PYROLYTIC REARRANGEMENTS OF HETERO-SUBSTITUTED VINYLCYCLOPROPANES AND CYCLOPROPANECARBONYL DERIVATIVES

by

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TO MY MOTHER

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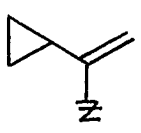
ABSTRACT

PYROLYTIC REARRANGEMENTS OF HETERO-SUBSTITUTED VINYLCYCLOPROPANES AND CYCLOPROPANECARBONYL DERIVATIVES

The pyrolytic rearrangement of hetero-substituted vinylcyclopropanes 93a-c (93a, Z= $OCOCH_3$; 93b, Z= OC_4H_9-n; 93c, Z= OCH_3), ketoesters 98a-d (98a, R_1= R_2= H; 98b, R_1= CH_3, R_2= H; 98c, R_1= H, R_2= CH_3; 98d, R_1= R_2= CH_3), cyclopropylketene (115) and vinyl cyclopropyl ketone (129) were investigated.



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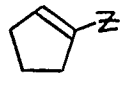

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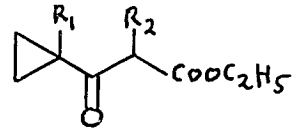

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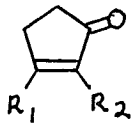

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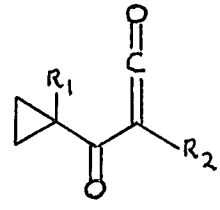

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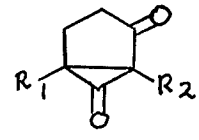

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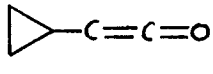

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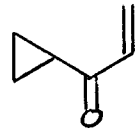

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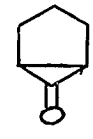

130

The conversion of enol derivatives 93a-c to 94a-c was investigated since 94a-c could readily be converted to cyclopentanone by treatment with aqueous acid, and consequently, the initial conversion (93 to 94) would provide a useful route to cyclopentanones if successful. Pyrolysis of 93a (Z= $OCOCH_3$) and 93c (Z= OCH_3) at 415-560° gave the corresponding derivatives of 94 in very moderate yields, while 93b (Z= OC_4H_9-n) gave cyclopropyl methyl ketone instead of the corresponding derivative of 94. Consequently, we focussed our attention on ketoester 98a (R_1= R_2= H) which was expected to be able to give the enol of 98a which could then undergo vinylcyclopropane rearrangement, affording 2-carbethoxycyclopentanone. Instead, pyrolysis of ketoesters 98a-d near 500° and 1-3 mm Hg gave cyclopentenones 99a-d in yields of 47-69%. Loss of ethanol from 98 would lead to the formation of acylketene 104 which could then rearrange to cyclopropanone 105. Decarbonylation of 105 would give 99. Evidence is presented for the intermediacy of acylketene 104, the formation of which is believed to be a surface catalyzed process. The substitution pattern of cyclopentenone 99d which requires the loss of the ketone carbonyl group rather than the carbonyl of the carboxyl group suggests that cyclopropanone 105 was also an intermediate in the conversion of 98 to 99.

Pyrolysis of related materials (ethyl cyclopropylacetate (114) and vinyl cyclopropyl ketone (129)) were also investigated. Pyrolysis of ester 114 at 587° and 0.25-2.00 mm Hg gave 2-cyclopentenone (99a) in

39% yield, and cyclopropylketene (115) was postulated as the intermediate involved in this conversion. Cyclopropylketene (115) was also generated by the familiar method of dimer cracking (537-560°, 0.20-1.80 mm Hg). Under these conditions, 2,4-dicyclopropyl-3-hydroxy-3-butenoic acid β-lactone (119) gave 2-cyclopentenone (99a) (13-31%), 1,6-spiro [4. 4] nonadiene (120) (3-14%), 1,3-dicyclopropylallene (121) (0-20%) and other minor products. Formation of 99a, 120, 121 and other minor products are discussed.

Pyrolysis of vinyl cyclopropyl ketone (129) at 610-664° and 0.20-1.00 mm Hg gave 2-cyclohexen-1-one (131) (7-27%), 3-cyclohexen-1-one (132) (7-13%), phenol (133) (4-19%), benzene (134) (6-31%) and 1,3-cyclohexadiene (135) (0-7%). The expected product, cyclopentene which would result from rearrangement of 129 to cyclopropanone 130, with subsequent decarbonylation, was not obtained. Mechanisms which would account for the formation of the observed products 131 to 135 are discussed.

The main objective of this work was to develop useful routes to cyclopentanones and/ or cyclopentenones. The pyrolytic rearrangement of 3-cyclopropyl-3-oxopropanoates to cyclopentenones has provided us with a useful route to cyclopentenones. Consequently, a review of the most useful methods for preparing cyclopentenones is presented so that a comparison can be made with the new method described in this dissertation.

Chapter 1

Synthetic Methods

Leading to Cyclopentenones

The objective of this work was to develop new synthetic routes to cyclopentanones and/ or cyclopentenones. The pyrolytic rearrangement of 3-cyclopropyl-3-oxopropanoates (See Chapter 3) has provided a route to cyclopentenones which may prove to be of considerable synthetic value. In view of this, a review of the most useful methods available for the preparation of cyclopentenones is presented so that a comparison can be made with the new method described in this dissertation.[1] The cyclopentenones that are to be considered may be divided into two categories: those which are substituted on the double bond (2-, 3-, or 2,3-dialkyl), and those which do not bear substituents on the olefinic double bond. We will refer to the former as type 'A' cyclopentenones and the latter as type 'B' cyclopentenones.

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(1) Two reviews[1a,b] merely list the methods available for the preparation of cyclopentenones. There is very little discussion of the scope and limitation of each method, and yields obtainable by each method are not available. Because of this, we think that it will be more useful if we listed the actual references whenever data is presented.

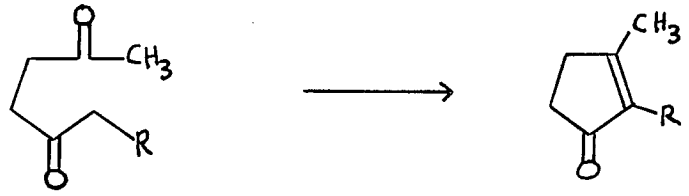
(1a) M. Green, G. R. Knox and P. L. Pauson, "Rodd's Chemistry of Carbon Compounds", ed., S. Coffey, 2nd edition, vol. IIA, Elsevier, Amsterdam, 1967, p. 168 et seq.

(1b) R. A. Raphael, "Rodd's Chemistry of Carbon Compounds", ed., E. H. Rodd, 1st edition, vol. IIA, Elsevier, Amsterdam, 1953, p. 95 et seq.

Method (1): Base Catalyzed Cyclization of 2,5-Diketones

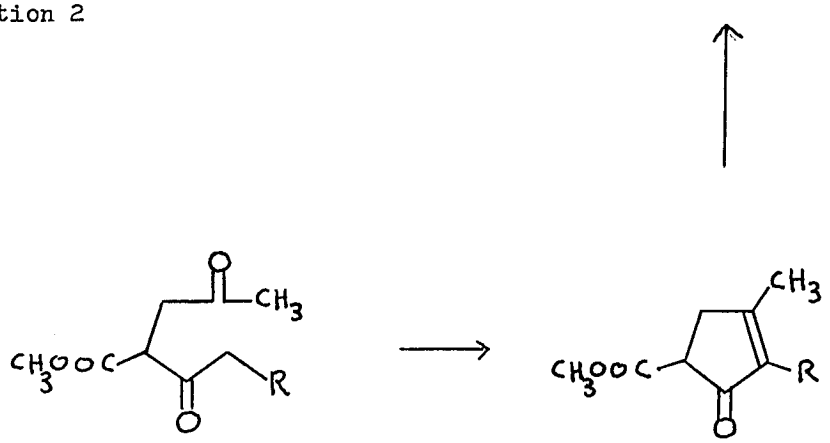
The base catalyzed cyclization of 2,5-diketones such as 1 and 3 have been extensively used for the preparation of 2-alkyl-3-methyl-2-cyclopentenones[1] (2) (equations 1 and 2).

Equation 1



1 2

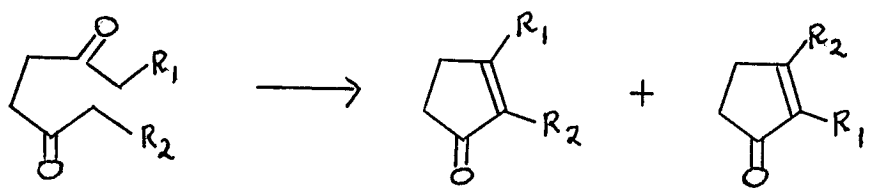
Equation 2



3 4

For example, 4-carbethoxydecan-2,5-dione (3, R= n-C_4H_9) was converted to 2-n-butyl-3-methyl-2-cyclopentenone (2a, R= n-C_4H_9) in 68% yield,[2] and 2,5-undecandione (1, R= n-C_5H_{11}) gave 2-amyl-3-methyl-2-cyclopentenone (2b, R= n-C_5H_{11}) in 92% yield.[2] In general, only 2,5-diketones are useful for this type of condensation since γ-diketones of the type 5 condense to give a mixture of the two possible products, 6 and 7 (equation 3).

Equation 3



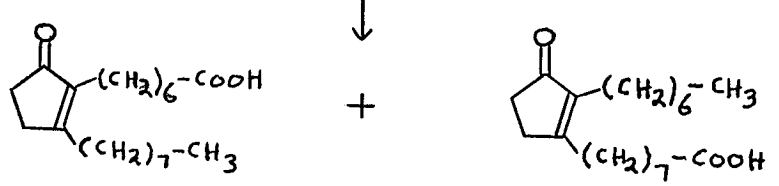
5 6 7

For instance, Samuelson obtained both 8 and 9 upon treatment of 10 with base[3] (equation 4).

Equation 4

$CH_3OOC-(CH_2)_7-CO-(CH_2)_2-CO-(CH_2)_7-CH_3$

10

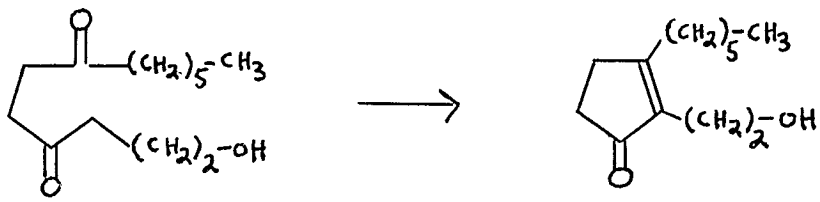


8 9

Relative Yield = 70% Relative Yield = 30%

An exception was found upon cyclization of 11, as Arndt and coworkers obtained 12 in quantitative yield[4] (equation 5).

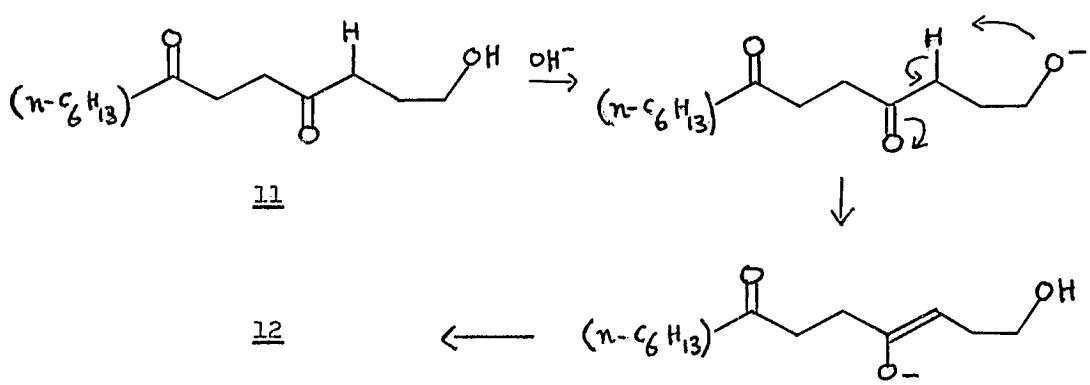
Equation 5



11 12

It is possible that the free hydroxyl acted as an internal base and preferentially formed the enolate anion of the nearer active methylene as shown in equation 6.

Equation 6



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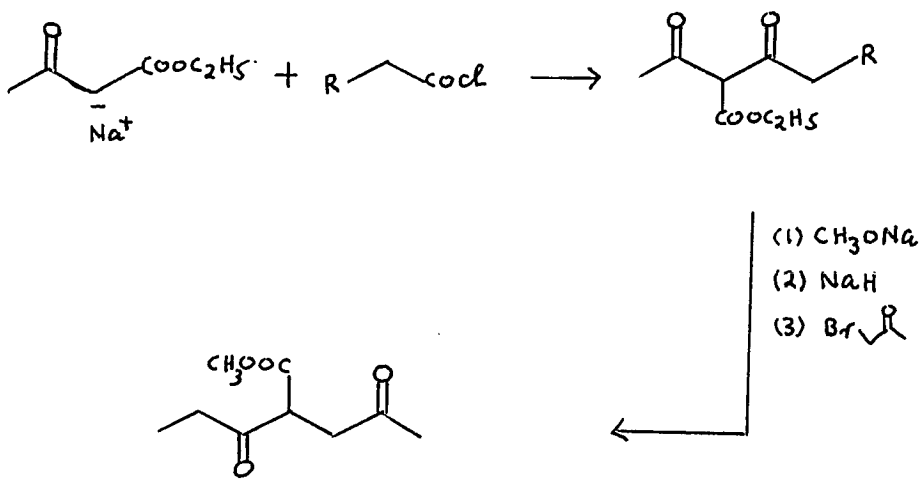
(2) H. Hunsdiecker, Ber. 75 B, 447, 455 (1942).
(3) B. Samuelson and G. Stallberg, Acta. Chem. Scand., 17, 810 (1963).
(4) F. Bohlman, P. Herbst, C. Arndt, H. Schoenowsky and H. Gleinig, Chem. Ber. 94, 3193 (1961).

Several routes have been developed for the preparation of the required 2,5-diketones 1 and 3 as shown in equations 7, 8 and 9.

Equation 7



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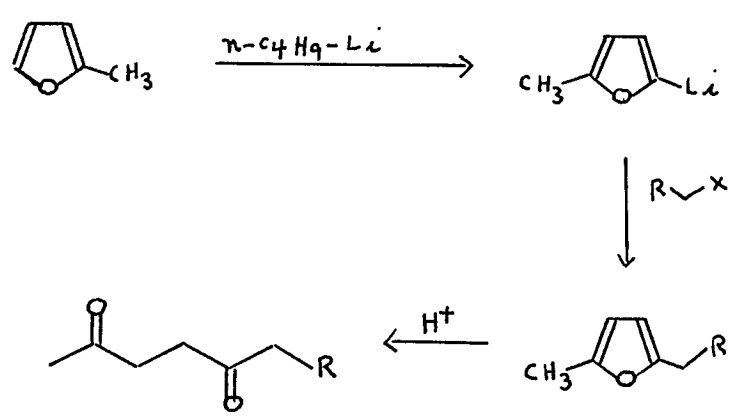
Equation 8



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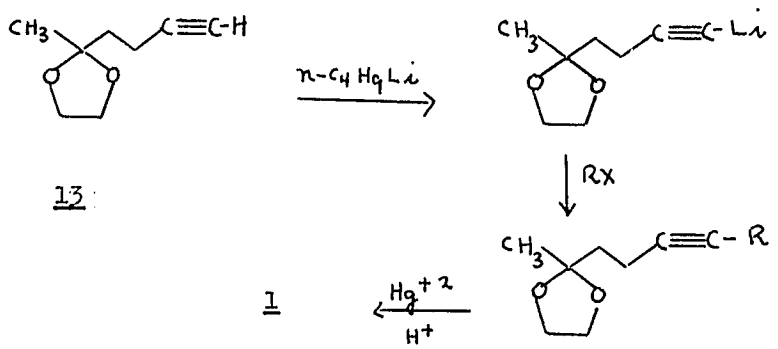
Equation 9



13

1

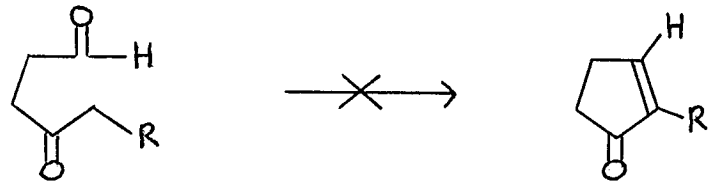
For example, Hunsdiecker obtained 3 (R= $n\text{-}C_4H_9$) from ethylacetoacetate and hexanoyl chloride in 26-42% yield (equation 7), and converted it to 2-n-butyl-3-methyl-2-cyclopentenone (2a, R= $n\text{-}C_4H_9$) in 18-28% overall yield.[2] Buchi and Wuest obtained 1 (R= cis-2-pentenyl) from 2-methylfuran (equation 8), and converted it to cis-jasmone (2, R= cis-2-pentenyl) in 40-5% overall yield.[5] Stork and Borch prepared the same diketone 1 (R= cis-2-pentenyl) in 42% yield from the acetylenic ketal 13 and cis-2-pentenyl tosylate (equation 9), and converted it to cis-jasmone in 32% overall yield.[6] Other methods have been developed for the preparation of 1[2,7] and 3,[8] but are less efficient.

---

(5) G. Buchi and H. Wuest, J. Org. Chem., 31, 977 (1966).
(6) G. Stork and R. Borch, J. Amer. Chem. Soc., 86, 935, 936 (1964).
(7) L. Crombie, P. Hemesley and G. Pattenden, J. Chem. Soc., C, 1024 (1969).
(8) L. Crombie, A. J. B. Edgar, S. H. Harper, M. W. Lowe and D. Thompson, ibid., 3552 (1950).

γ-Ketoaldehydes such as 14 which are not methyl ketones, do not condense to 2-alkyl-2-cyclopentenones (15) (equation 10).

Equation 10



14 15

Treatment of both 4-oxopentanal and 4-oxohexanal with base gave either unchanged starting material or polymeric products.[9] In contrast, Strike and Smith succeeded in preparing cyclopentenones 17a,b by treatment of γ-ketoaldehydes 16a,b with 0.5N sodium hydroxide for 15 minutes at 25° [10] (equation 11).

Equation 11

16 17

(a) $R_1 = R_2 = CH_3$

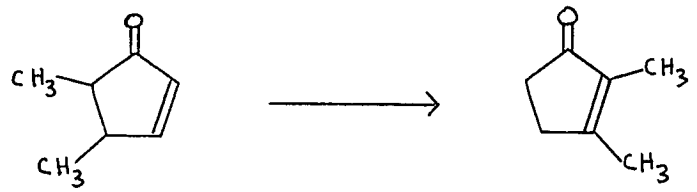
(b) $R_1 = (CH_2)_2\text{-}CHOPY^*\text{-}(CH_2)_4\text{-}CH_3$

$R_2 = (CH_2)_6\text{-}COOC_2H_5$

$PY^* = 2'$-tetrahydropyranyl

The success of the conversion of 16 to 17 is dependent on the exceedingly mild reaction conditions used, since it has been shown that more vigorous basic conditions converted initially formed 17a to 2,3-dimethyl-2-cyclopentenone[11] (equation 12).

Equation 12



17a

It is of interest to note that acids also isomerize 17a to 2,3-dimethyl-2-cyclopentenone.[12] Thus it appears that the requirement of exceedingly mild reaction conditions in the conversion of γ-ketoaldehydes (e.g. 16) to type 'B' cyclopentenones (e.g. 17) may limit the usefulness of this method.

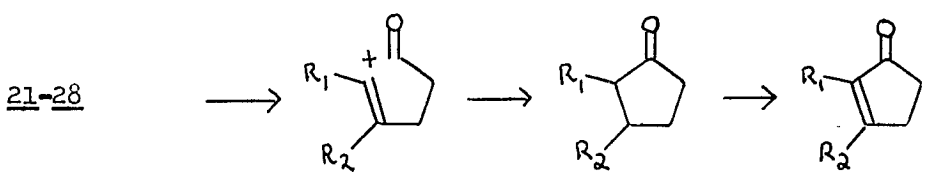
---

(9) G. W. K. Cavill, B. S. Goodrich and D. G. Laing, Australian J. Chem., 23, 83 (1970).
(10) D. P. Strike and H. Smith, Tetrahedron Lett., 4396 (1970).
(11) L. Ettlinger, E. Gaumann, R. Hutter, W. Keller-Schierlein, F. Kradolfer, L. Neip, V. Prelog and H. Zahner, Helv. Chim. Acta., 41, 216, 220 (1958).
(12) G. Stork and G. L. Nelson, J. Amer. Chem. Soc., 93, 3091 (1971).

Method (2): Acid Catalyzed Condensation of γ- and δ-Lactones

Various acid catalyzed processes lead to the formation of structures such as 18 and 19, resulting, ultimately, in 2-cyclopentenones 20 (equation 13)

Equation 13



18 19 20

Among these are the acid catalyzed reactions of Δ^4, Δ^5 and Δ^6-alkenoic acids[1a,13] (21, 22 and 23), γ- and δ-hydroxyacids[1a] (24 and 25), γ, δ-alkenoyl chlorides 26[1a] and γ- and δ lactones[1a,13] (27 and 28).

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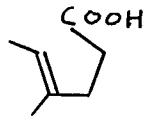
(13) M. F. Ansell, J. E. Emmet and B. E. Grimwood, J. Chem. Soc., C, 141 (1969) and references therein.



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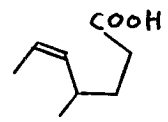

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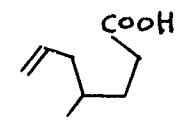

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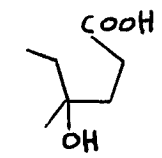

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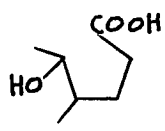

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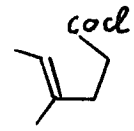

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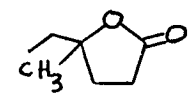

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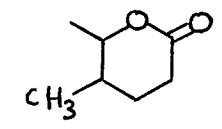
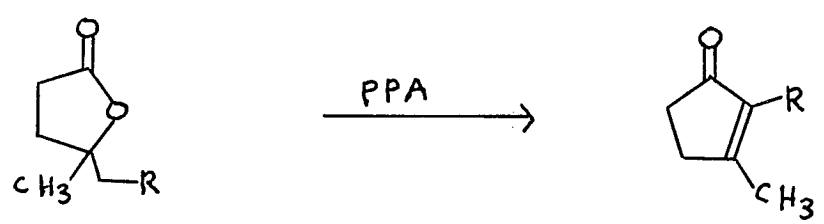


28

Of these, condensations of γ-lactones have proven to be of the greatest synthetic utility. For example, γ-methyl-γ-alkyl-γ-valerolactones 29 (29a, R= n-C_4H_9; 29b, R= n-C_5H_{11}) were converted to 2-alkyl-3-methyl-2-cyclopentenones (2a,b) in 92-5% yields[14a] (equation 14).

Equation 14

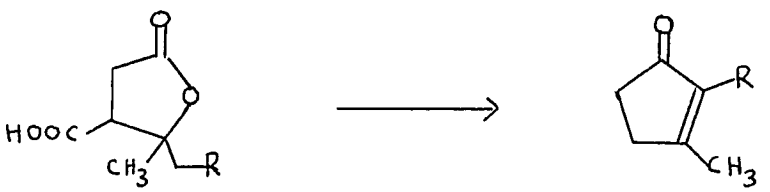


29 2

PPA = Polyphosphoric Acid

A certain variation in the γ-lactone structure is allowed. For example, paraconic acids 30 (30a, R= n-C_4H_9; 30b, R= n-C_5H_{11}) were converted to 2a and 2b in yields of 79% and 80% respectively[15] (equation 15).

Equation 15

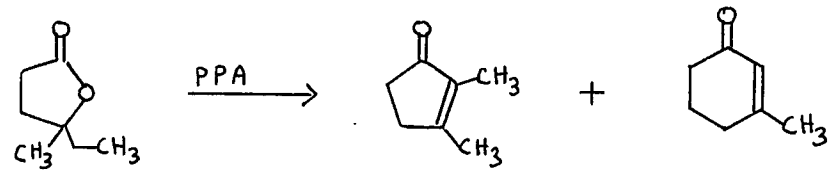


30 2

Neither Sukh[14] nor Sisido[15] have observed the formation of side products in the conversions of 29a,b to 2a,b and 30a,b to 2a,b . However, Ansell and coworkers noted that heating γ-methyl-γ-caprolactone with polyphosphoric acid gave 76% 2,3-dimethyl-2-cyclopentenone and 4% of a skeletally rearranged product, 3-methyl-2-cyclohexenone[13] (equation 16).

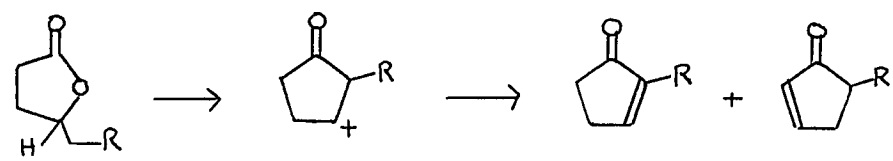
(14a) Ch. Rai and D. Sukh, Experientia, 11, 114 (1955).
(14b) Ch. Rai and D. Sukh, J. Indian Chem. Soc., 34, 178 (1957); Chem. Abstr. 52, 1977c (1958).
(15) K. Sisido, S. Torii and M. Kawanishi, J. Org. Chem., 29, 904 (1964).

Equation 16



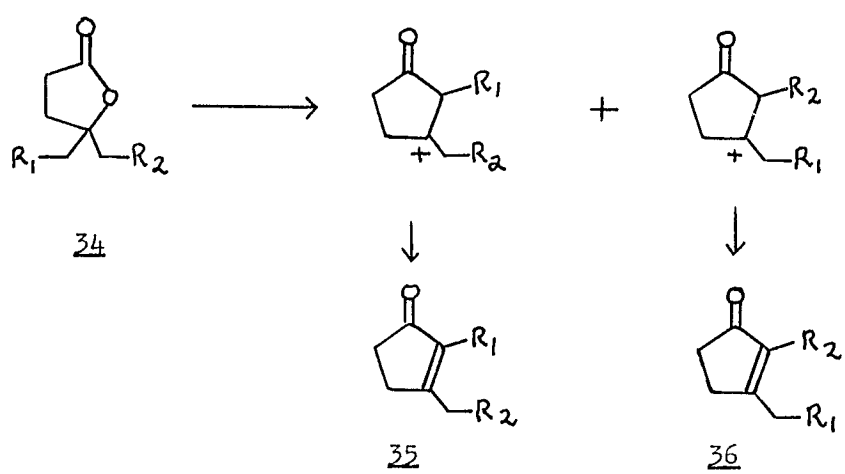
Attempts to prepare 2-alkyl-2-cyclopentenones and 2,3-dialkyl-2-cyclopentenones (alkyl larger than methyl) were only partially successful (equations 17 and 18).

Equation 17



31 32 33

Equation 18



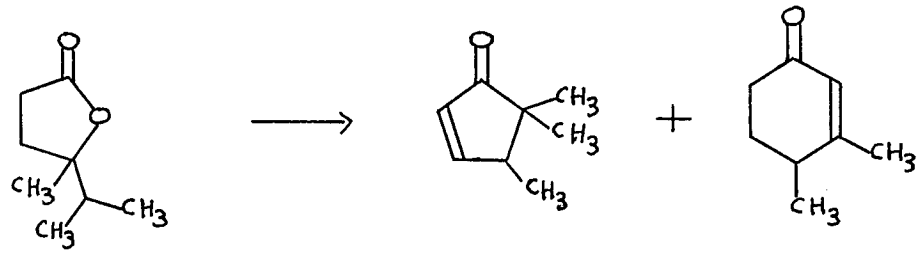
34 35 36

For instance, γ-undecanolactone (31, R= n-C_6H_{13}) gave 17% of 32 (R= n-C_6H_{13}) plus a small amount of 2-n-hexyl-4-cyclopentenone[16a] (33) (equation 17). Acid treatment of 34 (R_1= $(CH_2)_6$-CH_3, R_2= $(CH_2)_6$-$COOCH_3$) gave equal amounts of the cyclopentenones (as free acids) corresponding to 35 and 36.[3] It is reasonable to assume that in the first case, the formation of a secondary carbonium ion (equation 17), as in equation 13 (above), allowed competitive reactions to lower the yield of 32 (R= n-C_6H_{13}). On the other hand, formation of two equally probable carbonium ions in the latter example (equation 18) led to a mixture of the two possible products in approximately equal amounts.

Attempts to prepare 3-alkyl-2-cyclopentenones and type 'B' cyclopentenones have been unrewarding. Treatment of γ-valerolactone and γ-methyl-γ-valerolactone with phosphorous pentoxide gave only polymeric materials, instead of the expected 2-cyclopentenone and 3-methyl-2-cyclopentenone.[16a] In addition, γ, δ-dimethyl-γ-caprolactone which possesses a methyl and a methinyl group attached to the gamma carbon atom gave on treatment with phosphorous pentoxide equal amounts of 2,2,3-trimethyl-4-cyclopentenone and 3,4-dimethyl-2-cyclohexenone[16a] (equation 19).

(16a) R. L. Frank, R. Armstrong, J. Kwiatek and H. Price, J. Amer. Chem. Soc., 70, 1379 (1948).
(16b) R. L. Frank, P. G. Arvan, J. W. Richter and C. R. Vanneman, ibid., 66, 4 (1944).

Equation 19

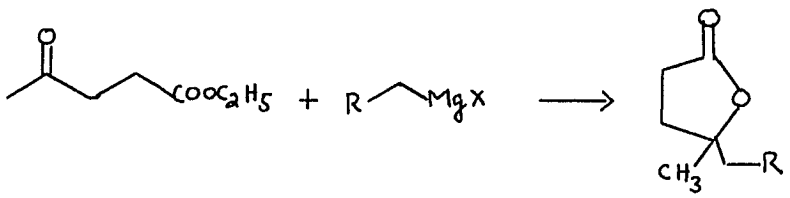


6% 6%

Sukh and Rai have found polyphosphoric acid to be superior to phosphorous pentoxide for the conversion of γ-methyl-γ-alkyl-γ-valerolactones 29 to 2-alkyl-3-methyl-2-cyclopentenones (2) (equation 14) and have suggested that this may be attributed to the fact that polyphosphoric acid is soluble in the reaction medium, and therefore permits a homogeneous reaction to occur.[14a] For example, they obtained 29a,b in 92-5% yields using polyphosphoric acid as the acid catalyst, while Frank and coworkers who used phosphorous pentoxide for this conversion, obtained 29a and 29b in yields of 30%[16a] and 50%.[16b]

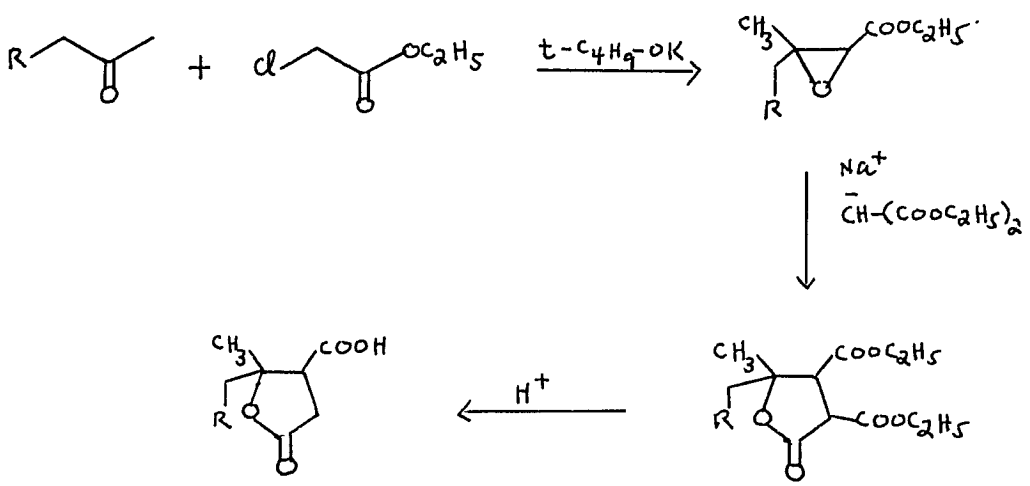
The methods used for the preparation of γ-methyl-γ-alkyl-γ-valerolactones (29) and paraconic acids 30 are depicted in equations 20 and 21.

Equation 20



29

Equation 21

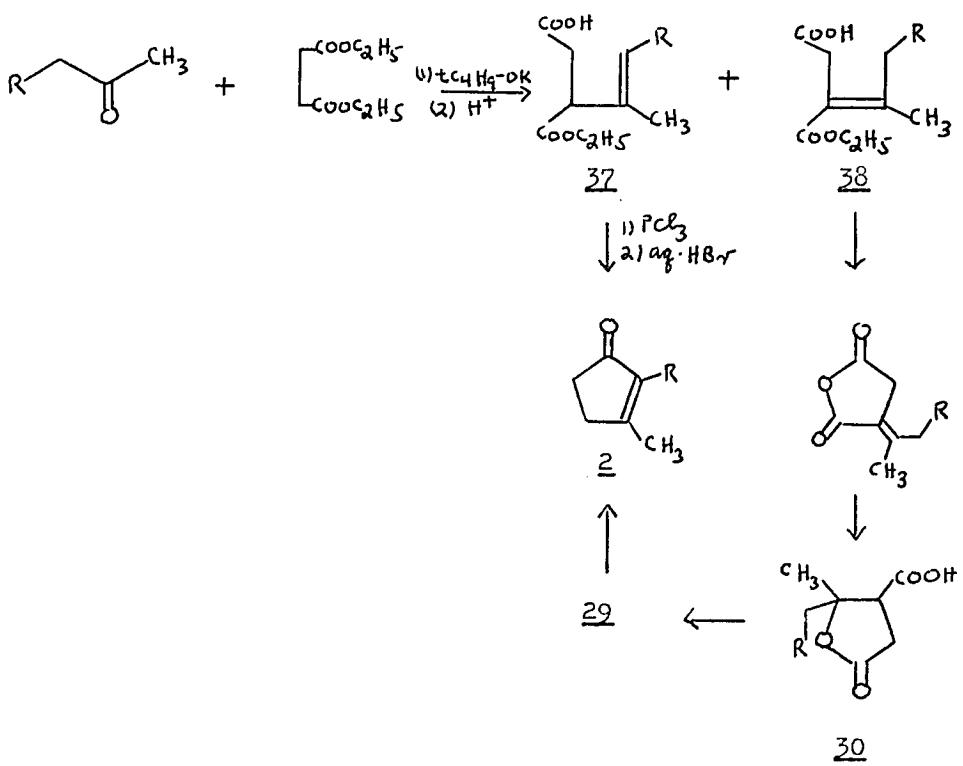


30

For instance, Sukh and Rai prepared 29a (R= n-C_4H_9) and 29b (R= n-C_5H_{11}) from ethyl levulinate and the appropriate Grignard reagents in 60% and 62% yields respectively (equation 20), and converted them to cyclopentenones 2a,b in overall yields of 55-75%.[14] Sisido and coworkers obtained the paraconic acids 30a (R= n-C_4H_9) and 30b (R= n-C_5H_{11}) from 2-heptanone and 2-octanone in yields of 42% and 41% respectively (equation 21), and converted them to 2a,b in overall yields of 33%[15] (for both cyclopentenones).

Elliot[17] has developed a procedure for preparing 2-alkyl-3-methyl-2-cyclopentenones (2) from Stobbe half esters 37 and 38 which is similar to the procedures of Sukh and Sisido (equation 22).

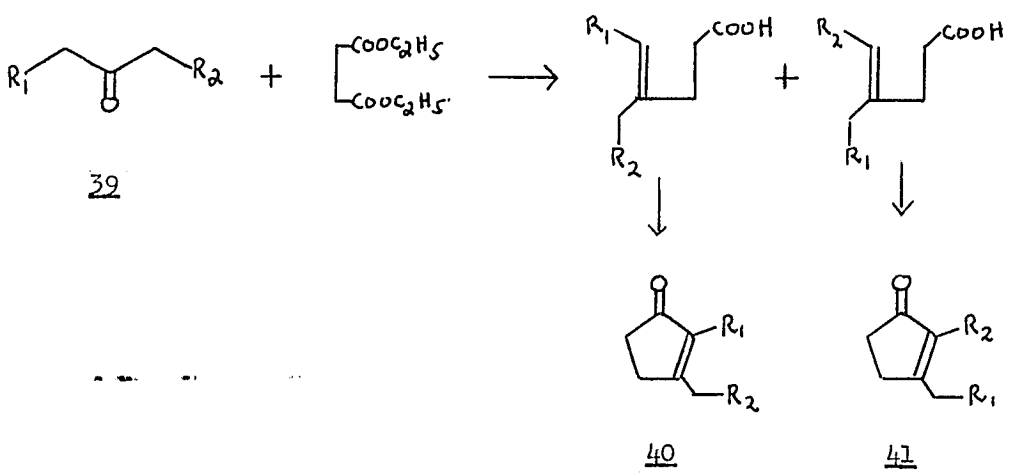
Equation 22



For example, condensation of 2-heptanone with diethyl succinate gave an 85% yield of a mixture consisting of 50% of 37 (R= n-C_5H_{11}) and 50% of 38 (R= n-C_5H_{11}). Compound 37 was converted to 2b (R= n-C_5H_{11}) in an overall yield of 34%, and 38 was converted to paraconic acid 30b (R= n-C_5H_{11}) which was subsequently transformed to 2b in an overall yield of 38%, based on 30b.

Elliot's procedure is also limited to the preparation of 2-alkyl-3-methyl-2-cyclopentenones (2) since the use of ketones (e.g. 39) other than methyl ketones as starting materials would probably lead to the formation of a mixture of cyclopentenones 40 and 41 (equation 23).

Equation 23

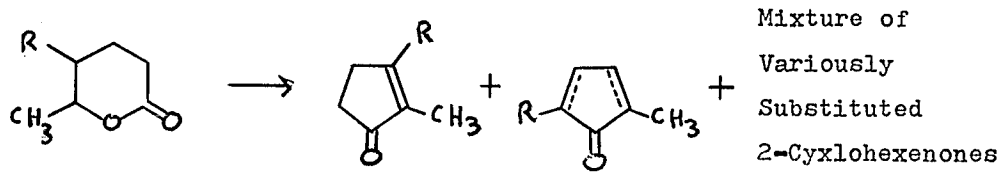


39 40 41

(17) M. Elliot, J. Chem. Soc., 2231 (1956).

Treatment of δ-methyl-γ-alkyl-δ-valerolactones (42) with polyphosphoric acid has led to the formation of 2-methyl-3-alkyl-2-cyclopentenones (43) in yields of 50-70%.[13] However, this method is not synthetically attractive since in addition to 43, a mixture of skeletally rearranged cyclopentenones (44) and 2-cyclohexenones were also obtained from the rearrangement of 42[13] (equation 24).

Equation 24



42 43 44

Preparation of cyclopentenones by the acid catalyzed cyclization of Δ^4, Δ^5 and Δ^6-alkenoic acids or γ- and δ-hydroxyacids is also synthetically unattractive since a mixture of products is obtained. For example, 5-heptenoic acid gave the mixture of products indicated in equation 25.[18]

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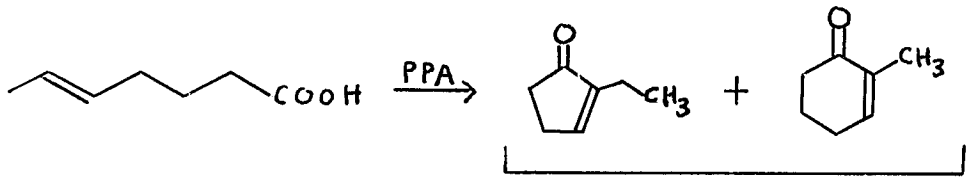
(18) M. F. Ansell and S. S. Brown, J. Chem. Soc., 2955 (1958).

Equation 25



55%

+ Unidentified Lactone
13%

Although formation of side products from the cyclization of γ, δ-alkenoyl chlorides has not been reported, this method has not been frequently used for preparing cyclopentenones since the yields are generally low. For instance, Ansell and Brown obtained 2-cyclopentenone from the aluminum chloride catalyzed cyclization of pent-4-enoyl chloride in a crude yield of 35%.[18]

Method (3): From 1,2-Cyclopentandiones

Ansell and Ducker have developed a general method for the preparation of 2-alkyl-2-cyclopentenones (45) from 1,2-cyclopentandione[19] (equation 26).

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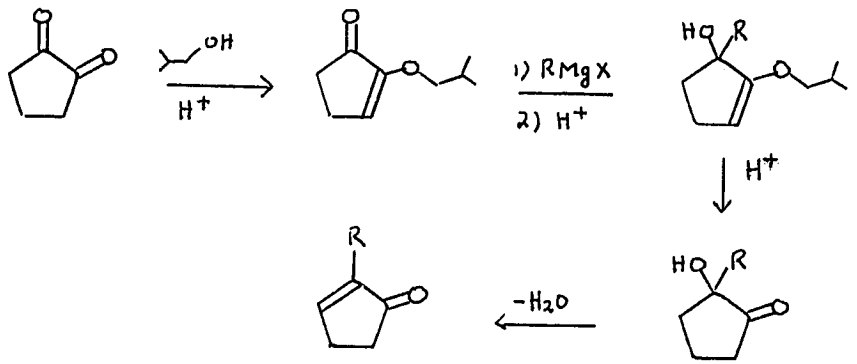
(19) M. F. Ansell and J. W. Ducker, J. Chem. Soc., 329 (1959).

Equation 26

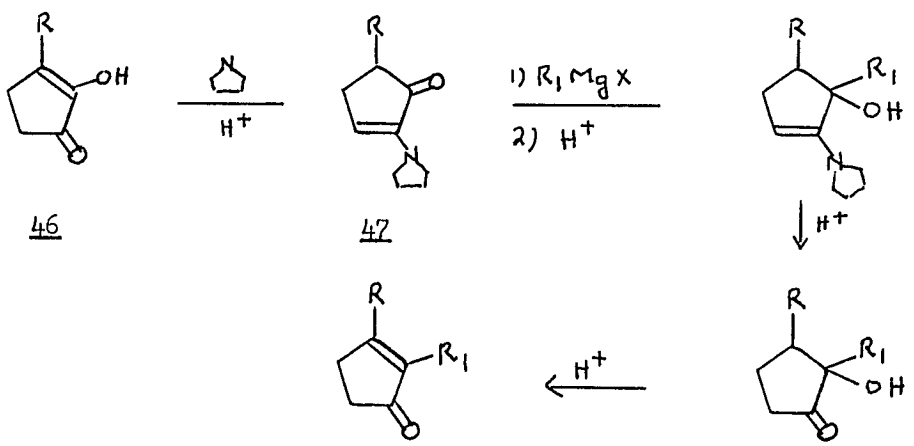


45

A number of 2-alkyl-2-cyclopentenones (45, R= CH_3 to n-C_6H_{13}) were obtained from 2-isobutoxycyclopent-2-en-1-one in yields of 45-75%. The overall yields of these products based on 1,2-cyclopentandione ranged from 30% to 50%.

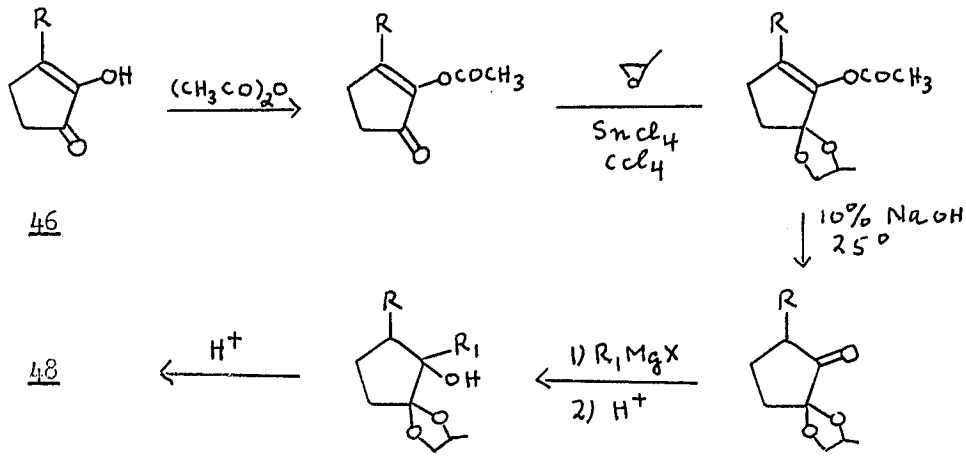
Similar procedures have been used to prepare 2,3-dialkyl-2-cyclopentenones (48) (equations 27 and 28).

Equation 27



46 47 48

Equation 28



46 48 49

For example, Gordon prepared enamine 47 (R= CH_3) from 46 (R= CH_3) in 90% yield, and converted it to cyclopentenone 48 (R= CH_3, R_1= n-C_5H_{11}) in 35% overall yield[20] (equation 27). Erickson prepared ketoketal 49 (R= CH_3) from 46 (R= CH_3) in 40% yield, and converted it to 48 (R= CH_3, R_1= n-C_5H_{11}) in 24% overall yield[21] (equation 28).

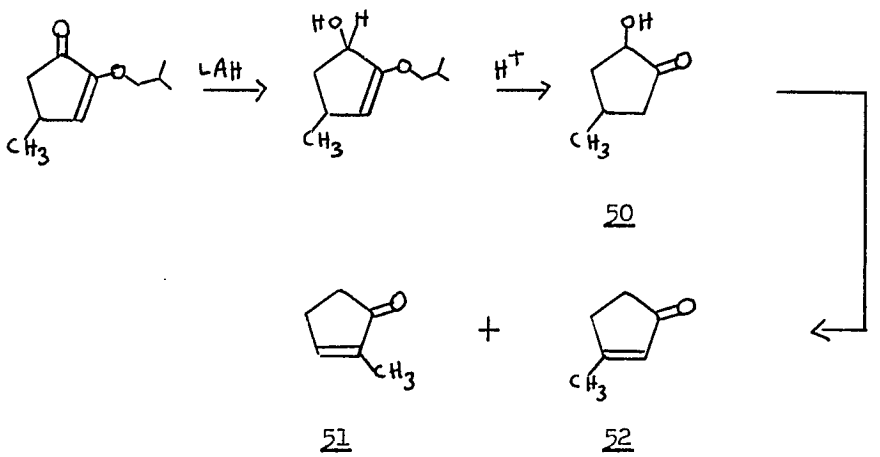
An attempt to prepare a 3-alkyl-2-cyclopentenone by an analogous procedure was only partially successful. Pollini and coworkers reported that treatment of hydroxyketone 50 with either potassium bisulfate or

---

(20) E. Gordon, F. Martens and H. Gault, Compt. Rend., 261, 4129 (1965).
(21) J. L. E. Erickson and F. E. Collins, Jr., J. Org. Chem., 30, 1050 (1965).

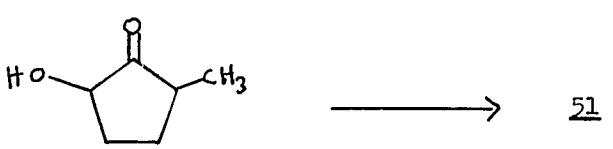
polyphosphoric acid gave 2-methyl-2-cyclopentenone (51) and 3-methyl-2-cyclopentenone (52) in the ratios of 7:3 and 4:6 respectively[22] (equation 29)

Equation 29



On the other hand, hydroxyketone 53 gave only 51 upon treatment with the same reagents[22] (equation 30).

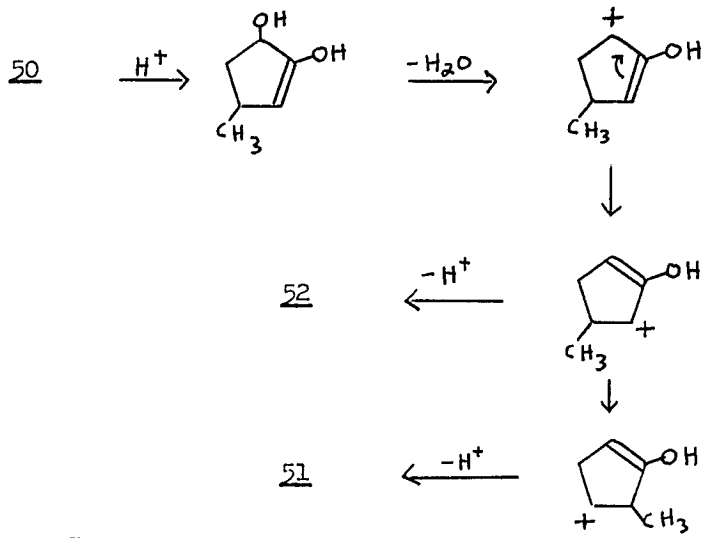
Equation 30



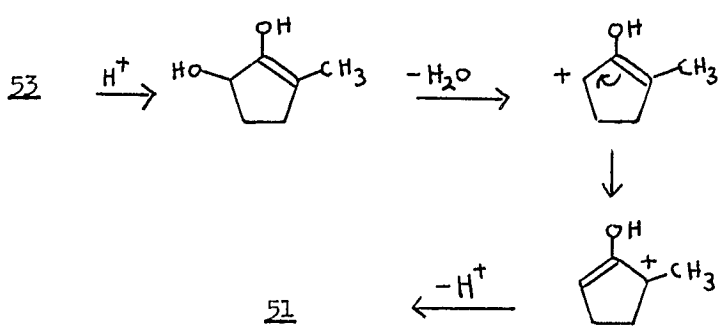
53

Pollini has suggested that formation of 51 and 52 from 50, and 51 from 53 may be accounted for as shown in eqautions 31 and 32.

Equation 31



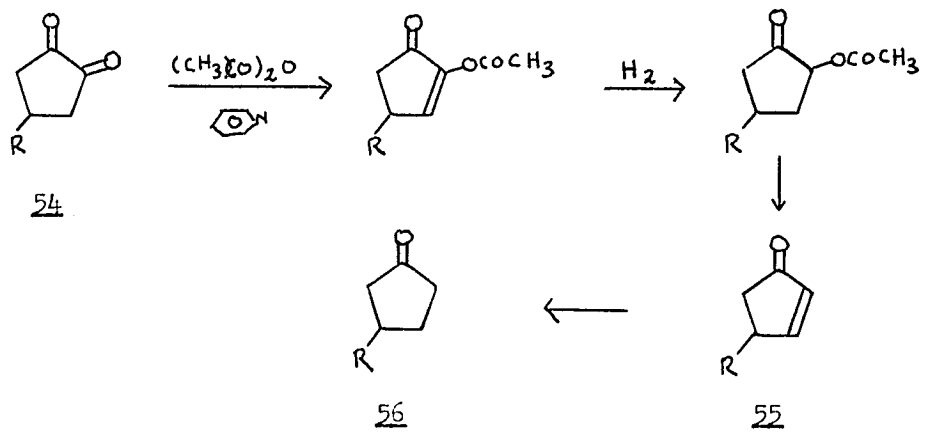
Equation 32



(22) G. P. Pollini, G. DeGiuli, G. Traverso and A. Barco, Chim. Ind. (Milan), 52, 1205 (1970); Chem. Abstr. 74, 53115a (1971).

Cavill and coworkers have recently shown that 4-alkyl- and subsequently 3-alkyl-2-cyclopentenones may be prepared by the procedure outlined in equation 33.

Equation 33

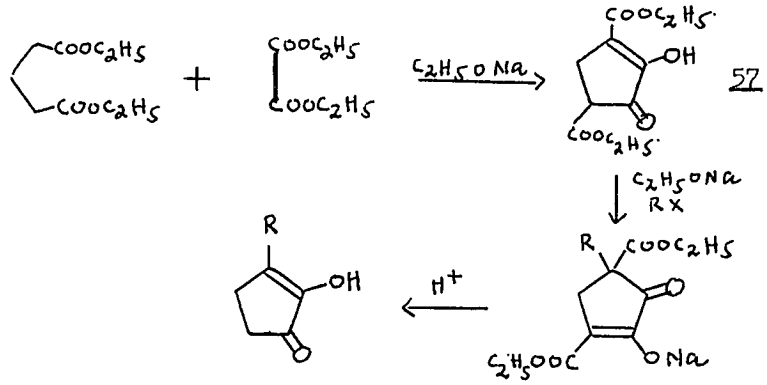


54 56 55

For instance, 4-methyl-2-acetoxycyclopentanone was prepared from cyclopentandione[22] 54 (R= CH_3) in 60% yield, and subsequently converted to cyclopentenone 55 (R= CH_3) in 51% overall yield.[9] Isomerization of 55 (R= CH_3) with p-toluenesulfonic acid monohydrate at 80° gave 56 (R= CH_3)[9] (80% conversion after two hours of heating as shown by gas liquiud chromatography).

Gordon[20] and Erickson[21] prepared 2-amyl-3-methyl-2-cyclopentenone (48, R= CH_3) from commercially available 46 (R= CH_3). However, other less readily available alkyl derivatives of 46 which are required for the preparation of 2,3-dialkyl-2-cyclopentenones (48) may be prepared by alkylation of 57 which is readily available from condensation of diethyl glutarate and diethyl oxalate in 65% yield[23] (equation 34).

Equation 34



46 58

Preparation of alkyl derivatives such as 46 by direct alkylation of 1,2-cyclopentandione may not be feasible since it has been reported that alkylation of 1,2-cyclohexandione gave mainly O-alkylated products.[24]

Condensation of diethyl β-methylglutarate (59, R= CH_3) with diethyl oxalate, followed by hydrolysis and subsequent decarboxylation of the diester intermediate, gave 4-methyl-1,2-cyclopentandione[23] (54, R= CH_3) which was required for the preparation of 4-methyl-2-cyclopentenone (55, R= CH_3) according to Cavill's procedure.[9] Less readily available alkyl derivatives of 59 which would be required for the preparation of 54 may be prepared by the route shown in equation 35.[25]

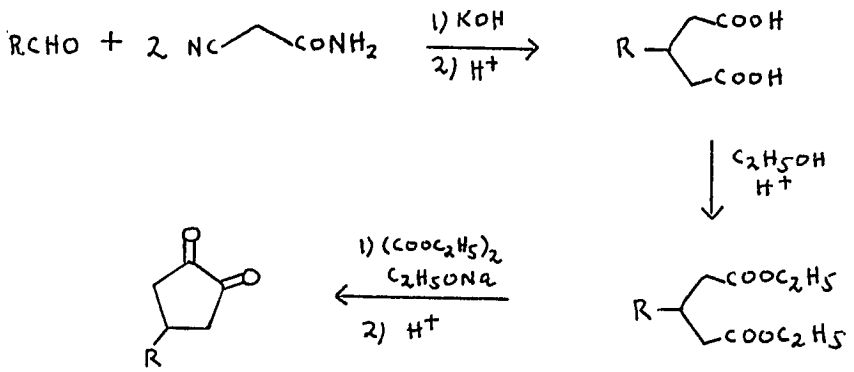
---

(23) G. Hesse and K. W. F. Bochmann, Ann., 563, 31, 37 (1949). The authors have methylated 57 and isolated 58 (R= methyl) in 67% yield, which was subsequently hydrolyzed to 46 (R= methyl). They also reported that methylation of 3-carbethoxy-2-hydroxy-2-cyclopentenone gave 5-methyl-5-carbethoxy-2-hydroxy-2-cyclopentenone in 70% yield.

(24) M. S. Gibson, J. Chem. Soc., 681 (1962).

(25) J. M. Osbond, J. D. Fulton and D. F. Spooner, ibid., 4785 (1952). The authors have prepared 59 (R= C_2H_5) from propionaldehyde in 55% overall yield.

Equation 35

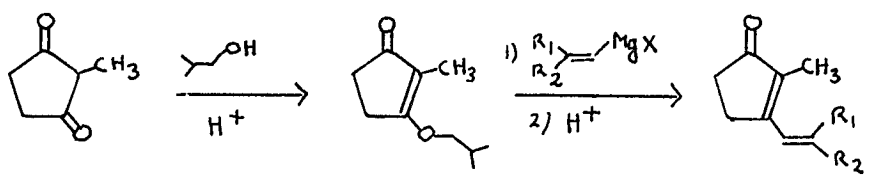


54 59

Method (4): From 1,3-Cyclopentandiones

Crisan and Normant prepared a series of 2-methyl-3-alkenyl-2-cyclopentenones (60) from commercially available 2-methyl-1,3-cyclopentandione by the following sequence of steps[26] (equation 36).

Equation 36



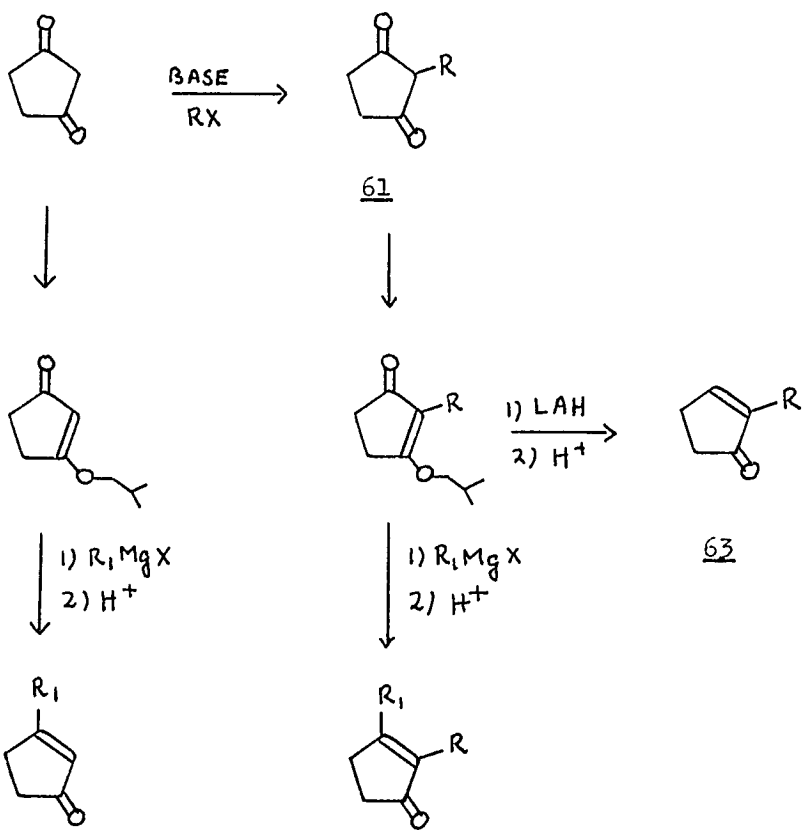
60

(26) C. Crisan and H. Normant, Bull. Soc. Chim. France, 1451 (1957).

For instance, 60a (R_1= R_2= H), 60b (R_1= CH_3, R_2= H) and 60c (R_1= R_2= CH_3) were obtained from 2-methyl-3-isobutoxycyclopent-2-en-1-one in yields of 35%, 50% and 72% respectively. The overall yields of 60a, 60b and 60c based on 2-methyl-1,3-cyclopentandione were 31%, 45% and 65% respectively.

It is obvious that method (4) may be applied to the preparation of 2-alkyl-, 3-alkyl- and 2,3-dialkyl-2-cyclopentenones (equation 37).

Equation 37



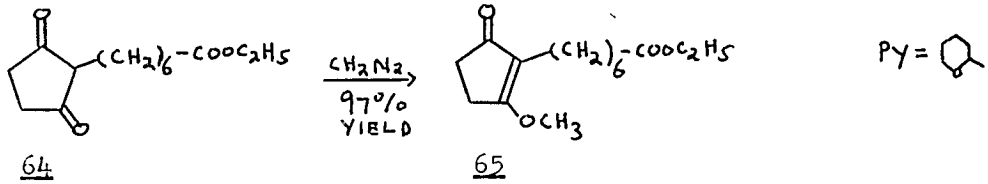
61

63

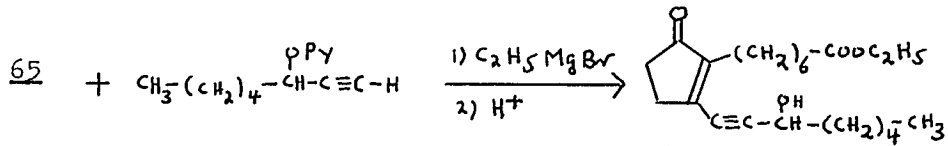
62

For instance, cyclopentenone 67 was prepared from 64 in an overall yield of 6% by the sequence of steps shown in equation 38.[27]

Equation 38



64 65

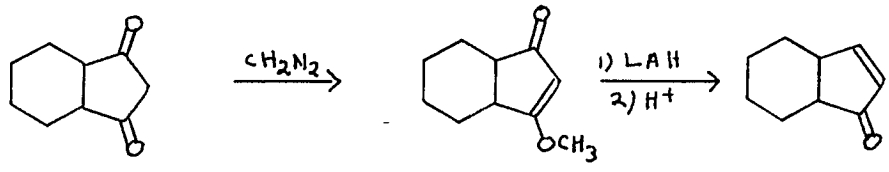


66 67

Part of the Grignard derivative from 66 may have reacted with the ester group of 65, resulting in the formation of an undesired product, and a consequent reduction in the yield of cyclopentenone 67.

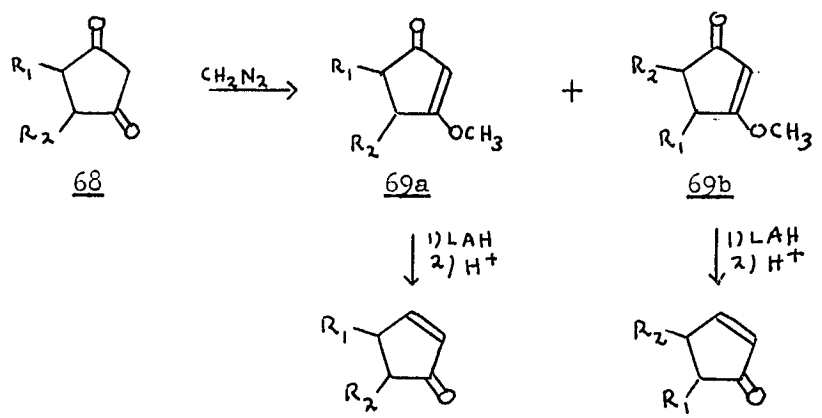
Compound 3a,4,5,6,7,7a-hexahydroindene-1-one, a type 'B' cyclopentenone, was prepared from 4,5,6,7-tetrahydroindanone in 60-70% overall yield by a similar sequence of steps[28] (equation 39).

Equation 39



However, the above procedure is not generally useful for the preparation of type 'B' cyclopentenones. For example, if formation of enol ethers 69a and 69b are equally favorable, then a mixture of products would arise as shown in equation 40.

Equation 40



68 69a 69b

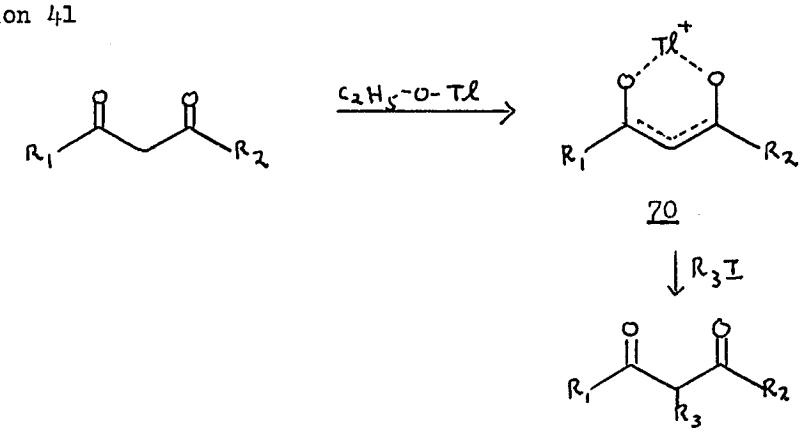
Alkylation of 1,3-diketones by the standard procedures often gives a mixture of C- and O-alkylated products. For instance, alkylation of 5-phenyl-1,3-cyclohexandione with 1-napthylmethyl chloride gave 48% C-alkylated and 18% O-alkylated materials.[29] However, Taylor and coworkers have shown that the thallium (I) enolates of 1,3-dicarbonyl compounds may be C-alkylated quantitatively[30] (equation 41).

---

(27) Y. Yura and J. Ide, Ger. Offen. 1, 925, 672 (Cl. C. 07c) 1969; Chem. Abstr. 72, 42931w (1970).

(28) V. F. Kucherov, L. N. Ivanova and I. A. Severina, Izvest. Akad. Nauk. S.S.S.R., Otdel. Khim. Nauk., 1348 (1961); Chem. Abstr. 56, 4636b (1962).

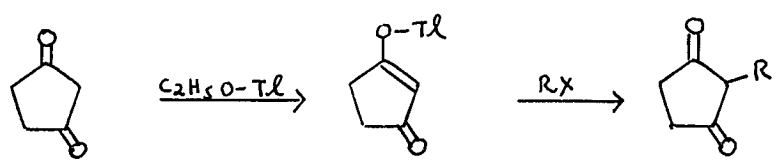
Equation 41



70

For example, the thallium enolate of acetylacetone (70, $R_1 = R_2 = CH_3$) which was prepared in very high yield, was quantitatively methylated to give 3-methyl-2,4-butandione.[30] Therefore it is anticipated that the alkyl derivatives of 61 which are required for the preparation of cyclopentenones 62 and 63 (see equation 37), may be prepared in good yield by the procedure shown in equation 42.

Equation 42



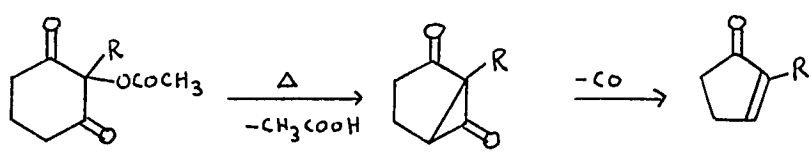
61

(29) A. Kotarska, Lodz. Towarz Nauk, Wydzial IIII, Acta. Chim. 7, 77 (1961).
(30) E. C. Taylor, G. H. Hawks, III, and A. M. McKillop, J. Amer. Chem. Soc., 90, 2421 (1968).

Method (5): From 1,3-Cyclohexandiones

Pyrolysis of 2-alkyl-2-acetoxy-1,3-cyclohexandiones (71) have led to the formation of 2-alkyl-2-cyclopentenones (73) in moderate yields, and cyclopropanones 72 have been postulated as the intermediates involved in these conversions[31] (equation 43). For instance, pyrolysis of 2-methyl-2-acetoxy-1,3-cyclohexandione (71, R= CH_3) at 350° gave 2-methyl-2-cyclopentenone (73, R= CH_3) in 42% yield.[31]

Equation 43



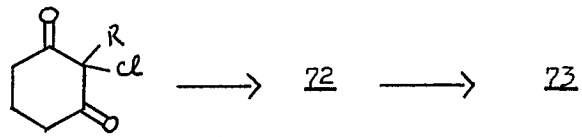
71 72 73

A similar reaction occured when 74 (R= 2-pentynyl) was treated with sodium carbonate in boiling xylene. Cyclopentenone 73 (R= 2-pentynyl) was then obtained in 74% yield[32] (equation 44).

---

(31) T. A. Spencer, A. L. Hall and C. Fordham Von Reyn, J. Org. Chem., 33, 3369 (1968).
(32) G. Buchi and B. Egger, ibid., 36, 2021 (1971).

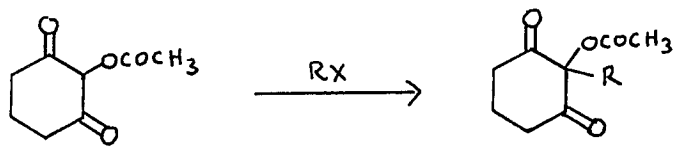
Equation 44



74

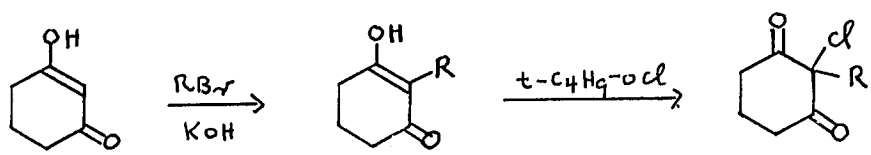
The methods used for the preparation of the starting materials 71 and 74 are shown in equations 45 and 46.

Equation 45



71

Equation 46

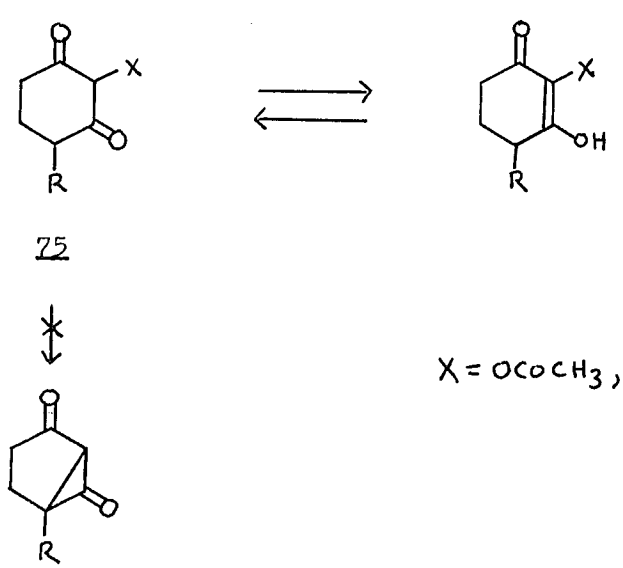


74

Spencer prepared 71 (R= CH_3) in 21% yield by methylation of 2-acetoxy-1,3-cyclohexandione, and converted it to 73 (R= CH_3) in 9% overall yield.[31] Buchi prepared 74 (R= 2-pentynyl) from 1,3-cyclohexandione and 2-pentynyl bromide in 62% yield as shown in equation 46, and converted it to cyclopentenone 73 (R= 2-pentynyl) in an overall yield of 46%.[32] Buchi's procedure is superior to Spencer's for the preparation of 2-alkyl-2-cyclopentenones (73) since the alkyl derivatives required in Spencer's method cannot be prepared in better than 20% yield.

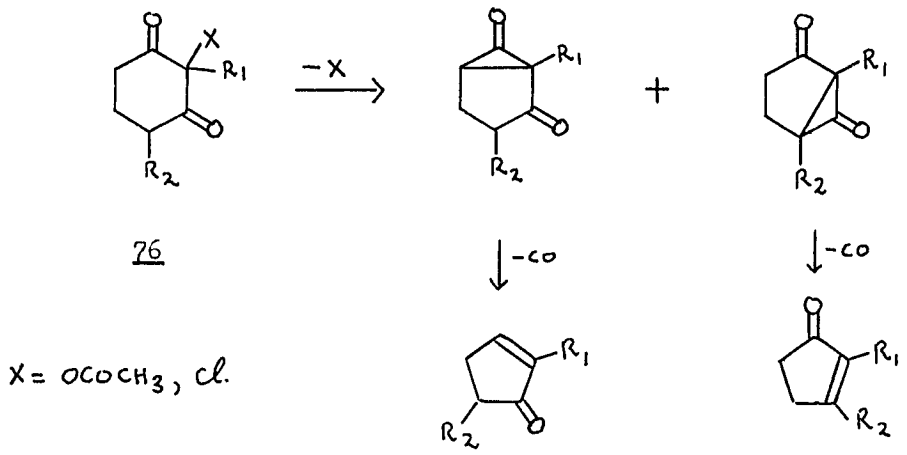
Preparation of 3-alkyl and 2,3-dialkyl-2-cyclopentenones from 75 and 76 respectively, is not feasible since in the former case the preferred reaction would probably be the enolization of 75 (equation 47), and in the latter case a mixture of products may arise (equation 48).

Equation 47



75

Equation 48



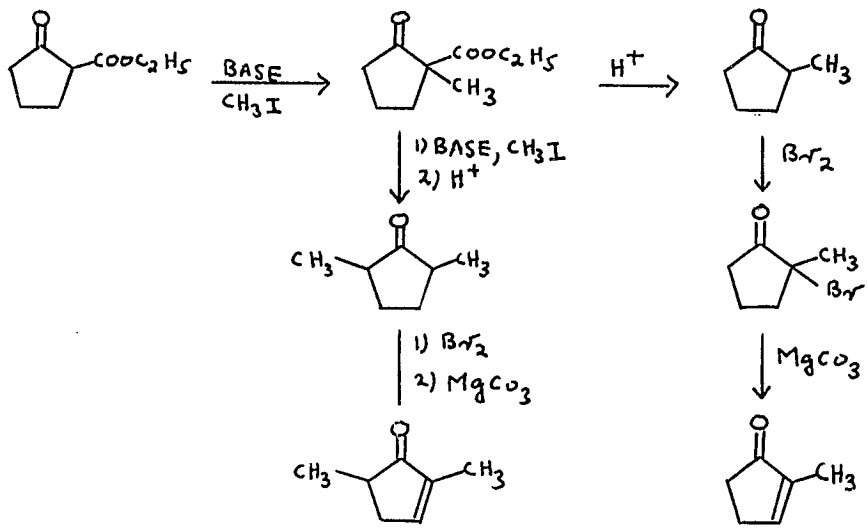
Method (6): From Cyclopentanones

Cyclopentenones have been prepared by halogenation of cyclopentanones, followed by dehydrohalogenation of the 2-halocyclopentanones.[1,33] For example, 2-methyl- and 2,5-dimethylcyclopentanones were prepared from 2-carbethoxycyclopentanone and 2-methyl-2-carbethoxycyclopentanone in yields of 46% and 57%, respectively, and converted to 2-methyl- and 2,5-dimethyl-2-cyclopentenones in overall yields of 24%[34] and 29%,[35] respectively. (equation 49).

---

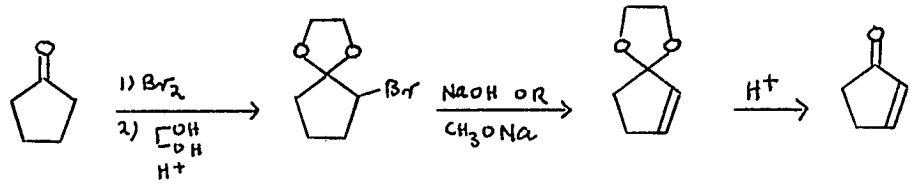
(33) C. Djerassi, J. Fajkos and A. R. Vanhorn, Steroids, 6, 239 (1965).
(34) I. N. Nazarov, L. D. Bergelson, I. V. Torgov and S. N. Ananchenko, Izvest. Akad. Nauk. S.S.S.R., Otdel Khim. Nauk., 889 (1953); Chem. Abstr. 49, 1082e (1955).
(35) V. A. Mironov, T. M. Fadeva, G. M. Kuz'yants and A. A. Akhreim, Izv. Akad. Nauk. S.S.S.R. Ser. Khim, 221 (1966); Chem. Abstr. 66, 75719 (1967).

Equation 49



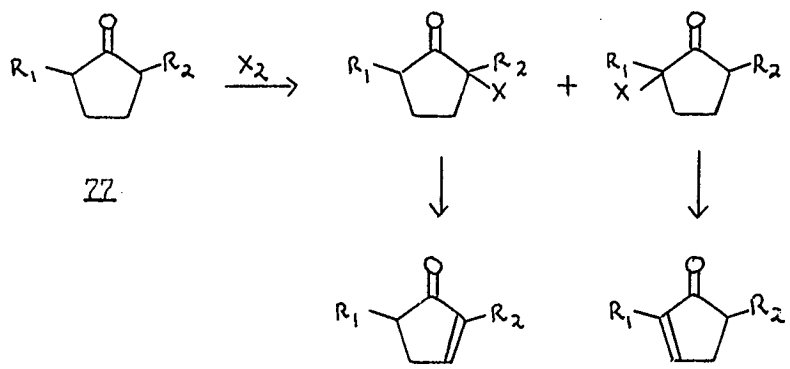
Our attempts to prepare 2-cyclopentenone by dehydrohalogenation of 2-chlorocyclopentanone with diethylaniline gave only polymeric material. However, initial conversion of 2-bromocyclopentanone to 1,1-ethylenedioxy-2-bromocyclopentane, followed by dehydrohalogenation of the ketal, with subsequent hydrolysis of 1,1-ethylenedioxy-2-cyclopentene, gave 2-cyclopentenone in 38% overall yield[36] (based on cyclopentanone) (equation 50). Thus it appears that this modified procedure is useful for the preparation of cyclopentenones which are susceptable to polymerization by base.

Equation 50



The conversion of unsymmetrical cyclopentanones (e.g. 77) to cyclopentenones is not feasible if halogenation at the 2- or 5-position is equally favorable, since a mixture of products would arise (equation 51).

Equation 51



77

However, the use of a protecting group (e.g. a carbethoxy group) would permit 78 and 81 which may be prepared by the routes shown in equation 52, to be selectively halogenated. Therefore both 79 and 82 may be obtained. The conversions of 79 to 80 or 82 to 83 may be done pyrolytically if the desired cyclopentenone is known to isomerize to the other isomer (e.g. 80 to 83) in the presence of aqueous acid[12] or base.[11] Cyclopentenones are known to be stable to double bond isomerization at temperatures as high as 500° [9] and 600°.[12]

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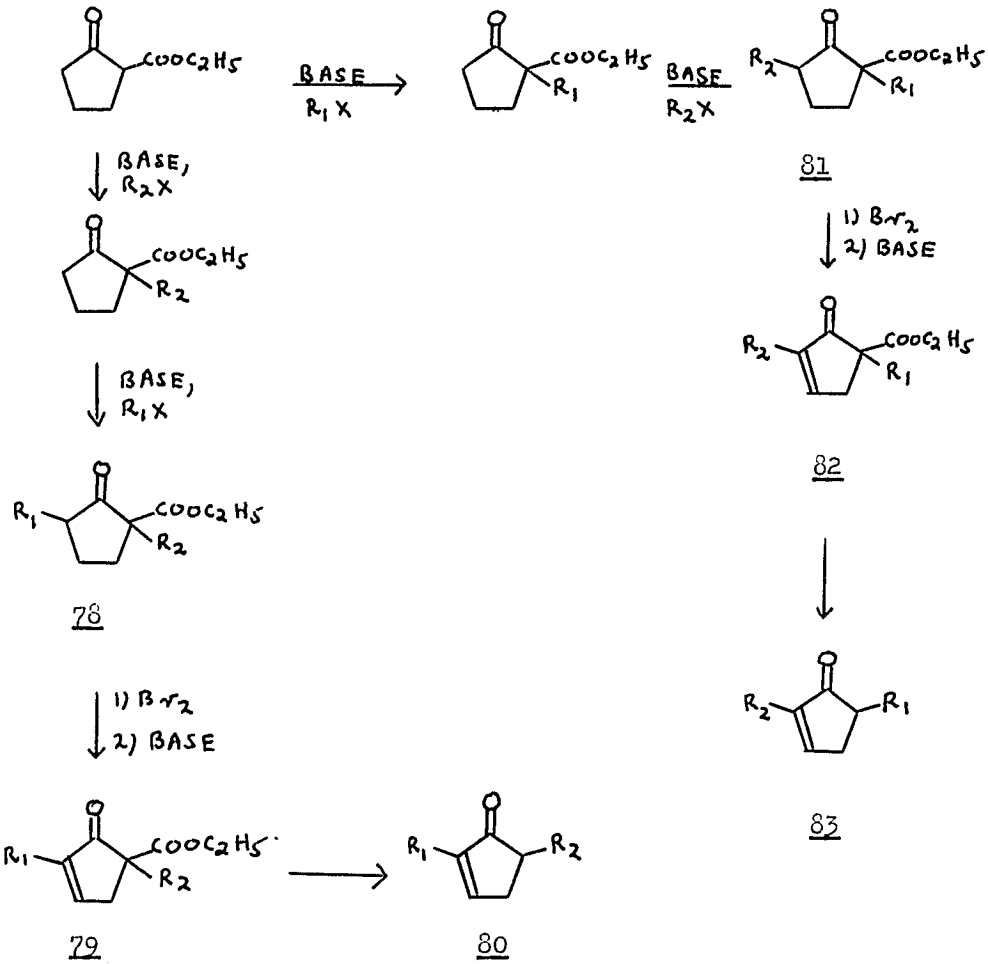
(36) E. W. Garbisch, Jr., J. Org. Chem., 30, 2109 (1965).

Equation 52



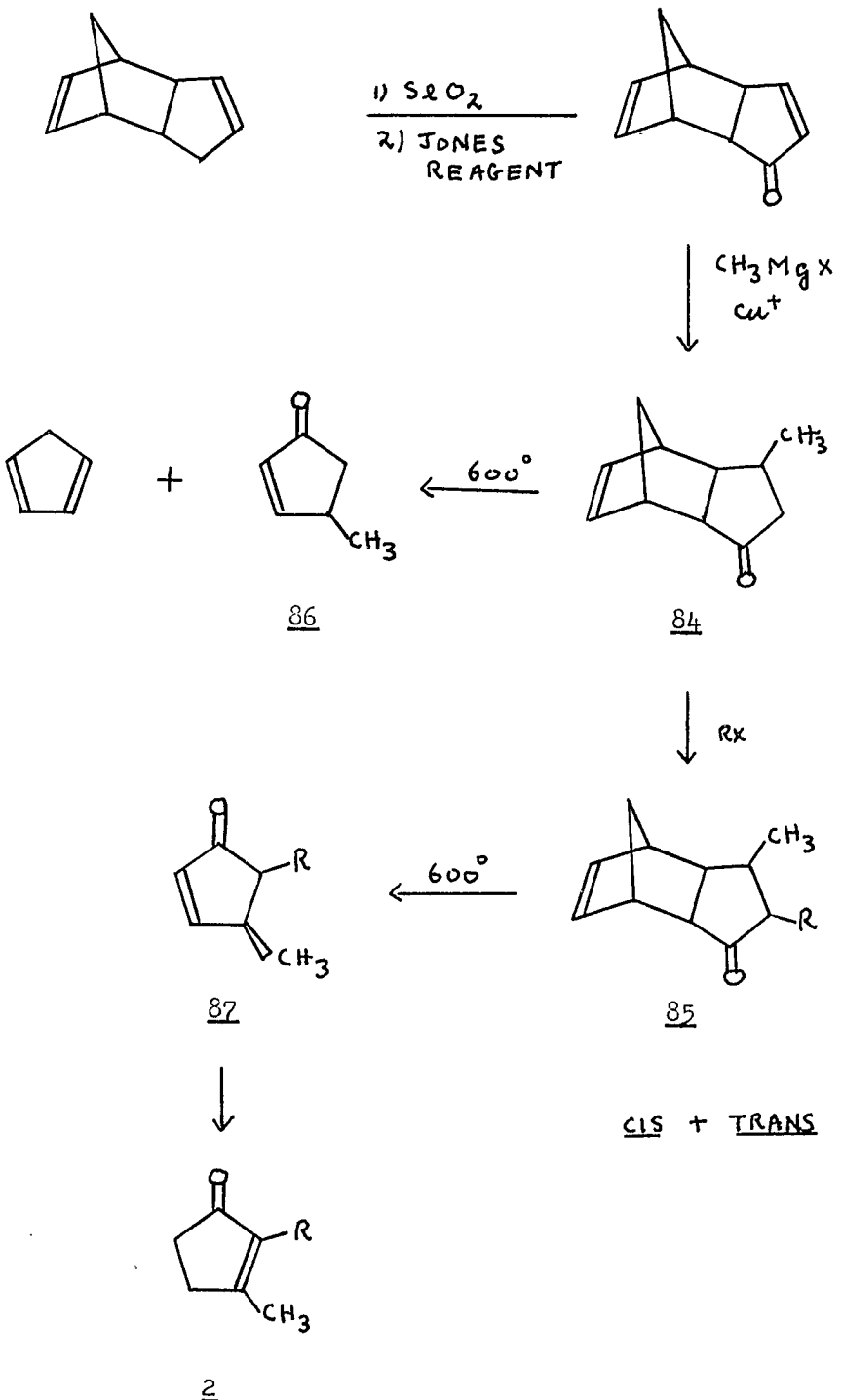
Method (6) is best suited for the preparation of 2-alkyl-2-cyclopentenones. Preparation of 3-alkyl- and 2,3-dialkyl-2-cyclopentenones by dehydrohalogenation of 2-halocyclopentanones is not the method of choice since the required cyclopentanones are often not readily available.

Method (7): From Dicyclopentadiene

Stork has recently shown that dicyclopentadiene may be converted to both types 'A' and 'B' cyclopentenones 2 and 87, respectively, by the elegant sequence of steps depicted in scheme 1.[12] The cis and trans mixture of 85 was equilibrated with base to give mainly the trans isomer of 85. Using this method, Stork prepared 4-methyl-2-cyclopentenone (87a, R= H), 4,5-dimethyl-2-cyclopentenone (87b, R= CH_3) and 4-methyl-5-(cis-2-pentenyl)-2-cyclopentenone (87c, R= cis-2-pentenyl). Cyclopentenone 87c was converted to cis-jasmone (2, R= cis-2-pentenyl) in an overall yield of 50% (based on 84).

It is obvious that method (7) may be used to prepare 3-alkyl- and 2,3-dialkyl-2-cyclopentenones other than 2. The most important feature of Stork's method is that it permits the preparation of 4-alkyl- and 4,5-dialkyl-2-cyclopentenones for which there are as yet few preparative procedures. However, 2-alkyl- and 5-alkyl-2-cyclopentenones may not be readily prepared by this method.

Scheme 1



86 84 87 85 2

Table I

Types and Yields of 2-Cyclopentenones Obtainable by Methods (1)-(7) and by the Method Developed in this Dissertation

Method	% Overall Yield[a] Route (a)	Route (b)	Route (c)	Type of 2-Cyclopentenone
1	40-5[b]	32[b]	18-28	2-alkyl-3-methyl
2	55-7[c,d]	35[c,d]	34[d]	2-alkyl-3-methyl
3	30-5			2-alkyl
3	51[e]			4-alkyl
3	*			3-alkyl
3	35[d]	24[d]		2-alkyl-3-methyl
3	**	**		2,3-dialkyl
4	31-65			2-methyl-3-alkyl
4	**			2,3-dialkyl
4	60-70[f]			4,5-dialkyl[g]
4	**			2-alkyl
4	**			3-alkyl
5	46[h]			2-alkyl
6	24[i], 29[j]			2-alkyl
7	50[b]			2-alkyl-3-methyl
7	**			2,3-dialkyl
7	*			3-alkyl
7	*			4-alkyl
7	*			4,5-dialkyl

Table I (continued)

Method	% Overall Yield[a] Route (a)	Route (b)	Route (c)	Type of 2-Cyclopentenone
Dissertation	41[k,l]			2-alkyl-3-methyl
"	13[k,m]			2,3-dialkyl
"		24[i,n]		2-alkyl
"	16[o,m]			3-alkyl

*This type of cyclopentenone has been prepared by the mentioned method, but the overall yield is not available.

**This type of cyclopentenone may also be prepared by the mentioned method. A distinction is made between 2-alkyl-3-methyl-2-cyclopentenones (2) and 2,3-dialkyl-2-cyclopentenones in methods (3) and (7), and 2-methyl-3-alkyl-2-cyclopentenones (60) and 2,3-dialkyl-2-cyclopentenones in method (4), since the reported overall yields of these cyclopentenones are based starting materials which may only be used to prepare derivatives of 2 and 60.

[a]Materials on which overall yields are based are mentioned in the discussions of each method. [b]3-Methyl-2-(cis-2-pentenyl)-2-cyclopentenone. [c]2-n-Butyl-3-methyl-2-cyclopentenone. [d]2-Amyl-3-methyl-2-cyclopentenone. [e]4-Methyl-2-cyclopentenone. [f]3a,4,5,6,7,7a-Hexahydroindene-1-one. [g]Special case; see Discussion Section. [h]2-(2-Pentynyl)-2-cyclopentenone. [i]2-Methyl-2-cyclopentenone. [j]2,5-Dimethyl-2-cyclopentenone. [k]2,3-Dimethyl-2-cyclopentenone. [l]Yield based on commercially available 1-methylcyclopropyl methyl ketone; see equation 60. [m]Yield based on 2-acetylbutyrolactone; see equation 60.

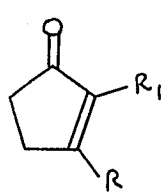
Table I (continued)

[n]Yield based on cyclopropanecarboxylic acid; see equation 61.

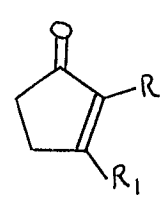
[o]3-Methyl-2-cyclopentenone.

Summary of Scope and Limitation of Methods (1)-(7)

The various types of cyclopentenones which may be prepared by each method are listed in Table I. Methods (1) and (2) are generally limited to the preparation of 2-alkyl-3-methyl-2-cyclopentenones (2), while methods (5) and (6) are most useful for the preparation of 2-alkyl-2-cyclopentenones (45) which as we have noted previously, may not be prepared by method (1), and only in low yield by method (2). Although alkyl derivatives of (2) are readily prepared by methods (1) and (2), 2-methyl-3-alkyl-2-cyclopentenones (60) in which the order of the alkyl substituents are merely reversed, may not be prepared by these methods. Methods (3), (4) and (7) do not possess this limitation since the 2- and 3-alkyl substituents are introduced separately. For example, both 48 and 62 may be prepared by these methods.



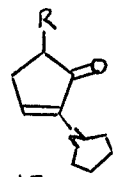
48



62

For the preparation of a series of 2-cyclopentenones possessing a common 2- or 3-alkyl substituent it is obvious that methods (3) and (4) complement each other (equation 53).

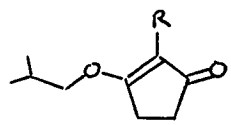
Equation 53



47

1) R_1MgX
2) H^+

48



1) R_1MgX
2) H^+

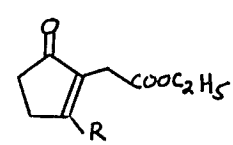
62

The use of Grignard reagents to introduce a 2- and 3-alkyl substituent by methods (3) and (4), respectively, precludes the possibility of preparing either 88a or 88b since these reagents are not compatible with esters. However, use of Reformatsky reagents may permit the preparation of 88a,b by both methods (3) (equation 54) and (4) (equation 55).

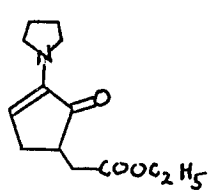
Equation 54

47

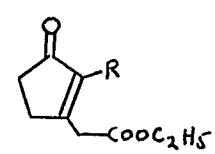
1) $Br\text{-}Zn\text{-}CH_2\text{-}COOC_2H_5$
2) H^+



88a

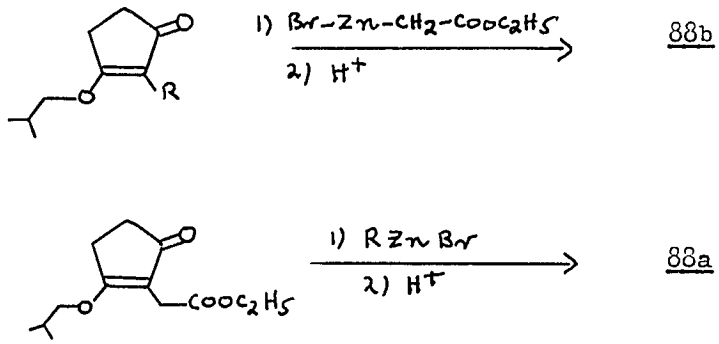


1) $R\text{-}Zn\text{-}Br$
2) H^+



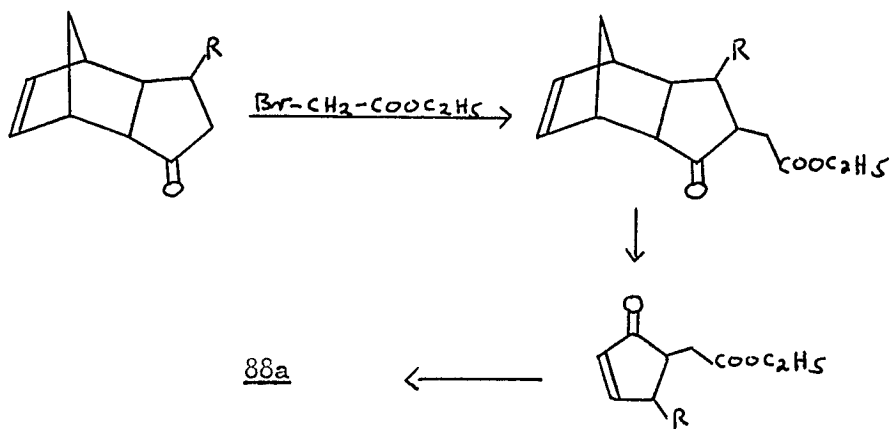
88b

Equation 55



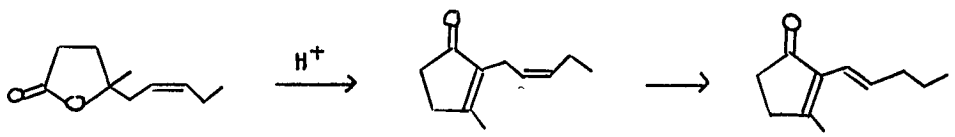
Method (7) permits the preparation of 88a, but not 88b (equation 56).

Equation 56



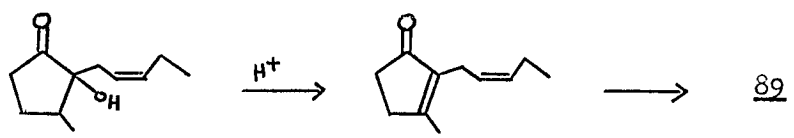
Finally, methods (2)-(4) may not permit the preparation of cyclopentenones such as cis-jasmone since the moderately vigorous acidic conditions used in these methods would probably isomerize it to 89 (equations 57 and 58).

Equation 57



89

Equation 58

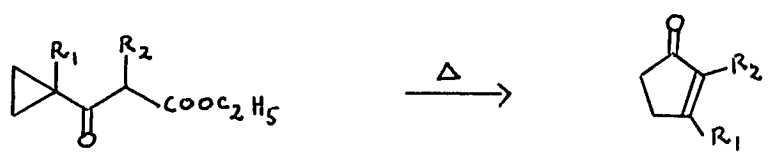


89

Cyclopentenones from 3-Cyclopropyl-3-oxopropanoates

In this dissertation it is shown that the pyrolysis of keto-esters 90a (R_1= CH_3, R_2= H), 90b (R_1= H, R_2= CH_3) and 90c (R_1= R_2= CH_3) near 500° and 1-3 mm Hg give cyclopentenones 91a, 91b and 91c in yields of 69%, 56% and 68% respectively (equation 59).

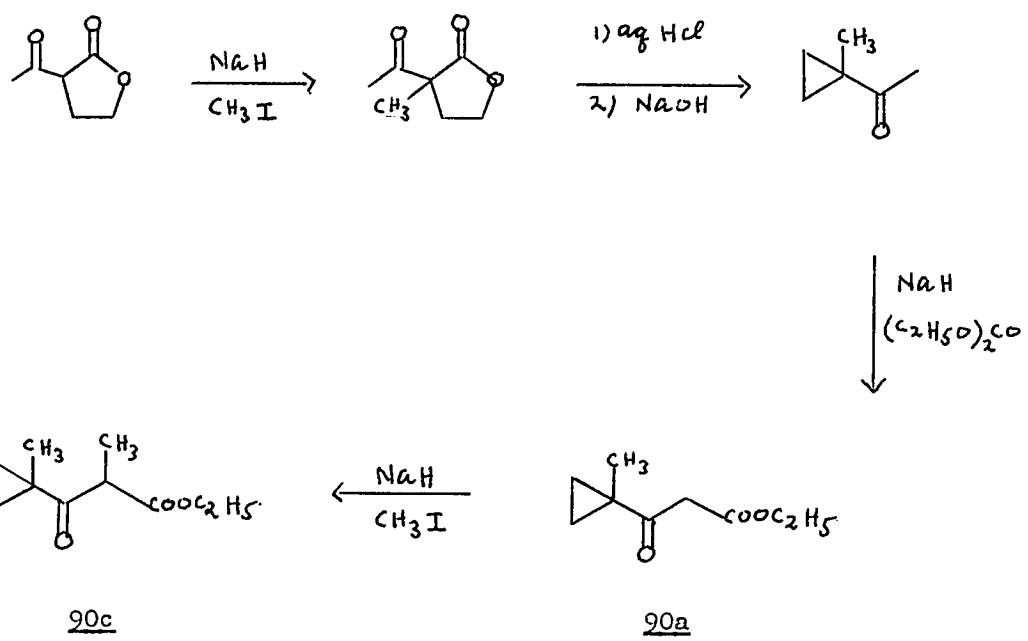
Equation 59



90 91

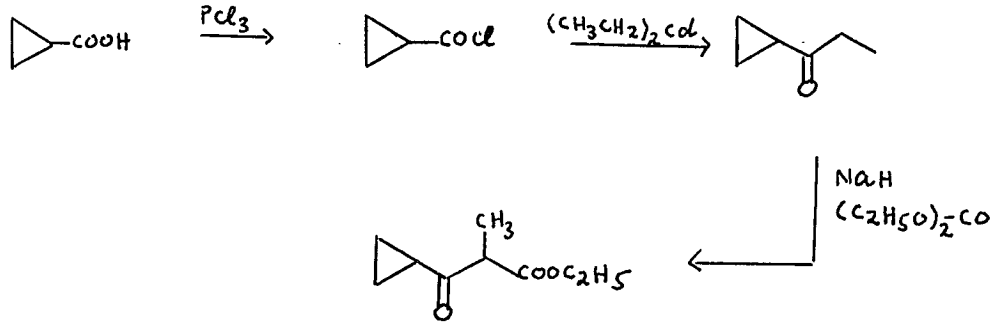
The methods used for the preparation of ketoesters 90a,b,c are depicted in equations 60 and 61. Ketoester 90b was also prepared by the route shown in equation 62, but the product was slightly contaminated with unmethylated starting material which could not be removed by distillation since the boiling point of both the product and the starting ketoester were extremely close. However, ethyl 2-alkyl-3-cyclopropyl-3-oxopropanoates with boiling points sufficiently removed from that of ethyl 3-cyclopropyl-3-oxopropanoate to permit separation by distillation, may be prepared by this route.

Equation 60



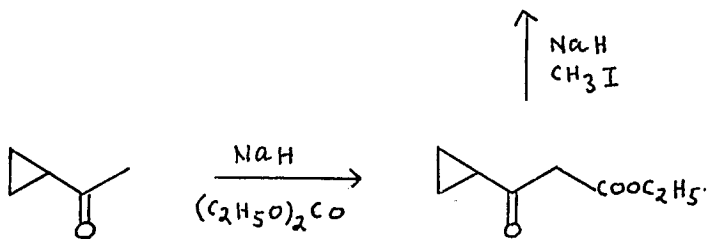
90c 90a

Equation 61



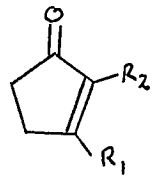
90b

Equation 62

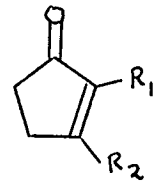


Ketoesters 90a and 90c were prepared from 2-acetylbutyrolactone as shown in equation 60, and converted to 91a and 91c in overall yields of 16% and 13% respectively. Ketoester 90b was obtained from cyclopropanecarboxylic by the route depicted in equation 61, and converted to 91b in 24% overall yield. Thus it appears that judicious choice of the appropriate route to the required ketoester allows for a general route to the preparation of 2-alkyl, 3-alkyl and 2,3-dialkyl-2-cyclopentenones.

As in methods (3), (4) and (7), the 2- and 3-alkyl substituents of a 2-cyclopentenone are introduced separately, and therefore both 91 and 92 may be prepared.



91



92

Furthermore, cis-jasmone, which may not be prepared by methods (2)-(4), has been prepared by Prof. W. F. Berkowitz from 1-methylcyclopropyl methyl ketone in 29-32% overall yield subsequent to the development of the sequence shown in equation 63.

Equation 63

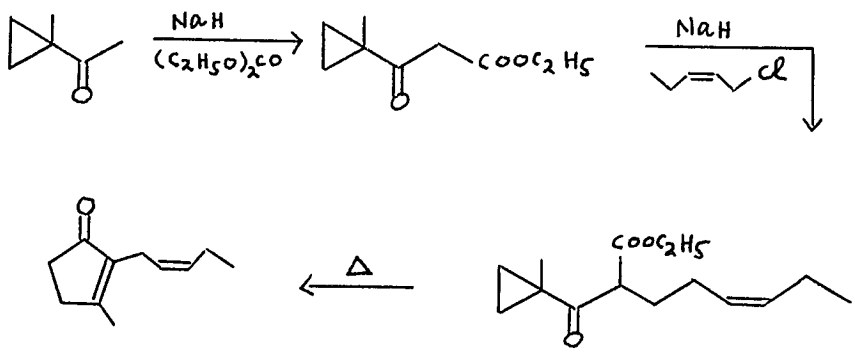


Table I shows that the overall yield of a 2-alkyl-2-cyclopentenone (45) obtained by the dissertation method compares favorably with the overall yields of 45 obtainable by methods (3) and (6), but not with those obtained by method (5). The overall yield of a 2-alkyl-3-methyl-2-cyclopentenone (2) obtained by the dissertation procedure also compares favorably with those obtained by methods (1)- (3) and (7).

Comparison of the overall yield of a 2,3-dialkyl-2-cyclopentenone obtained by the dissertation method with those of 2 and 2-methyl-3-alkyl-2-cyclopentenones (60) is not valid since the reported overall yields of these cyclopentenones are based on starting materials which may onle be used to prepare alkyl derivatives of 2 and 60 (see Discussion). Table I also shows that the overall yields of 3-alkyl- and 2,3-dialkyl-2-cyclopentenones obtained by the dissertation method are at present low. However, further improvements in the yields for the conversion of 2-acetylbutyrolactone to 1-alkylcyclopropyl methyl ketone (e.g. 1-methyl-cyclopropyl methyl ketone in equation 60), and ketoesters 90 to cyclopentenones 91 (equation 59) would increase the overall yields, and thus offer a useful procedure for the preparation of 2-alkyl-, 3-alkyl- and 2,3-dialkyl-2-cyclopentenones.

Miscellaneous methods which have been used, or may be used for the preparation of cyclopentenones include: (a) Acid catalyzed rearrangement of α , β -unsaturated esters,[37] and acid catalyzed cyclization of dienones[1a] and dienynes;[38] (b) Reaction of alkenoyl chlorides with acetylene;[39] (c) Reaction of cyclopentenes with nitrosyl chloride, followed by conversion of the product to a cyclopentenone;[40] (e) Pyrolysis of 2-acetoxycyclopentanones,[1a] 4-oxohexanal[9] and dicyclopentadien-1-ol.[1a]

Miscellaneous reactions which have given cyclopentenones among other products, or in low yields, include: (a) Treatment of 2,2-dibromodimedone with sodium acetate;[41] (b) Rearrangement of allene oxides;[42] (c) Acid catalyzed rearrangement of 2-cyclohexenone,[43] and the oxime of 2,2-dimethylcyclohexanone;[44] (d) Nitrous acid deamination of 2-aminocyclohexanones;[45] (e) Reaction of phenylacetylene with allyl chloride in the presence of nickel carbonyl;[46] (f) Pyrolysis of thujone[47] and 3-methylene-1,5-benzodioxepane;[48] (g) Irradiation of 2,4,6-tri-t-butyl-3-methoxy-4-hydroxy-2,5-cyclohexadien-1-one,[49] 4,5-di-t-butylresorcinol[50] and 5-methylhex-4-en-2,3dione;[51] (h) Base induced rearrangements of 2,6-di-t-butyl-p-quinone,[52] 2,3,4,5-tetramethyl-2,5-diperoxydihydrofuran[53] and methyl 2-(2'-carbomethoxy-1'-isopropyl-cyclopropyl)-acetate;[54] (i) Reaction of diphenylcyclopropenone with 2,6-dimethylisocyanide.[55]

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(37) J. M. Conia and M. L. Leriverend, Bull. Soc. Chim. France, 2992 (1970).
(38) G. F. Hennion and R. B. Davis, J. Org. Chem., 16, 1289 (1951).
(39) G. J. Marten and G. Daviayd, Bull. Soc. Chim. France, 3198 (1970).
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(40b) A. V. Zakharychev and I. V. Torgov, Izv. Akad. Nauk. S.S.S.R. Otdel. Khim. Nauk., 1682 (1962); Chem. Abstr. 58, 3323 (1963).
(41) H. DePooter and N. Scham, Bull. Soc. Chim. Belg. 77, 377 (1968).
(42) J. Grimaldi and M. Bertrand, Bull.Soc. Chim. France, 957 (1971).
(43) H. Hogeveen, Rec. Trav. Chim. Pays-Bas, 87, 1295 (1968).
(44) R. T. Conley and B. E. Nowak, J. Org.Chem., 27, 3196 (1962).
(45) O. E. Edwards and M. Lesage, Can. J. Chem., 41, 1592 (1963).
(46) G. P. Chiusoli, G. Bottaccio and C. Venturello, Tetrahedron Lett., 2875 (1965).
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(49) K. Ogura and T. Matsura, Bull. Chem. Soc. Japan, 43, 3181, 3187 (1970).
(50) T. Matsura, A. Akira, N. Yoshimura, T. Arai, K. Omura, H. Matsushima, S. Kato and I. Saito, Tetrahedron Lett., 1673 (1969).

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(52) U. Cuntze, D. Maassen and H. Musso, Chem. Ber., 102, 2851 (1969).
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Chapter 2

Vinylcyclopropane Rearrangement of Hetero-substituted Vinylcyclopropanes

The thermal conversion of vinylcyclopropanes to cyclopentenes[56] has received considerable attention and has been thoroughly reviewed.[57] Vinylcyclopropanes possessing a variety of substituents on the double bond as well as on the cyclopropane ring have been successfully isomerized to cyclopentenes.[57,58] In particular, Ketley has noted that electron donating substituents on the double bond of vinylcyclopropanes favored formation of cyclopentenes.[59] However, isomerization of enol (93a-d) or enamine (93e) analogs to the corresponding cyclopentanone derivatives (94a-e) have not yet been reported (equation 64). Such rearrangements would provide an attractive route to cyclopentanone derivatives (Scheme 2).

---

(56) C. G. Overberger and A. E. Borchert, J. Amer. Chem. Soc., 82, 4896 (1960).
(57a) C. D. Gutche and D. Redmore, "Carbocyclic Ring Expansion Reactions", Academic Press, New York, N. Y., 1968, chap. IX.
(57b) G. L. Closs, "Advances in Alicyclic Chemistry", H. H. Hart and G. J. Karabatos, ed., Academic Press, New York, N. Y., 1966, vol. I, chap. 2.
(57c) R. Breslow, "Molecular Rearrangements, Part I", P. deMayo, ed., Interscience Publishers, New York, N. Y., 1963, chap. 4.
(58a) Wu Yih-Hsien, A. S. Koz'min and R. Ya Levina, Zh. Org. Khim., 5, 1707 (1969).
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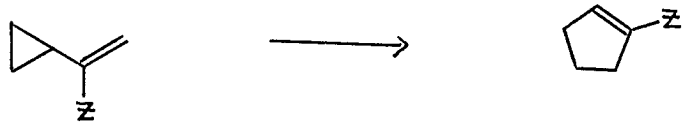
(58d) P. H. Mazzocchi and R. C. Ladenson, J. Chem. Soc., D, 468 (1970).
(59) A. D. Ketley, A. J. Berlin and L. P. Fischer, J. Org. Chem., 31, 305 (1966).

Equation 64



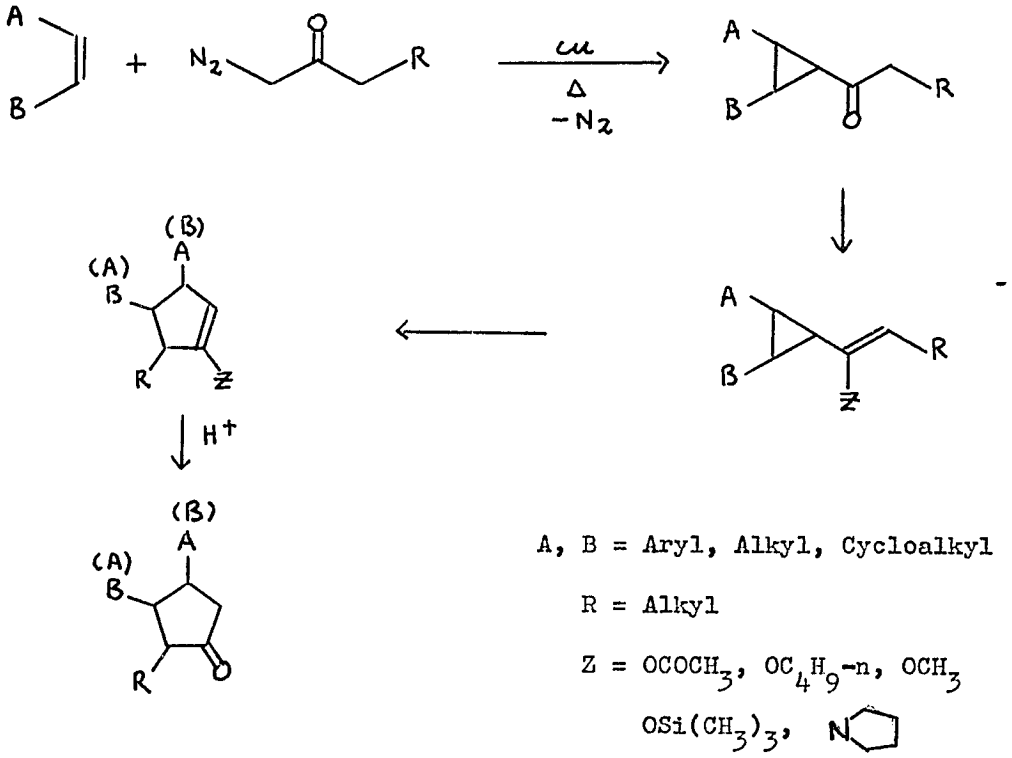
93 94

a : Z= $OCOCH_3$ d : Z= $OSi(CH_3)_3$

b : Z= OC_4H_9-n e : Z= 

c : Z= OCH_3

Scheme 2



A, B = Aryl, Alkyl, Cycloalkyl

R = Alkyl

Z = $OCOCH_3$, OC_4H_9-n, OCH_3

$OSi(CH_3)_3$,

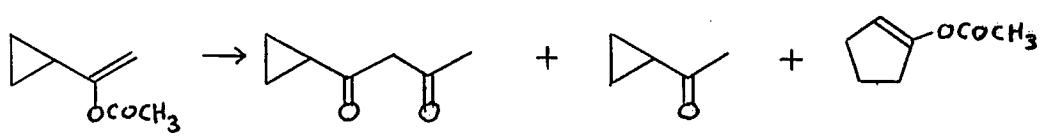
Results and Discussion

We prepared and pyrolyzed the enol derivatives 93a-c. Since we learned of parallel studies on 93d by Professor S. Monti of the University of Texas (Austin), we did not pursue the subject. All attempts to prepare the enamine derivative 93e by an associate at Queens College failed. However, Cook and coworkers have recently achieved the synthesis of 93e, but in very low yield.[60]

Enol Acetate (93a)

Pyrolysis of 93a at 415° and 1 atm. gave the products shown in equation 65.

Equation 65



93a 95 (70%) 96 (12%) 94a (4%)

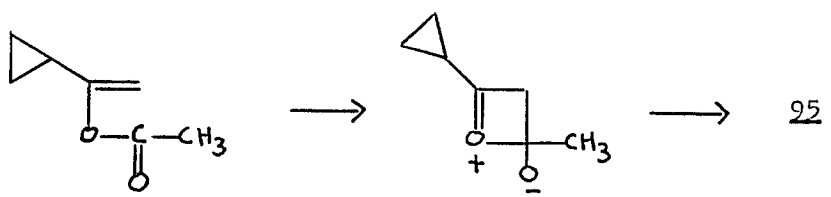
+ CH_3COOH (Trace)

(60) A. G. Cook, S. B. Herscher, D. J. Schultz and A. J. Burke, J. Org. Chem., 35, 1550 (1970).

Formation of diketone 95 was not unexpected as the rearrangement of enol acetates to 1,3-diketones at 400-550° have been reported.[61] Ritchie has shown that this isomerization is an equilibrium process in which the 1,3-diketone is highly favored.[61c] Pyrolysis of 1,3-diketones did indeed yield small amounts of enol acetates.[61c] Young and coworkers have demonstrated the intramolecular nature of the rearrangement by pyrolyzing a mixture of isopropenyl benzoate and styrene acetate at 500°.[61a] Acetylacetophenone was the only product and no dibenzoylmethane was detectable. Therefore they suggested that the isomerization of enol acetates to 1,3-diketones occur by way of a cyclic four-membered transition state.[61a]

The rearrangement of 93a to 95 may therefore be depicted as indicated in equation 66.

Equation 66

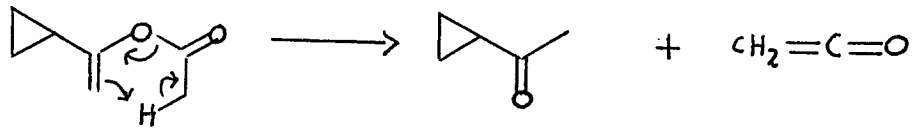


93a

(61a) F. G. Young, F. C. Frostick, Jr., J. J. Sanderson and C. R. Hauser, J. Amer. Chem. Soc., 72, 3635 (1950).
(61b) R. J. P. Allan, R. L. Forman and P. D. Ritchie, J. Chem. Soc., 2717 (1955).
(61c) R. J. P. Allan, J. McGee and P. D. Ritchie, ibid., 4700 (1957).

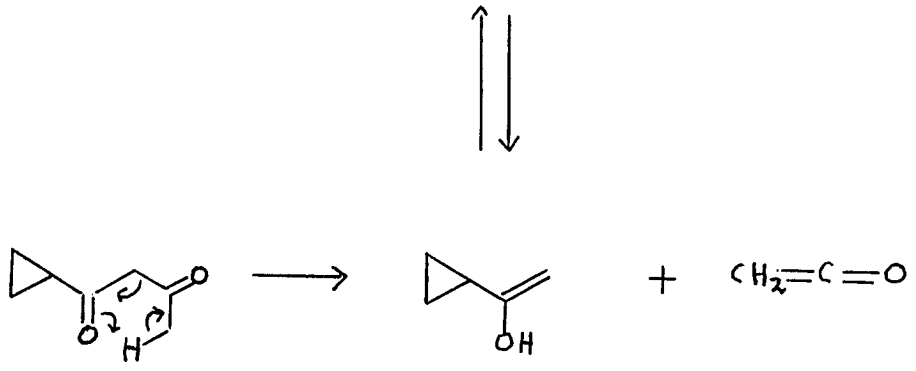
Formation of the parent ketone 96 could have resulted from the rearrangement of either 93a or 95 as shown in equations 67 and 68 respectively.

Equation 67



93a 96

Equation 68



95

It has been shown that enol acetates are able to undergo acyl-oxygen scission which results in the formation of a ketone and a ketene[61b] (equation 67). An alternative route involves the initial formation of 95, which then decomposes to ketone 96 and ketene (equation 68). Hurd and Tallyn have observed that the pyrolysis of acetylacetone gave small amounts of acetone and ketene.[62] Although ketene, itself, was not detected, traces of acetic acid were detected in the pyrolyzate of 93a. Reaction of ketene with traces of water[63] would result in the formation of acetic acid. Acetic acid has been detected among the pyrolysis products of vinylacetate.[61b]

It is of interest that no cyclopentanone was detected in the pyrolyzate of 93a although it might have arisen from enol acetate 94a by analogous routes. Apparently the products were swept out of the hot tube too quickly.

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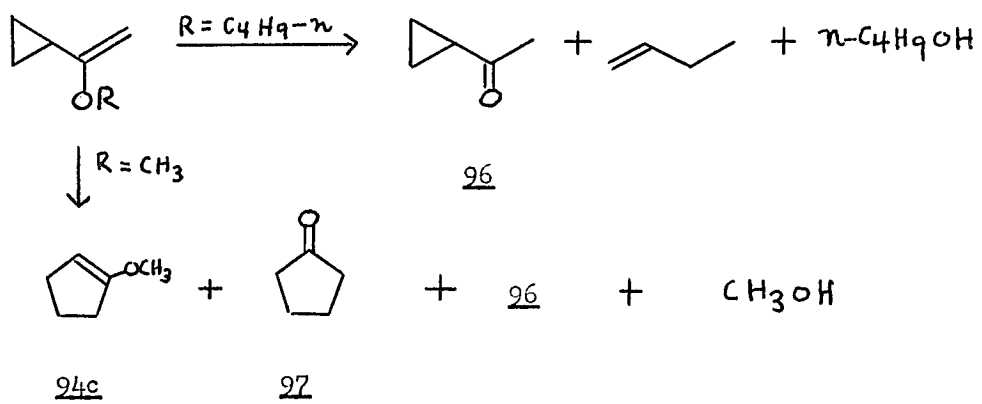
(62) C. D. Hurd and W. H. Tallyn, J. Amer. Chem. Soc., 47, 1779 (1925).

(63) The pyrolysis system was either flushed with nitrogen or maintained at 0.25-0.50 mm Hg for at least 30 min. prior to use. Despite these precautions it is possible that not all traces of water were removed from the system.
Alternately, it is possible that ketene reacted with atmospheric moisture upon opening the pyrolysis traps.

Enol Ethers 93b and 93c

Pyrolysis of enol ether 93b at 455° and 1 atm. gave the parent ketone 96 in 80% yield and n-butanol in 7% yield (equation 69). The product of rearrangement, 1-butoxycyclopentene-1 (94b) was not detected in the pyrolyzate.

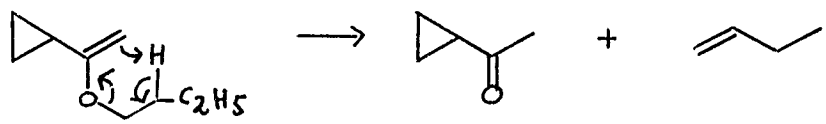
Equation 69



Formation of 95 from 93b probably occurs as shown in equation 70.[64] The presumed by-product, 1-butene was not identified. Formation of n-butanol may be attributed to hydrolysis of unreacted starting material.[63]

(64a) A. T. Blades and G. W. Murphy, J. Amer. Chem. Soc., 74, 1039 (1952).
(64b) A. T. Blades, Can. J. Chem., 31, 418 (1953).
The authors have shown that an enol ether which possesses a hydrogen atom in the β-position (e.g. 93b) thermally decomposes to a ketone and an olefin by way of a cyclic six-membered transition state.

Equation 70



93b 96

On the other hand, optimum conditions for pyrolysis of 93c gave 1-methoxycyclopentene-1 (94c) in 30% yield (equation 69). Formation of cyclopentanone (97) (6%), parent ketone 96 (21%) and methanol (11%) may again be attributed to hydrolysis.[63]

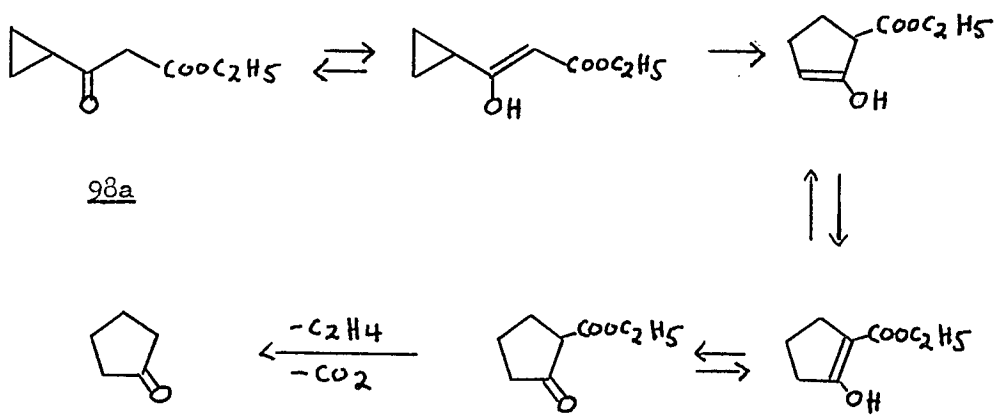
Several unsuccessful attempts to increase the yield of 94c by increasing contact time in the hot tube, either by slowing the nitrogen flow rate or by lengthing the tube, resulted in lower percentage recoveries and increased amounts of non-volatile products which were not identified (Table V, runs 1-3 and 6). In addition, increasing the packing surface area or using a basic packing material did not improve the yield of 94c (Table V, runs 4, 5 and 7).

Chapter 3

2-Cyclopentenones from 3-Cyclopropyl-3-oxopropanoates

It has been shown that at 180° gaseous ethyl acetoacetate is 14% enolic.[65] In view of this fact, we expected the vapor phase pyrolysis of ketoester 98a to be able to give the enol of 98a which could then undergo vinylcyclopropane rearrangement, affording 2-carbethoxy-cyclopentanone, or perhaps cyclopentanone (equation 71). However, neither of these products was obtained from the pyrolysis of 98a.

Equation 71

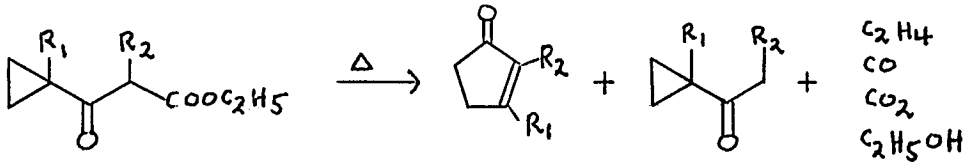


(65) G. Brigleb and H. Rebelein, Z. Naturforsch, 2a, 562 (1947).

Results and Discussion

The products of pyrolysis of ketoesters 98 near 500° at 1-3 mm Hg included cyclopentenones 99, ketones 100, carbon monoxide, carbon dioxide, ethanol and ethylene (equation 72).

Equation 72



98 99 100

Table VII

Pyrolysis of Ketoesters 98a-d

Starting Material 98	R_1	R_2	T°C[a]	Yield of 99	T°C[a] (continued)	Yield of 99 (continued)
a	H	H	565	51[b]	540	47[c]
b	CH_3	H	500	65[b]	500	60[c]
c	H	CH_3	585	65[b]	585	58[c]
d	CH_3	CH_3	535	81[b]	570	69[c]

[a]Pyrolysis temperature affording greatest glpc yield. [b]Glpc yields based upon unrecovered starting material. [c]Isolated yields based upon weight of product recovered by distillation.

Table VIII

Pyrolysis of Ketoester 98a under Various Conditions[a]

Run	Packing Material[b]	T°C[c]	Products: % Yield[d] 99a	100a	C_2H_5OH	% Unchanged 98a	Pyrolyzate Total Wt. %
1	A	470	14	36	56	48	68
2	A	575	5	18	37	80	88
3	A	625	8	30	58	78	84
4	B	600	20	16	42	19	69
5	C	460	27	31	65	21	70
6[e]	C	525	54	0	76	17	66
7[e]	C	540	52	0	85	8	79
8	C	565	51	7	74	0	73
9	C	625	46	5	75	0	63
10[f]	C	525	35	1	53	0	78
11[f]	C	575	45	1	73	0	70
12[g]	C	450	14	19	57	0	37[h]
13[i]	A	410	1	9	50	1	48[g]
14[j]	D	400	—	—	—	30	69

[a]Material entered the pyrolysis tube in the vapor state at 1-3 mm Hg unless otherwise noted.

[b]A: 6 X 6 mm Pyrex Raschig Rings; B: 6 mm Pyrex helices; C: Pyrex glass wool; D: Pumice.

Table VIII (continued)

[c]Maximum temperature, ± 10°, at the center of the tube oven prior to pyrolysis. The temperature was approximately 50-70° lower at a distance of 15 cm from the center.

[d]Glpc yield based on unrecovered 98a. For glpc conditions see Experimental Section.

[e]Yields based upon weights of isolated products produced from unrecovered 98a.

[f]98a methyl ester was pyrolyzed.

[g]Pyrolysis at 100 mm Hg.

[h]Low recoveries were due to cooler tube ends which condensed and charred products.

[i]Pyrolysis at 760 mm. A Pyrandione (108) was obtained in 20% yield. See Experimental Section.

[j]Pyrolysis at 760 mm over pumice.[79] Pyrandione 108 was obtained in 79% yield based on unrecovered 98a. See Experimental Section.

Table VIII presents evidence that the ratio of ketones 99a and 100a varied only slightly with temperature, but increased dramatically with an increase in the surface area of the pyrolysis packing material. This leads us to believe that the reaction affording 99 is catalyzed by glass surfaces,[66] while that leading to 100 is not, and thus 99 and 100 are produced by competitive routes (equation 75).

The substitution pattern of cyclopentenones (99a-d) produced requires the loss of the ketone carbonyl group rather than the carbonyl of the carboxyl group. In the latter case, the methyl groups of 99d would appear in the 1- and 5- positions of the product (e.g. 101a,b) rather than in adjacent positions 2- and 3- as in 99d. This result precludes mechanisms involving the direct conversion of 100 to 99 (equation 73) or ones involving prior conversion of 98 to a cyclopentanone carboxylate (102), decarboxylation[67] to 103 and subsequent formation of 101a,b[68] (equation 74).

---

(66) Acid or base washing, followed by thorough washing with distilled water, apparently had little effect on either the percentage conversion or the ratio of 99a to 100a.

(67) Thermal decarboxylation, while not observed heretofore with 2-carbethoxycyclopentanone, is a common reaction of β-ketoesters (reference 67a,d), malonates (reference 67b) and α-cyanoesters (reference 67c).

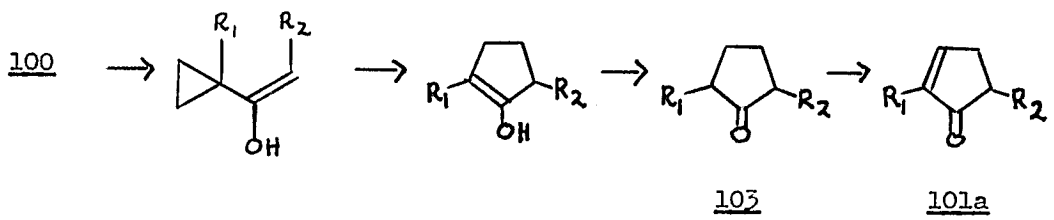
(67a) W. J. Bailey and J. J. Daly, Jr., J. Org. Chem., 22, 1189 (1957).

(67b) W. J. Bailey and J. J. Daly, Jr., ibid., 29, 1249 (1964).

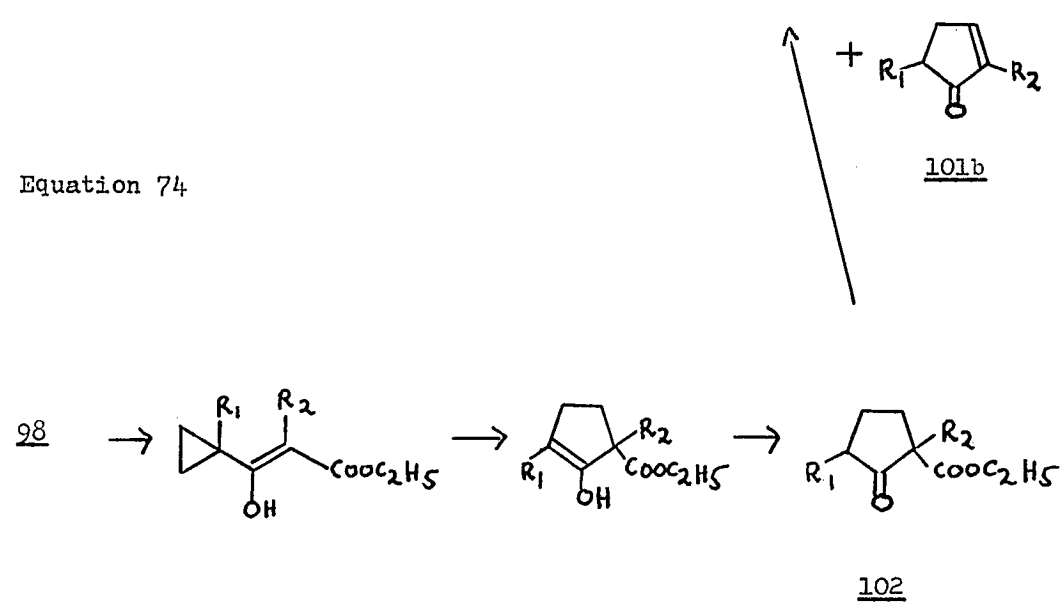
(67c) W. J. Bailey and J. J. Daly, Jr., J. Amer. Chem. Soc., 81, 5397 (1959).

(67d) H. O. House, "Modern Synthetic Reactions", W. A. Benjamin, New York, N. Y., 1965, p. 171.

Equation 73



Equation 74

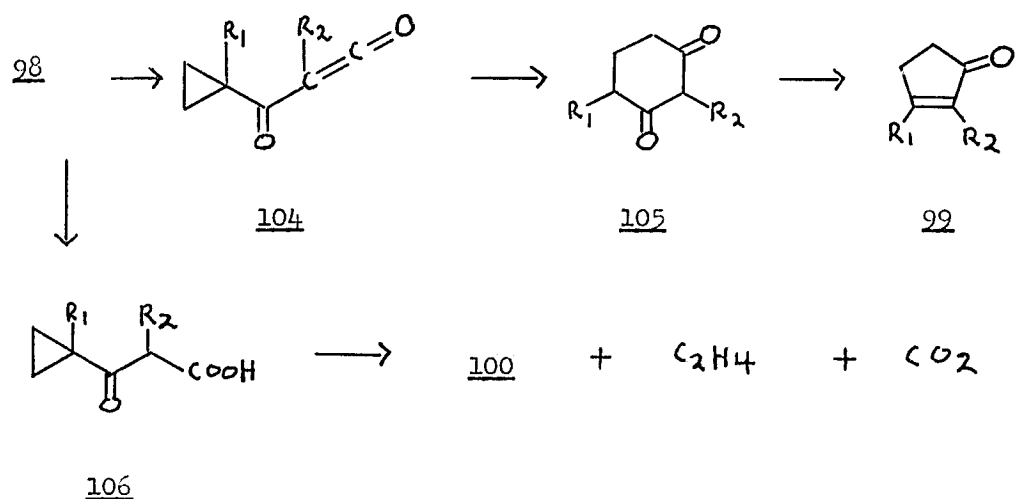


(68) Pyrolytic dehydrogenation of cyclopentanone to cyclopentenone was noted at 488-543 degrees (99-314 mm) by E. R. Johnson and W. D. Walters, J. Amer. Chem. Soc., 76, 6266 (1954), and at 532-581 degrees (11-30 mm) by F. M. Delles et al, ibid., 91, 7645 (1969). A static system was used in these investigations with much longer contact times than in our flow system.

Furthermore, using conditions which would have converted 98 to 99,[69] we found that cyclopropyl methyl ketone (100a) and cyclopentanone were recovered unchanged by pyrolysis (99 and 96% recovery, respectively), and 2-carbethoxycyclopentanone (102, R_1= R_2= H) was converted to cyclopentanone (103, R_1=R_2= H) in 48% yield. In none of these reactions was 2-cyclopentenone detectable in the pyrolyzate.[70]

We suggest the following mechanism for the conversion of 98 to 99 and 100 (equation 75).

Equation 75



(69) See Experimental Section.
(70) Glpc conditions used enabled the easy detection of less than 1% of 98a in a mixture of 99a, 100a, 101a and 102.

Formation of 100 from 98 (via 106) is the expected behavior of a β-ketoester.[67a,d] The mechanism is believed to consist of formation of a β-ketoacid with subsequent decarboxylation, both steps proceeding by way of cyclic six-membered transition states.[71-73]

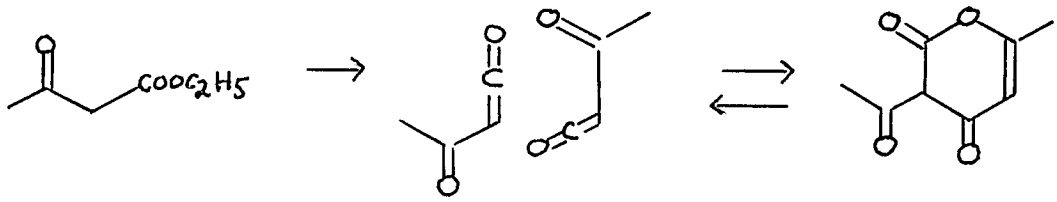
Formation of acylketenes (e.g. 104) from β-ketoesters has never been observed; on the other hand, ketenes[77] have been obtained by pyrolysis of esters in competition with olefin formation.[78]

---

(71) A. Macoll and P. J. Thomas, Prog. Reaction Kin., 4, 119 (1967).
(72) E. M. Hodnet and R. L. Rowton, Radioisotopes Phys. Sci. Ind. Proc. Conf. Uses, Copenhagen, 3, 225 (1960); Chem. Abstr. 58, 4400b (1963).
(73a) D. B. Bigley and J. C. Thurman, Tetrahedron Lett., 2377 (1967).
(73b) D. B. Bigley and J. C. Thurman, J. Chem. Soc., B, 941 (1967).
(73c) D. B. Bigley and J. C. Thurman, ibid., 436 (1968).
Whereas catalytic effects of glass surfaces have not been reported, it is reasonable to assume that they should be minimal since normal ester pyrolysis has been shown to be insensitive to changes in the (clean) surface area of silaceous packing materials (references 74-76).
(74) E. U. Emovan, J. Chem. Soc., 1246 (1963).
(75) D. H. R. Barton, A. J. Head and R. J. Williams, ibid., 1715 (1953).
(76) M. Szwarc and J. Murawski, Trans Faraday Soc., 47, 269 (1951).
(77a) W. E. Hanford and J. C. Sauer, "Organic Reactions", John Wiley and Sons, Inc., New York, N. Y., 1946, vol. III, chap. 3.
(77b) H. M. MacKinnon and P. D. Ritchie, J. Chem. Soc., 2564 (1967).
(77c) R. N. Bennet, A. A. Deans, J. G. H. Harris, P. D. Ritchie and J. S. Shim, ibid., 4508 (1958).
(77d) A. L. Brown and P. D. Ritchie, ibid., C, 2007, 2013 (1968).
(78) C. H. Depuy and R. W. King, Chem. Revs., 60, 431 (1960).

It appears reasonable that the increased acidity of the α-hydrogens of β-ketoesters would facilitate the loss of ethanol from 98, and consequently enhance the ease of ketene formation (e.g. 98 to 104). Pyrolysis of acetoacetic ester has given dehydroacetic acid,[79,80] which, it may be noted, can be considered as a Diels-Alder dimer of acylketene 107[81] (equation 76). In addition, dehydroacetic acid has been depolymerized to ketene,[82] presumably by way of the acylketene 107 (equation 76).

Equation 76

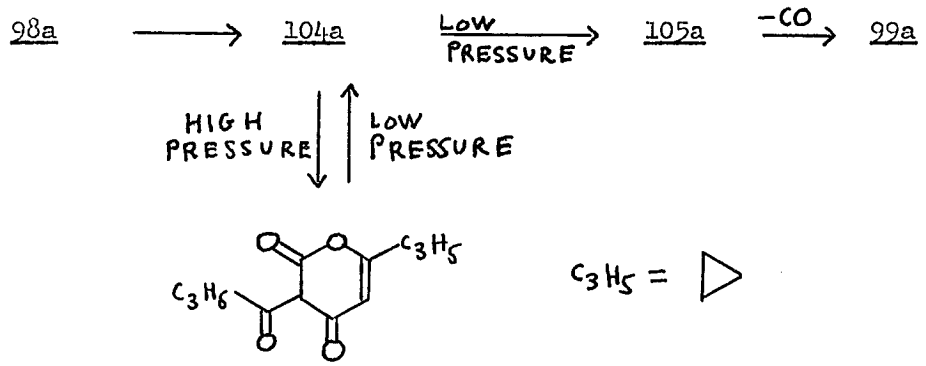


107

Similarly, pyrolysis of β-ketoester 98a at 760 mm (Table VIII, run 13) gave a white solid which we believe to be the analogous pyrandione 108 (See Experimental Section).

(79a) S. Nakamura, S. Ishidoya and U. Okubo, Japan, 2375 (1955); Chem. Abstr. 51, P14826b (1957).
(79b) S. Nakamura and S. Ishidoya, Japan, 1884 (1955); Chem. Abstr. 51, P4442d (1957).
(80) F. Arndt, Org. Syn., 20, 26 (1940).
(81a) H. Stetter and K. Kiehs, Tetrahedron Lett., 3531 (1964).
(81b) H. Stetter and K. Kiehs, Chem. Ber., 98, 1181, 2099 (1965).
(82) A. B. Boese, Jr., Ind. Eng. Chem., 32, 16 (1940).

Equation 77

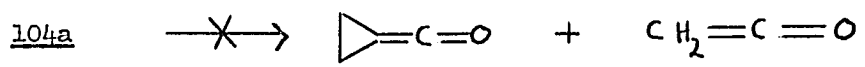


108

Thus at low pressure (1-3 mm) the formation of acylketene 104a from 98a led to 99a as in equation 77, while at high pressure (760 mm), the higher concentration of 104a would permit dimerization leading to 108. Furthermore, pyrolysis of the dimer itself (108) at low pressure gave 99a in 48% yield (Table IX, run 24 in Experimental Section), presumably by way of a retro-Diels-Alder reaction leading to 104a with subsequent rearrangement to 105a and extrusion of carbon monoxide as in equation 77. Formation of ketone 100a (3%) can be attributed to hydrolysis[63] of acylketene 104a to ketoacid 106 which then decarboxylates to 100a .

The further rearrangement of 104a to 109 and ketene is less likely because the methine proton of the cyclopropane ring is known to be weakly acidic[83] (equation 78).

Equation 78



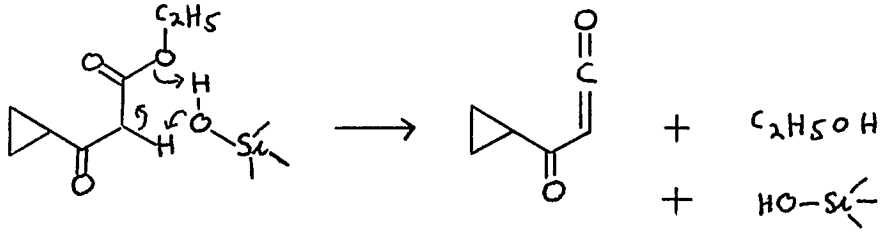
104a 109

It is possible to suggest that the loss of ethanol from 98 to give 104 is catalyzed by the silanol groups of the glass surface. Two mechanisms involving this type of catalysis may be postulated. The first facilitates the loss of ethanol from 98 to give 104 (equation 79), while the second catalyzes the enolization of 98 to give 110,[84] which is then converted to 104 by elimination of ethanol (equation 80).

It is less likely that the unimolecular rearrangement of 104 to 105 (equation 75), or the decarbonylation of 105 to 99 would be affected by a catalyst since they are presumably concerted processes.

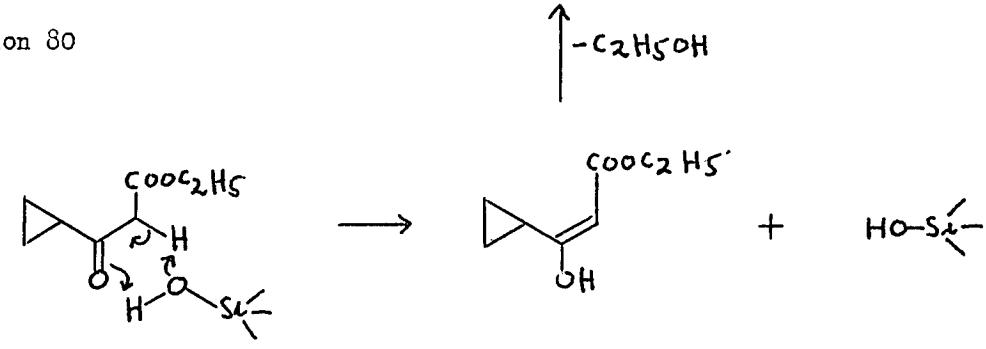
(83a) C. Agami and M. Audouin, Compt. Rend., C, 268, 1267 (1969).
(83b) H. W. Amburn, K. C. Kaufmann and H. Schecter, J. Amer. Chem. Soc., 91, 530 (1969).
(83c) C. Rappe and W. H. Sachs, Tetrahedron, 24, 6287 (1968).
(83d) W. T. Van Wijnen, H. Steinberg and J. J. de Boer, Rec. Trav. Chim., 87, 844 (1968).
(84) We are grateful to the referee who read the manuscript of this work which was submitted for publication, and suggested the second type of catalysis (equation 80) to us.

Equation 79



98 104

Equation 80



98 110

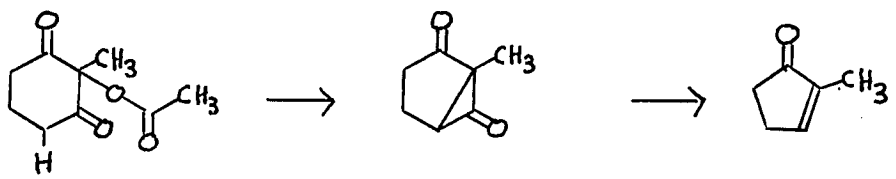
The rearrangement of 104 to 105 has, of course, no precedent as neither acylketenes nor cyclopropanones similar to 105 have ever been isolated. However, it may be a thermally allowed[85] $\sigma_{2s} + \pi_{2a}$ electrocyclic reaction with subsequent, or perhaps, simultaneous non-linear chelotropic elimination of carbon monoxide.

---

(85) R. B. Woodward and R. Hoffman, "The Conservation of Orbital Symmetry", Academic Press, New York, N. Y., 1970.

Intermediate 105c (R_1= H, R_2= CH_3) has been proposed[86] as the preliminary product of the pyrolytic loss of acetic acid from 111 giving, ultimately 99c (equation 81).

Equation 81



111 105c 99c

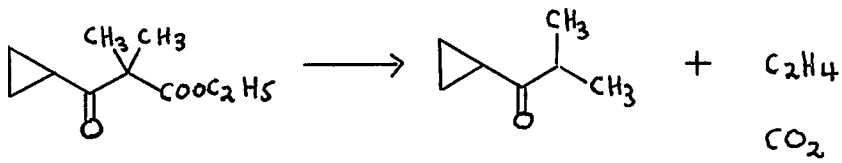
The formation of alkenes by the pyrolytic extrusion of a carbonyl adjacent to an acetoxy group has been noted in other instances, and preliminary formation of cyclopropanones were also proposed.[87,88]

Finally, β-ketoester 112, with no α-hydrogens afforded only ketone 113 in 77% yield upon pyrolysis (Table IX, run 23 in Experimental Section). No cyclopentenones or ethanol were observed in the pyrolyzates (equation 82).

---

(86) T. A. Spencer, A. L. Hall and C. F. von Reyn, J. Org. Chem., 33, 3369 (1968).
(87) R. G. Carlson and J. H. Bateman, ibid., 32, 1608 (1967) and references cited therein.
(88) See also A. S. Kende, Chem. and Ind., 1053 (1956).

Equation 82



112 113

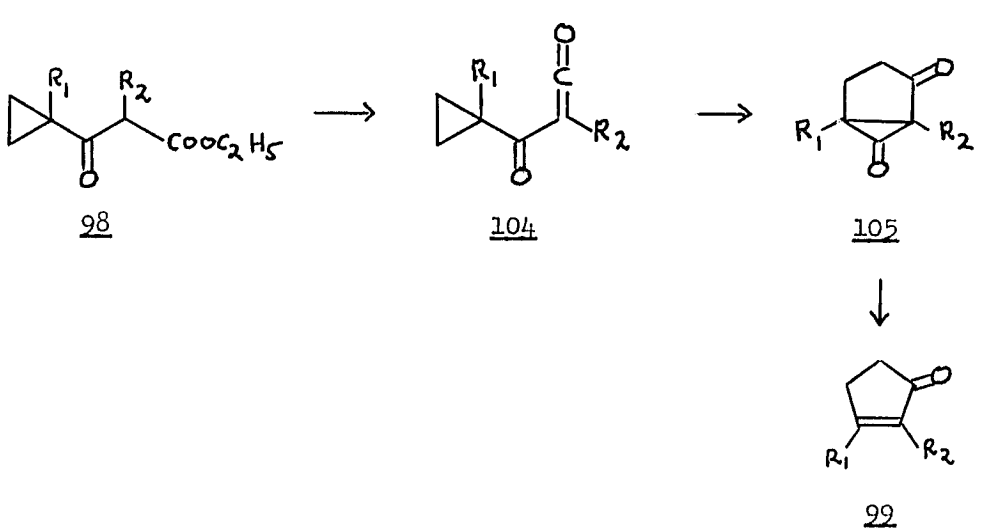
Chapter 4

Thermal Isomerization of Cyclopropylketene to 2-Cyclopentenone

The studies of the rearrangement of ketoesters 98 to cyclopentenones 99 indicated an intermediate rearrangement of acylketene 104 (equation 84) strongly reminiscent of the vinylcyclopropyl rearrangement (equation 83). Analysis of this relationship led to investigations of the pyrolysis of related materials, 114 (equation 85) and 129 (equation 86) (129 will be discussed in chapter 5).

Equation 83

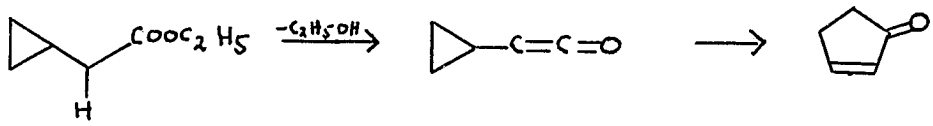
Equation 84



98 104 105

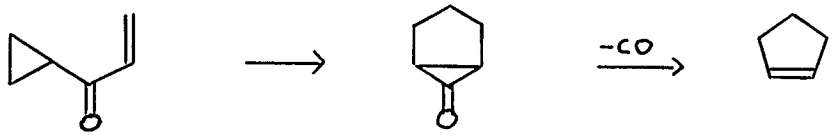
99

Equation 85



114 115 99a

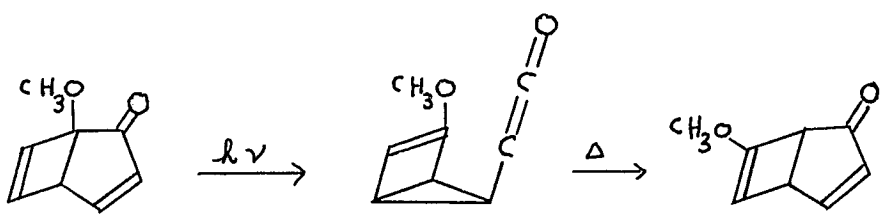
Equation 86



129 130

Recently there has been considerable interest in the isomerization of cyclopropylketenes to cyclopentenones.[89] For example, Chapman has provided evidence indicating that the photochemically generated ketene 116 rearranges spontaneously to 7-methoxybicyclo[3. 2. 0]hepta-3,6-dienone[89d,e] (equation 87). Other examples of this type of isomerization have been reported.[89b,c,f]

Equation 87

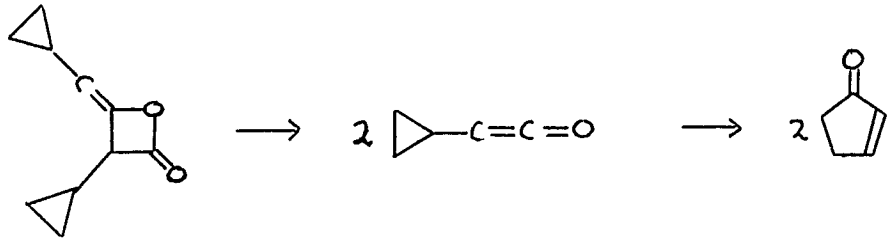


116

(89a) W. C. Agosta, A. B. Smith, III, A. S. Kende, R. G. Eilerman and J. Benham, Tetrahedron Lett., 4517 (1969).
(89b) T. H. Kinstle and P. D. Carpenter, ibid., 3943 (1969).
(89c) M. J. Goldstein and B. G. Odell, J. Amer. Chem. Soc., 89, 6356 (1967).
(89d) O. L. Chapman and J. D. Lassila, ibid., 90, 2449 (1968).
(89e) O. L. Chapman, M. Kane, J. D. Lassila, R. L. Loeschen and H. E. Wright, ibid., 91, 6857 (1969).
(89f) A. S. Kende, Z. Goldschmidt and P. T. Izzo, ibid., 91, 6858 (1969).

The pyrolytic decomposition of esters to give acids and olefins is, of course, well known.[78] However, ketenes have also been obtained from the pyrolysis of esters. An 84% yield of ketene was obtained from the pyrolysis of phenylacetate.[77a] Aliphatic esters have generally given low yields of ketenes,[77] the preferred reaction being olefin formation.[78] Therefore it appeared reasonable to attempt preparation of cyclopropylketene (115), with subsequent rearrangement to cyclopentenone (99a), by pyrolysis of ethyl cyclopropylacetate (114) (equation 85). The preparation of 115 by the familiar method of dimer cracking[77a] was also investigated. (equation 88).

Equation 88



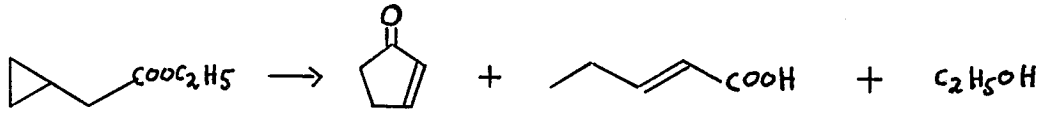
119 115 99a

Results and Discussion

Ethyl Cyclopropylacetate (114)

Pyrolysis of 114 at 587° and 0.25-2.00 mm Hg gave yields of 39% 2-cyclopentenone (99a), 5% 2-pentenoic acid (117), 18% ethanol and 42% unreacted ester 114 (equation 89).

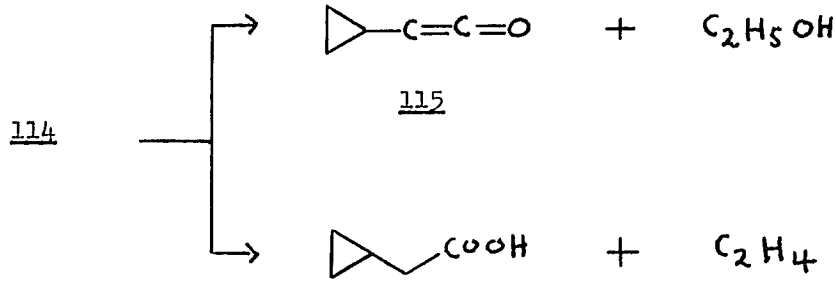
Equation 89



114 99a 117

Ester 114 could either undergo alkyl-oxygen scission to give cyclopropylacetic acid (118) and ethylene, or acyl-oxygen cleavage to give cyclopropylketene (115) and ethanol (equation 90).

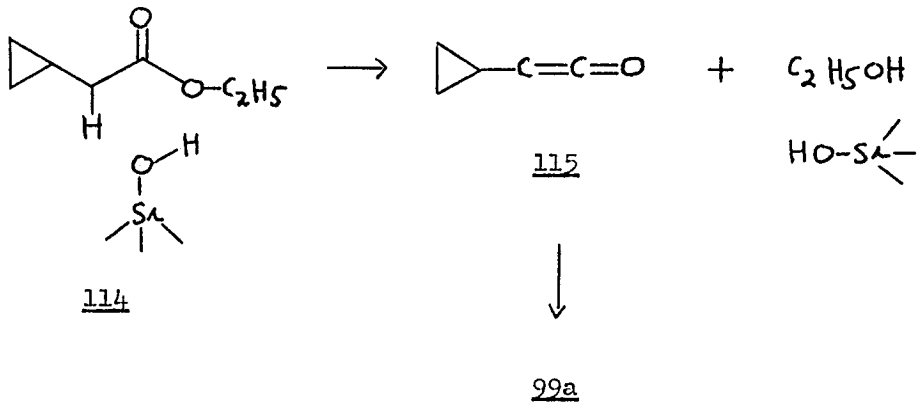
Equation 90



115 118

Normally, alkyl-oxygen scission predominates.[78] However, in our case it appears that alkyl-oxygen and acyl-oxygen scission are at least equally favorable, as evidenced by the yield of ketone 99a obtained. The increased amount of acyl-oxygen cleavage observed can be attributed to catalysis by the silanol groups of the glass surface (equation 91) (See pyrolysis of 3-cyclopropyl-3-oxopropanoates in chapter 3).

Equation 91



The intermediate 115 could then rearrange to ketone 99a as was previously suggested.

Two possible routes which would lead to the formation of acid 117 are depicted in scheme 3. Route (a) which involves the ring opening of acid 118, has been proposed by Bigley and Thurman to account for the formation of 1-butene from the pyrolysis of 118.[90] However, the isomerization of 4-pentenoic acid, produced by route (a), to acid 117 is also possible.

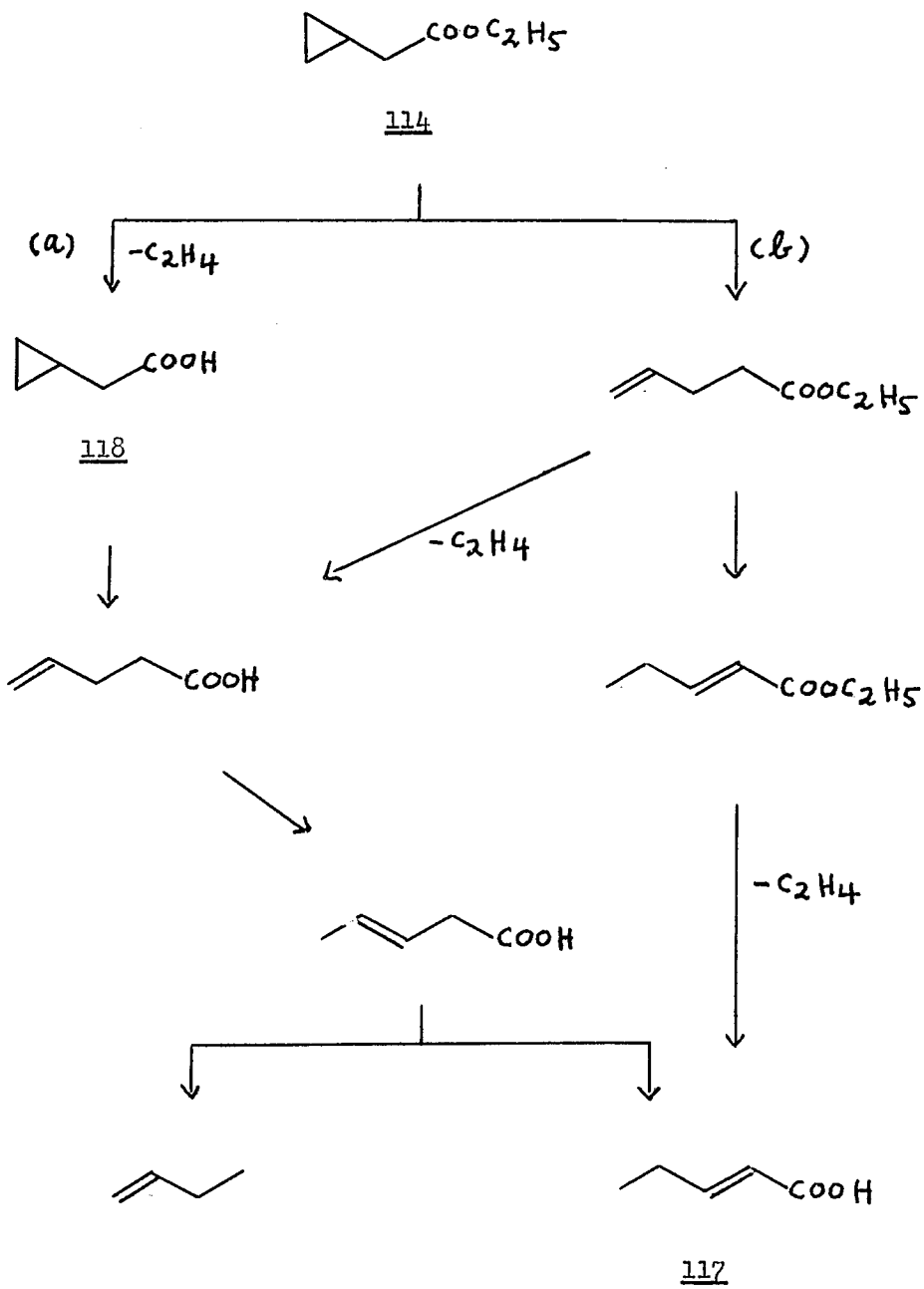
Alternatively, ring opening of ester 114[91] would lead to the formation of ethyl 4-pentenoate which could then be converted to acid 117 as shown in route (b).

---

(90) D. B. Bigley and J. C. Thurman, Tetrahedron Lett., 4687 (1965).

(91) Cyclopropane and its alkyl derivatives are known to undergo ring opening to give propene derivatives in the vicinity of 400-500 degrees. For references see, R. Breslow, "Molecular Rearrangements, Part I", P. deMayo, ed., Interscience Publishers, New York, N. Y., 1963, chap. 4; and "Organic Reaction Mechanisms, 1969", B. Capon and C. W. Rees, eds., Interscience Publishers, New York, N. Y., 1969, p. 274.

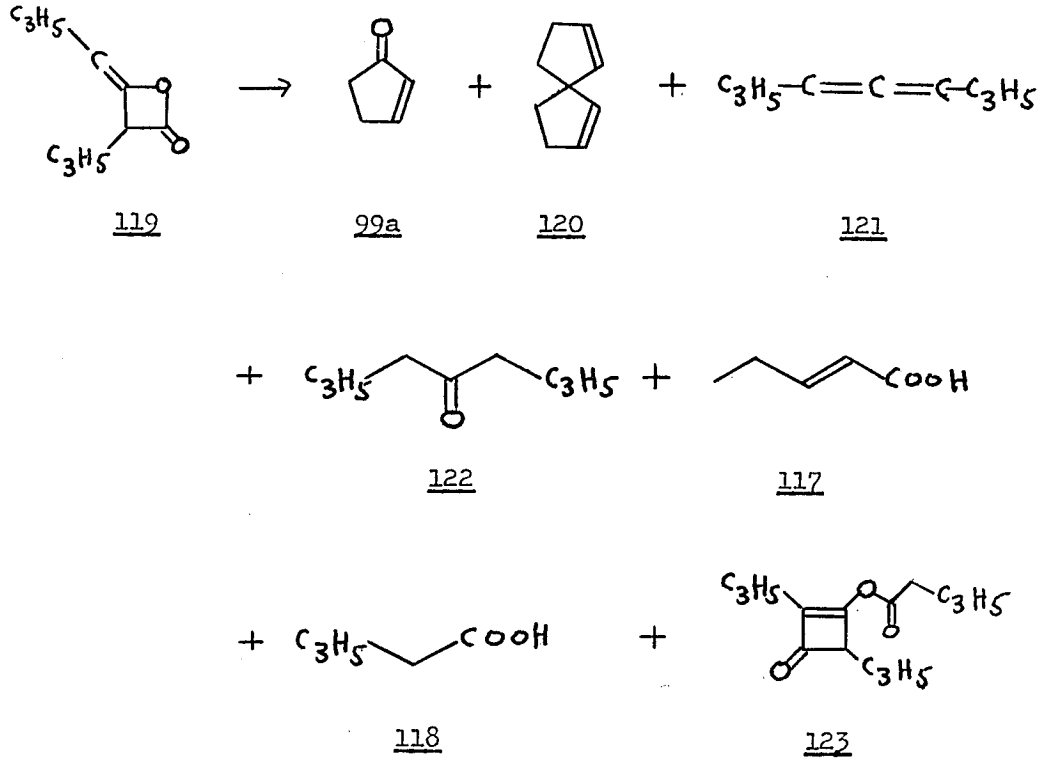
Scheme 3



2,4-Dicyclopropyl-3-hydroxy-3-butenoic acid β-lactone (119)

The products of the pyrolysis of 119 at 537-560° and 0.20-1.80 mm Hg included 2-cyclopentenone (99a) (13-31%), 1,6-spiro [4. 4] nonadiene (120) (3-14%), 1,3-dicyclopropylallene (121) (0-20%), 1,3-dicyclopropylpropan-2-one (122) (1-4%), 2-pentenoic acid (117) (1-5%), cyclopropylacetic acid (118) (0-1%) and 2,4-dicyclopropyl-3-cyclopropylacetoxycyclobut-2-en-1-one (123) (See Tables XIV and XV in Experimental Section).

Equation 92



119 99a 120 121

122 117

118 123

C_3H_5 = ▷

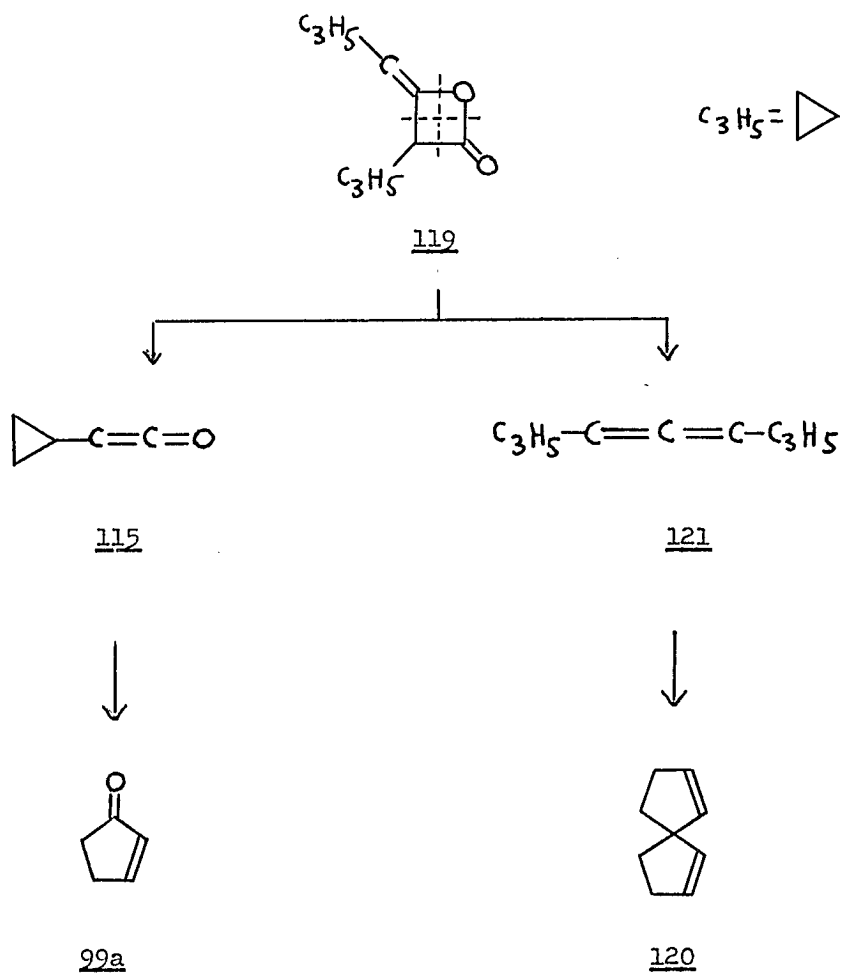
The formation of ketenes from the pyrolysis of their dimers is known.[77a] The dimers of ketene, methylketene and dimethylketene have been converted to their monomers in yields of 86-100% by decomposition over hot filaments or in hot tubes[77a] (550-600°).

Allenes have also been obtained from the pyrolysis of ketene dimers.[92] The proportion of allene formed depends upon the degree of alkyl substitution[92d] as well as experimental conditions.[92a,b] Pyrolysis of diketene over an electrically heated (55 volts) nichrome wire in a flow system, gave the following relative yields of products: Allene (45% = 8-18% molar yield), carbon dioxide (54%), ketene (0.1%) and acetone (0.4%).[92a] On the other hand, pyrolysis of 2,2,4,4-tetra-alkyl-3-hydroxy-3-butenoic acid β-lactones over vycor chips at 150-550° and 5-760 mm Hg (flow system with contact time of 0.5-10 sec.) gave tetraalkylallenes in yields of 91-94%.[92c]

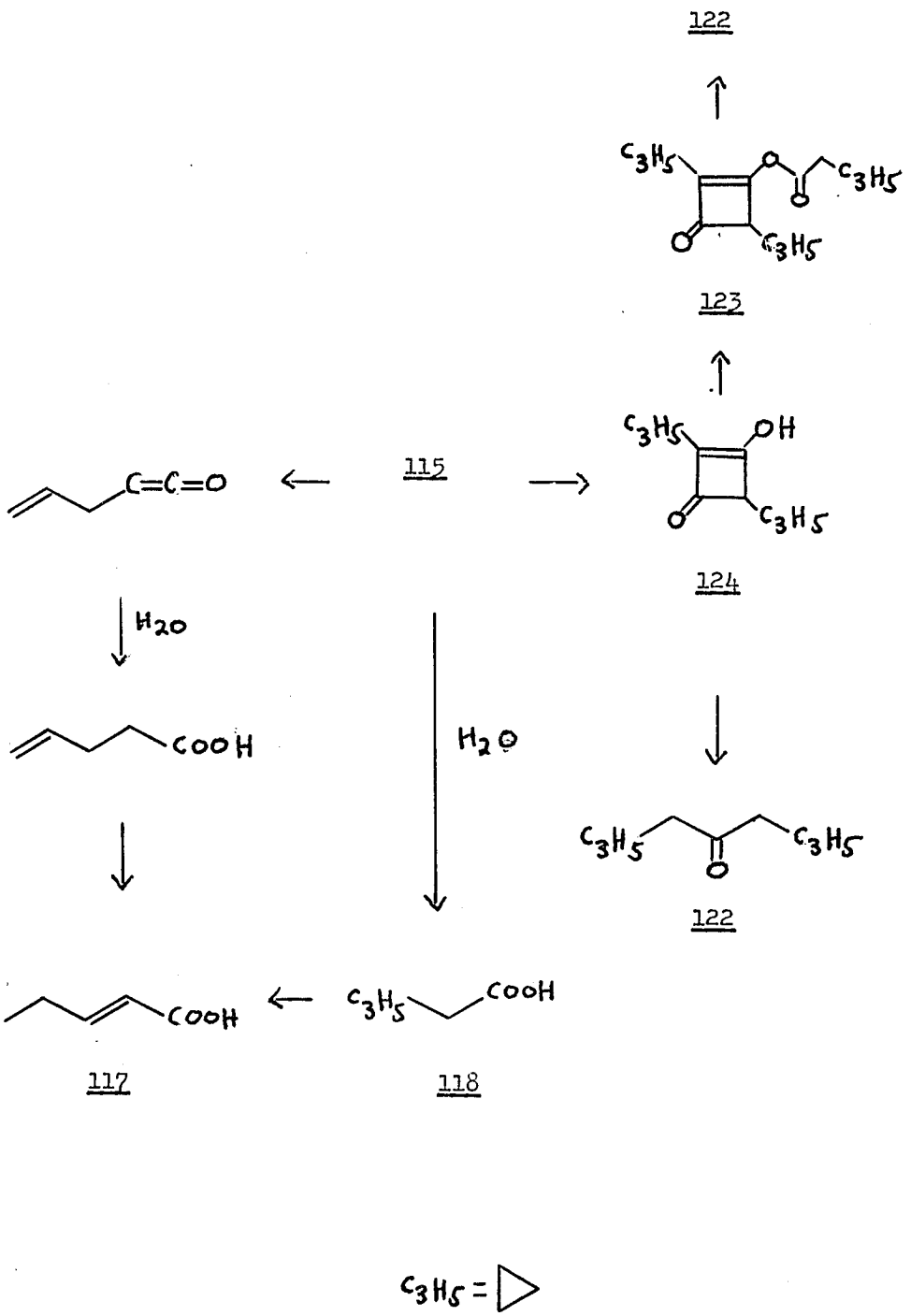
(92a) J. T. Fitzpatrick, J. Amer. Chem. Soc., 69, 2236 (1947).
(92b) W. B. Guenther and W. D. Walters, ibid., 81, 1310 (1959).
(92c) J. C. Martin, U.S. Patent, 3, 131, 234; Chem. Abstr. 61, 2969 (1964).
(92d) D. R. Taylor, Chem. Revs., 67, 317 (1967).

It is therefore apparent that ketene dimer 119 decomposed by two competitive pathways leading either to cyclopropylketene (115) or 1,3-dicyclopropylallene (121) which further rearranged, condensed or hydrolyzed[63] to the products obtained (See schemes 4 and 5).

Scheme 4



Scheme 5



C_3H_5 = △

It is noteworthy that the yield of cyclopentenone (99a) was affected by the rate of distillation of ketene dimer 119 through a vycor tube packed with glass wool. Table XIV (Experimental Section) shows that a threefold increase in the rate of distillation increased the yield of 99a from 13% to 31% (runs 1 and 6).

Evidence that spirodiene 120 arises from allene 121 by a double vinylcyclopropane-cyclopentene rearrangement was obtained by variation of contact times and surface area of the packing material. Distillation of ketene dimer 119 through a tube packed with pyrex helices gave allene 121 in 20% yield and 120 in 3% yield. A similar distillation of 119 through a glass wool packed tube (longer contact time and more surface area) gave 121 in 0.2% yield and 120 in 14% yield (See Table XIV, runs 1 and 4 in Experimental Section).

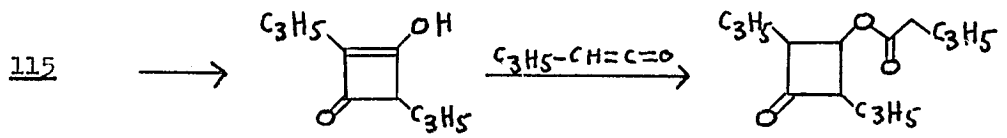
Formation of trimer 123 may be attributed to liquid phase trimerization of unreacted cyclopropylketene (115) in the cooler region of the pyrolysis tube, or perhaps in the trap.
Farnum and coworkers have pointed out that with the exception of ketene itself, liquid phase dimerization of aldoketenes in the absence of catalysts such as triethylamine or aluminum chloride, afford 3-hydroxy-cyclobut-2-en-1-ones, which may react further to give trimers.[93]

---

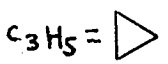
(93) D. G. Farnum, J. R. Johnson, R. E. Hess, T. B. Marshall and B. Webster, J. Amer. Chem. Soc., 87, 5191 (1965).

Therefore, trimer 123 may arise as shown in equation 93.

Equation 93

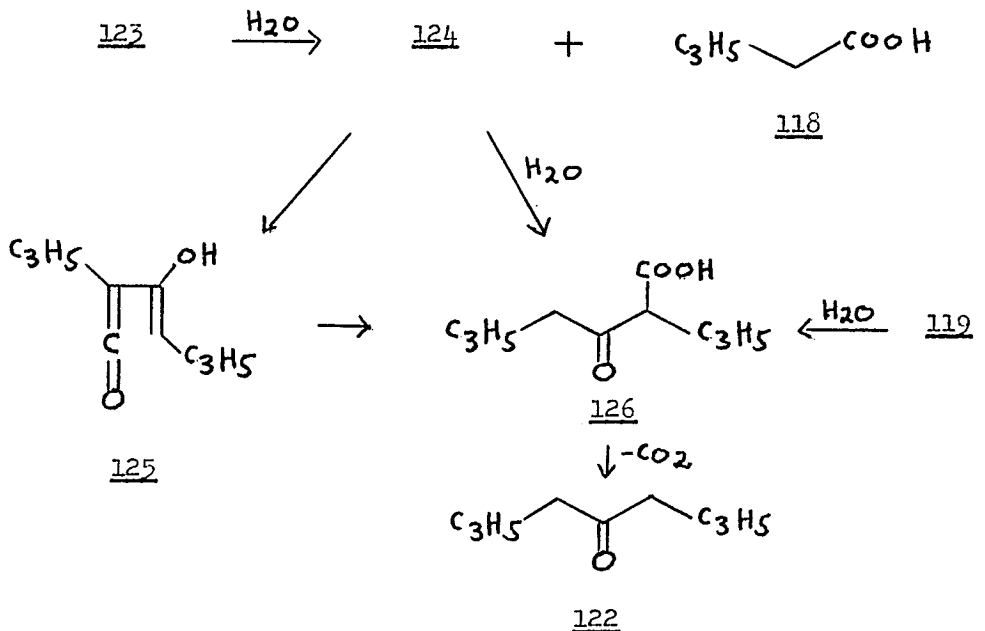


124 123



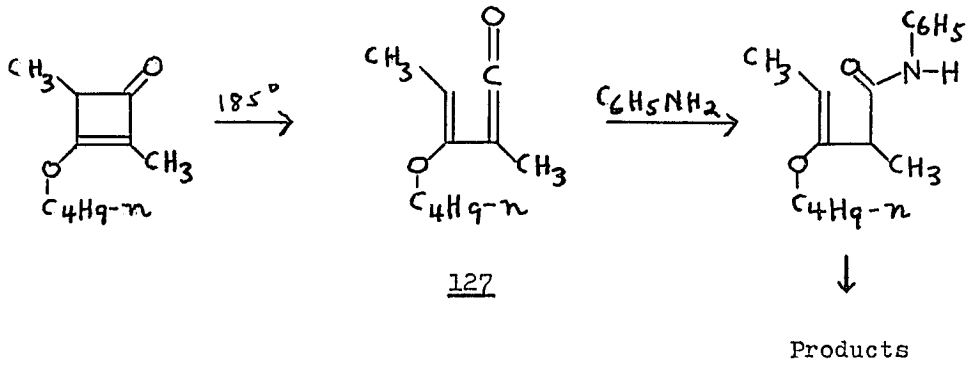
Hydrolysis[63] of 123 or 124 or unchanged dimer 119 would account for the formation of both ketone 122 and part of the acid 118 (scheme 6).

Scheme 6



Ring opening of 124 to give 125 is not unprecedented since Arens postulated a similar intermediate (127) in order to account for the products obtained from the pyrolysis of 2,4-dimethyl-3-butoxycyclobut-2-en-1-one in the presence of aniline[94] (equation 94).

Equation 94



127

Products

It has also been shown that cyclobutenones are thermally unstable, and undergo ring opening at low temperatures to give vinylketenes[95] (e.g. 124 to 125 in scheme 6).

---

(94) J. J. Van Daalen, A. Kraak and J. F. Arens, Rec. Trav. Chim., 80, 810 (1961).
(95a) E. Silversmith, Y. Kitahara and J. D. Roberts, J. Amer. Chem. Soc., 80, 4088 (1958).
(95b) J. E. Baldwin and M. C. McDaniel, ibid., 89, 1537 (1967).

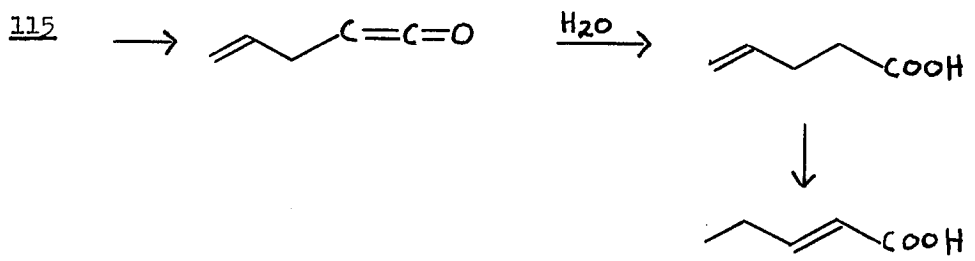
An alternative route which involves the hydrolysis of 124 to ketoacid 126 (scheme 6) is also to be expected since alcoholysis of 1,3-dialkylcyclobut-1-en-2-ol-4-ones have led to good yields of α, γ-disubstituted acetoacetic esters.[96] Alkylidene β-lactone type dimers (e.g. 119 in scheme 6) are known to hydrolyze in a similar manner.[82,97]

Formation of 2-pentenoic acid (117) may occur by isomerization of cyclopropylacetic acid (118) (produced by hydrolysis[63] of cyclopropylketene (115) or trimer 123, as previously discussed; see pyrolysis of ester 114, or by prior rearrangement of cyclopropylketene (115) to allylketene, with subsequent hydrolysis[63] of the ketene to 4-pentenoic acid, followed by isomerization of the acid to 117 (equation 95).

---

(96) Wacker-Chemie G.m.b.H., Brit. 994, 64 (Cl. C. 07c), 1965; Chem. Abstr. 63, P5531c (1965).
(97) S. Piekarski, Compt. Rend., 241, 210 (1955).

Equation 95

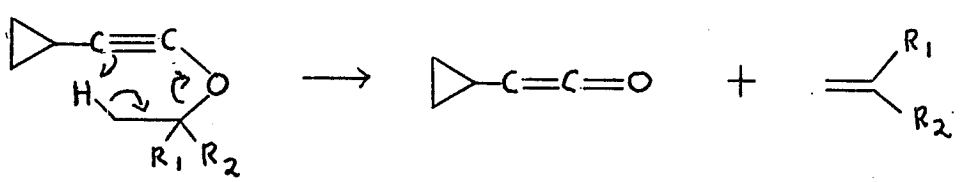


117

Proposal

An attractive source of cyclopropylketene (115) would be the pyrolysis of the cyclopropylacetylenic ether 128 (equation 96).

Equation 96



128 115

$R_1 = R_2 =$ H or CH_3

It has been shown that 1-alkoxy-1-alkynes[98] are thermally unstable and decompose to aldoketenes by elimination of alkene at 80-140°.[94] For instance, pyrolysis of 1-n-butoxy-1-propyne at 130-140° gave methylketene which further reacted with starting material, affording 2-n-butoxy-1,3-dimethylcyclobut-2-en-4-one in 52% yield.[94] The decomposition is a cis-elimination, probably involving a cyclic six-membered transition state[99] (e.g. 128 in equation 96). Arens has noted the following order of thermal stability of 1-alkoxy-1-alkynes: C_2H_5O-, > $i-C_3H_7O-$, > $t-C_4H_9O$.[94]

The thermal instability of 128 may offer the advantage of a clean and efficient method of generating cyclopropylketene (115) in good yield and at low temperatures.

---

(98) For reviews of the chemistry of acetylenic ethers see (a) J. F. Arens, "Ethynyl Ethers and Thioethers as Synthetic Intermediates", Advances in Organic Chemistry, Methods and Results, ed., R. A. Raphael, E. C. Taylor and H. Wynber, Interscience Publishers Inc., New York, N. Y., vol. II, 1960, p. 117-212. (b) T. F. Rutledge, "Acetylenic Compounds", Reinhold Book Corporation, New York, Amsterdam, London, 1968, p. 35-36, (c) T. F. Rutledge, "Acetylenes and Alleneś", Reinhold Book Corporation, New York, Amsterdam, London, 1969, p. 229.

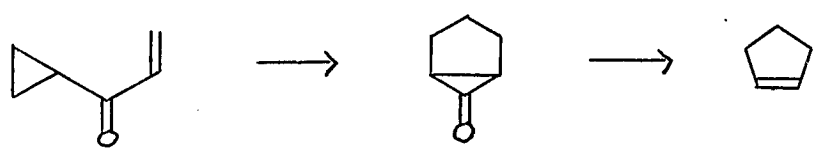
(99) H. Olsman, A. Graveland and J. F. Arens, Rec. Trav. Chim., 83, 301 (1964).

Chapter 5

Thermal Rearrangement of Vinylcyclopropyl Ketone

The relationship between vinylcyclopropyl ketone (129) (equation 86), acylketene 104 (equation 84) and cyclopropylketene (115) (equation 85) was previously noted in Chapter 4. In particular, it was felt that replacing the ketene moiety in acylketene 104 with a vinyl group (as in 129) might not affect the basic course of the reaction, namely the formation of the cyclopropanone 130, which could subsequently decarbonylate to cyclopentene (equation 97).

Equation 97

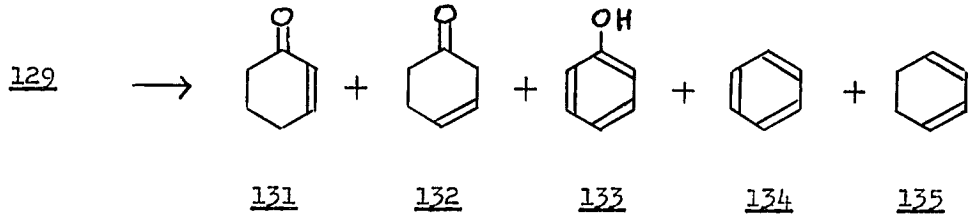


129 130

Results and Discussion

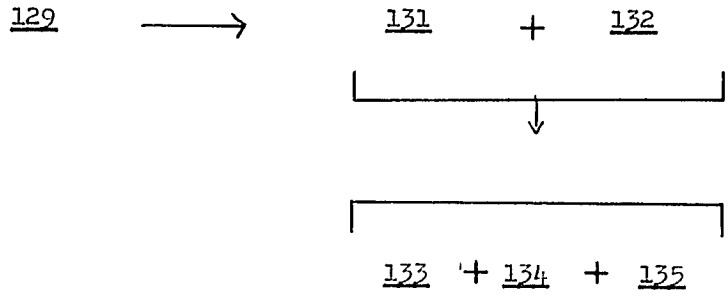
The products of the pyrolysis of vinylcyclopropyl ketone (129) at 610-664° and 0.20-1.00 mm Hg included 2-cyclohexenone (131) (7-27%), 3-cyclohexenone (132) (7-13%), phenol (133) (4-19%), benzene (134) (6-31%) and 1,3-cyclohexadiene (135) (0-7%) (See Table XVII in Experimental Section).

Equation 98



Ketone 129 was pyrolyzed under various conditions. It was observed that when glass wool (which provided longer contact time and more surface area) was used as the packing material, the combined yields of aromatics 133, 134 and 135 exceeded the combined yields of ketones 131 and 132 (See Table XVII, runs 1-4 in Experimental Section). When a mixture of pyrex helices and glass wool (which provided shorter contact time and less surface area) was used as packing material, 131 was the major product (See Table XVII, runs 5 and 6 in Experimental Section). These observations suggest that 129 is initially converted to 131 and 132, which are further converted to 133, 134 and 135 (equation 99).

Equation 99



Compounds 133, 134, 135 and cyclohexene were obtained from the pyrolysis of 2-cyclohexenone (131) over an aluminum catalyst at 400° and 760 mm Hg[100] (a flow system was used). Furthermore, we pyrolyzed a commercial sample of 2-cyclohexenone (131) under conditions which would have converted ketone 129 to the observed products, and obtained 132 (5%), 133 (26%), 134 (37%) and 10% unchanged starting material 131 (See Table XVII, run 7 in Experimental Section).

A possible mode of formation of 133, 134 and 135 is shown in scheme 7. A disproportionation reaction between two molecules of 2-cyclohexenone (131) could give 2-cyclohexen-1-ol (136) and 2,4-cyclohexadien-1-one (137). Enolization of 137 leads to the formation of phenol (133). Dehydration of 136 would yield 1,3-cyclohexadiene (135) which could either lose hydrogen or disproportionate with itself or 2-cyclohexenone (131) to give benzene (134). That 134 did not arise from phenol (133) was shown by pyrolysis of 133 itself at 664° and 0.20-1.00 mm Hg (60% recovery of unchanged 133 was obtained).
Formation of 133, 134 and 135 from 3-cyclohexenone (132) can be accounted for by a similar scheme.

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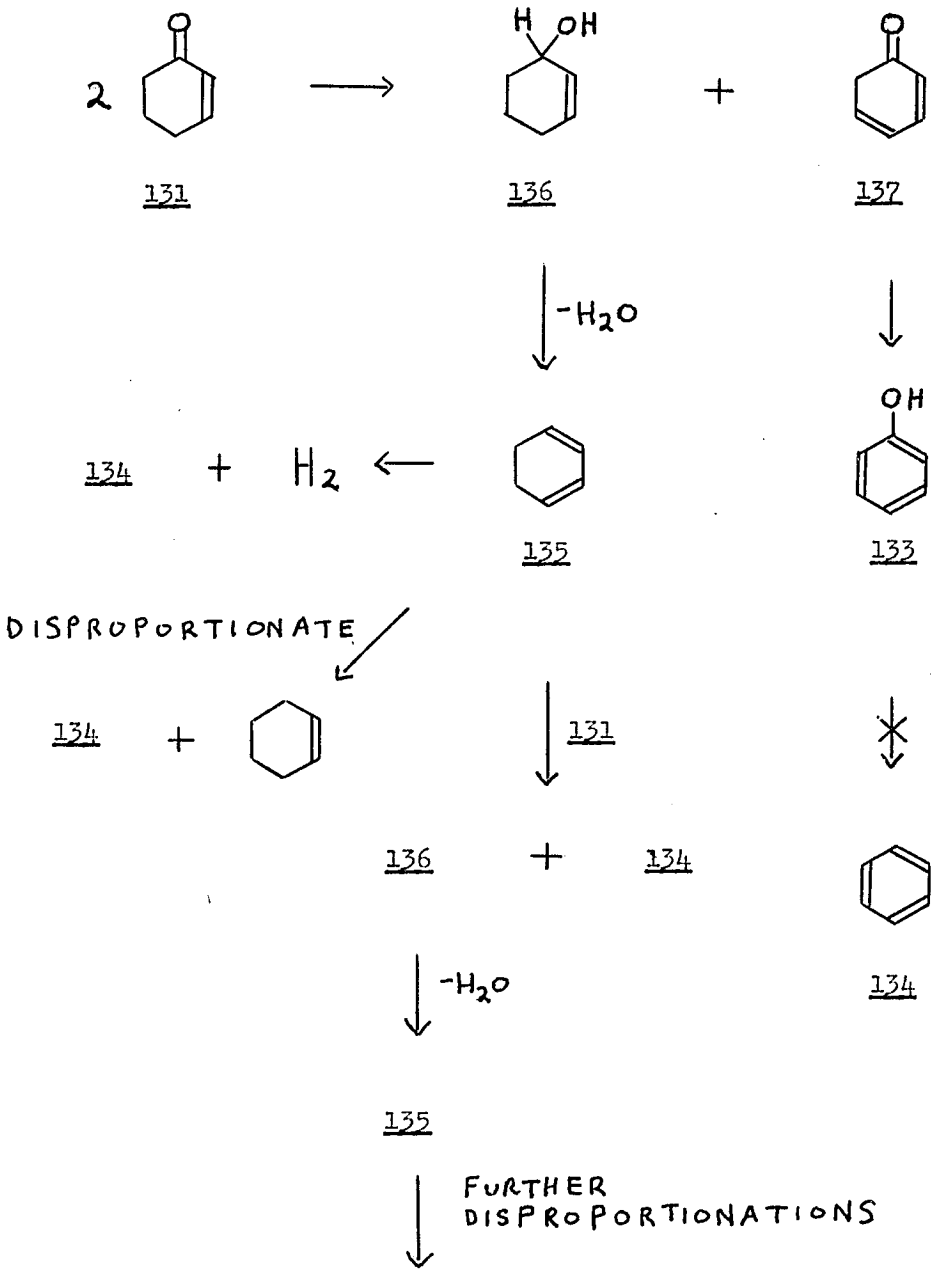
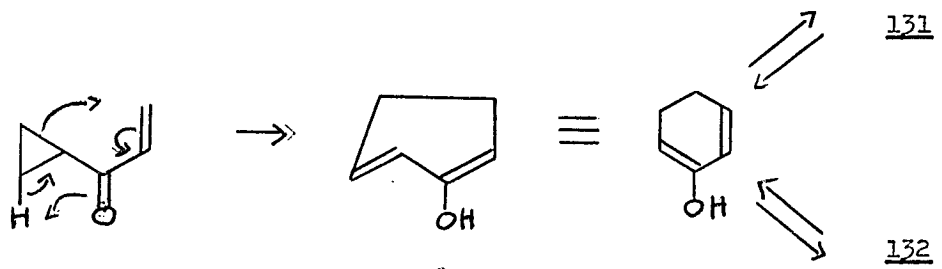
(100) G. Forrest Woods , U. S. Dept. Com. Office Techn. Serv. A. D., 278, 110 (1962); Chem. Abstr. 60, 5381h (1964).

Scheme 7

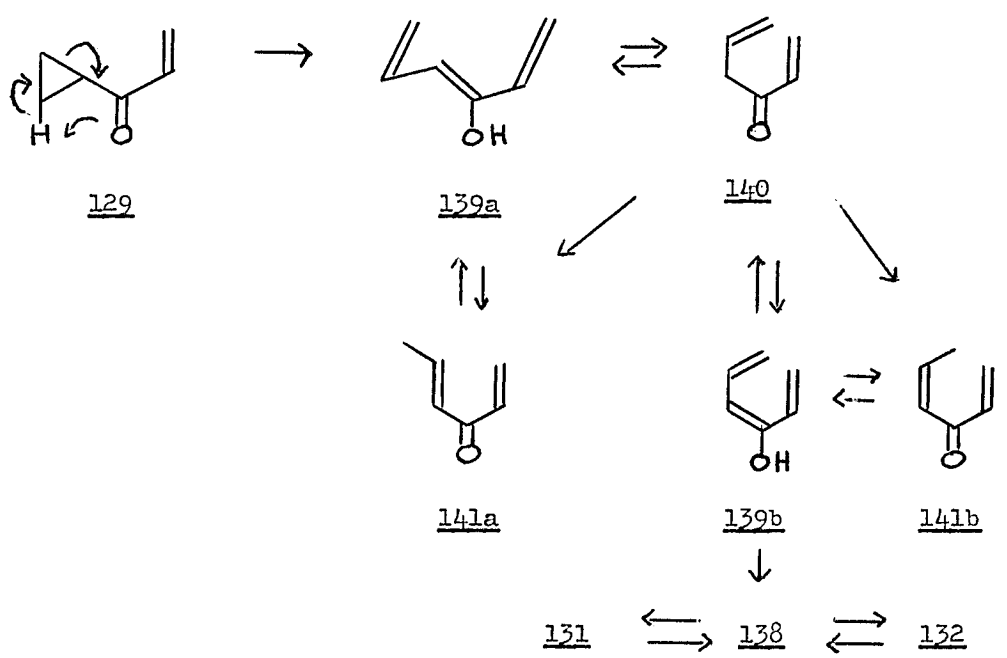


Three mechanisms that can be postulated to account for the formation of ketones 131 and 132 from 129 are shown in schemes 8, 9 and 10.

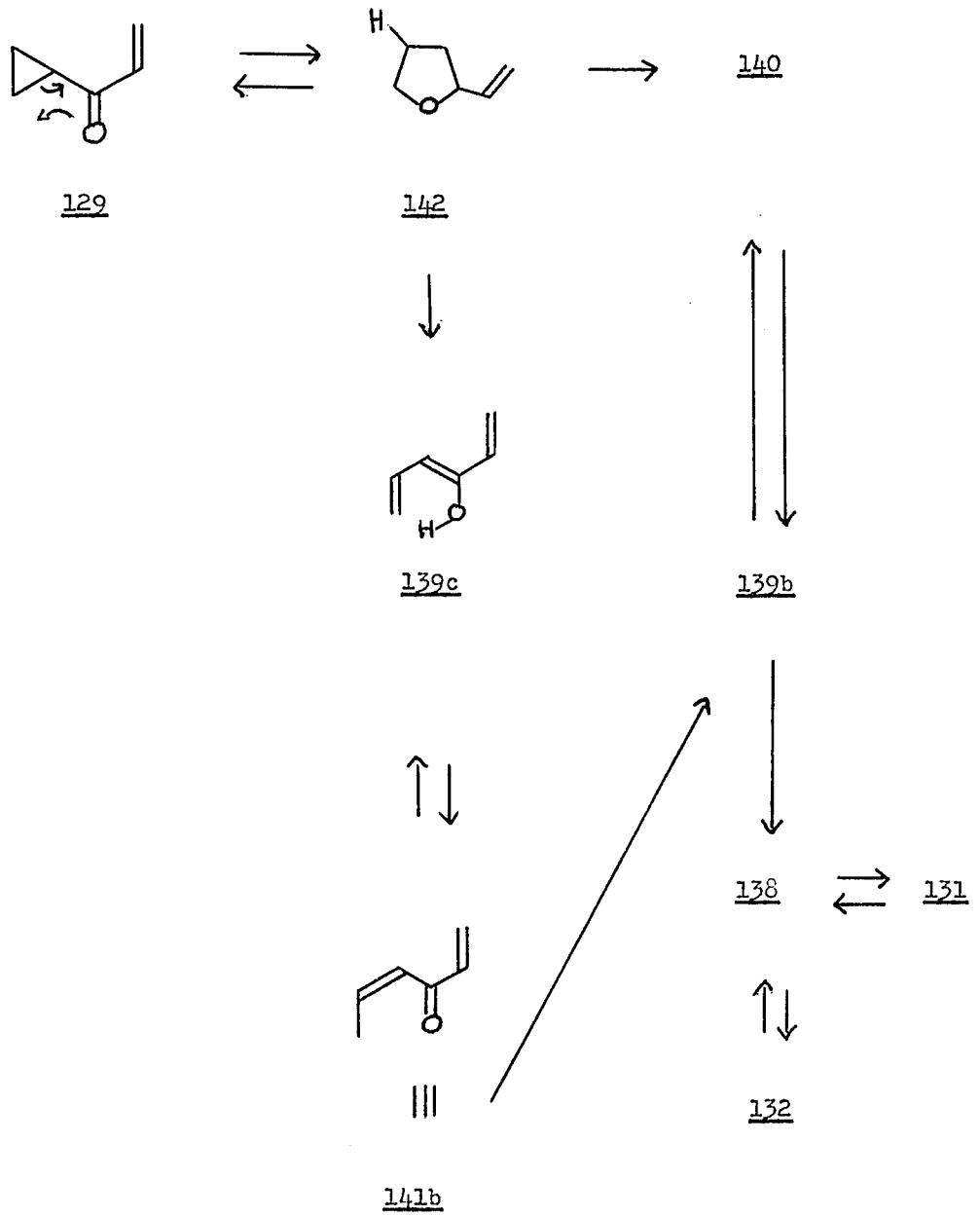
Scheme 8



Scheme 9



Scheme 10



Pyrolysis of a mixture consisting of 44% 140 and 50% 141a,b[101] at 585° and 0.20-1.00 mm Hg gave 131 (31%), 132 (2%), 133 (6%), 134 (3%), 135 (4%) and 14% unchanged starting material 141a,b (See Table XVII, run 9 in Experimental Section). Although this result does preclude entirely the possibility of direct conversion of 129 to 131 and 132 (See scheme 8), it suggests that ketone 129 may have been converted to 131 and 132 through the intermediacy of a dienone 140 or 141a,b or both (See schemes 9 and 10).

Although thermal ring opening of cyclopropyl ketones involving a 1,5-hydrogen shift[102] (equation 100) have been observed, unassisted thermal ring opening of cyclopropyl ketones,[103] or ring openings involving a 1,4-hydrogen shift (See scheme 9, e.g. 129 to 139a), have never been observed.

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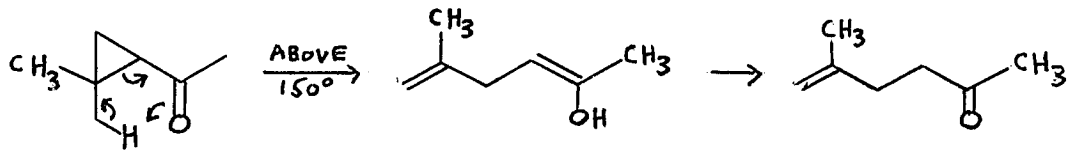
(101) It was not possible to determine from the nmr spectrum of the mixture of 140 and 141 whether we had 141a or 141b. It is possible that both were present, with 141a predominating.

(102) R. M. Roberts and R. G. Landolt, J. Amer. Chem. Soc., 87, 2281, 2282 (1965).

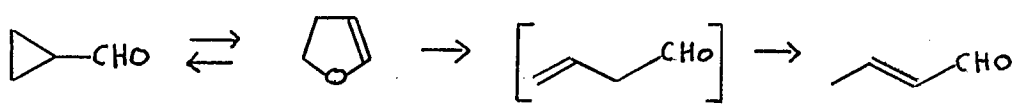
(103) It is of interest that cyclopropyl methyl ketone undergoes ring opening leading to 3-penten-2-one upon irradiation. For references see D. C. Neckers, "Mechanistic Organic Photochemistry", eds., C. A. Vanderwerf and H. H. Sisler, Reinhold Publishing Corporation, New York, N. Y., 1967, p. 57.

Equation 100



Wilson[104] has shown that pyrolysis of cyclopropanecarboxaldehyde (143) at 500° and 760 mm Hg through a tube packed with glass chips gave small amounts of 2,3-dihydrofuran (144) and crotonaldehyde, and mostly unreacted starting material (equation 101). Pyrolysis of 2,3-dihydrofuran (144) under similar conditions gave mostly cyclopropanecarboxaldehyde (143) and a smaller amount of crotonaldehyde. These observations suggested that at high temperature, 143 and 144 were in equilibrium, and crotonaldehyde resulted from the rearrangement of 144[104] (equation 101).

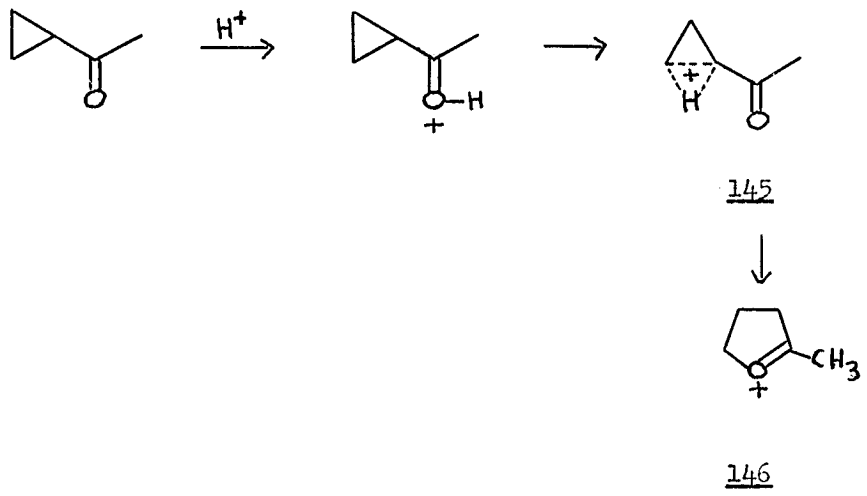
Equation 101



143 144

Nmr studies have shown that cyclopropyl methyl ketone is quantitatively converted to oxonium ion 146 upon treatment with 90% sulfuric acid at 81°.[105] One of the mechanisms suggested by Pittman and McMannus involves the initial protonation of cyclopropyl methyl ketone, with subsequent formation of the edge-protonated cyclopropane intermediate 145 which further rearranges to 146[105] (equation 102).

Equation 102



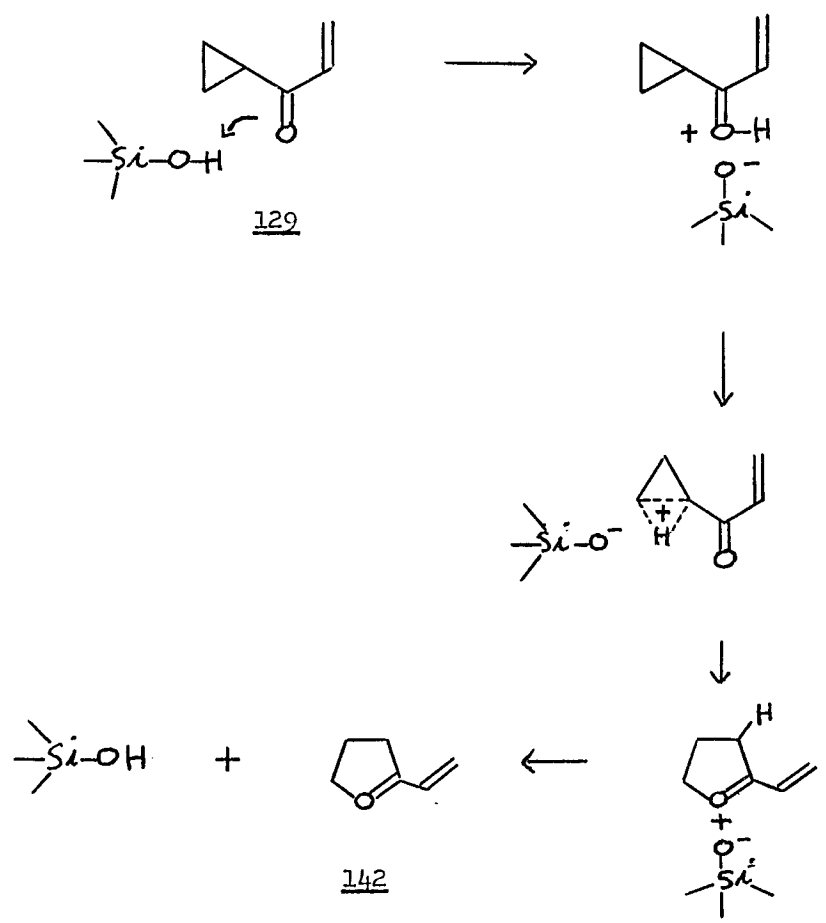
145

146

(104) C. L. Wilson, J. Amer. Chem. Soc., 69, 3002 (1947).
(105) C. U. Pittman and S. P. McMannus, ibid., 91, 5915 (1969).

In view of the above observations, it appears reasonable to suggest that ketone 129 is either directly converted to the dihydrofuran derivative 142 (See scheme 10), or by a pathway which involves catalysis by the silanol groups of the glass surface (equation 103).

Equation 103



Further rearrangement of 142 would lead to the formation of either enol 139c or ketone 140 (See scheme 10). Formation of enol 139b from 139c or 140, with subsequent valence-bond isomerization[106] of 139b would lead to the formation of 138 which could enolize to give ketones 131 and 132[107] (See scheme 10).

Conclusion

The cycloaddition reaction between two olefins leading to a cyclobutane, and the cycloaddition reaction between ketene and an olefin to give a cyclobutanone derivative are considered to be thermally allowed $\pi_{2s}+\pi_{2a}$ reactions, with ketene participating as the π_{2a} component in the latter case.[85] Analysis of the appropriate bonding orbitals for both systems (Fig. 147 and 148) reveals that the ketene molecule possesses a low-lying $\pi^*_{C=O}$ orbital which permits additional bonding between ketene and the olefin component (Fig. 147a) to take place, and therefore greatly enhances the $\pi_{2s}+\pi_{2a}$ process.[85] It is this additional bonding, absent in the reaction path for simple olefins (e.g. Fig. 148), which partly accounts for the formation of cyclobutanones

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(106) For a discussion of valence-bond isomerization of trienes see S. J. Rhoads, "Molecular Rearrangements, Part I", P. deMayo, ed., Interscience Publishers, New York, N. Y., 1963, chap. 11, p. 696.

(107) N. Heap and G. W. Whitham, J. Chem. Soc., B, 164 (1966). The equilibrium between ketones 131 and 132 (See scheme 10) has been demonstrated, and it has been suggested that they equilibrate through the common intermediate 138.

to the exclusion of cyclohexenones when ketenes react with simple dienes.[85]

Reaction of Ketene with an Olefin

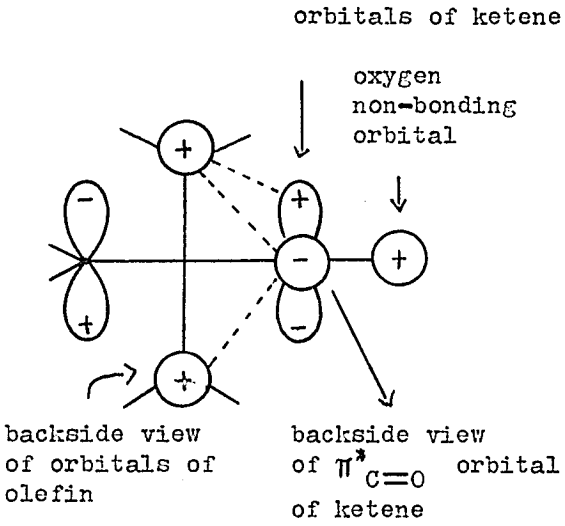


Fig. 147a

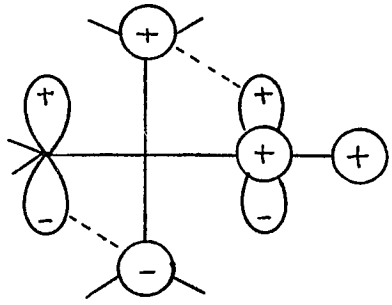


Fig. 147b

Reaction of Two Olefins

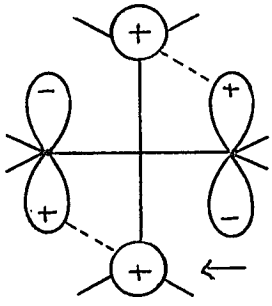


Fig. 148a

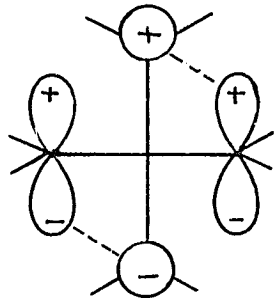
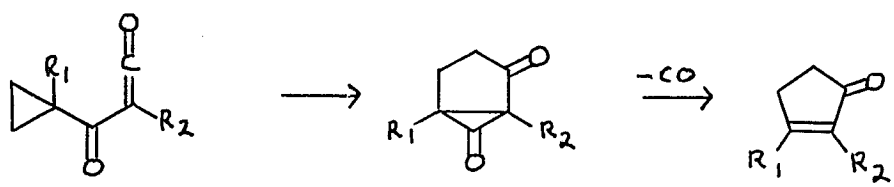


Fig. 148b

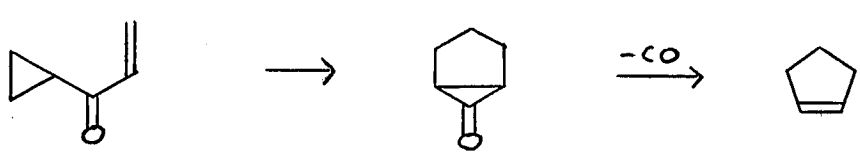
Formation of cyclopropanones 105 and 130 from acylketene 104 (equation 104) and cyclopropyl vinyl ketone (129) (equation 105) may be considered to be thermally allowed $\sigma_{2s} + \pi_{2a}$ processes, with the ketene moiety participating as the π_{2a} component in the former case and an olefin moiety in the latter case.

Equation 104



104 105 99

Equation 105



129 130

Formation of cyclopropanone 130 from 129, a thermally allowed process, does not occur, as evidenced by the absence of cyclopentene in the pyrolyzate of 129. This may partly be attributed to the absence of a low-lying $\pi^*_{C=O}$ orbital in 129, which is present in acylketene 104, and thereby enhances the $\sigma_{2s} + \pi_{2a}$ process, leading to the formation of cyclopropanone 105, by providing additional bonding to the orbitals of the cyclopropane ring.

Experimental Section

All melting points were obtained on a Mel-Temp apparatus, and neither melting points nor boiling points are corrected. Microanalysis were performed by Spang Microanalytical Laboratory, Ann Arbor Michigan. Gas-liquid phase chromatography (glpc) was done with a Varian-Aerograph Model A-700, thermal conductivity apparatus. Areas of glpc records were integrated with a planimeter and adjusted for differing response factors by inclusion of an internal standard. Infrared spectra were determined with a Perkin-Elmer Model 237B, or a Beckman IR-20, grating spectrophotometer. IR values were recorded in Microns (u). Ultraviolet spectra were determined with a Carry Model 14, or Bausch and Lomb Spectronic 505, recording spectrophotometer. U.V. maxima were recorded in nanometers (nm). Proton magnetic resonce spectra were obtained with a Varian Model A60-A, spectrometer. Peak positions were recorded in parts per million using tetramethylsilane as the internal standard, and J values were recorded in Hz. Pyrolysis were done with a Heavy-Duty Electric Co Type 77-T (600 watt, "Multi-Unit") tube oven.

Materials

Cyclopropyl methyl ketone, cyclopentanone, isopropenyl acetate, triethylorthoformate, trimethylorthoformate, 3-butenonitrile, methylene iodide, p-bromoaniline, 3-methyl-2-cyclopentenone, dialkyl carbonates, methyl iodide, benzaldehyde, 2-acetylbutyrolactone, paraformaldehyde, dimethylamine hydrochloride, acrolein, allyl chloride and anisole were

obtained from the Aldrich Chemical Company, Cedar Knolls, New Jersey. The liquid materials were distilled prior to use. 2-Cyclopentenone was obtained from K. and K. Laboratories, Plainview, New York, and was distilled and then further purified by preparative glpc.[108] Ethyl 2-cyclopentanone-1-carboxylate (2-carbethoxycyclopentanone) was obtained from K. and K. Laboratories and was distilled prior to use.

Pyrex Raschig rings and helices were obtained from the Ace Glass Company, Vineland, New Jersey; pyrex glass wool (Corning 3950) was obtained from The Scientific Glass Apparatus Company, Bloomfield, New Jresey. Pumice stone (4-8 mesh) was obtained from Matheson, Coleman and Bell. Catalytic activity of the glass surface appeared to be unaltered by either acid or base washing (followed by thorough rinsing with distilled water), and were simply washed and oven dried prior to use. The vycor tubes were manufactured by Mr. Carl Schuman, Columbia University, New York, N. Y. The tubes were packed with fresh packing material for each run. 2,4-Dinitrophenylhydrazone derivatives were prepared by the procedure of Shriner, Fuson and Curtin.[109]

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(108) A 5ft X 0.25 inch column packed with 60/80 Chromosorb W coated with 20% by weight of SE-30 silicone gum rubber was used for both analysis and isolation. The internal standard used was 4-methylcyclohexanone.

(109) R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds", John Wiley and Sons Inc., 5th edition, New York, N. Y., 1964.

General Pyrolysis Procedure

The material to be pyrolyzed was introduced into the top end of a 37 X 2.5 cm vycor tube packed with a specified packing material, and heated over a length of 30 cm by a tube oven mounted horizontally at a 10-15° angle. The temperature was measured by a thermocouple at the center of the tube oven prior to insertion of the pyrolysis tube, which was temperature equilibrated for at least 30 minutes prior to use. The maximum temperature range at the center of the tube oven was ± 10° prior to pyrolysis. The temperature was approximately 50-70° lower at a distance of 15 cm from the center. When pyrolysis was conducted at reduced pressure, the material to be pyrolyzed was degassed prior to pyrolysis, and the pressure was measured by a Mcleod gage on the line between the cold trap and the mechanical pump. When pyrolysis was conducted at atmospheric pressure with nitrogen as the carrier gas, the flow rate of nitrogen was equilibrated for at least 15 minutes. The product vapor was collected in a dry ice-trichloroethylene, dry ice-acetone or liquid nitrogen cooled trap. The products of pyrolysis were isolated for identification by preparative glpc of the pyrolyzate. On small runs, the yields of products were estimated by glpc using an appropriate internal standard. On preparative runs, the pyrolyzate was distilled through a Teflon Annular spinning band column, and yields were based on isolated material.

Except for the method of introducing the material to be pyrolyzed, and the type of packing material used for individual pyrolyses, the

procedure mentioned above applies to all of the pyrolyses which will be mentioned.

Materials Mentioned in Chapter 2

1-Acetoxy-1-cyclopropylethylene (93a) was prepared from cyclopropyl methyl ketone and isopropenyl acetate by a modification of the procedure of Hagemeyer and Hull.[110] 1-Acetoxycyclopentene-1 (94a) was prepared from cyclopentanone and isopropenyl acetate by the procedure of Goodman.[111] 1,1-Dibutoxy-1-cyclopropylethane was prepared from cyclopropyl methyl ketone and tri-n-butylorthoformate by the procedure of Julia.[112] 1-Butoxycyclopentene-1 (94b) was prepared from cyclopentanone and tri-n-butylorthoformate by adaptation of the procedure of MacKenzie and Stocker.[113] Ketals 1,1-dimethoxy-1-cyclopropylethane and 1,1-dimethoxycyclopentane were prepared from cyclopropyl methyl ketone, cyclopentanone and trimethylorthoformate by a modification of the procedure of MacKenzie and Stocker.[113] 1-Butoxy-1-cyclopropylethylene (93b), 1-methoxy-1-cyclopropylethylene (93c) and 1-methoxycyclopentene-1 (94c) were prepared by dealcoholysis of their corresponding ketals over Woelm alumuna (activity 1). 1-Cyclopropyl-1,3-butandione (95) was prepared by acylation of cyclopropyl methyl ketone with ethyl acetate.

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(110) H. J. Hagemeyer and D. C. Hull, Ind. Eng. Chem., 41, 2920 (1949).
(111) L. Goodman, A. Benitz, C. D. Anderson and B. R. Baker, J. Amer. Chem. Soc., 80, 6587 (1958).
(112) S. Julia, M. Julia, Song-Yu Tchen and P. Graffin, Bull. Soc. Chim. France, 3207 (1964).
(113) C. A. MacKenzie and J. H. Stocker, J. Org. Chem., 20, 1695 (1955).

1-Acetoxy-1-cyclopropylethylene (93a)

A mixture of 30.0 g (0.36 mole) of cyclopropyl methyl ketone, 72.0 g (0.72 mole) of isopropenyl acetate, 150 ml of anhydrous benzene and 18 drops of concentrated sulfuric acid was subjected to distillation through a Teflon annular spinning band column at a reflux ratio of 9:1. The distillate which consisted mainly of benzene and acetone, boiled at 74° (760 mm). After two hours of distillation, the reaction mixture was cooled to room temperature, and an additional 150 ml of benzene and 18 drops of concentrated sulfuric acid were added. The distillation was continued for two hours after which time the above procedure was repeated, and the distillation was allowed to proceed overnight at a reflux ratio of 9:1. The reaction mixture was washed with saturated sodium bicarbonate, dried over magnesium sulfate, and benzene and excess isopropenyl acetate were removed through a Teflon annular spinning band column at atmospheric pressure. Vacuum distillation of the residue furnished 18.0 g (41%) of 93a, bp 60° (30 mm) (lit.[114] bp 78-83°(54 mm)).

Anal. Calcd. for $C_7H_8O_2$: C, 66.65; H, 7.99. Found: C, 66.72; H, 8.03.

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(114) J. A. Landgrebe and L. W. Becker, J. Amer. Chem. Soc., 90, 395 (1968).

Enol acetate 93a has ir (CCl_4) 3.22 (vinyl C-H), 3.23 (cyclopropyl C-H), 5.58 (C=O), 6.04 (C=C) and 11.42 (terminal vinyl) u; (consistent with lit.[114] ir values); nmr, δ^{CDCl_3} 0.48-0.87 (m, 4, cyclopropyl CH_2), 1.33-1.86 (m, 1, cyclopropyl methine), 2.23 (s, 3, $-O-\overset{O}{\overset{\|}{C}}-CH_3$), 4.47-4.89 (d, 1, J= 7Hz, vinyl H) and 4.89-4.98 (a doublet which is further split into a doublet of doublets by cyclopropyl methine, 1, J= 3Hz, vinyl H) (consistent with lit.[114] nmr values).

1-Acetoxycyclopentene-1 (94a)

Enol acetate (94a) was prepared by Goodman's procedure[111] using 10.0 g (0.12 mole) of cyclopentanone, 20.0 g (0.20 mole) of isopropenyl acetate and 2drops of concentrated sulfuric acid. Workup gave 10.0 g (66%) of 94a, bp 62° (30 mm) (lit.[111] bp 84-87° (69 mm)).

Enol acetate 94a has ir (CCl_4) 3.25 (vinyl C-H), 5.70 (C=O), 6.02 (C=C) and 8.30, 9.95 (C-O-C) u (consistent with lit.[111] ir values); nmr, δ^{CCl_4} 1.60-2.67 (m, 6, ring CH_2), 2.07 (s, 3, CH_3COO) and 5.32-5.46 (m, 1, vinyl H).

1,1-Dibutoxy-1-cyclopropylethane

This ketal was prepared by Julia's procedure[112] using 41.0 g (0.49 mole) of cyclopropyl methyl ketone, 88.0 g (0.59 mole) of triethylorthoformate, 222.0 g (3 moles) of n-butanol and 0.60 g of p-toluenesulfonic acid monohydrate. Workup of the reaction mixture gave 56.1 g (54%) of 1,1-dibutoxy-1-cyclopropylethane, bp 52° (0.50 mm) (lit.[112] bp 72-75° (0.90 mm)).

Anal. Calcd. for $C_{13}H_{26}O_2$: C, 72.85; H, 12.23. Found: C, 73.00; H, 12.21.

1,1-Dibutoxy-1-cyclopropylethane has ir (CCl_4) 3.25 (cyclopropyl C-H), and 9.35 (C—O) u (consistent with lit.[112] ir values); nmr, δ^{CDCl_3} 0.20-0.60 (m, 4, cyclopropyl CH_2), 0.68-1.11 (triplet (centered at 0.92) superimposed on a multiplet, 7, J for triplet = 5Hz, $(\underline{CH_3}CH_2CH_2CH_2O)_2$- and cyclopropyl methine), 1.17-1.82 (singlet (centered at 1.33) superimposed on a multiplet, 11, CH_3-$\overset{|}{C}$-, and $(CH_3\underline{CH_2}\underline{CH_2}CH_2O)_2$) and 3.14-3.95 (m, 4, $(CH_3CH_2CH_2\underline{CH_2}O)_2$-).

2,4-Dinitrophenylhydrazone Derivative: 154-55° (lit.[112] mp of 2,4-DNP, 154°).

1,1-Dimethoxy-1-cyclopropylethane

A mixture consisting of 50.7 g (0.60 mole) of cyclopropyl methyl ketone, 80.0 g (0.76 mole) of trimethylorthoformate, 200.0 g (6.24 moles) of anhydrous methanol, 250 ml of benzene and 200 mg of p-toluenesulfonic acid monohydrate was subjected to a slow distillation through a 30 cm vigreux column under nitrogen. The distillate (300 ml), bp 54° (760 mm), which consisted of benzene and methanol, was collected over a period of 4 hours. The reaction mixture was cooled to room temperature, an additional 100.0 g (3.16 moles) of methanol, 60 ml of benzene and 40 mg of p-toluenesulfonic acid monohydrate were added, and the distillation was continued for 2.5 hours during which time 150 ml of distillate were collected. The reaction mixture was cooled, neutralized

with 0.02 mole of sodium methoxide, and then poured into 250 ml of water. The aqueous layer was extracted twice with 80 ml portion of benzene which were combined with organic layer and dried over anhydrous potassium carbonate. Benzene and excess trimethylorthoformate were removed through a 30 cm vigreux column, and the residue was vacuum distilled to give 40.3 g (52%) of 1,1-dimethoxy-1-cyclopropylethane, bp 63-5° (90 mm).

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.67; H, 10.91.

1,1-Dimethoxy-1-cyclopropylethane has ir (CCl_4) 3.22 (cyclopropyl C-H), 3.52 (CH_3O) and 8.10-9.50 (C—O) u; nmr, δ^{CDCl_3} 0.25-0.58 (m, 4, cyclopropyl CH_2), 0.70-1.10 (m, 1, cyclopropyl methine), 1.28 (s, 3, CH_3-$\overset{1}{C}$-) and 3.23 (s, 6, $(CH_3O)_2$-C-).

2,4-Dinitrophenylhydrazone Derivative: 153.5-54° (lit.[115] mp of 2,4-DNP of authentic cyclopropyl methyl ketone, 150°).

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(115) H. D. Cheronis, J. B. Entrikin and E. M. Hodnett, "Semimicro Qualitative Organic Analysis, The Systematic Identification of Organic Compounds", 3rd edition, Interscience Publishers, New York, London, Sydney, 1964, p. 892.

1,1-Dimethoxycyclopentane

This ketal was prepared by a procedure similar to that used for the preparation of 1,1-dimethoxy-1-cyclopropylethylene. Using 10.0 g (0.12 mole) of cyclopentanone, 12.7 g (0.12 mole) of trimethylorthoformate, 100.0 g (3.31 moles) of methanol, 100 ml of benzene and 25 mg of p-toluenesulfonic acid monohydrate, 11.8 g (76%) of 1,1-dimethoxycyclopentane,[116] bp 78° (95 mm) was obtained.

1,1-Dimethoxycyclopentane has ir (CCl_4) 3.50 (CH_3-O) and 8.40-9.54 (C—O) u; nmr, δ^{CCl_4} 1.65 (s, 8, ring CH_2) and 3.14 (s, 6, $(CH_3O)_2$-C-).

2,4-Dinitrophenylhydrazone Derivative: 140-42° (lit. mp of 2,4-DNP of cyclopentanone, 142°,[109] 146°[115]).

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(116) M. Verzele, M. Acke and M. Anteneunis, J. Chem. Soc., 5598 (1963). The authors have prepared this ketal and the corresponding enol ether 94c, but they did not report any physical or spectral data for them.

1-Butoxy-1-cyclopropylethylene (93b)

A mixture consisting of 22.9 g (0.11 mole) of 1,1-dibutoxy-1-cyclopropylethane and 0.6 g of Woelm alumuna (activity 1) was heated at 13 mm Hg with distillation of enol ether 93b and n-butanol (bp 55-60° (13 mm)) as they were formed. Redistillation of the 11.1 g of distillate through a Teflon annular spinning band column gave 1.7 g of n-butanol, bp 33° (13 mm), 1.8 g of unreacted ketal, bp 90-100° (13 mm) and

5.7 g (41%) of 93b, bp 54-5° (13 mm) (lit.[112] bp 55° (13 mm)).

Anal. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.80; H, 11.48.

Enol ether 93b has ir (CCl_4) 3.22, 3.33 (vinyl C-H), 3.24 (cyclopropyl C-H), 6.10 (C=C) and 11.25 (terminal vinyl) u (consistent with lit.[112] ir values); nmr, δ^{CDCl_3} 0.37-1.82 (m, 12, cyclopropyl CH_2, cyclopropyl methine and $\underline{CH_3CH_2CH_2CH_2}O$-), 3.18-3.95 (triplet (centered at 3.63) superimposed on vinyl multiplet, 4, J for triplet = 7Hz, $CH_3CH_2CH_2\underline{CH_2}O$- and -$\overset{|}{C}$=$\underline{CH_2}$).

2,4-Dinitrophenylhydrazone Derivative: 154-5° (lit.[112] mp of 2,4-DNP, 154°).

1-Methoxy-1-cyclopropylethylene (93c)

Woelm alumina (2.26 g, activity 1) was placed at the center portion of a vycor tube and the remainder of the tube was packed with Pyrex glass wool. 1,1-Dimethoxy-1-cyclopropylethane (20.0 g) was distilled at 3.5-4.0 mm Hg and at a rate of 5.0 g per hour through the packed tube which was pre-heated to 210°. The pyrolyzate (19.2 g) which was collected in a liquid nitrogen cooled trap, was dried over anhydrous potassium carbonate, and distilled through a Teflon annular spinning band column to give 4.9 g of methanol, bp 56° (760 mm) and 10.2 g (68%) of 93c, bp 90-5° (760 mm).

Enol ether 93c has ir (CCl_4) 3.20 (vinyl C-H), 3.22 (cyclopropyl C-H), 3.52 (CH_3-O), 6.11 (C=C) and 11.90 (terminal vinyl) u; nmr, δ^{CCl_4} 0.38-0.98 (m, 4, cyclopropyl CH_2), 1.16-1.67 (m, 1, cyclopropyl methine), 3.50 (s, 3, CH_3O-) and 3.68-3.89 (two doublets, 2, J= 2Hz, -C=CH_aH_b).

2,4-Dinitrophenylhydrazone Derivative: 152-3° (lit.[115] mp of 2,4-DNP of cyclopropyl methyl ketone, 150°).

1-Methoxycyclopentene-1 (94c)

Enol ether 94c was prepared by a procedure similar to that used for the preparation of 93c. From 8.7 g of 1,1-dimethoxycyclopentane, 2.9 g (44%) of 94c,[116] bp 108° (760 mm) was obtained.

Enol ether 94c has ir (CCl_4) 3.25, 3.33 (vinyl C-H), 3.51 (CH_3-O) and 6.09 (C=C) u; nmr, δ^{CDCl_3} 1.22-2.22 (m, 6, ring CH_2), 3.27 (s, 3, CH_3-O-) and 4.00-4.22 (m, 1, vinyl H).

2,4-Dinitrophenylhydrazone Derivative: 141-41.5° (lit. mp of 2,4-DNP of cyclopentanone, 142°,[109] 146°[115]).

1-Butoxycyclopentene-1 (94b)

MacKenzie's procedure[113] for the preparation of 1-butoxycyclohexene-1 was adapted to the preparation of 94b. Using 8.4 g (0.10 mole) of cyclopentanone, 35.0 g (0.15 mole) of tri-n-butylorthoformate, 22.2 g (0.30 mole) of n-butanol and 0.05 g of p-toluenesulfonic acid monohydrate, 7.6 g (54%) of 94b, bp 37° (1.50 mm) was obtained.

Enol ether 94b has ir (CCl_4) 3.26 (vinyl C-H) and 6.10 (C=C) u; nmr, δ^{CDCl_3} 0.76-2.10 (triplet (centered at 0.93) superimposed on multiplet, 9, J for triplet = 6Hz, $\underline{CH_3}\underline{CH_2}\underline{CH_2}CH_2O$- and ring CH_2), 2.10-2.55 (m, 4, ring allylic CH_2), 3.74 (t, 2, J= 6Hz, -O$\underline{CH_2}CH_2$-) and 4.42 (broad s, 1, vinyl H).

2,4-Dinitrophenylhydrazone Derivative: 141-41.5° (lit. mp of 2,4-DNP of cyclopentanone, 142°,[109] 146°[115]).

1-Cyclopropyl-1,3-butandione (95)

Cyclopropyl methyl ketone (25.0 g, 0.30 mole) was added dropwise to a stirred suspension of 14.3 g (0.60 mole) of sodium hydride (50% dispersion in mineral oil) in 800 ml of anhydrous benzene at room temperature under nitrogen. The mixture was heated to 40° during which time hydrogen evolved rapidly. When hydrogen evolution ceased, 52,8 g (0.60 mole) of ethyl acetate was added dropwise and the resulting mixture was stirred overnight at room temperature under nitrogen, then cautiously

acidified with dil. hydrochloric acid. The separated organic layer was washed with saturated sodium bicarbonate and then with water, and finally dried over magnesium sulfate. Benzene and unchanged ethyl acetate were removed on a Teflon annular spinning band column, and the residue was distilled to give 17.3 g (46%) of 95, bp 48° (3mm) (lit.[117] bp 78-9° (8 mm)).

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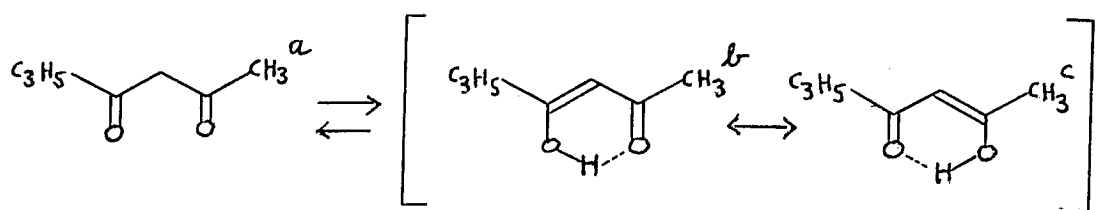
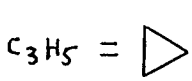
(117) G. W. Cannon and H. L. Whidden, J. Org. Chem., 17, 685 (1952).

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.67; H, 8.06.

Diketone 95 has ir (CCl_4) 2.78-3.12 (O-H of enol), 3.25 (cyclopropyl C-H), and 6.23 (C=O) u; nmr, δ^{CDCl_3} 0.75-1.18 (m, 4, cyclopropyl CH_2), 1.18-1.85 (m, 1, cyclopropyl methine), 2.02 (s, 2.37, CH_3^b and CH_3^c), 2.24 (s, 0.81, CH_3^a), 3.67 (s, 0.41, $-CO\underline{CH_2}CO-$) and 5.60 (s, 0.69, vinyl H) (enol content = 69%). Ratio of 95a to (95b + 95c) is 1:3.



95a 95b 95c

C_3H_5 = 

Pyrolysis of 1-Acetoxy-1-cyclopropylethylene (93a) at 760 mm Hg

A stream of nitrogen was bubbled through 93a (2.1 to 3.6 g used) while it was maintained at a certain temperature (see Table II). The vapor of 93a was swept into the pyrolysis tube which was packed with Raschig rings.

Table II

Pyrolysis of 1-Acetoxy-1-cyclopropylethylene (93a)

Run	°C	Pot °C	Nitrogen Flow Rate[a] in ml per min	Products[b] % Yield 95	94a	96	Unchanged 93a	Total Pyrolyzate Wt. %
1	369	85-7	193	41	3	17	72	94
2	407	139-40	93	47	3	12	38	75
3	415	145-60	47	70	4	12	2	85

[a]The flow rate of nitrogen was measured with a previously calibrated flowmeter. [b]Yields of products and unchanged 93a were estimated by glpc[118] using diethylmalonate as the internal standard. Yields of products have been corrected for unreacted 93a.

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(118) A 20ft X 3/8 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L at 110 degrees with a flow rate of helium of 170 ml per min. was used for analysis and collection.

Table III

Retention Times of Acetic Acid, Cyclopropyl Methyl Ketone (96), 1-Acetoxy-1-cyclopropylethylene (93a), 1-Acetoxycyclopentene-1 (94a) and 1-Cyclopropyl-1,3-butandione (95)(min.)[118]

Acetic Acid	6.2
96	9.0
93a	23.7
94a	40.0
95	70.0

Products of Pyrolysis of 1-Acetoxy-1-cyclopropylethylene (93a)

Acetic acid, cyclopropyl methyl ketone (96) and 1-acetoxy-cyclopentene-1 (94a) were identified by comparison of their glpc retention times and their ir spectra with those of authentic samples. 1-Cyclopropyl-1,3-butandione (95) was identified by comparison of its glpc retention time, ir and nmr spectra with those of an authentic sample.

Pyrolysis of 1-Butoxy-1-cyclopropylethylene (93b) at 760 mm Hg

Enol ether 93b (3.0 g) was dripped at a rate of one drop per minute into the top end of a vycor tube packed with Pyrex Raschig rings and pre-heated to 454°. A stream of nitrogen at a flow rate of 100 ml per minute, was used to keep the vapor of 93b flowing through the tube. The pyrolyzate, 1.86 g (62% recovery), was analysed by glpc[119] using

diethylmalonate as the internal standard. The products included cyclopropyl methyl ketone (96) (81%), n-butanol (7%) and unchanged 93b (15%).

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(119) A 20ft X 3/8 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L at 150 degrees with a flow rate of helium of 140 ml per minute was used for analysis and collection.

Table IV

Relative Retention Times[119] of Unknown (possibly 1-butene), n-Butanol, Cyclopropyl Methyl Ketone (96) and 1-Butoxy-1-cyclopropylethylene (93b).

Unknown	1.0
n-Butanol	1.7
96	2.1
93b	9.3

Products of Pyrolysis of 1-Butoxy-1-cyclopropylethylene (93b)

Cyclopropyl methyl ketone (96) and n-butanol were identified by comparison of their glpc retention times and ir spectra with those of authentic samples.

Pyrolysis of 1-Methoxy-1-cyclopropylethylene (93c)

Pyrolysis were conducted using 1.14 to 1.50 g of 93c. The methods used ti introduce 93c into the pyrolysis tube are mentioned in Table V.

Table V

Pyrolysis of 1-Methoxy-1-cyclopropylethylene (93c)

Run	Packing Material[a]	°C	Products:[b] % Yield 94c	97	96	CH_3OH	93c	Total Pyrolyzate Wt. %	Total Wt. %[c] Accounted for
1[d]	A	397	12	7	24	10	23	74	77
2[d]	B[f]	500	10	3	9	7	7	48	57
3[d]	C	476	4	2	17	22	0	45	61
4[e]	C[f]	560	26	4	18	10	36	84	80
5[e]	C[f]	588	23	7	25	10	44	85	87
6[e]	C	(560, 575)[g]	31	7	23	18	37	80	96
7[e]	C	535	30	6	21	11	40	79	93

[a]A: 6 X 6 mm Pyrex Raschig Rings; B: 6 mm Pyrex helices; C: Pyrex glass wool. [b]Yields of products and unchanged 93c were estimated by glpc[120] using 2-pentanone as the internal standard. Yields of products have been corrected for unchanged 93c. [c]Represents total weight of material that has been accounted for by glpc.[120]

[d]Enol ether 93c was dripped into the pyrolysis tube at 760 mm Hg while a stream of nitrogen was used to keep the vapor of 93c flowing through the tube. The corresponding flow rates of nitrogen for runs 1, 2 and 3 were: 25, 10 and 35 ml per min. [e]Enol ether 93c was introduced into the pyrolysis tube at 31 mm Hg (run 4) and 1-3 mm Hg (runs 5-7) by distillation at room temperature. [f]Packing material was washed with saturated sodium bicarbonate and rinsed with water until the washings indicated a PH of 10. [g]Enol ether 93c was passed through two tubes which were connected in series.

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(120) A 20ft X 3/8 inch column packed with 60/80 Chromosorb W coated with 20% by weight Apiezon L at 110 degrees with a flow rate of helium of 153 ml per min. was used for analysis and collection.

Table VI

Retention Times of Methanol, Cyclopropyl Methyl Ketone (96), Cyclopentanone (97), 1-Methoxy-1-cyclopropylethylene (93c) and 1-Methoxycyclopentene-1 (94c) (min.).[120]

Methanol	1.3
96	5.3
93a	7.0
97	8.5
94c	10.6

Products of Pyrolysis of 1-Methoxy-1-cyclopropylethylene (93c)

Methanol, cyclopropyl methyl ketone (96), cyclopentanone (97) and 1-methoxycyclopentene-1 (94c) were identified by comparison of their glpc retention times and ir spectra with those of authentic samples.

Materials Mentioned in Chapter 3

Ethyl 3-cyclopropyl-3-oxopropanoate (98a), ethyl 3-(1'-methylcyclopropyl)-3-oxopropanoate (98b) and ethyl 3-cyclopropyl-3-oxo-2-methylpropanoate (98c) were prepared by carbethoxylation of cyclopropyl methyl ketone (100a), 1-methylcyclopropyl methyl ketone (100b) and cyclopropyl ethyl ketone (100c), respectively, using a slight modification of the procedure of Johnson.[121]

Ethyl 3-(1'-methylcyclopropyl)-3-oxo-2-methylpropanoate (98d) was prepared from 98c, and was freed of traces of 98c by treatment with benzaldehyde. Ethyl 3-cyclopropyl-3-oxo-2,2-dimethylpropanoate (112) was prepared by exhaustive methylation of 98c. Thiouracil derivatives were prepared by the appropriate modification of the procedure of Spitzmiller.[122]

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(121) S. F. Brady, M. A. Ilton and W. S. Johnson, J. Amer. Chem. Soc., 90, 2882 (1968).
(122) E. R. Spitzmiller, ibid., 69, 2073 (1947).

Ethyl 3-Cyclopropyl-3-oxopropanoate (98a)

Ketoester 98a was prepared by modification of the procedure of Johnson[121] using 25.0 g (0.30 mole) of cyclopropyl methyl ketone, in 70 ml of anhydrous ether and 1 ml of absolute ethanol with a mixture of 55.2 g (1.15 moles) of sodium hydride (50% dispersion in mineral oil) and 260.0 g (2.20 moles) of diethyl carbonate in 300 ml of anhydrous ether. After stirring at room temperature for 36 hrs., ethanol was added to the ice-cooled reaction mixture and the resulting mixture was acidified with dil. hydrochloric acid. The aqueous layer was extracted several times with 100 ml portions of ether which were combined with the organic layer, washed with saturated sodium bicarbonate, dried over magnesium sulfate, and concentrated under reduced pressure to an oil which was distilled, affording 35.0 g (75%) of ketoester 98a, bp 70° (2.8 mm) (lit.[123] bp 99-101° (11 mm)) which was 99.5% pure[108] after one distillation. Repetition of this procedure gave ketoester 98a in 82% after one distillation.

(123) M. Jackman, A. J. Bergman and S. Archer, J. Amer. Chem. Soc., 70, 497 (1948).

Methyl 3-Cyclopropyl-3-oxopropanoate (98a, methyl ester)

Replacement of the diethyl carbonate by 200.0 g (2.20 moles) of dimethylcarbonate in the procedure used for 98a, gave, after 72 hrs. stirring at room temperature and workup 32.0 g (75%) of 99.5% pure[108] 98a, methyl ester after one distillation, bp 58° (1.5 mm). Stirring for 24 hrs. reduced the yield to 56%.

Anal. Calcd. for $C_7H_{10}O_3$: C, 59.14; H, 7.09. Found: C, 59.17; H, 7.03.

Ethyl ester 98a has ir (CCl_4) 5.75 (ester C=O), 5.88 (ketone C=O) and 3.24 (cyclopropyl C-H) u. The methyl ester 98 has ir (CCl_4) 5.72 (ester C=O), 5.87 (ketone C=O) and 3.24 (cyclopropyl C-H) u. The nmr spectrum of 98a (ethyl ester) shows δ^{CCl_4} 0.74-1.09 (m, 4, cyclopropyl CH_2), 1.22 (t, 3, J= 7Hz, $-CH_2\underline{CH_3}$), 1.78-2.24 (m, 1, cyclopropyl methine), 3.41 (s, 2, $-CO\underline{CH_2}COO-$) and 4.06 (q, 2, J= 7Hz, $-\underline{CH_2}CH_3$). The nmr spectrum of 98a, methyl ester, shows δ^{CCl_4} 0.77-1.10 (m, 4, cyclopropyl CH_2), 1.84-2.32 (m, 1, cyclopropyl methine), 3.54 (s, 2, $-CO\underline{CH_2}COO-$) and 3.70 (s, 3, $-COO\underline{CH_3}$).

Both esters gave a positive ferric chloride test. Both esters were converted to 2-thio-6-cyclopropyluracil.[122,123] The identity of the derivatives was established by comparison of ir spectra and mixture melting points (mmp 239-41° (lit. mp 234-5°,[123] 239-40[122])).

Ethyl 3-(1'-Methylcyclopropyl)-3-oxopropanoate (98b)

Ketoester 98b was prepared by Johnson's procedure[121] using 25.0 g (0.255 mole) of 1-methylcyclopropyl methyl ketone,[124] 260.0 g (2.2 moles) of diethyl carbonate and 26.0 g (1.08 moles) of sodium hydride (50% dispersion in mineral oil) in 300 ml of anhydrous ether. Stirring for 24 hrs. at room temperature and workup gave 31.2 g (73%) of ketoester 98b, bp 73-4° (0.25 mm). A second distillation through a spinning band column gave 29.68 g (70%) of 98b, bp 51.5-52° (0.025 mm).

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(124) N. L. Goldman, Chem. and Ind. (london), 1036 (1963).

Ketoester 98b gave a positive ferric chloride test; ir (CCl_4) 3.25 (cyclopropyl C-H), 5.76 (ester C=O), 5.92 (ketone C=O) and 6.20 (enol C=C) u; nmr, δ^{CCl_4} 0.53-0.93 (m, 4, cyclopropyl CH_2), 1.17-1.53 (singlet (centered at 1.40) superimposed on triplet (centered at 1.30), 6, J for triplet = 7Hz, $\underline{CH_3}$-$\overset{|}{C}$-, -$COOCH_2\underline{CH_3}$), 3.46 (s, 1.6, -$CO\underline{CH_2}COO$-), 4.31 (q, 2, J= 7Hz, -$COO\underline{CH_2}CH_3$), 5.21 (s, 0.16, $\underline{H}$-C=C-OH) and 12.80 (s, 0.24, H-C=C-O$\underline{H}$) (enol content = 20%).

2-Thio-6-(1'-methylcyclopropyl)-uracil

The thiouracil derivative was obtained in 18% yield,[122] mp 212-13°; ir (KBr) 6.11 (C=O), 6.46 (C=S), 8.45 (C—S) and 13.25 (C—S) u; nmr, $\delta^{DMSO\text{-}d_5}$ 0.52-1.15 (m, 4, cyclopropyl CH_2), 1.31 (s, 3, CH_3-$\overset{|}{C}$-),

3,32 (s, 2, NH, disappears with addition of D_2O) and 5.70 (s, 1, vinyl H); uv, $\lambda_{max}^{CH_3OH}$ 276 nm (ε 20,350), 219 nm (ε 20,860); $\lambda_{max}^{CH_3OH, PH 12}$ 258 nm (ε 17,320), 316 nm (ε 16,020).

Anal. Calcd. for $C_8H_{10}N_2SO$: C, 52.60; H, 5.49; N, 15.36; S, 17.55.
Found: C, 52.62; H, 5.45; N, 15.19; S, 17.49.

Ethyl 3-Cyclopropyl-3-oxo-2-methylpropanoate (98c)

Ketoester 98c was prepared from 20.7 g (0.211 mole) of cyclopropyl ethyl ketone,[125,126] 26.0 g (1.08 moles) of sodium hydride (50% dispersion in mineral oil) and 260.0 g (2.20 moles) of diethyl carbonate in 300 ml of anhydrous ether. The mixture was stirred at room temperature for 48 hrs., and workup gave 26.2 g (73%) of 98c, bp 72-4° (1.3-1.5 mm) after one distillation through a Teflon annular spinning band column.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.75; H, 8.31.

Ketoester 98c gave a positive ferric chloride test; ir (CCl_4) 3.25 (cyclopropyl C-H), 5.75 (ester C=O), 5.86 (ketone C=O) u; nmr, δ^{CCl_4} 0.73-1.10 (m, 4, cyclopropyl CH_2), 1.10-1.33 (triplet (centered at 1.26) and doublet (centered at 1.30) overlap, 6, J for triplet = 7Hz, J for doublet = 7Hz, $-COOCH_2\underline{CH_3}$, $-CH\underline{CH_3}$), 1.80-2.28 (m, 1, cyclopropyl methine), 3.58 (q, 1, J= 7Hz, $-\underline{CH}CH_3$) and 4.20 (q, 2, J= 7Hz, $-COO\underline{CH_2}CH_3$).

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(125) P. Bruylants, Bull. Soc. Chim. Belg., 36, 519 (1927); Chem Abstr. 22, 582 (1928).

(126) M. Julia, S. Julia and S. -Y. Tchen, Bull. Soc. Chim. France, 1849 (1961).

2-Thio-5-methyl-6-cyclopropyluracil

The thiouracil derivative was prepared in 17% yield,[122] mp 238-9°; ir (KBr) 6.16 (C=O), 6.50 (C=S), 8.33 (C—S) and 12.68 (C—S) u; nmr, δ^{DMSO-d_5} 0.75-1.17 (m, 4, cyclopropyl CH_2), 1.58-2.16 (singlet (centered at 1.90) superimposed on multiplet, 4, $-\overset{|}{C}=\overset{|}{C}-\underline{CH_3}$ and cyclopropyl methine) and 3.30 (s, 2, NH, disappears upon addition of D_2O); uv, $\lambda_{max}^{CH_3OH}$ 280 nm (ε 21,390), 223 nm (ε 18,230); $\lambda_{max}^{CH_3OH,\ PH\ 12}$ 261 nm (ε 18,570) and 318 nm (ε 17,160).

Anal. Calcd. for $C_8H_{10}N_2SO$: C, 52.72; H, 5.53; N, 15.37; S, 17.59.

Found: C, 52.64; H, 5.54; N, 15.40; S, 17.67.

Ethyl 3-(1'-Methylcyclopropyl)-3-oxo-2-methylpropanoate (98d)

Ketoester 98c (90.28 g, 0.531 mole) was added dropwise to a stirred suspension of 14.0 g (0.584 mole) of sodium hydride (50% dispersion in mineral oil) in 1.5 l of benzene at room temperature under nitrogen. When hydrogen evolution ceased, 141.9 g (1.00 mole) of methyl iodide was added rapidly and the resulting mixture was refluxed overnight under nitrogen, then poured into 1 l of dilute aqueous acid. The aqueous layer was extracted twice with 100 ml portions of ether which were combined with the organic layer, dried over magnesium sulfate, and concentrated under reduced pressure to an oil which was distilled, affording 85.60 g

(87%) of crude 98d, bp 69-70° (1 mm). Further distillation on a Teflon annular spinning band column did not separate a small amount of unmethylated 98c, and the crude ketoester 98d was therefore purified as follows: A Mixture of 25.17 g (ca. 0.137 mole) of crude 98d, 2.91 g (0.0275 mole) of benzaldehyde, 109 microliters (1.1 mmole) of piperidine and 300 microliters (5.2 mmole) of glacial acetic acid in 200 ml of benzene was refluxed for 3 hrs. with removal of water (0.34 ml). The reaction mixture was washed with 5% hydrochloric acid, saturated aqueous sodium bicarbonate and water, dried over magnesium sulfate, and concentrated in vacuo to an oil which upon spinning band distillation, gave 20.4 g (81%)recovery) of 98d, bp 67-67.5° (0.9 mm).

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.30; H, 8.77.

Ketoester 98d gave a negative ferric chloride test; ir (CCl_4) 3.24 (cyclopropyl C-H), 5.74 (ester C=O), 5.90 (ketone C=O) u; nmr, δ^{CCl_4} 0.58-1.00 (m, 4, cyclopropyl CH_2), 1.10-1.46 (overlapping triplet (centered at 1.24), doublet (centered at 1.24) and singlet (centered at 1.36), 9, J for triplet and doublet = 7Hz, $-COOCH_2\underline{CH_3}$, $-\overset{|}{C}H\underline{CH_3}$ and $\underline{CH_3}-\overset{|}{C}-$), 3.67 (q, 1, J= 7Hz, $-\underline{\overset{|}{C}H}CH_3$) and 4.13 (q, 2, J= 7Hz, $-COO\underline{CH_2}CH_3$).

2-Thio-5-methyl-6-(1'-methylcyclopropyl)-uracil

The thiouracil was prepared in 20% yield,[122] mp 225-6°; ir (KBr) 6.14 (C=O), 6.45 (C=S), 8.23 (C—S) and 12.94 (C—S) u; nmr, δ^{DMSO-d_5} 0.65-0.94 (m, 4, cyclopropyl CH_2), 1.26 (s, 3, CH_3- ), 1.90

(s, 3, -C≡C-$\underline{CH_3}$), 3.32 (s, 2, NH, disappears upon addition of D_2O); uv, $\lambda_{max}^{CH_3OH}$ 279 nm (ε 21,010), 219 nm (ε 19,190); $\lambda_{max}^{CH_3OH}$ PH 12 263 nm (ε 16,170) and 320 nm (ε 11,770).

Anal. Calcd. for $C_9H_{12}N_2SO$: C, 55.08; H, 6.16; N, 14.29; S, 16.35. Found: C, 55.03; H, 6.20; N, 14.37; S, 16.41.

Ethyl 3-Cyclopropyl-3-oxo-2,2-dimethylpropanoate (112)

Ketoester 112 was prepared by the methylation procedure used for 98d with 9.65 g (0.0567 mole) of ketoester 98c, 2.86 g (0.059 mole) of sodium hydride (50% dispersion in mineral oil) and 24.2 g (0.17 mole) of methyl iodide in 500 ml of benzene, affording 8.38 g (84%) of ketoester 112 after one distillation, bp 55-7° (1.2 mm). Redistillation through a Teflon annular spinning band column using a reflux ratio of 50:1 gave 7.40 g (71%) of ketoester 112, bp 52-3° (1.0 mm) (no difficulty was encountered in separating 112 from traces of 98c).

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.26; H, 8.76. Found: C, 65.15; H, 8.85.

Ketoester 112 gave a negative ferric chloride test; ir (CCl_4) 3.25 (cyclopropyl C-H), 5.76 (ester C=O), 5.87 (ketone C=O) and 7.23, 7.27 (gem dimethyl) u; nmr, δ^{CCl_4} 0.68-1.00 (m, 4, cyclopropyl CH_2), 1.08-1.42 (triplet (centered at 1.25) and singlet (centered at 1.32) overlap, 9, J for triplet = 7Hz, -COOCH$_2\underline{CH_3}$, $>C(CH_3)_2$), 1.70-2.16 (m, 1, cyclopropyl methine) and 4.18 (q, 2, J= 7Hz, -COO$\underline{CH_2}CH_3$).

Pyrolysis Procedure for Ketoesters 98a-d, 112 and 3-Cyclopropanecarbonyl-6-cyclopropyl-2H-pyran-2,4(3H)-dione (108)

The degassed materials to be pyrolyzed were distilled at a rate of 1-3 g/hr, at 1-3 mm Hg, into the top end of a vycor tube packed with glass wool (16-18 g in 33 cm) or other packing material (98, runs 1-4, 13 and 14, Table VIII). On small runs (1-2 g) the pyrolyzate was analyzed by glpc and yields were calculated using internal standards. On preparative runs (10-38 g) the trapped pyrolyzate was distilled through a Teflon annular spinning band column and yields were based on isolated material. Individual conditions and product yields are summarized in Table IX.

Table IX

Pyrolysis of Ketoesters 98a-d, 112 and 3-Cyclopropanecarbonyl-6-cyclopropyl-2H-pyran-2,4(3H)-dione (108); Glass Wool Packing, 1-3 mm.

Run	Starting Material	°C	99	100	C_2H_5OH	(Other Compound)	% Recovery of Starting Material	Total Pyrolyzate Wt. %
15[a]	98a	565	51	7	74	—	0	73
16[b]	98a	540	47	0	78	—	8	79
17[a]	98b	500	65	9	86	—	0	67
18[b]	98b	500	60	0	82	—	0	68
19[a]	98c	585	65	2	87	—	0	66
20[b]	98c	585	60	0	83	—	0	70
21[a]	98d	535	81	2	61	—	9	71

Table IX (continued)

Run	Starting Material	°C	99	100	C_2H_5OH	(Other Compound)	% Recovery of Starting Material	Total Pyrolyzate Wt. %
22[b]	98d	570	68	2	75	—	0	75
23[a]	112	610	—	—	—	(21)77	8	58
24[a]	108	600	48	3	—	—	0	51

[a]Glpc yields based on unrecovered starting material. For individual glpc conditions see Experimental Section. [b]Yields based on weight of material isolated by distillation and ketoester committed to pyrolysis.

Products of Pyrolysis of Ketoesters 98a-d, 112 and 3-Cyclopropanecarbonyl-6-cyclopropyl-2H-pyran-2,4(3H)-dione (108)

2-Cyclopentenone (99a), 3-methyl-2-cyclopenten-1-one (99b), 2-methyl-2-cyclopenten-1-one (99c), 2,3-dimethyl-2-cyclopenten-1-one (99d), cyclopropyl methyl ketone (100a), 1-methylcyclopropyl methyl ketone (100b), cyclopropyl ethyl ketone (100c), 1-methylcyclopropyl ethyl ketone (100d), cyclopropyl isopropyl ketone (113) and cyclopentanone were isolated by preparative glpc of the corresponding ketoesters (98a-d, 112 and 2-carbethoxycyclopentanone (102)). Although a trace of what is probably 4-methyl-2-cyclopenten-1-one was isolated from the pyrolyzate of 98b, no isomeric ketone was detected in the pyrolyzate of 98c. Ethanol was isolated by preparative glpc and identified by comparison of glpc retention times and ir spectra with a commercial sample.

Table X

Retention Times of Ketones 99a-d (min.)[a]

99a	7.5
99b	11.1
99c	16.0
99d	23.4

[a]A 10ft X 0.25 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L at 130 degrees with a flow rate of helium of 57 ml per min. was used.

Table XI

Retention Times of Ketones 100a-d and 113 (min.)[b]

100a	5.1
100b	7.6
100c	8.6
100d	11.0
113	12.6

[b]A 10ft X 0.25 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L at 130 degrees with a flow rate of helium of 38 ml per min. was used.

2-Cyclopenten-1-one (99a)[108,127] and 3-Methyl-2-cyclopenten-1-one (99b)[127]

Ketone 99a was isolated from the pyrolyzates of 98a and 108. Ketone 99b was isolated from the pyrolyzate of 98b. Both ketones were identified with commercial samples by comparison of glpc retention times, ir, uv and nmr spectra and by mixture melting points of the 2,4-dinitrophenylhydrazone derivatives.

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(127) A 10ft X 0.25 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L was used for analysis and collection. The internal standard was 4-methylcyclohexanone.

2-Methyl-2-cyclopenten-1-one (99c)[127]

The ketone was obtained from the pyrolyzates of 98c, with bp 42-3° (0.25 mm) (lit. bp 46-48° (0.2 mm),[128] 59.1° (18.5 mm)[129]); ir (CCl_4) 5.86 (C=O), 6.11 (C=C) u (lit. 1705 cm^{-1} (5.86 u), 1640 cm^{-1} (6.10 u);[130] 1711 cm^{-1} (5.84 u), 1642 cm^{-1} (6.09 u)[128]); uv, $\lambda_{max}^{C_2H_5OH}$ 227 nm (ε 14,700) (lit. $\lambda_{max}^{95\%\ C_2H_5OH}$ 227 nm (ε 11,220);[130] 226 nm (ε 8550)[128]); nmr, δ^{CCl_4} 1.70 (d, 3, J= 2Hz, small side bands, -CH=C—$\underline{CH_3}$, cis), 2.25-2.78 (m, 4, J= 2Hz, -$\underline{CH_2}\underline{CH_2}$-) and 7.26-7.48 (m, 1, J= 1.5Hz, -$\underline{CH}$=C—CH_3, cis) (consistene with lit. nmr values[128,130]).

2,4-Dinitrophenylhydrazone Derivative: mp 223.5-224° (lit. mp of 2,4-DNP, 221-2°,[129] 219-20°[131]).

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(128) H. N. A. Al-Jallo and E. S. Waight, J. Chem. Soc., B, 73 (1966).

(129) V. A. Mironov, E. V. Sobolev and A. N. Elizarova, Izv. Akad. Nauk. S.S.S.R., Ser. Khim. 1607 (1963); Bull. Acad. Sci. USSR, 1467 (1963).

(130) O. E. Edwards and M. Lesage, Can. J. Chem., 41, 1592 (1963).
(131) I. N. Nazarov, L. A. Kazitsyna and I. I. Zaretskaya, Zhur. Obshchei Khim., 27, 606 (1957); J. Gen. Chem., USSR, 27, 675 (1957).

2,3-Dimethyl-2-cyclopenten-1-one (99d)[132]

The ketone was isolated from the pyrolyzates of 98d, with bp 50° (0.1 mm) (lit. bp 80° (10 mm);[133] 90-2° (25 mm);[134] 87-9° (20 mm)[135]); ir (CCl_4) 5.86 (C=O), 6.05 (C=C) u (lit. 1701 cm^{-1} (5.87 u), 1656 cm^{-1} (6.04 u)[128]); uv, $\lambda_{max}^{C_2H_5OH}$ 234 nm (ε 14,500) (lit. 235 nm (log ε 3.04);[134] 234 nm (ε 13,660);[133] 235 nm (ε 11,784);[136] 234 nm (ε 13,580)[128]); nmr, δ^{CCl_4} 1.63 (s, 3, $\underline{CH_3}$), 2.04 (s, 3, $\underline{CH_3}$), 2.10-2.67 (m, 4, $-\underline{CH_2}\underline{CH_2}-$) (consistent with lit. nmr values[128]).

2,4-Dinitrophenylhydrazone Derivative: 231-2° (lit. mp of 2,4-DNP, 233°,[137] 230-1°[136]).

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(132) A 5ft X 0.25 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L was used for both analysis and collection. The internal standard used was 4-methylcyclohexanone.
(133) S. Dev and C. Rai, J. Indian Chem. Soc., 34, 266 (1957).
(134) R. L. Frank, R. Armstrong, J. Kwiatek and H. A. Price, J. Amer. Chem. Soc., 70, 1379 (1948).
(135) M. V. Mavrov and V. F. Kucherov, Izv. Akad. Nauk. S.S.S.R., Ser. Khim., 164 (1964); Bull. Acad. Sci., USSR, 145 (1964).
(136) M. Ansell, J. E. Emmet and B. E. Grimwood, J. Chem. Soc., C, 141 (1969).
(137) H. Strickler, G. Ohloff and E. sz Kovats, Tetrahedron Lett., 649 (1964).

Cyclopropyl Methyl Ketone (100a)[108]

Ketone 100a was isolated from the pyrolyzates of 98a and was identified by comparison of glpc retention times, ir and nmr spectra and mixture melting point of the 2,4-dinitrophenylhydrazone derivatives with a commercial sample. Ketone 100a was also recovered unchanged (99% recovery) when pyrolyzed at 575° (1-3 mm) with glass wool packing.

1-Methylcyclopropyl Methyl Ketone (100b)[127]

Ketone 100b was isolated from the pyrolyzates of 98b and was identified by comparison of glpc retention times, ir and nmr spectra, and mixture melting point of the 2,4-dinitrophenylhydrazone derivatives[138,139] with a sample prepared by the procedure of Goldman.[124]

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(138) M. Julia, S. Julia and M. Y. Noel, Bull. Soc. Chim. France, 1708 (1960).
(139) H. Monti., Comptes Rend. Acad. Sci., Paris, Ser. C, 265, 522 (1967).

Cyclopropyl Ethyl Ketone (100c)

Ketone 100c was isolated from the pyrolyzates of 98c and was similarly identified with a sample prepared by the procedure of Julia[140] (cadmium method).

2,4-Dinitrophenylhydrazone Derivative: mp 167.5-168° (lit.[140] mp of 2,4-DNP, 162-3°).

Anal. Calcd. for $C_{12}H_{14}N_4O_4$: C, 51.80; H, 5.07; N, 20.13.

Found: C, 51.51; H, 4.98; N, 20.13.

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(140) M. Julia, S. Julia and S. -Y. Tchen, Bull. Soc. Chim. France, 1849 (1961).

1-Methylcyclopropyl Ethyl Ketone (100d)[132]

Ketone 100d was isolated from the pyrolyzates of 98d and was identified by the following data: ir (CCl_4) 3.24 (cyclopropyl C-H), 5.92 (C=O) u; nmr, δ^{CCl_4} 0.48-0.73 (m, 2, cyclopropyl CH, cis or trans to C=O), 0.81-1.28 (triplet (centered at 0.98) superimposed on multiplet, 5, J for triplet = 7.5Hz, $-CH_2\underline{CH_3}$, cyclopropyl CH, cis or trans to C=O), 1.35 (s, 3, $\underline{CH_3}-\overset{|}{C}-$) and 2.43 (q, 2, J= 7.5Hz, $-\underline{CH_2}CH_3$).

Anal. Calcd. for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 75.09; H, 10.87.

2,4-Dinitrophenylhydrazone Derivative: mp 120.5-121°

Anal. Calcd. for $C_{13}H_{16}N_4O_4$: C, 53.42; H, 5.52; N, 19.17.

Found: C, 53.17; H, 5.47; N, 19.23.

Cyclopropyl Isopropyl Ketone (113)[127]

Ketone 113 was isolated from the pyrolyzates of 112 and was identified by the following data: ir (CCl_4) 3.24 (cyclopropyl C-H), 5.88 (C=O), 7.20, 7.33 ($>C(CH_3)_2$) u; nmr, δ^{CCl_4} 0.56-1.02 (m, 4, cyclopropyl CH_2), 1.13 (d, 6, J= 7Hz, $-CH(\underline{CH_3})_2$), 1.68-2.16 (m, 1, cyclopropyl methine) and 2.45-2.99 (quintet, 1, J= 7Hz, $-\underline{CH}(CH_3)_2$).

Anal. Calcd. for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.85; H, 10.65.

2,4-Dinitrophenylhydrazone Derivative: mp 83° (sharp).

Anal. Calcd. for $C_{13}H_{16}N_4O_4$: C, 53.42; H, 5.52; N, 19.17.
Found: C, 53.25; H, 5.51; N, 19.22.

Cyclopentanone (103)[108]

Cyclopentanone was recovered in 96% yield from the pyrolyzates[141] of cyclopentanone and was produced in 48% yield by pyrolysis[141] of 2-carbethoxycyclopentanone (102). The compound was identified by comparison of glpc retention times, ir and nmr spectra, and mixture melting point of the 2,4-dinitrophenylhydrazone derivatives with a commercial sample. No cyclopentenone was observed in either pyrolyzates.[70]

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(141) The pyrolysis was done at 575° at 1-3 mm with glass wool packing.

3-Cyclopropanecarbonyl-6-cyclopropyl-2H-pyran-2,4(3H)-dione (108)

This dehydroacetic acid analog was obtained by pyrolysis of 98a at 760 mm. The ketoester was carried through the hot tube by a stream of prepurified nitrogen (25 ml/min.). Part of the pyrolyzate solidified, and upon filtration and recrystallization (ethanol), afforded a white solid, mp 66-66.5°, in 20% yield. This material gave a positive ferric chloride test, ir (CCl_4) 3.24 (cyclopropyl C-H), 5.82, 6.16, 6.52, 10.19 u; uv, $\lambda_{max}^{C_2H_5OH}$ 319 nm (ε 14,200), 233.5 nm (ε 13,500); $\lambda_{max}^{C_2H_5OH}$ PH 12 298 nm (ε 15,200), 232 nm (ε 20,200);[142] nmr, δ^{CDCl_3} 0.94-1.37 (m, 8, cyclopropyl CH_2), 1.56-2.05 (m, 2, cyclopropyl methine), 3.29-3.80 (m, 1, Vinyl H) and 5.99 (s, 1, enolic H).

Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49. Found: C, 65.39; H, 5.43.

Pyrandione 108 was also prepared in 80% yield by passing 39.2 g (0.25 mole) of ketoester 98a, on a stream of prepurified nitrogen at 1 atm, over a 6 inch segment of pumice[79] at 400°. The pyrolyzate was distilled under reduced pressure giving 11.7 g (29.8%) of unreacted 98a and 15.2 g (55.5%) of 108, bp 125-6°(0.05 mm), which solidified upon cooling, mp 65-6°. This material was identified with the above sample by comparison of ir, nmr and uv spectra.

Gases

Carbon monoxide, carbon dioxide and ethylene were identified in the untrapped pyrolysis product stream (1-3 mm) by comparison of glpc

retention times with those of commercial samples. A 6ft X 0.25 inch column packed with Porak Q at room temperature was used for these analyses in a Gow-Mac, Model 69-100, thermal conductivity instrument. A gas sample volume of 7.5 ml was used.

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(142) Dehydroacetic acid $\lambda_{max}^{95\% C_2H_5OH}$ 310 nm (ε 11, 200), $\lambda_{max}^{C_2H_5OH, NaOH}$ 294 nm (ε 8,150); J. A. Berson, W. M. Jones and L. F. O'Callaghan, C. S. J., J. Amer. Chem. Soc., 78, 622 (1956).

Materials Mentioned in Chapter 4

Goering's procedure[143] for the preparation of methyl 3-pentenoate from 3-pentenonitrile was adapted to the preparation of ethyl and methyl 3-butenoate from 3-butenonitrile. Ethyl and methyl cyclopropylacetates were prepared from ethyl and methyl 3-butenoates by the procedure of Kochi and Bacha.[144]

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(143) H. L. Goering, S. J. Cristol and K. Dittmer, J. Amer. Chem. Soc., 70, 3314 (1948).
(144) J. K. Kochi and J. D. Bacha, J. Org. Chem., 33, 2754 (1968).

Ethyl 3-Butenoate

Dry hydrogen chloride was rapidly bubbled into a solution consisting of 149.5 g (2.22 moles) of 3-butenonitrile, 40.0 g (2.22 moles) of water and 3 l of absolute ethanol. After 2 hrs. ammonium chloride began to precipitate, and stirring was started. When the reaction mixture began to subside, it was heated for an additional 2 hrs, after which time it was allowed to stand overnight at room temperature, then poured into 6 l of saturated sodium chloride solution. The aqueous layer was extracted with three 250 ml portions of ether which were combined with the organic layer, washed with saturated sodium bicarbonate, water and saturated sodium chloride solutions, and finally dried over magnesium sulfate. Ether was removed through a 30 cm vigreux column, and the residue was distilled to give 135.3 g (60%) of ethyl 3-butenoate, bp 120-21.5° (760 mm) (lit.[145] bp 125-25.5° (760 mm)).

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(145) G. E. Cartier and S. C. Bunce, J. Amer. Chem. Soc., 85, 935 (1963).

Ethyl 3-butenoate has ir (CCl_4) 3.24 (vinyl C-H), 5.75 (C=O), 6.09 (C=C) and 10.10, 10.89 (terminal vinyl).

Methyl 3-Butenoate

This ester was prepared by a procedure similar to that used for the preparation of ethyl 3-butenoate. Using 162.6 g (2.4 moles) of

3-butenonitrile, 43.5 g (2.40 moles) of water and 3 l of dry methanol, 140.0 g (58%) of methyl 3-butenoate, bp 108-108.5° (760 mm) (lit.[146] bp 107° (742 mm) was obtained. Repetitions of this procedure gave methyl 3-butenoate in yields of 53%, 60% and 65% after one distillation.

Methyl 3-butenoate has ir (CCl_4) 3.23, 3.30 (vinyl C-H), 5.74 (C=O), 6.10 (C=C) and 10.13, 10.86 (terminal vinyl) u; nmr, δ^{CCl_4} 3.06 (d, 2, J= 6.8Hz, CH_2=CH-$\underline{CH_2}$-), 3.65 (s, 3, -COO$\underline{CH_3}$), 4.93-5.34 (m, 1, CH_2=$\underline{CH}$-CH_2-) and 5.53-6.33 (m, 2, $\underline{CH_2}$=CH-CH_2-).

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(146) E. J. Corey, J. Amer. Chem. Soc., 75, 2251 (1953).

Ethyl Cyclopropylacetate (114)

Ester 114 was prepared by the procedure of Kochi and Bacha[144] using 117.0 g (1.79 g atoms) of zinc-copper couple, 480.0 g (1.79 moles) of methylene iodide and 136.6 g (1.20 moles) of ethyl 3-butenoate in 100 ml of anhydrous ether. The reaction mixture was poured into 500 ml of saturated ammonium chloride solution and the resulting mixture was extracted once with a 500 ml portion of ether which was then washed with three 200 ml portions of saturated ammonium chloride, once with saturated sodium bicarbonate, twice with water, and finally dried over magnesium sulfate. Ether was removed through a 30 cm vigreux column, and the residue was distilled to give 97.2 g (64%) of 114, bp 145-47° (760 mm) (lit.[144] bp 146-49° (760 mm)).

Ester 114 has ir (CCl_4) 3.23 (cyclopropyl C-H) and 5.75 (C=O) u; nmr, δ^{CCl_4} 0.05-1.10 (m, 5, cyclopropyl H), 1.28 (t, 3, J= 8Hz, $COOCH_2\underline{CH_3}$), 2.23 (d with fine splitting, possibly due to further splitting of doublet by cyclopropyl CH_2, 2, J for doublet = 6.5Hz, $C_3H_5\underline{CH_2}$-) and 4.16 (q, 2, J= 8Hz, $COO\underline{CH_2}CH_3$).

Methyl Cyclopropylacetate

This ester was prepared by a procedure similar to that used for the preparation of 114. Using 200.0 g (2.0 moles) of methyl 3-butenoate, 800.0 g (3.0 moles) of methylene iodide and 196.0 g (3.0 g atoms) of zinc-copper couple in 300 ml of anhydrous ether, 150.3 g (67%) of methyl cyclopropylacetate, bp 126-7° (760 mm) (lit.[147] bp 132° (745 mm)) was obtained. Repetition of this procedure gave methyl cyclopropylacetate in 65% yield after one distillation.

Methyl cyclopropylacetate has ir (CCl_4) 3.24 (cyclopropyl C-H), 3.51 (CH_3-O) and 5.75 (C=O) u; nmr, δ^{CCl_4} 0.04-1.40 (m, 5, cyclopropyl H), 2.17 (d, 2, J= 6.5Hz, $C_3H_5\text{-}\underline{CH_2}$-) and 3.64 (s, 3, $-COO\underline{CH_3}$).

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(147) L. I. Smith and S. McKenzie, Jr., J. Org. Chem., 15, 78 (1950).

Cyclopropylacetic Acid (118)

A mixture consisting of 148.6 g of methyl cyclopropylacetate and 1.6 l of 20% aqueous potassium hydroxide was refluxed with stirring for 3 days. Then most of the water was removed by distillation, the residue was cautiously acidified with 50% sulfuric acid, and then stirred vigorously with 700 ml of ether for 0.5 hr. The ethereal extract was decanted and the procedure was repeated. The collected potassium sulfate was washed several times with 200 ml portions of ether which were combined with the previous extracts, dried over magnesium sulfate, and concentrated under reduced pressure to an oil which was distilled, affording 104.3 g (80%) of 118, bp 90-1° (12 mm) (lit.[144] bp 86-7° (9 mm)).

Acid 118 has ir (CCl_4) 3.24 (cyclopropyl C-H), 3.74-3.90 (O-H) and 5.85 (C=O) u; nmr, δ^{CCl_4} 0.05-3.32 (doublet (centered at 2,33) with fine splitting, possibly due to further splitting of doublet by cyclopropyl CH_2; doublet is superimposed on multiplet; 7H, J for doublet= 7Hz, C_3H_5-$\underline{CH_2}$-, cyclopropyl $\underline{H}$) and 11.37 (s, 1, O$\underline{H}$).

Cyclopropylacetyl Chloride

Acid 118 (71.3 g, 0.71 mole) and 65.0 g (0.47 mole) of phosphorous trichloride were maintained at 50° under nitrogen for one hour. Distillation of the reaction mixture gave 70.3 g (84%) of cyclopropylacetyl chloride,[148] bp 57-8° (47 mm). A second distillation gave 65.6 g (78%) of the acid chloride, bp 56-7° (45 mm). Repetition of the above procedure gave the acid chloride in yields of 75%, 72% and 83% after one distillation.

Cyclopropylacetyl chloride has ir (CCl_4) 3.24 (cyclopropyl C-H) and 5.54, 5.62 (shoulder) (C=O) u; nmr, δ^{CCl_4} 0.07-1.42 (m, 4, cyclopropyl CH_2), 1.92-2.37 (m, 1, cyclopropyl methine) and 2.80 (d, 2, J= 6.8Hz, C_3H_5-$\underline{CH_2}$-).

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(148) J. H. Turnbull and E. S. Wallis, J. Org. Chem., 21, 663 (1956). The authors prepared cyclopropylacetyl chloride, but gave no physical constants for it.

Cyclopropylacetamide

Ammonia was bubbled into a solution of 50.5 mg (0.43 mmole) of cyclopropylacetyl chloride in 5 ml of benzene for 10 minutes. Benzene was removed at reduced pressure and the resulting oil was washed once with 2 ml of water, and extracted from the aqueous layer with ether. Removal of ether left an oil which upon trituration with petroleum ether (bp 30-60°) gave 13.5 mg (31%) of cyclopropylacetamide, mp 119-21° (lit.[149] mp 122-23.7°).

Cyclopropylacetamide has ir ($CHCl_3$) 2.82-3.11 (N-H), 5.96 (C=O) and 6.32 (amide II band).

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(149) G. E. Cartier, Renssalaer Polytechnic Institute, PHD 1962, microfilm of thesis, No 62-6439, University Microfilms, Inc., Ann Arbor, Michigan.

2,4-Dicyclopropyl-3-hydroxy-3-butenoic acid β-lactone (119)

Triethylamine (30.4 g, 0.30 mole) was added dropwise to 35.6 g (0.30 mole) of cyclopropylacetyl chloride in 250 ml of anhydrous ether at 0°C. The mixture which was protected from moisture, was stirred overnight at room temperature, then filtered under nitrogen. The collected precipitate of triethylammonium chloride was washed with small portions of ether which were combined with the organic layer and washed once with a 2% solution of sulfuric acid, once with a 2% solution of sodium bicarbonate, and once with water. The ethereal extracts were dried over magnesium sulfate, ether was removed through a 30 cm vigreux column, and the residue was distilled, affording 11.4 g (46%) of 119, bp 80-1° (0.20-0.25 mm). A second distillation gave 10.1 g (41%) of 119, bp 79-80° (0.20 mm). Repetition of this procedure gave 119 in 40% yield after two distillations.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.00; H, 7.45.

Dimer 119 has ir (CCl_4) 3.23 (cyclopropyl C-H), 5.32 (C=O) and 5.80 (C=C) u; nmr δ^{CCl_4} 0.12-1.92 (m, 10, cyclopropyl H), 3.88 (dd(split by cyclopropyl methine into a doublet which is further split by allylic H), 1, J= 1.5Hz, C_3H_5-CH=C(-CH-)) and 4.35 (dd (split by cyclopropyl methine into a doublet which is further split by vinyl H), 1, J= 1.5Hz, C_3H_5-CH=C(-CH-)); uv, $\lambda_{max}^{C_2H_5OH}$ 210 nm (ε 2,400); mass spectrum, order of intensity of m/e ratios are: 82 > 54 > 39 > 164 ≈ 41 (parent peak, m/e, 164).

N-p-Bromophenyl-2,4-dicyclopropyl-3-oxobutyramide Derivative

Dimer 119 (1.0 g, 6.1 mmoles) and 1.7 g (9.9 mmoles) of p-bromoaniline were refluxed in 10 ml of anhydrous benzene for 0.5 hr. Removal of benzene at reduced pressure, followed by addition of petroleum ether (bp 30-60°) to the resulting oil, gave a white solid which was recrystallized from a 1:1 mixture of ethanol and water, affording 1.6 g (78%) of the amide derivative, mp 130-31°. A second recrystallization from the same solvent mixture gave 1.2 g (59%) of the amide derivative, mp 132-32.5°.

Anal. Calcd. for $C_{16}H_{18}NO_2Br$: C, 57.09; H, 5.39; N, 4.16; Br, 23.76.
Found: C, 56.88; H, 5.34; N, 4.14; Br, 23.69.

This amide derivative has ir (CCl_4) 3.05 (N-H), 5.95 (C=O), 6.60 (amide II band), 6.29 (C=C of phenyl) and 12.14 (phenyl, p-substituted) u; nmr, δ^{CDCl_3} 0.35-1.67 (m, 10, cyclopropyl H), 2.60 (d, 2, J= 6.5Hz, C_3H_5-CH_2-CO-), 2.83 (d, 1, J= 10Hz, C_3H_5-CH-CO-NH-) and 7.45 (s, 4, phenyl H).

1,3-Dicyclopropylpropan-2-one (122)

A mixture consisting of 730 mg (4.45 mmoles) of dimer 119 and 2 ml of 5% aqueous sodium hydroxide was refluxed for one hour. The cooled mixture was extracted with small portions of ether, and the combined extracts were dried over magnesium sulfate. Ether was removed at reduced

pressure leaving 436 mg of crude ketone 122. The yield of pure 122, 405 mg (66%), was estimated by glpc[150] using ethyl benzoate as the internal standard.

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(150) A 10ft X 0.25 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L at 135 degrees with a flow rate of helium of 79 ml per min. was used for analysis and collection.

Ketone 122 has ir (CCl_4) 3.24 (cyclopropyl C-H) and 5.83 (C=O) u (consistent with lit.[151] ir values); nmr δ^{CCl_4} -0.10-0.65 (m, 8, cyclopropyl CH_2), 0.65-1.37 (m, 2, cyclopropyl methine) and 2.28 (d, 4, J= 6.3Hz, $(C_3H_5-\underline{CH_2})_2-CO$) (lit.[151] nmr values: 0.3-0.9 (m, 8, cyclopropyl CH_2), 2.2-2.7 (m, 2, cyclopropyl methine) and 3.2 (d, 4, $(C_3H_5-\underline{CH_2})_2-CO$); mass spectrum, order of intensity of m/e ratios are: 55 > 83 > 29 > 27 > 39 > 138 (parent peak, m/e, 138).

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(151) M. Hanack and H. M. Ensslin, Justus Liebigs Ann. Chem., 697, 109 (1966).

2,4-Dinitrophenylhydrazone Derivative of 122: 93.5° (sharp).

Pyrolysis of Ethyl Cyclopropylacetate (114)

Ester 114 (0.93 to 1.00 g used) was distilled at 0.25-2.00 mm Hg and over a period of approximately one hour, into a vycor tube packed with glass wool.

Table XII

Pyrolysis of Ethyl Cyclopropylacetate (114)

Run	°C	Products: % Yield[a] 99a	117	C_2H_5OH	% Unchanged 114	Pyrolyzate Total Wt. %	Wt. % Accounted for[b]
1	587	39	5	18	42	64	99
2	610	34	4	26	30	60	91
3	624	27	10	31	20	51	95

[a]Yields of products and unchanged 114 were estimated by glpc[152] using 4-methylcyclohexanone as the internal standard. Yields of products have been corrected for unchanged 114. [b]Represents total Wt. % of material that has been accounted for by glpc.[152]

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(152) A 5ft X 0.25 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L at 115 degrees with a flow rate of helium of 23 ml per min. was used for analysis and collection.

Table XIII

Retention Times of 2-Cyclopentenone (99a), 2-Pentenoic Acid (117), Ethyl Cyclopropylacetate (114) and Ethanol (min.)[152]

C_2H_5OH	0.3
117	1.2
99a	1.8
114	2.5

Products of Pyrolysis of Ethyl Cyclopropylacetate (114)

2-Cyclopentenone (99a) and ethanol were identified by comparison of their glpc[152] retention times and ir spectra with those of authentic samples.

Trans-2-pentenoic Acid (117)[152]

Acid 117 was isolated from the pyrolyzate of 114 and was identified by its ir spectrum (CCl_4): 3.50, 3.18 (O-H), 5.94 (C=O, conjugated), 6.12 (C=C, conjugated) and 10.45 (-CH=CH-, trans disubstituted).

Pyrolysis of 2,4-Dicyclopropyl-3-hydroxy-3-butenoic acid β-lactone (119)

Dimer 119 (1.0 to 3.0 g used) was distilled at 0.20-1.80 mm Hg into a vycor tube packed either with glass wool or Pyrex helices. The pyrolyzate of 119 was separated by short path distillation into a volatile fraction (V. F.) and a non-volatile fraction (R(x)) (see Table XV). The volatile fraction was analyzed by glpc (see Table XIV) and the non-volatile fraction was hydrolyzed with 5% aqueous sodium hydroxide, affording 1,3-dicyclopropylpropan-2-one (122) and cyclopropylacetic acid (118).

Table XIV

Pyrolysis of 2,4-Dicyclopropyl-3-hydroxy-3-butenoic acid β-lactone (119)

Run	°C	Packing Material[a]	Products: % Yield[b] 99a	120	121	122	117	118	Unchanged[c] 119	Pyrolyzate Total Wt. %
1[d]	560	C	31	14	0.21	3	5	0	0	63
2[d]	567	C	27	13	0	3	4	0	0	58
3[e]	537	C	17	9	0	1	3	0	0	63
4[d]	554	B	15	3	20	4	2	1	—	78
5[d]	554	B	15	3	18	3	2	1	—	76
6[e]	560	B	13	3	14	1	1	1	—	61

[a]B: 6 mm Pyrex helices; C: Pyrex glass wool. [b]Yields of products were estimated by glpc[153] using ethyl benzoate as the internal standard.

Table (XIV) (continued)

[b]Yields of products for runs 4,5 and 6 were not corrected for unchanged 119. [c]The presence of unreacted 119 in runs 4,5 and 6 was shown by the ir spectra of the pyrolyzates, but 119 was not recovered (see Experimental). [d]Dimer 119 was distilled into the vycor tube at an average rate of 0.035 g/min. [e]Dimer 119 was distilled into the vycor tube at an average rate of 0.013 g/min.

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(153) A 10ft X 0.25 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L at 136 degrees with a flow rate of helium of 81 ml per min. was used for analysis and collection.

Table XV

Wt. % of Material that has been accounted for in the Pyrolysis of Dimer 119

Run[a]	Pyrolyzate Total Wt. in g	Wt. % Volatile Fraction[b] (V.F.)	Wt. % Accounted[c] for in (V.F.)	Wt. % of Residue (x)[b] R(x)	Wt. %[d] Accounted for in R(x)	Total Wt. % Accounted for
1	1.89	85	75	15	3[e]	78
2	1.22	80	71	20	5[f]	76
3	0.82	—	45[g]	—	—	45[g]
4	2.35	53	47	47	28[h]	75
5	2.29	52	45	48	—[i]	45
6	0.61	—	48[g]	—	—	48[g]

Table XV (continued)

[a]Numbered runs correspond numerically to those in Table XIV. [b]Total pyrolyzate was separated by short path distillation into a volatile fraction (V.F.) and a non-volatile fraction (R(x)). For example, R(1) corresponds to the residue obtained from the pyrolyzate of run 1. [c]Represents the Wt. % of material that has been accounted for by glpc (see Table XIV). Weight percentages are fractions of the total Wt. of recovered pyrolyzate. [d]Residues (R(x)) were refluxed with 5% aqueous sodium hydroxide, affording ketone 122 and acid 118. Yields of 122 and 118 were determined by glpc, or were isolated and weighed. Wt. percentages listed represent the sum of the Wt. percentages of individual products. They are also fractions of the total weight of recovered pyrolyzate. [e]Only acid 118 was obtained from the hydrolysis of R(1) (see Experimental). [f]Acid 118 and ketone 122 were obtained from the hydrolysis of R(2) (see Experimental). [g]Total pyrolyzate was not separated into two fractions by short path distillation, but was analysed directly. [h]Acid 118, ketone 122 and a small amount of allene 121 were obtained from the hydrolysis of R(4). [i]R(5) was not treated with boiling 5% aqueous sodium hydroxide. An attempt to isolate products by simply extracting R(5) with either dil. acid or base was unsuccessful.

Table XVI

Retention Times of 2-Cyclopentenone (99a), 2-Pentenoic Acid (117), Cyclopropylacetic Acid (118), 1,6-Spiro [4. 4] -nonadiene (120), 1,3-Dicyclopropylallene (121) and 1,3-Dicyclopropylpropan-2-one (122) (min.)[153]

117	3.5
99a	5.5
120	8.7
118	10.9
121	13.2
122	23.1

Products of Pyrolysis of Dimer (119)

2-Cyclopentenone (99a) and cyclopropylacetic acid (118) were identified by comparison of their glpc[153] retention times and ir spectra with those of authentic samples. 1,3-Dicyclopropylpropan-2-one (122) was identified by comparison of its ir and nmr spectra, and glpc[153] retention time with those of an authentic sample.

1,6-Spiro [4. 4] -nonadiene (120)[153,154]

Compound 120 was isolated from the pyrolyzate of 119 and was identified by the following data: ir (CCl_4) 3.28 (vinyl C-H) and 6.22 (C=C) u; nmr, δ^{CCl_4} 1.63-1.97 (m, 4, ring CH_2), 2.17-2.53 (m, 4, ring allylic CH_2) and 5.38-5.72 (m, 4, J= 2Hz, vinyl H); mass spectrum,

order of intensity of m/e ratios are: 105 > 120 > 91 > 90 > 79 > 77 > 78 > 65 > 64 (parent peak, m/e, 120).

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(154) D. J. Cram and B. L. Van Duuren, J. Amer. Chem. Soc., 77, 3578 (1955). The authors have prepared 120, but did not report any spectral data.

1,3-Dicyclopropylallene (121)[153]

Allene 121 was isolated from the pyrolyzate of 119 and was identified by the following data: ir (CCl_4) 3.23 (cyclopropyl C-H), 5.11 (C=C=C), and 9.8 (cyclopropyl) u; nmr, δ^{CCl_4} 0.10-1.43 (m, 10, cyclopropyl H) and 5.00 (dd (allene H is first split by cyclopropyl methine into a doublet which is further split into a doublet of doublets by other allene H), 2, J= 3Hz, CH=C=CH-); uv, $\lambda_{max}^{C_2H_5OH}$ 213 nm (ε 1,490); mass spectrum, order of intensity of m/e ratios are: 91 > 39 > 77 > 105 > 65 ≈ 51 ≈ 41 > 120 (parent peak, m/e, 120).

Anal. Calcd. for C_9H_{12}: C, 89.93; H, 10.06. Found: C, 89.93; H, 9.92.

Trans-2-pentenoic Acid (117)[153]

Acid 117 was isolated from the pyrolyzate of 119 and was identified by its ir (CCl_4) spectrum. For ir values of 117 see products of pyrolysis of ethyl cyclopropylacetate (114).

Non-Volatile Products of the Pyrolysis of Dimer (119)

Residue (4) (R(4)) exhibited ir (CCl_4) absorption bands with the following order of intensity: 5.72 ≈ 5.52 ≈ 5.60 (shoulder of 5.52) ≈ 5.82 (shoulder of 5.72) > 6.08 > 5.33 u. Absorption bands at 5.52-5.82[155] and 6.08 u were attributed to 2,4-dicyclopropyl-3-cyclopropylacetoxy-cyclobut-2-en-1-one (123) (ir (neat) absorption bands of 2,4-dimethyl-3-propionoxy-cyclobut-2-en-1-one[93] are: 5.6-5.8 and 6.0-6.1 u), while those at 5.33 and 5.82[155] u were attributed to unreacted dimer 119.

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(155) The absorption at 5.82 u which was attributed to 123 overlaps with a similarly positioned band which may be attributed to 119.

Residue (4) (1.10 g used) was refluxed in 10 ml of 5% aqueous sodium hydroxide for 2.5 hrs. The cooled mixture was extracted with two 5 ml portions of ether and the combined extracts were dried over magnesium sulfate. Ether was removed at reduced pressure, leaving 296 mg of residue which contained 249 mg of 1,3-dicyclopropylpropan-2-one (122) and 10.3 mg of 1,3-dicyclopropylallene (121),[156] as estimated by glpc[153] (internal standard was ethyl benzoate). The aqueous layer was acidified with concentrated hydrochloric acid and worked up in the manner indicated above, affording 634.4 mg of residue which contained 403 mg of cyclopropylacetic acid (118), as indicated by glpc[153] (internal standard was ethyl benzoate). The combined weight of products (663 mg) is 60% of the weight of R(4) hydrolysed, and 28% of the total weight of recovered pyrolyzate (see Table XV, run 4).

Residue (1) and (2) exhibited ir (CCl_4) absorption bands with the following order of intensity: 5.84> 5.71≈5.64 (shoulder of 5.71)> 5.52 (shoulder of 5.71) u. These absorptions were attributed to the trimer 123. Hydrolysis of 270 mg of R(1) with 5% aqueous sodium hydroxide gave 59 mg of acid 118 (21% of the weight of R(1) hydrolysed, and 3% of the total weight of recovered pyrolyzate; see Table XV, run 1). A similar hydrolysis of 238 mg of R(2) gave 44.6 mg of acid 118 and 14.3 mg of ketone 122 (26% of the weight of R(2) hydrolysed, and 5% of the total weight of recovered pyrolyzate; see Table XV, run 2).

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(156) Incomplete separation during the short path distillation of the pyrolyzate of 119 accounts for the presence of allene 121.

Materials Mentioned in Chapter 5

Cyclopropyl 2-dimethylaminoethyl ketone was prepared from cyclopropyl methyl ketone, paraformaldehyde and dimethylamine hydrochloride by the procedure of Smith and Rogier.[157] Vinyl cyclopropyl ketone (129) was prepared from cyclopropyl 2-dimethylaminoethyl ketone by the procedure of Smith and Showell.[158] The alcohol 1,5-hexadien-3-ol was prepared from acrolein and allyl chloride by the Organic Synthesis procedure.[159] Oxidation of 1,5-hexadien-3-ol using Bond's procedure[160] gave a mixture consisting of 1,5-hexadien-3-one (140) and 1,4-hexadien-3-one (141). The Jones reagent used was prepared by the procedure of Bowden et al.[161]

The compound 2,5-dihydroanisole was prepared from anisole by the procedure of Wilds and Nelson.[162] The ketone 3-cyclohexen-1-one (132) was obtained from 2,5-dihydroanisole by the procedure of Birch.[163]

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(157) L. I. Smith and E. R. Rogier, J. Amer. Chem. Soc., 73, 3842 (1951).
(158) L. I. Smith and J. S. Showell, J. Org. Chem., 17, 839 (1952).
(159) J. C. H. Hwa and H. Sims, Org. Syn., 41, 49 (1961).
(160) F. T. Bond and H. L. Jones, Tetrahedron Lett., 4685 (1965).
(161) K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Werdon, J. Chem. Soc., 39 (1946).
(162) A. L. Wilds and N. A. Nelson, J. Amer. Chem. Soc., 75, 5360 (1953).
(163) A. J. Birch, J. Chem. Soc., 593 (1946).

Cyclopropyl 2-Dimethylaminoethyl Ketone

This ketone was prepared by the procedure of Smith and Rogier[157] using 84.0 g (1.00 mole) of cyclopropyl methyl ketone, 25.0 g (0.28 mole) of paraformaldehyde and 50.0 g (0.62 mole) of dimethylamine hydrochloride in 100 ml of isopropanol. Workup gave 57.8 g (66%) of the ketone, bp 63-5° (1.1 mm) (lit.[157] bp 63-6° (1 mm)).

Cyclopropyl 2-dimethylaminoethyl ketone has ir (CCl_4) 3.24 (cyclopropyl C-H), 3.52, 3.60 ($(CH_3)_2$-N-) and 5.88 (C=O) u; nmr, δ^{CCl_4} 0.51-1.17 (m, 4, cyclopropyl CH_2), 1.70-2.27 (singlet (centered at 2.16) superimposed on multiplet, 7, $(CH_3)_2$-N-, cyclopropyl methine) and 2.35-2.78 (poorly resolved A_2B_2 multiplet, 4, $-CH_2CH_2-$).

Vinyl Cyclopropyl Ketone (129)

Ketone 129 was prepared by the procedure of Smith and Showell[158] using 40.0 g (0.28 mole) of cyclopropyl 2-dimethylaminoethyl ketone, 42.5 g (0.30 mole) of methyl iodide and 61.0 g (0.30 mole) of potassium hydrogen phthalate. Workup gave 8.5 g (31%) of 129, bp 66° (60 mm) (lit.[158] bp 63-5° (60 mm)).

Ketone 129 has ir (CCl_4) 3.23 (cyclopropyl C-H), 3.28 (vinyl C-H), 5.99 (C=O), 6.21 (C=C) and 10.20, 11.30 (terminal vinyl) u; nmr, δ^{CCl_4} 0.63-1.22 (m, 4, cyclopropyl CH_2), 1.73-2.38 (m, 1, cyclopropyl methine), 5.80 (dd (H_a is split by H_b into a doublet which is further split into a doublet of doublets by H_c), 1, J= 4Hz, $\underline{CH}_a{=}CH_bH_c$) and 6.05-6.81 (m, 2, $CH_a{=}\underline{CH}_b\underline{H}_c$).

1,5-Hexadien-3-ol

This alcohol was prepared by the Organic Synthesis procedure[159] using 115.0 g (1.51 moles) of allyl chloride, 38.4 g (1.60 g atoms) of magnesium turnings and 60.0 g (1.10 moles) of acrolein in 600 ml of anhydrous ether. Workup gave 44.0 g (41%) of the alcohol, bp 67° (75 mm) (lit.[159] bp 62-5° (50 mm)).

This alcohol has ir (CCl_4) 2.78, 2.94 (O-H), 3.25 (vinyl C-H), 6.11 (C=C) and 10.10, 10.86 (terminal vinyl) u.

Oxidation of 1,5-Hexadien-3-ol[160]

Jones reagent[161] prepared from 13.6 g of chromic oxide and 10 ml of concentrated sulfuric acid in 15 ml of water, was added dropwise to 13.6 g (0.14 mole) of 1,5-hexadien-3-ol in 30 ml of acetone at 0°C. The mixture was stirred at 0°C for 2.5 hrs., then poured into 100 ml of water. The aqueous layer was extracted with ether and the combined extracts were dried over magnesium sulfate. Ether was removed through a 30 cm vigreux column, and the residue was distilled, affording 6.0 g (44%) of a mixture, bp 44° (19 mm), which consisted of 44% 1,5-hexadien-3-one (140) and 50% 1,4-hexadien-3-one (141) (shown by nmr).

Infrared (CCl_4) absorption bands which were attributed to 140 are: 3.23 (vinyl C-H), 5.89, 5.95 (C=O), 6.12, 6.20 (C=C) and 10.10, 10.88 (terminal vinyl) u (consistent with lit.[164] ir values); the nmr spectrum of the mixture of 140 and 141 shows δ^{CCl_4} 2.14 (dd (methyl hydrogens are split by H_a into a doublet which is further split by H_b into a doublet of doublets), 3, J= 1Hz, $\underline{CH_3}$-CH$_a$=CH$_b$- of 141) (lit.[164] 2.1 ppm), 3.32 (d further split by long range coupling, 2, J= 1Hz, CH_2=CH-$\underline{CH_2}$- of 140) (lit.[164] 3.34 ppm) and 4.89-6.50 (vinyl H's of 140 and 141).

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(164) A. Viola and J. Iorio, J. Org. Chem., 35, 856 (1970).

2,5-Dihydroanisole

This compound was prepared by the procedure of Wilds and Nelson[162] using 30.0 g (0.28 mole) of anisole and 9.0 g (1.3 g atoms) of lithium wire in 400 ml of liquid ammonia. Workup gave 25.0 g (81%) of 2,5-dihydroanisole, bp 150° (760 mm) (lit.[162] bp 148-9° (745 mm)).

Dihydroanisole has ir (CCl_4) 3.28, 3.33 (vinyl C-H), 3.52 (CH_3-O), and 6.07, 6.30 (C=C) u.

3-Cyclohexen-1-one (132)

The procedure of Birch[163] was used to convert 24.9 g (0.23 mole) of 2,5-dihydroanisole to the bisulfite derivative of 132 which was then treated with 50% aqueous sodium carbonate, affording after workup, 9.12 g (42%) of ketone 132, bp 53-4° (35 mm) (lit.[165] bp 53° (35 mm)).

Ketone 132 has ir (CCl_4) 3.29 (vinyl C-H), 5.31 (C=O) and 6.06 (C=C) u.

2,4-Dinitrophenylhydrazone Derivative: mp 130-31° (lit.[163] mp of 2,4-DNP, 132-33°).

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(165) H. J. Shine and R. H. Snyder, J. Amer. Chem. Soc., 80, 3064 (1958).

Pyrolysis of Vinyl Cyclopropyl Ketone (129), 2-Cyclohexen-1-one (131), The Mixture of 1,5-Hexadien-3-one (140) and 1,4-Hexadien-3-one (141), and Phenol (133).

The compound (1.0 to 2.0 g used) to be pyrolyzed was distilled at 0.20-1.00 mm Hg over a period of 2-2.5 hrs. into a vycor tube packed either with glass wool or a mixture of glass wool and Pyrex helices. Individual pyrolysis conditions are mentioned in Table XVII.

Table XVII

Pyrolysis of Ketones 129, 131, (140 and 141) and Phenol (133)

Run	°C	Packing Material[a]	Products: % Yield[d] 131	132	133	134	135	Unchanged Material	Pyrolyzate Total Wt. %
1[e]	610	C	19	7	19	5	4	(129) 18	86
2[e]	663	C	18	8	13	19	5	(129) 6	70
3[e]	(610, 610)[f]	C	19	8	11	11	7	(129) 11	57
4[e]	(610, 675)[f]	C	7	5	17	31	0	(129) 1	65
5[e]	664	(C + B)[b]	26	13	6	13	4	(129) 31	83
6[e]	664	(C + B)[c]	27	9	4	6	6	(129) 27	89
7[g]	665	C		5	26	37	0	(131) 10	47
8[h]	664	C	—	—	—	—	—	(133) 60	60
9[i]	585	(C + B)[c]	31	2	6	3	4	(141) 14	95

Table XVII (continued)

[a]B: 6 mm Pyrex helices; C: Pyrex glass wool. [b]Half of the pyrolysis tube (16 cm of the entrance side) was packed with glass wool, and the other half (16 cm of the side leading to traps) was packed with Pyrex helices. [c]The center portion (12 cm) of the vycor tube was packed with glass wool and the remainder of the tube (entrance and exit sides) was packed with Pyrex helices. [d]Yields of products and unchanged starting material were estimated by glpc[166] using cycloheptanone and acetophenone (for phenol) as the internal standards. Yields of products have been corrected for unchanged starting material. [e]Ketone 129 was pyrolyzed. [f] Ketone 129 was passed through two pyrolysis tubes connected in series. [g]The ketone 2-cyclohexen-1-one (131) was pyrolyzed. [h]Phenol (133) was pyrolyzed. [i]A mixture consisting of 44% 1,5-hexadien-3-one (140) and 50% 1,4-hexadien-3-one (141) was pyrolyzed.

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(166) A 5ft X 0.25 inch column packed with 60/80 Chromosorb W coated with 20% by weight of Apiezon L at 126 degrees with a flow rate of helium of 30 ml per min. was used for analysis and collection.

Table XVIII

Retention Times of Vinyl Cyclopropyl Ketone (129), 2-Cyclohexen-1-one (131), 3-Cyclohexen-1-one (132), Phenol (133), Benzene (134) and 1,3-Cyclohexadiene (135) (min.).[166]

135	1.2
134	2.0
129	3.4
132	5.5
131	7.2
133	9.1

Products of Pyrolysis of (129), (131), (140 and 141) and (133).

2-Cyclohexen-1-one (131),[166] 3-Cyclohexen-1-one (132),[166] Phenol (133),[166] Benzene (134)[166] and 1,3-Cyclohexadiene (135).[166]

Compounds 132, 133 and 134 were isolated from the pyrolyzates of 129 and the mixture of (140 and 141). Compounds 131 and 135 were isolated from the pyrolyzates of 129 and the mixture of (140 and 141). Phenol (133) was recovered in 60% yield from the pyrolysis of 133 at 664° and 0.20-1.00 mm Hg (see Table XVII, run 8). These compounds were identified by comparison of their glpc retention times and ir spectra with those of authentic samples.

2,4-Dinitrophenylhydrazone Derivative of 131: mp 161-62° (lit.[162] mp of 2,4-DNP, 162-63.5°).

2,4-Dinitrophenylhydrazone Derivative of 132: mp 133-34° (lit.[163] mp of 2,4-DNP, 132-33°).

3,5-Dinitrobenzoate Derivative of 133: mp 142-43° (lit.[115] mp of 3,5-dinitrobenzoate, 145.8°).

1,4-Hexadien-3-one (141)[166]

Ketone 141 was isolated from the pyrolyzate of the mixture of (140 and 141) and was identified by the following data: ir (CCl_4) 3.28 (vinyl C-H), 6.00 (C=O), 6.12, 6.20 (C=C), 10.20, 10.74 (terminal vinyl) and 10.37 (trans -CH=CH-) u; nmr, δ^{CDCl_3} 1.99 (dd (methyl hydrogens are split by H_a into a doublet which is further split by H_b into a doublet of doublets), 3, J= 1Hz, CH_3-CH_a=CH_b-) and 5.72-7.40 (m, 5, vinyl H's).