0.813 mmol) of KF. The work-up was identical and yielded 61.0 mg (61%) of unracemized (–)-**60**: $[\alpha]_{546}$–106 (c 1.75, ethyl acetate); mp 124–125.5 °C; ^{1}H NMR identical to that of a known sample.

22. Reaction of (–)-60 with $NaSC_6H_6$/MeOH at Reflux. A piece of sodium metal (14.7 mg, 0.640 g-atoms) was cut under mineral oil, rinsed twice with hexane, and transferred to a preweighed 50-mL round-bottom flask. The flask was fitted with a reflux condenser and was evacuated to remove residual hexane using a syringe inserted through a rubber septum at the top of the condenser. The flask was filled with nitrogen and weighed. The weight of the sodium was determined by difference . The flask was cooled to –5° and 1 mL of absolute methanol was added with a syringe. After the sodium had reacted completely, 210 mg (1.91 mmol) of thiophenol was added with a syringe as a methanolic solution. The total volume was 30 mL. (–)-**60** (100 mg, 0.212 mmol; $[\alpha]_D$–79.9, ethyl acetate) was transferred to the flask, and the flask was quickly fitted with a reflux condenser and flushed with nitrogen. The pale yellow solution was heated to reflux for 14 h. No change was observed other than a slight darkening. The solution was allowed to cool to room temperature and methanol was removed on a rotary evaporator. The residue was transferred to a separatory funnel using 100 mL each of benzene and 50% saturated Na_2CO_3. The benzene layer was washed with 3 x 100 mL 50% saturated Na_2CO_3, once with 100 mL saturated NaCl, dried over $MgSO_4$, filtered, and evaporated. The residue was heated in vacuo (0.1 torr, 65 °C, 4 h) to yield 88.0 mg (88%) of unracemized (–)-**60**: mp 124.5–125.5 °C; $[\alpha]_D$–79.7 (c 2.38, ethyl acetate).

23. Preparation of Methyl 2-Chloro-3,5-dinitrobenzoate. 2-Chloro-3,5-dinitrobenzoic acid (20.0 g, 81.0 mmol; 97%, Aldrich Chemical Co., Milwaukee, Wisconsin 53233) was dissolved in 100 mL of ether. The solution was dried over $MgSO_4$, filtered, and evaporated. The residue was heated in vacuo (70 °C, 0.2 torr, 1 h) to yield 16.7 g (67.6 mmol) of dry acid. The acid was dissolved in 50 mL of acetone. The solution was stirred magnetically while ethereal diazomethane was added with a Pasteur pipet. Reaction progress was monitored by analytical TLC (silica gel plate, eluent: neat chloroform). Excess diazomethane was destroyed by adding several drops of acetic acid. The solution was evaporated, and the residue was dissolved in 70 mL of chloroform and decolorized using 200 mg of Norit-A. The filtrates were evaporated, and the residue was crystallized from 50 mL of methanol to yield 15.0 g: mp 89.5–90.5 °C. The mother liquors were concentrated to 10 mL to yield a second crop, 1.45 g: mp 88.5–89.5 °C (lit. 87 °C[139]). Total yield based on dry acid: 94%.

24. Preparation of (±)-Dimethyl 4,4',6,6'-Tetranitrobiphenyl-2,2'-dicarboxylate (64). Activated copper was prepared by stirring 50 g of copper powder (Aldrich Chemical Co., 99%) in a solution of 13 g iodine in 100 mL of acetone for 1 h. The supernatant liquid was decanted and the copper was washed with 6 x 25 mL of acetone and 2 x 25 mL of benzene. Residual solvent was removed on a rotary evaporator and by heating in vacuo (85 °C, 0.8 torr, 2 h). In a 100-mL round-bottom flask were combined 15.0 g (57.4 mmol) of methyl 2-chloro-3,5-dinitrobenzoate, 20.0 g (315 mg-atoms) of activated copper powder, 40 mL of distilled reagent grade nitrobenzene (bp 210 °C), and a magnetic stirrer. The mixture was heated at reflux for 30 minutes with vigorous stirring. Reaction progress was monitored by dipping a microspatula into the reaction mixture

and swirling the microspatula in a centrifuge test tube containing 1 mL of $CDCl_3$. The test tube was centrifuged and the supernatant liquid was analyzed by ^1H NMR . The reaction mixture was allowed to cool to room temperature, and was filtered through a Büchner funnel containing two sheets of filter paper to prevent clogging. The copper powder in the funnel was washed with a total of 150 mL of acetone. The filtrates were combined, and acetone was removed on a rotary evaporator. Nitrobenzene was removed by distilling at 5 torr. The residue was purified by column chromatography with 135 g of silica gel (230–400 mesh, E-M 60, E. Merck, Darmstadt, West Germany) in a 2 x 60 cm column eluted with chloroform. Fractions containing product were combined and evaporated. Traces of starting material and nitrobenzene were easily removed by extracting the residue once with 50 mL of methanol. Pale yellow crystals of (±)-**64** were collected on a Büchner funnel and washed with 5 x 20 mL of methanol to yield 9.96 g (77%): mp 174–175 °C (lit. 176.1 °C,[140] 175 °C[141]); IR (KBr) 3100, 2950, 1730, 1620, 1600, 1540, 1440, 1350, 1310, 1270, 1160, 1100, 930, 890, 820, 800, 740, 730, 720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ9.22 (m, 4H), δ3.80 (s, 6H).

25. Preparation of (±)-4,4',6,6'-Tetranitrobiphenyl-2,2'-dicarboxylic Acid (67). (±)-Dimethyl ester **64** (4.34 g, 9.64 mmol) was combined with 100 mL of glacial acetic acid and 120 mL of 65% concentrated H_2SO_4 in a 500-mL round-bottom flask. The mixture was heated in an oil bath set at 120° for 13.5 h. After 1 h a solution was obtained. The solution was poured into 250 mL of water and extracted twice with 200 mL of ether. The ether layer was washed with 5 x 100 mL of 50% saturated NaCl, dried over $MgSO_4$, filtered, and evaporated to yield 4.04 g. When an attempt was made to crystallize the crude product from water, much of the sample oiled out. Unsuccessful attempts were made to

crystallize the crude acid from $CHCl_3$/MeOH, $CHCl_3$/ether, and $CHCl_3$/acetic acid. Finally, the remaining 2.72 g of crude product was purified by column chromatography with 70 g of silica gel (230–400 mesh, E-M 60, E. Merck, Darmstadt, West Germany) in a 2.4 x 31 cm column eluted with 10% acetic acid/benzene. The fractions containing product as determined by analytical TLC (silica gel plates, eluent: 10% acetic acid/$CHCl_3$) were combined and evaporated. The residue was heated in vacuo (90 °C, 0.4 torr, 22 h) to yield 1.97 g: mp 280.5–290.5 °C [lit. 284 °C (decomp.)[141] and 288–289 °C (decomp)[123]].

26. Resolution of (±)-67. A solution of 1.50 g (3.56 mmol) of (±)-**67** in 25 mL of ethanol was poured into a solution of 2.70 g (7.21 mmol) of brucine (anhydrous, 99%, Aldrich Chemical Co.) in 75 mL of ethanol. The thick yellow brucine salt was collected on a Büchner funnel, washed with 5 x 25 mL of ethanol, and heated in vacuo (75 °C, 0.5 torr, 1.5 h) to yield 3.97 g (92%): mp 232 °C. A sample of this salt (3.13 g, 2.58 mmol) was treated with 250 mL of boiling *n*-propanol for 5 min and filtered hot through a Büchner funnel. The pale orange salt in the funnel was washed with 3 x 50 mL of boiling *n*-propanol and 3 x 10 mL of methanol to yield 1.60 g of the (+)-diacid/brucine salt. This salt was dissolved in 100 mL of 10% HCl, and the free acid was extracted into 100 mL of ether. The layers were separated. The ether layer was washed with 100 mL 10% HCl, 100 mL saturated NaCl, dried over $MgSO_4$, filtered, and evaporated. The residue was heated in vacuo (60 °C, 0.15 torr, 2 h) to yield 546 mg of (+)-**67**: $[\alpha]_D$+73.7 (*c* 2.55, acetone). The filtrates of the *n*-propanol extraction were combined and evaporated, and the residue was dried in vacuo to yield 1.06 g of the (–)-diacid/brucine salt. This salt was hydrolyzed by the same method as the (+)-diacid/brucine salt to yield 406 mg of (–)-**67**: $[\alpha]_D$–81.2 (*c* 2.66, acetone).

27. Preparation of (–)-Dimethyl 4,4',6,6'-Tetranitrobiphenyl-2,2'-dicarboxylate (64). (–)-67 (372 mg, 0.880 mmol; $[\alpha]_D$–81.2, c 2.66, acetone) was dissolved in 5 mL of acetone, and ethereal diazomethane was added dropwise using a Pasteur pipet. Reaction progress was monitored by analytical TLC (silica gel plates, eluent: 10% acetic acid/chloroform). Excess diazomethane was destroyed by adding several drops of glacial acetic acid. The solution was evaporated on a rotary evaporator. The residue was dissolved in 50 mL of chloroform, and the solution was washed twice with 50 mL of saturated $NaHCO_3$, once with 50 mL of water, dried over $MgSO_4$, filtered, and evaporated to yield 304 mg. Preparative TLC was carried out on the residue using a 1000 micron silica gel plate (20 x 20 cm with preadsorbent, Analtech, Newark, Delaware 19711) eluted twice with chloroform. The product was recovered by extracting in 100 mL of acetone, filtering, and evaporating the filtrates. The residue was heated in vacuo (70 °C, 0.15 torr, 2 h) to yield 220 mg (56%): mp 61–63 °C; $[\alpha]_D$–74.8 (c 2.08, acetone).

28. Reaction of (±)-64 with Potassium Methoxide/Methanol. A piece of potassium metal (101 mg, 2.58 g-atom) was cut under mineral oil, rinsed twice with hexane, and quickly transferred to a preweighed 50-mL round-bottom flask under an atmosphere of nitrogen fitted with a rubber septum. The flask was evacuated to remove residual hexane using a syringe inserted through the rubber septum, flushed with nitrogen, and the potassium was weighed by difference. Absolute methanol (2 mL) was added using a syringe. After the reaction was completed, (±)-64 (169 mg, 0.376 mmol) was transferred to the flask. Another 25 mL of methanol was added to the flask using a syringe. The mixture was heated to reflux under a nitrogen atmosphere. The ester

dissolved to give a red solution. After 1 h, 13.5 mL was drawn out with a syringe. The solution was acidified to pH 1 with concentrated HCl. Methanol was removed on a rotary evaporator. Chloroform (50 mL) was added to the residue and the solution was washed with 2 x 50 mL of water and 2 x 50 mL of saturated Na_2CO_3. The aqueous layers were combined and acidified to pH 1 with concentrated HCl and extracted twice with 100 mL of chloroform, which were combined, dried over $MgSO_4$, filtered, and evaporated. The residue was heated in vacuo (70 °C, 0.6 torr, 1.5 h) to yield 22 mg of unidentified hydrolysis products. The chloroform layer of the initial extraction was dried over $MgSO_4$, filtered, and evaporated. Analytical TLC (silica gel plate, eluent: benzene) of the residue contained spots at R_f 0.0, 0.2 and 0.28. Preparative TLC was carried out on the residue using a 1000 micron silica gel plate (20 x 20 cm with preadsorbent, Analtech, Newark, Delaware 19711) eluted 3x with neat benzene. Two bands appeared at R_f 0.50 and 0.75. To recover each component, the silica gel was extracted with 50 mL of acetone, which was filtered and evaporated. The component with R_f 0.75 was identified as (±)-dimethyl 4-methoxy-4',6,6'-trinitrobiphenyl-2,2'-dicarboxylate (23.6 mg): mp 134.5–136 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ9.09 (2H), δ7.93 (2H), δ4.01 (s, 3H), δ3.73 (d, 6H); IR (KBr) 3100, 2950, 1720, 1610, 1520, 1430, 1340, 1300, 1250, 1230, 1150, 1080, 1040, 980, 920, 880, 790, 740, 710 cm^{-1}; MS (CH_4/CI+) calcd for $(M+H)^+$ 436.0628, found 436.0591. The component with R_f 0.5 was identified as (±)-dimethyl 4,4'-dimethoxy-6,6'-dinitrobiphenyl-2,2'-dicarboxylate (5.0 mg): mp 131-132 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ7.80 (m, 4H), δ3.97 (s, 6H), δ3.66 (s, 6H); IR (KBr) 3100, 2950, 3850, 1720, 1610, 1520, 1420, 1340, 1290, 1250, 1220, 1090, 1050, 870, 860, 780, 750, 710 cm^{-1}; MS (CH_4/CI+) calcd for $(M+H)^+$ 421.0883, found 421.0907. After 13 h the remaining 13.5 mL of the reaction solution was worked up in the same way. This yielded 15 mg of (±)-dimethyl 4,4'-dimethoxy-6,6'-

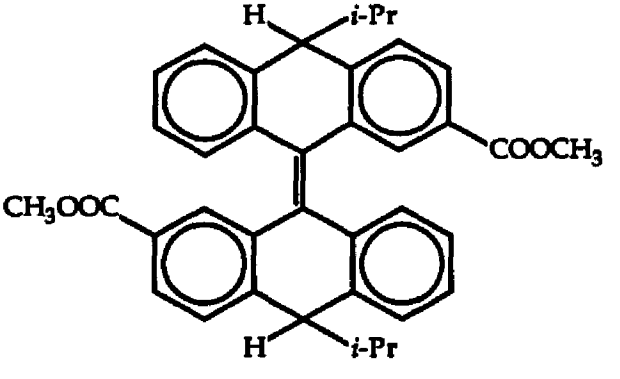
dinitrobiphenyl-2,2'-dicarboxylate (identified by ^{1}H NMR) and 46 mg of unidentified hydrolysis products.

29. Reaction of (–)-64 with KF/18-Crown-6/Acetonitrile. KF (35.5 mg, 0.611 mmol) and 297 mg (1.12 mmol) of 18-crown-6 (Aldrich Chemical Co., Milwaukee, Wisconsin 53233) were combined in a 50-mL round-bottom flask fitted with a condenser. The apparatus was flushed with nitrogen using a syringe inserted through a rubber septum at the top of the condenser. (–)-Dimethyl ester **64** (162 mg, 0.359 mmol; $[\alpha]_D$–74.8, c2.08, acetone) was dissolved in 10 mL of acetonitrile and transferred to the reaction flask using a syringe. The pale red solution turned deep red when heated to reflux. Reflux was continued for 23 hours. The solution was allowed to cool to room temperature and was poured into a separatory funnel containing 25 mL of saturated NaCl and 5 drops of concentrated HCl. The organic layer was separated, washed twice with 25 mL of saturated NaCl, and evaporated. The residue was dissolved in 50 mL of chloroform and washed twice with 50 mL of saturated $NaHCO_3$. The aqueous layers were combined, acidified to pH 1 with concentrated HCl, and extracted twice with 100 mL ether. The combined ether layers were dried over $MgSO_4$, filtered, and evaporated to yield 17.7 mg. The ^{1}H NMR spectrum was not consistent with hydrolyzed starting ester. The initial chloroform layer was dried over $MgSO_4$, filtered, and evaporated to yield 97.4 mg. Preparative TLC was run on the residue using a 1000 micron silica gel plate with preadsorbent (20 x 20 cm, Analtech, Newark, Delaware 19711). Five elutions with benzene were necessary to separate two components.(final R_f values 0.7 and 0.9). To recover the band at R_f 0.9, the silica gel was extracted in 100 mL of acetone, which was filtered and evaporated. The residue was heated in vacuo (55 °C, 0.3 torr, 1 h) to yield

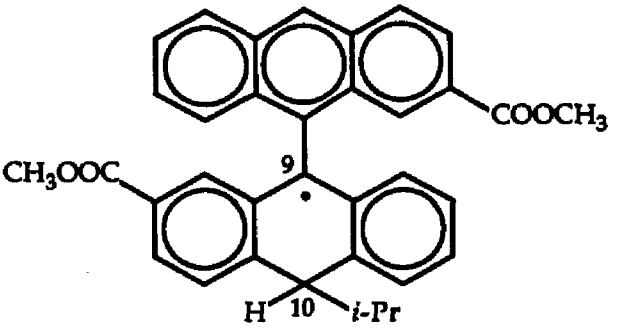
53.5 mg of semi-solid: ^{1}H NMR (60 MHz, $CDCl_3$) δ9.2–8.0 (m), δ3.7 (m); analytical TLC (silica gel, 2:1 hexane/$CHCL_3$) produced three spots of approximately the same size at R_f 0.36 (same as starting material), 0.42, and 0.50. Repeated preparative TLC and column chromatography were unsuccessful in isolating the components of the mixture.

Appendix

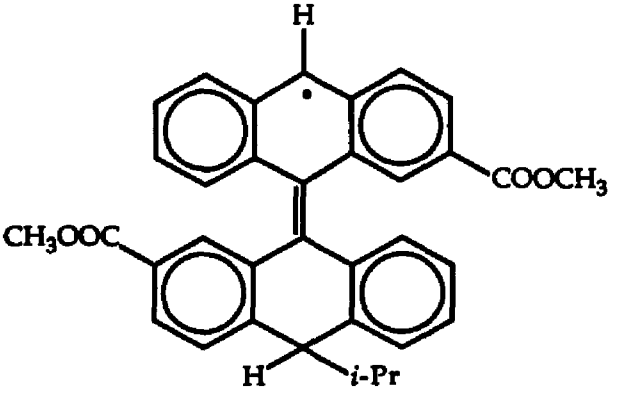
The ^{1}H-NMR spectrum of one of the products isolated from the racemization of **11** by diisopropylmercury indicates the presence of two isopropyl groups. Note that ca. 90% of **11** was recovered, and the product represents only 1% of the mass of **11** used. The mass spectrum (see page 120) has a molecular ion which is two mass units higher than expected for the product of displacement of two hydrogen atoms by isopropyl radicals. The structure shown as **66** is consistent with this information. The 10-position on the anthracene ring is the most reactive, and it is likely that most addition by isopropyl radical takes place at this position. The resulting methyne hydrogen at the 10 position in **67** is not easily abstracted because it is in a sterically crowded environment.[142] Delocalization of the odd electron in **67** could lead to appreciable electron density at the 10' carbon as shown in **68**. Addition of an isopropyl radical at C(10') would then lead to **66**. Addition at the 9-carbon is less likely because approach is more highly hindered. Compounds such as **69** are known.[143]



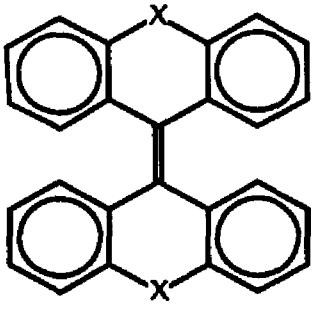
66



67



68



69 (X = O, NH, CO)

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