Acid-Catalyzed Rearrangements of Cyclobutanones[1]

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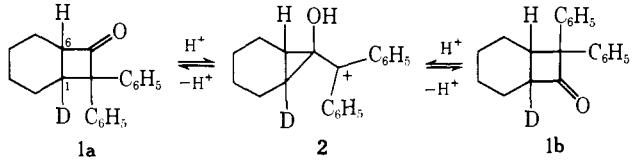
Abstract: Under controlled conditions and at room temperature, (−)-chrysanthenone (**3**) and (+)-2,4,4-trimethylbicyclo[3.1.1]hept-2-en-6-one (**11**) undergo boron trifluoride catalyzed rearrangement to (+)-2,6,6-trimethylbicyclo[3.2.0]hept-2-en-7-one (**4**) and (−)-2,4,4-trimethylbicyclo[3.2.0]hept-2-en-7-one (**12**), respectively, with high retention of optical activity. On prolonged treatment with the same reagent, (+)-ketone **4** is converted to (−)-2,7,7-trimethylbicyclo[3.2.0]hept-2-en-6-one (**8**) and the monocyclic compounds (+)-isopiperitenone (**5**), piperitenone (**6**), and thymol (**7**). The related *exo*-chlorobicyclo[3.1.1]heptanone derivatives **13** and **17** undergo similar stereospecific rearrangement to the corresponding *exo*-chlorobicyclo[3.2.0]heptanone derivatives **14** and **18**, respectively. In order to account for the observed absolute configurations and stereochemistry of products, a mechanism which involves sequential 1,2-alkyl shifts and intermediate cyclopropylcarbinyl cations is proposed for each of these conversions. When (−)-**3** is treated with acid at elevated temperatures (>50°), the same products are produced but with partial loss of optical activity. Data are presented which indicate that racemization occurs by thermal cleavage of **3** to the ketene **23** which undergoes rapid recyclization to **3** exclusive of **4**.

Although cyclobutanol derivatives are known to undergo facile Wagner–Meerwein rearrangement in acid, probably *via* bicyclobutonium ions, to the corresponding cyclopropylcarbinyl derivatives,[3] similar transformations of cyclobutanones have not been reported. One isolated observation by Katz and Dessau[4] suggested to us that such ketones might have the potential to undergo Wagner–Meerwein rearrangement; *i.e.*, when the cyclobutanone **1a** was heated in the presence of a protic acid the deuterium atom located at the C-1 position was exchanged. These results suggested to these authors that the isomer **1a** is converted, *via* a 1,2-alkyl shift involving the cyclopropylcarbinyl cation **2**, to **1b** which can then undergo exchange *via* a normal keto-enolization process.[4]



1a **2** **1b**

We report here our studies of the behavior of certain bicyclo[3.1.1]heptenones and bicyclo[3.1.1]heptanones toward acid. These studies indicate that strained cyclobutanones undergo generally Wagner–Meerwein rearrangement with remarkable facility.

Results

When (−)-chrysanthenone (**3**)[5,6] ([α]^{25}D −12.3°) was heated at 60° in acetic acid for 77 hr, (+)-2,6,6-trimethylbicyclo[3.2.0]hept-2-en-7-one (**4**)[7] ([α]^{25}D +24.2°; *ca.* 30% relative retention[8]), isopiperitenone (**5**),[9] piperitenone (**6**),[10] and recovered **3** were produced in yields of 31, 3, 5, and 12%, respectively.[11] At 118°, consumption of (−)-chrysanthenone ([α]^{25}D −12.3°) was essentially complete in 60 min and the four ketones, **4** ([α]^{25}D +17.7°; *ca.* 22% relative retention[8]), **5**, **6**, and **3**, were isolated in 38, 2, 10, and 2% yields, respectively. Catalysis by a stronger Lewis acid allowed rapid isomerization of **3** at room temperature with relatively less racemization. Thus, treatment of (−)-**3** ([α]^{25}D −26.6°) with a solution of 10% boron trifluoride etherate in 1,2-dichloroethane at 26–27° for 30 min afforded (+)-**4** ([α]^{25}D +174°; 100% relative retention[8]) (26%), **5** (10%), and no **6** or recovered **3**. Prolonged treatment (2.5 hr) of (−)-**3** ([α]^{25}D −12.3°) under the same conditions produced **4** (4–6%), (+)-**5** ([α]^{25}D +10.2°)[12] (20–38%), **6** (6–11%), thymol (**7**) (1–2%), and (−)-2,7,7-trimethylbicyclo[3.2.0]hept-2-en-6-one (**8**) (1–2%) ([α]^{25}D −16.4°). Treatment of ketone **4** with boron trifluoride etherate as above for 2.5 hr did not afford even traces of **3**, but did produce **5**, **6**, **7**, and **8** in yields comparable to those obtained from chrysanthenone (**3**).

The structure of the ketone **8** was assigned on the basis of spectral data. The infrared spectrum showed absorption at 5.63, 7.25, and 12.30 μ, indicative of a cyclobutanone,[13a] *gem*-dimethyl,[13b] and trisubstituted

(1) For a preliminary account of part of this work, see W. F. Erman, *J. Amer. Chem. Soc.*, **91**, 779 (1969); W. F. Erman, Abstracts, 5th International Symposium on Natural Products, London, England, July 8–13, 1968, p 383.

(2) (a) Procter & Gamble Co. (b) Indiana University. (c) P. B. and E. W. acknowledge support of part of this work by the National Science Foundation.

(3) For examples, see (a) R. Breslow in "Molecular Rearrangements," P. de Mayo, Ed., Interscience, New York, N. Y., 1963, Chapter 4, pp 259–276; (b) M. S. Silver, M. C. Caserio, H. E. Rice, and J. D. Roberts, *J. Amer. Chem. Soc.*, **83**, 3671 (1961).

(4) T. J. Katz and R. Dessau, *ibid.*, **85**, 2172 (1963).

(5) W. F. Erman, *ibid.*, **89**, 3828 (1967).

(6) J. J. Hurst and G. H. Whitham, *J. Chem. Soc.*, 2864 (1960).

(7) J. J. Beereboom, *J. Amer. Chem. Soc.*, 85, 3525 (1963); *J. Org. Chem.*, 30, 4230 (1965).

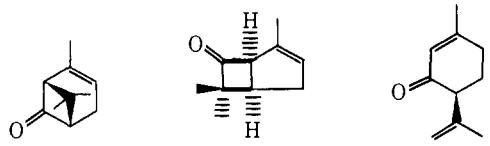
(8) For a discussion of the absolute configurations of ketones **3** and **4**, see the section on absolute configurations of cyclobutanones (*vide infra*). Since the rotation of optically pure **4** has not been established, per cent optical retentions, as recorded here, are relative to the maximum rotation of **4** observed when **3** is rearranged at room temperature with boron trifluoride etherate.

(9) G. O. Schenck, O.-A. Neumüller, G. Ohloff, and S. Schroeter, *Justus Liebigs Ann. Chem.*, 687, 26 (1965).

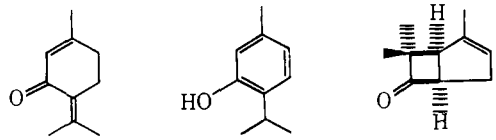
(10) Ch. Balant, Ch. A. Vodoz, H. Kappeler, and H. Schinz, *Helv. Chim. Acta*, 34, 722 (1951).

(11) The formation of ketone **6** by the action of acid on chrysanthenone (**3**) is not unprecedented. Interaction of **3** with refluxing aqueous sulfuric acid is reported to yield piperitenone (**6**) and two degradation products of **6**: methylcyclohexanone and acetone; M. Kotake and H. Nonaka, *Justus Liebigs Ann. Chem.*, 607, 153 (1957).

(12) The absolute configuration of (+)-**5** has been established by chemical means.[9]

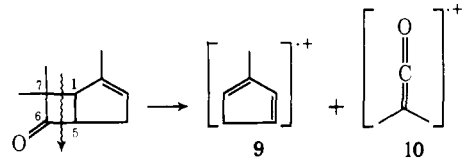


(−)-3 (+)-4 (+)-5



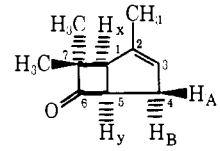
6 7 (−)-8

olefin,[13c] respectively. Both the position and intensity of bands of the ultraviolet spectrum and CD and ORD curves were consistent with (−)-**8**. (For a discussion of this point see the section on absolute configurations.) A high-resolution mass spectral element map revealed a molecular ion peak of empirical formula $C_{10}H_{14}O$ and two major fragments of empirical formulas C_6H_8 and C_4H_6O. This observed fragmentation is consistent with structure **8** which would be expected to undergo cleavage at the 1,7 and 5,6 bonds to produce methylcyclopentadienyl (**9**) $(C_6H_8)\cdot^+$ and dimethylketenyl (**10**) $(C_4H_6O)\cdot^+$ ions.[14]



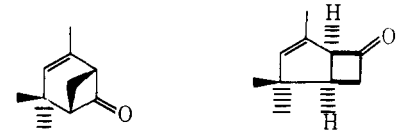
8 9 10

Final confirmation of structure was based upon a careful analysis of the nmr spectrum of **8**. Signals displayed at τ 8.24 and at 8.71 and 8.95 are assigned to the C-2 methyl hydrogens and the C-7 methyl hydrogens, respectively. Signals due to the C-3 olefinic hydrogen and the C-4 allylic hydrogens (H_A and H_B in structure **8**, below) appeared as complex multiplets at τ 4.60 and 7.3–7.7, respectively. The C-1 hydrogen (H_x) signal occurred as a broad doublet, J_1 = 8.0 Hz, at τ 7.05 and that of the C-5 hydrogen (H_y) as a sextet, $J_1 = J_2$ = 8.0 Hz, J_3 = 3.0 Hz, at τ 6.13. Irradiation of the C-5 hydrogen at τ 6.13 converted the doublet at τ 7.05 to a broad singlet; irradiation of the C-1 hydrogen at τ 7.05 transformed the sextet at τ 6.13 to a quartet, J_{BY} = 8.0 Hz, J_{AY} = 3.0 Hz; and irradiation of the multiplet at τ 7.3–7.7 produced sharp doublets, J = 8.0 Hz, at τ 7.05 and at τ 6.13. The coupling constant J_{XY} thus is defined clearly as 8.0 Hz, indicative of a cis-fused ring juncture.[5,15]



8

In like manner, (+)-2,4,4-trimethylbicyclo[3.1.1]hept-2-en-6-one[5] (**11**), $[\alpha]^{25}D$ +29.1°, was rearranged with boron trifluoride etherate to (−)-2,4,4-trimethylbicyclo[3.2.0]hept-2-en-7-one (**12**),[5] $[\alpha]^{25}D$ −328°. (For a discussion of the absolute configurations of **11** and **12** see the section on absolute configurations.)

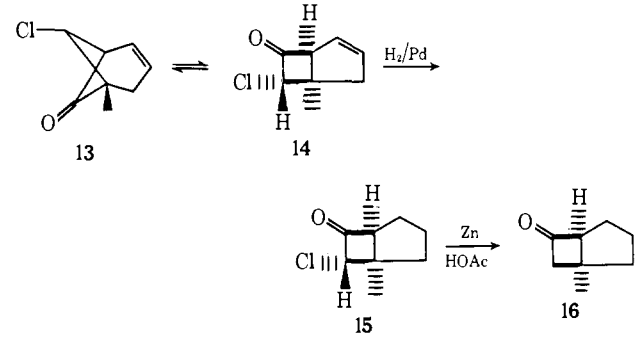


(+)-11 (−)-12

Treatment of the racemic olefinic ketone 7-*exo*-chloro-5-methylbicyclo[3.1.1]hept-2-en-6-one (**13**)[16] with boron trifluoride etherate in dichloroethane afforded a mixture of 85% 6-*exo*-chloro-5-methylbicyclo[3.2.0]hept-2-en-7-one (**14**) and 15% **13**. Prolonged treatment of **13** with boron trifluoride etherate did not change the ratio of **14** to **13** or cause epimerization of the chloro function. Treatment of **14** with boron trifluoride etherate afforded the two ketones in the same ratio, 85:15.

The gross structure of **14** was confirmed by its stepwise conversion to the known 1-methylbicyclo[3.2.0]heptan-6-one (**16**).[17] Catalytic reduction produced the saturated chloro ketone **15** which was reduced cleanly to **16** with zinc in acetic acid.

Further support for the position of the chloro function was given by the nmr spectra of both the unsaturated ketone **14** and the saturated analog **15**. The signal for the chloromethine hydrogen of each isomer appeared as a doublet of 3–3.5 Hz. Long-range couplings of 2–6 Hz have been observed for 1,3-oriented hydrogens in other cyclobutanones.[5,18] A tentative assignment of stereochemistry is based upon the ease with which the chloro function of **15** undergoes zinc dust reduction. Reduction of the saturated *exo*-chloro ketone **18** (*vide infra*) and the ketone **15** proceeded at room temperature; in contrast, the *endo*-chloro ketone was reduced only at elevated temperature (60°). Further support for the exo assignment is provided by the observed behavior of the related saturated analog **17**, discussed below, and mechanistic arguments (see Discussion).



13 14 15 16

The analogous saturated racemic chloro ketone 7-*exo*-chloro-1-methylbicyclo[3.1.1]heptan-6-one (**17**)[19] be-

(13) (a) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, Wiley, New York, N. Y., 1958, p 132; (b) p 13; (c) p 34.

(14) We are indebted to Dr. J. H. Collins and associates for the mass spectral data and interpretation.

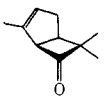
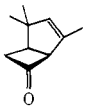
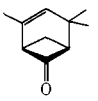
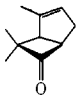
(15) Further confirmation of structure was obtained by comparison of spectral data (nmr, ir) with that of **8** prepared by an independent route and provided to us by Professor Dr. André Dreiding, Organisch-Chemisches Institut der Universität Zürich. We thank Professor Dreiding for these comparisons (*cf.* U. A. Huber, Ph.D. Dissertation, University of Zürich, 1970, pp 37, 85).

(16) E. Wenkert, P. Bakuzis, R. J. Baumgarten, C. L. Leicht, and H. P. Schenk, *J. Amer. Chem. Soc.*, in press.

(17) (a) K. B. Wiberg and G. W. Klein, *Tetrahedron Lett.*, 1043 (1963); (b) S. Julia and C. Gueremy, *Bull. Soc. Chim. Fr.*, 2994 (1965); (c) F. Nerdel, D. Frank, and H. Marschall, *Chem. Ber.*, 100, 720 (1967).

(18) (a) V. Georgian, L. Georgian, A. V. Robertson, and L. F. Johnson, *Tetrahedron*, 19, 1219 (1963); (b) K. Griesbaum, W. Naegele, and G. G. Wanless, *J. Amer. Chem. Soc.*, 87, 3151 (1965).

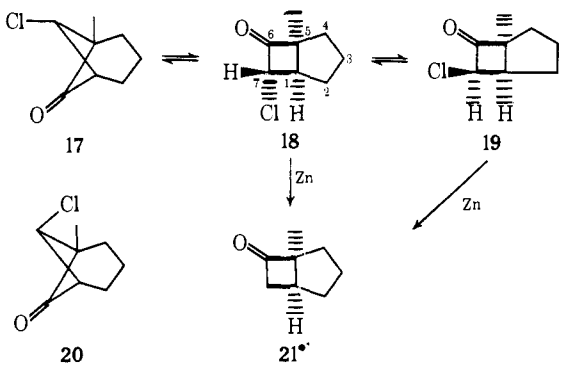
Table I. ORD, CD, and Uv Data for the Olefinic Cyclobutanones[a]

Compd	Chromophore type	$[\alpha]^{25}D$, deg	$[\phi] \times 10^3$	$(\epsilon_l - \epsilon_r)_{max}$	ϵ_{max}
(+)-**4** 	+A	+174[b]	+9.04 (329) −7.20 (292)	+3.75 (313)	260 (310)
(−)-**12** 	−A	−328[c]	−17.1 (322) +14.7 (283)	−6.83 (304)	289 (307)
(+)-**11** 	+B	+29.1	+2.96 (309) −3.38 (272)	+1.35 (293)	102 (293)
(−)-**3** 	−B	−26.6	−2.56 (311) +2.78 (277)	−1.16 (296)	126 (295)
(−)-**8** 	−C	−16.4[d]	−1.01 (321) +1.09 (281)	−0.45 (307)	35 (301)

[a] Values in parentheses are wavelengths in nanometers. [b] Prepared from (−)-**3**, $[\alpha]^{25}D$ −26.2°. [c] From (+)-**11**, $[\alpha]^{25}D$ +29.1°. [d] From (−)-**3**, $[\alpha]^{25}D$ −12.3°.

haves in a similar manner toward acid except that more vigorous conditions are required to effect rearrangement. Thus, only after exposure for 22–23 hr to a refluxing solution of boron trifluoride etherate in dichloroethane was **17** converted to a mixture containing 86% 7-*exo*-chloro-5-methylbicyclo[3.2.0]heptan-6-one (**18**), 4% of the 7-endo isomer **19**, and 10% recovered ketone **17**. When **17** was heated at reflux with 97% formic acid for 108 hr, the two epimers **18** and **19** were produced in about equal quantities (39 and 35% yields, respectively) accompanied by a significant quantity of **17** (9% yield). When either **18** or **19** was heated in formic acid for extended periods (5–9 days) an apparent equilibrium was reached in which the ratio of **19**:**18**:**17** was approximately 12:6:1. Even after careful analysis of product mixtures, no evidence for the presence of the *endo*-chloro epimer **20** could be found in any of these three runs.

The base structures of ketones **18** and **19** were established by zinc reduction to the known 5-methylbicyclo-[3.2.0]heptan-6-one (**21**).[20] The stereochemistry and position of the chloro function in each case was established rigorously by nmr spectroscopy. The chloromethine hydrogen signals in **18** and **19** appeared as doublets with coupling constants of 4.0 and 9.5 Hz, respectively. Regardless of how the four-membered ring is puckered, the coupling between the vicinal cis-oriented C-7 chloromethine hydrogen and C-1 bridge hydrogen should be greater than that of the trans-oriented hydrogens. Thus, the isomer with the larger coupling, 9.5 Hz, is assigned the structure **19** and that with the smaller coupling, 4.0 Hz, the structure **18**.[21]



Absolute Configuration of Cyclobutanones. The absolute configurations of the β,γ-unsaturated ketones were deduced from the observed Cotton effect signs (Table I) by application of the appropriate "octant" rule.[22,23] The positive Cotton effects of (+)-**4** and (+)-**11** indicate that the olefinic bonds lie to the upper left of the carbonyl bonds, while the negative Cotton effects of (−)-**12** and (−)-**3** place the olefinic bonds to the upper right.[24] Unlike the other compounds, (−)-**8** has the olefinic bond in the γ,δ position. Moving the double bond to this position reduces its influence on the sign of the Cotton effect and increases the relative importance of the methylene group of the cyclopentene ring. Fortunately, whichever of the two groups is considered to be the principal asymmetric perturber, a negative Cotton effect is expected for the enantiomer having the cyclopentene ring to the upper right. Thus, (−)-**8** confidently can be assigned this absolute configuration.

(19) (a) R. M. Dodson, J. R. Lewis, W. P. Webb, E. Wenkert, and R. D. Youssefyeh, *J. Amer. Chem. Soc.*, **83**, 938 (1961); (b) E. Wenkert, P. Bakuzis, R. J. Baumgarten, D. Doddrell, P. W. Jeffs, C. L. Leicht, R. A. Mueller, and A. Yoshikoshi, *ibid.*, **92**, 1617 (1970).

(20) E. Wenkert, B. L. Mylari, and L. L. Davis, *ibid.*, **90**, 3870 (1968).

(21) (a) These values are consistent with previous assignments for cis and trans vicinal couplings of four-membered ring ketones. See, for example, W. Brügel, Compiler, "Nuclear Magnetic Resonance Spectra and Chemical Structure," Vol. I, Academic Press, New York, N. Y., 1967, p 55 and ref 5.

(22) A. Moscowitz, K. Mislow, M. A. W. Glass, and C. Djerassi, *J. Amer. Chem. Soc.*, **84**, 1945 (1962).

(23) R. C. Cookson and S. MacKenzie, *Proc. Chem. Soc.*, 423 (1961); R. C. Cookson and J. Hudec, *J. Chem. Soc.*, 429 (1962); S. F. Mason, *ibid.*, 3285 (1962); R. E. Ballard, S. F. Mason, and G. W. Vane, *Trans. Faraday Soc.*, **59**, 775 (1963).

(24) (a) In agreement with these assignments, the absolute configurations of (+)-**4**[24b] and (+)-**3**[5,6,22,23] have been deduced previously by chemical and optical means; (b) R. B. Bates, M. J. Onore, S. K. Paknikar, and C. Steelink, *Chem. Commun.*, 1037 (1967).

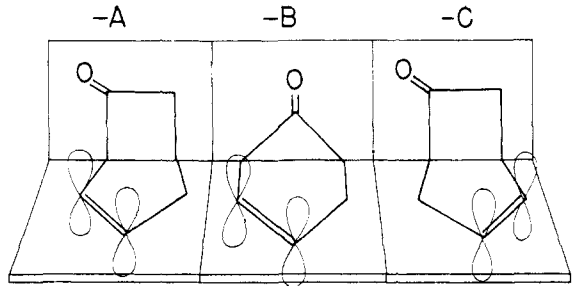
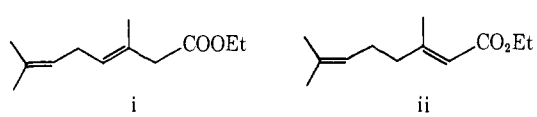


Figure 1. Unsaturated ketone chromophore types, illustrating enantiomers giving negative n–π^* Cotton effects.

The magnitudes of the n → π^* absorption bands and rotational strengths are consistent with the proposed geometric structures. The unusually high magnitudes of ORD, CD, and absorption bands in unsaturated ketones result from coupling of the forbidden n → π^* transition with the allowed π → π^* charge-transfer band.[22,23,25,26] A geometry is required in which: (1) overlap of the olefinic π and π^* orbitals creates the intense charge-transfer band and (2) overlap of the nonbonded p and olefinic π orbitals causes coupling of the transitions. Type A chromophores (Figure 1) have a favorable geometry for satisfying both overlap requirements. Type B chromophores suffer from a decrease in p–π overlap, and C chromophores are poor in both requirements. Absorption intensities and rotational strengths of the cyclobutanones (Table I) vary in the manner expected from their assignment as A, B, and C chromophores.

Racemization of Cyclobutanones. Before considering the mechanism of the above cyclobutanone interconversions, it was essential to establish the cause of partial racemization of the ketone **4** when prepared from (−)-**3**. Since the degree of racemization was temperature dependent, we assumed that either the products or the starting ketone underwent racemization by a thermal process. When (−)-**3** was heated at reflux (81°) under a nitrogen atmosphere in cyclohexane for periods of 16 and 77 hr, the recovered chrysanthenone (75–80% recovery) was 29 and 71% racemized, respectively. Not even trace amounts of the ketone **4** were observed in the reaction mixture. Treatment of **3** with methanol at reflux (65°) for 16 hr produced (*Z*)-3,7-dimethylocta-3,6-dienoate (**22**)[5] (37% yield), and 43% recovered **3**.[27] In contrast, (+)-**4** was recovered in high yield with complete retention of configuration by similar treatment in cyclohexane. Attempted thermolysis of **4** in methanol gave only recovered **4** with no evidence for even trace amounts of the ester **22**. Pyrolysis of (−)-**3** ($[\alpha]^{25}D$ −36.6°) at 250° for 20 min afforded **4**, **5**, and **6** in yields of 16, 3, and 18%, respectively. The ketone **4**, though partially racemized, showed significant optical activity ($[\alpha]^{25}D$ +1.8°).

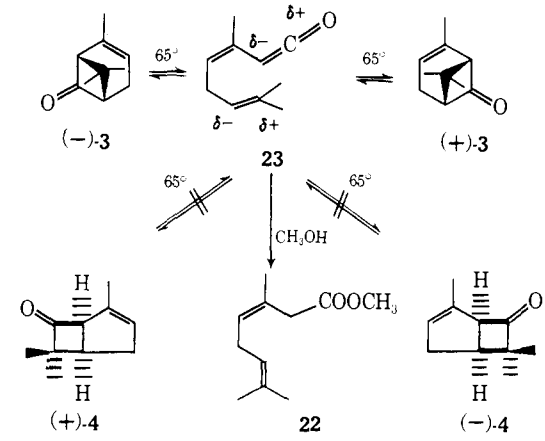
(25) H. Labhart and G. Wagniere, *Helv. Chim. Acta*, **42**, 2219 (1959).
(26) A. Moscowitz, A. E. Hansen, L. S. Forster, and K. Rosenheck, *Biopolym., Symp.*, **No. 1**, 75 (1964).
(27) Extended treatment of ketone **3** with refluxing ethanol is reported to yield a mixture of nonconjugated and conjugated esters i and ii of undesignated geometric configuration.[6]



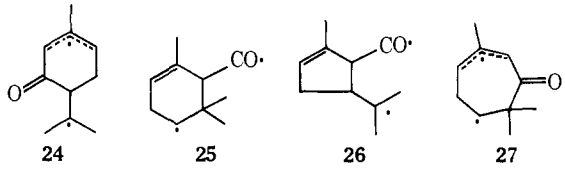
i ii

These observations suggest that **3** undergoes rapid thermal cleavage to ketene **23**[28] at temperatures as low as 65°. Ketene **23** must then undergo thermal recyclization to **3** at a much faster rate than it undergoes cyclization to **4**. Although **4** may be produced to some extent from **23** at higher temperatures (*i.e.*, at 250° or greater),[29] loss of optical activity at the temperatures utilized for the rearrangement experiments must be the consequence of the rapid interconversion of **3** and **23**[31] (Scheme I).

Scheme I



The cycloaddition of ketenes to olefins has been treated as a two-step process involving both biradical[1,32] and ionic intermediates[32,33] and, more recently, as a "near-concerted" or concerted process involving charge separation in the transition state.[34,35] The preferential formation of **3** (rather than **4**) from **23** may be predicted regardless of whether a biradical, ionic, or charge separation concerted mechanism is involved in the cycloaddition process. Thus, of the four possible biradical intermediates—**24**–**27**—which would be formed by stepwise bond formation from **23**, **24** is the anticipated most stable and this radical leads only to ketone **3**.



24 25 26 27

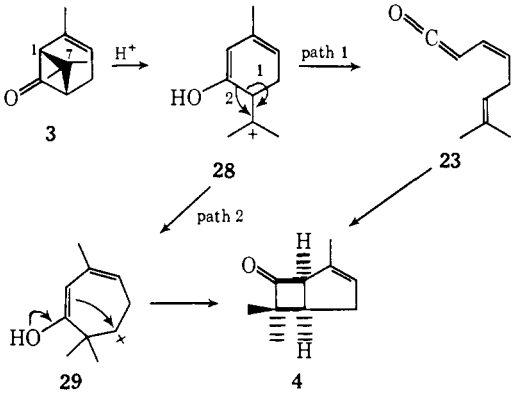
(28) The ketene **23** has been proposed as an intermediate in the conversion of **3** to geranic acid in refluxing 5% aqueous potassium hydroxide; E. P. Blanchard, Jr., *Chem. Ind. (London)*, 293 (1958).
(29) Since the ketone **4** retains some optical activity, it is perhaps more likely that **4** is produced by an ionic process from **3** at 250° even in the absence of added acid. Acid-catalyzed rearrangements which occur at low temperature in the presence of strong acids have been known to be induced by glass surfaces at higher temperatures.[30]
(30) W. Reusch, D. F. Anderson, and C. K. Johnson, *J. Amer. Chem. Soc.*, 90, 4988 (1968).
(31) Optically active ketones **3** and **4** on gas chromatography have been reported to yield (±)-**4**. Ketene **23** has been implicated as an intermediate in this process.[24b]
(32) For a discussion of the biradical and ionic mechanisms for cycloaddition of ketenes to olefins see the review of J. D. Roberts and C. M. Sharts, *Org. React.*, **12**, 1 (1962).
(33) R. H. Hasek and J. C. Martin, *J. Org. Chem.*, **28**, 1468 (1963).
(34) W. T. Brady and H. R. O'Neal, *ibid.*, **32**, 612, 2704 (1967).
(35) (a) R. Huisgen, L. A. Feiler, and P. Otto, *Tetrahedron Lett.*, 4485 (1968); (b) R. Huisgen and P. Otto, *ibid.*, 4491 (1968); (c) G. Binsch, L. A. Feiler, and R. Huisgen, *ibid.*, 4497 (1968); (d) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 847 (1969); (e) M. Rey, S. Roberts, A. Dieffenbacher, and A. S. Dreiding, *Helv. Chim. Acta*, **53**, 417 (1970); (f) P. R. Brook, J. M. Harrison, and A. J. Duke, *Chem. Commun.*, 589 (1970).

Correspondingly, a charge separation concerted mechanism would favor formation of **3** (*cf.* Scheme I).

Discussion

A priori three reaction pathways logically can be proposed for the conversion of the bicyclo[3.1.1]heptanones to the corresponding bicyclo[3.2.0]heptanones. As depicted for ketone **3** (Scheme II), the first two of these involves cleavage of the 1,7 bond to produce an intermediate cation **28**.[36] This cation could undergo cleavage to the ketene **23** with subsequent recyclization to **4** (path 1), or it could undergo ring expansion to **29** with rebonding to **4**[37] (path 2). Both processes involve optically inactive intermediates. Since the rearrangement reactions proceed with apparent retention of optical activity at room temperature, both processes are precluded.[38]

Scheme II

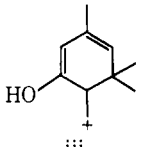


A reaction pathway that is consonant with the observed stereochemistry and relative configuration of products involves a series of sequential 1,2-alkyl shifts. Migration of the 1,7 bond in **3** would produce the optically active intermediate cyclopropanol **30**;[39] subsequent shift of the 1,6 bond in **30** would afford **4** with the observed absolute configuration (path a, Scheme III). Migration of the 5,6 bond in **4** would produce the intermediate **31** which would undergo further rearrangement to **8** (Scheme III). By the same type of sequences of 1,2-alkyl shifts, **12** would be produced from **11** *via* the cation **32**; **14**, from **13** *via* **33**; and **18**, from **17** *via* **34**.

(36) Cleavage of the 1,7 bond of pinene and related derivatives by acid is a well-documented process. For examples, see J. A. Berson in "Molecular Rearrangements," P. de Mayo, Ed., Interscience, New York, N. Y., 1963, Chapter 3, p 187.

(37) The latter sequence is analogous to that proposed by Wiberg[17a] for the solvolytic conversion of 2-methyl-2-tosyloxymethylcyclohexanones to 1-methylbicyclo[3.2.0]heptan-6-ones.

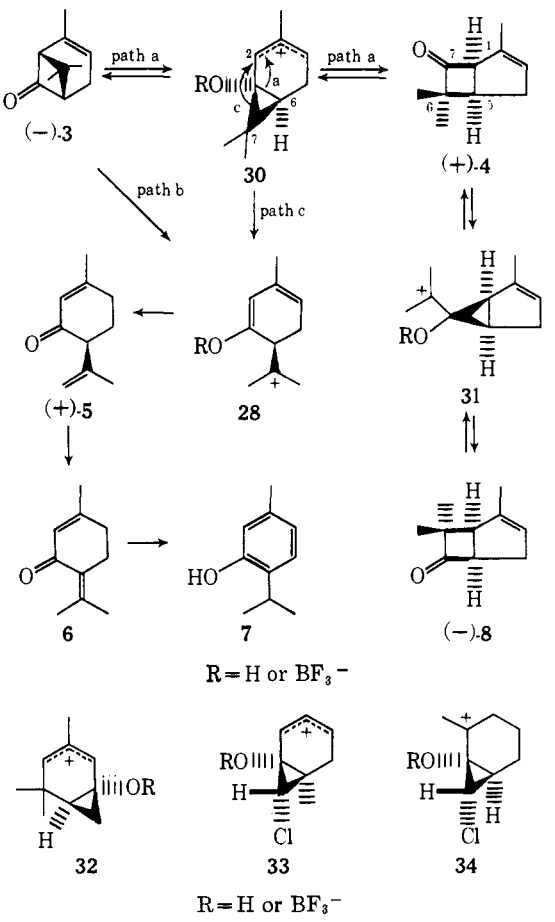
(38) The first mechanism is also voided by the earlier mentioned observation that ketene **23** is not thermally converted to **4** at the temperatures employed for the rearrangement reactions. The fact that ketone **11** undergoes facile rearrangement to **12** further precludes the second mechanism since conversion of **11** to **12** requires formation of the high-energy primary carbonium ion iii.



iii

(39) Similar mechanisms recently have been proposed for the transformation of phorbol to phorbobutanone and crotophorbolone: H. W. Thielmann and E. Hecker, *Justus Liebigs Ann. Chem.*, **728**, 158 (1969).

Scheme III



Two different reaction pathways, both involving the intermediacy of the cation **28**, can be proposed to explain the production of the monocyclic products **5**, **6**, and **7** from **3** and **4**. In the first (path b, Scheme III), **28** is depicted as arising by direct cleavage of the 1,7 bond of **3**, as previously mentioned; in the second (path c), **28** is produced by scission of the 1,7 bond of **30**.[39]

The transformation of **3** or **30** to isopiperitenone (**5**) is essentially irreversible under the conditions employed for the boron trifluoride etherate experiments since **5** on treatment with this reagent afforded only **6** and **7** with no evidence for **3**, **4**, or **8**. Similarly, **6** is isomerized to **7** but not back to **5** under these conditions. These observations suggest that the latter three compounds are generated *via* the progression **28** → **5** → **6** → **7**.

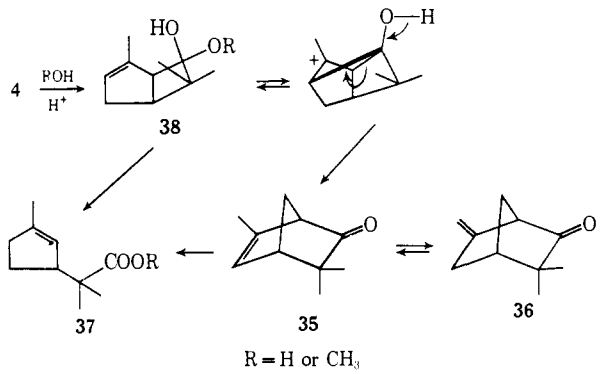
Extended treatment of **4** with boron trifluoride etherate in refluxing toluene gave no evidence of **4** and **8** and produced **6** and **7** in yields of 22 and 5%, respectively. This observation implies that the conversions of **4** to **8** and of **30** to **4** are reversible if path c is the operative mechanism for the generation of **5**, **6**, and **7**. If path a is in effect then the transformation of **3** to **30** must also be a reversible step.

The fact that **4**, on treatment with boron trifluoride etherate, produced only **5**, **6**, **7**, and **8** and not even traces of **3** *a priori* suggests that the conversion of **3** to **30** is irreversible and that path c is the preferred reaction pathway. On the other hand, an accumulation of **3** would not be anticipated if the rate of conversion of **3** to **28** were faster than the rate of conversion of **4** to **3** (*i.e.*, if the ground-state energies of the ketonic products are of the relative order 3 > 4 > 5). That **3** could be con-

verted to **4** and **5** at a faster rate than the reverse process is suggested by the behavior of **4** and **5** in acetic acid. Both **4** and **5** are stable on extended exposure (24 hr) to refluxing acetic acid, conditions which almost completely transform **3** to **4**, **5**, and **6**. Although one cannot state with certainty that the overall transformation of **3** to **4** with boron trifluoride etherate is a reversible process, the fact that the transformations of the related bicyclo[3.1.1]heptanones **13** and **17** to the bicyclo[3.2.0]heptanones **14** and **18**, respectively, are reversible, suggests that the conversion of **4** to **3** is not energetically prohibitive. Unfortunately, however, it is impossible to distinguish between the two possible mechanisms from the data at hand.

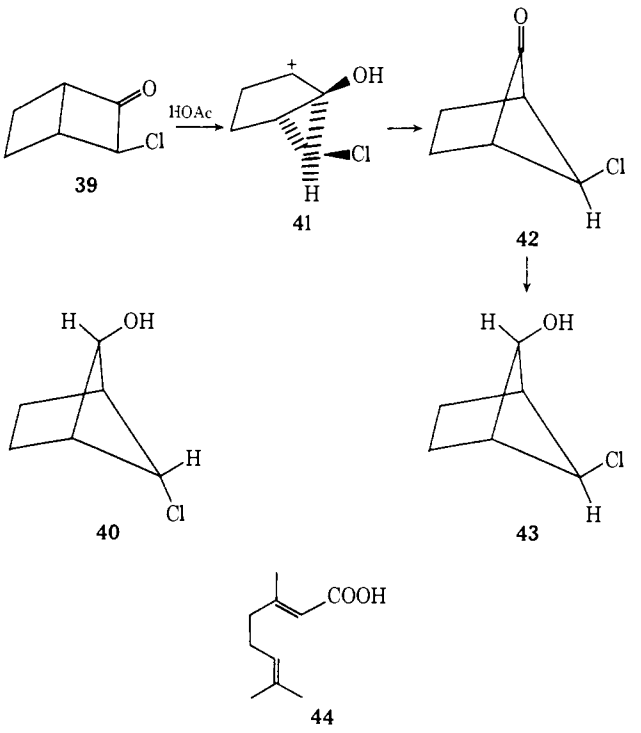
In contrast to the observations reported here, Beereboom[7] has found that **4** when treated with *p*-toluenesulfonic acid monohydrate in refluxing benzene for 24 hr affords only the olefinic ketones **35** and **36** with no evidence for formation of **4**, **5**, **6**, **7**, or **8**. Acidic degradation of **4** with methanolic hydrogen chloride led to methyl α-fencholenate (**37**). Since the mechanistic details of the conversion of **4** to **35**, **36**, and **37** have not been ascertained, it is difficult to speculate on the reasons for these apparent anomalies. Possibly in the presence of nucleophilic solvents the hemiketal **38** is produced from the initially protonated ketone **4** and undergoes fragmentation to **37** or rearrangement to **35** and **36** (Scheme IV). The ester **37** could also be produced from **35**.

Scheme IV



Although the reactions discussed here are the only well-defined examples of acid-catalyzed Wagner–Meerwein rearrangements of cyclobutanones, certain previously reported transformations of cyclobutanones probably involve similar type 1,2-alkyl shifts. For example, the ketone **39** on treatment sequentially with zinc in acetic acid and lithium aluminum hydride is reported to yield the chloro alcohol **40**.[40] More likely the ketone **39** is converted *via* the intermediates **41** and **42** to the epimeric compound **43**. The spectral properties of the alcohol product in fact are better aligned with the latter structure. Finally, the reported[7] transformation of geranic acid (**44**) to ketone **4** with 1 equiv of acetic anhydride–sodium acetate undoubtedly proceeds *via* the ketene **23**. A previous proposal[7] that **4** is produced by direct thermal cyclization of **23** seems untenable in view of the observations reported here. An alternate sequence **44** → **23** → **3** → **4** is in better accord with our findings.

(40) R. N. McDonald and C. E. Reineke, *J. Org. Chem.*, **32**, 1888 (1967).



Experimental Section

General. Infrared spectra were recorded on Perkin-Elmer Model 137 or 257 infrared spectrophotometers. Nuclear magnetic resonance spectra were run on Varian HA-100 or A60 spectrometers using tetramethylsilane as internal reference or sulfuric acid as external reference. Chemical shifts are recorded as parts per million on the τ scale and coupling constants as hertz (Hz). Nuclear magnetic resonance data are recorded in the order: chemical shift (multiplicity, integration, coupling constant, interpretation). Gas-chromatographic analyses and preparations were performed on one of four columns at the temperatures and flow rates as indicated: column 1, a 10 ft × 0.25 in. stainless steel column packed with 20% Reoplex 400 on 60–80 mesh Anakrom ABS-300; column 2, a 10 ft × 0.25 in. stainless steel column packed with 20% SF-96 silicon oil on 60–80 mesh Anakrom ABS-300; column 3, a 10 ft × 0.25 in. stainless steel column packed with 20% Reoplex 400 on 60–80 mesh Chromosorb AWDMCS; column 4, a 5 ft × 0.125 in. column packed with 15% Carbowax 20M. Unless otherwise indicated, compounds collected by preparative glc were subjected to further purification by recollection on a 10 ft × 0.25 in. stainless steel column packed with 20% DC-200 silicon oil on 60–80 mesh Chromosorb W followed by flash distillation. Gas-chromatographic retention times are recorded relative to air. ORD and CD curves were obtained on a JASCO ORD/CD/UV-5 spectropolarimeter at 25°. Measurements were made in 0.1-, 1-, and 5-cm cells at 1–2 mg/ml in $CHCl_3$. Specific rotations were obtained on the JASCO instrument at 25° or on a Rudolph Model 70 precision polarimeter. Mass spectral data were obtained on a Varian-MAT SM1 mass spectrometer.

Treatment of Chrysanthenone (3) with Acetic Acid. A. At 60° for 77 Hr. A solution of 502 mg of chrysanthenone (**3**),[5,6] $[\alpha]^{25}D$ −12.3°, in 15 ml of glacial acetic acid was heated to 60° under a nitrogen atmosphere for 77 hr. The reaction mixture was cooled to 26–27°, diluted with 15 ml of water, and extracted with 75 ml of ether. The ethereal layer was washed with two 10-ml portions of water, seven 10-ml portions of aqueous sodium bicarbonate, and three 10-ml portions of water, and dried over magnesium sulfate. Evaporation of ether under reduced pressure afforded 464 mg of residual oil, which, on analysis by glc on column 1 at a helium flow of 60 ml/min and programmed temperature between 100 and 150°, indicated the presence of 2,6,6-trimethylbicyclo[3.2.0]hept-2-en-7-one (**4**, 71%), chrysanthenone (**3**, 20%), isopiperitenone (**5**, 3%), and piperitenone (**6**, 6%). Short-path distillation of the residue afforded 218 mg of liquid, bp 100–125° (11.4–10.2 mm), consisting of ketone **4** (72%; 31% yield) and **3** (28%; 12% yield) and 39 mg of liquid, bp 125–150° (10.2 mm), consisting of **5** (32%; 2.5% yield) and **6** (68%; 5% yield).

Each of the two ketones **3** and **4** was collected by preparative glc on the same column, above, and identified by comparison of the infrared and nmr spectral parameters and glc retention times with those of authentic specimens of **4**[7] and **3**.[5,6] The ketone **4** showed $[\alpha]^{25}D$ +24.2° (*c* 0.242, $CHCl_3$). The ketones **5** and **6** were collected by preparative glc on the same column, above, at 150° and were identified by comparison with authentic specimens of isopiperitenone[9] and piperitenone,[10] respectively.

B. At 118° for 1 Hr. A solution of 505 mg of chrysanthenone (**3**) in 15 ml of glacial acetic acid was heated at reflux for a period of 60 min. After work-up as described for the above run at 60°, there was isolated 448 mg of residual oil which was shown by glc analysis to consist of **3** (75%), **4** (3%), **5** (7%), and **6** (15%). Short-path distillation of the residual liquid afforded 200 mg of liquid, bp 105–120° (10.6–11.6 mm), consisting of **4** (96%; 38% yield) and **3** (4%; 2% recovery) and 59 mg of liquid, bp 120–140° (10.6 mm), consisting of **5** (17%; 2% yield) and **6** (83%; 10% yield). The products were isolated and identified as in the previous run A, above.

Treatment of Chrysanthenone (3) with Boron Trifluoride Etherate. A. At 25–26° for 30 Min. To a solution of 500 mg of chrysanthenone ($[\alpha]^{25}D$ −26.6°; *c* 2.11, $CHCl_3$) in 15 ml of 1,2-dichloroethane was added 1.5 ml of boron trifluoride etherate. This mixture was maintained under a nitrogen atmosphere with stirring for a period of 30 min. The mixture was poured into 20 ml of cold water and extracted with ether. The ethereal layer was washed with 10 ml of saturated sodium bicarbonate solution and four 20-ml portions of water, and dried over magnesium sulfate. Evaporation of ether under reduced pressure afforded 478 mg of liquid consisting of ketone **4** (78%) and ketone **5** (22%). Short-path distillation afforded 130 mg (26%) of ketone **4**, bp 110–115° (10.2–11.6 mm), and 52 mg (10%) of ketone **5**, bp 125–130° (9.2 mm). Final purification of **4** by preparative glc on column 1 at 100° afforded **4**, $[\alpha]^{25}D$ +174° (*c* 0.122, $CHCl_3$). In a separate run, repurification of **4** by glc under the same conditions as above did not change its optical rotation. In order to preserve optical retention in these glc collections the injection port and detector cells must be maintained below 150°. Both ketones were collected by preparative glc and identified by spectral means as above.

B. At 25–26° for 2 Hr 25 Min. A solution of 500 mg of (−)-chrysanthenone (**3**) ($[\alpha]^{25}D$ −12.3°) and 1.5 ml of boron trifluoride etherate in 15 ml of 1,2-dichloroethane was stored at 25–26° for a period of 2 hr 25 min. Work-up as above afforded 455 mg of liquid consisting of **4** (13%), 2,7,7-trimethylbicyclo[3.2.0]hept-2-en-6-one (**8** (4%), **5** (63%), and **6** (20%)). Short-path distillation afforded 155 mg (32%) of liquid, bp 100–155° (11.0 mm), consisting of **4** (13%; 4% yield), **8** (4%; 1% yield), **6** (63%; 20% yield), and **8** (20%; 6% yield). In separate runs starting with 400–500 mg of **3**, the products **4**, **8**, **5**, **6**, and **7** were obtained in yields of 4–6, 1–2, 20–30, 6–10, and 1–2%, respectively. Each of the compounds **4**–**8** was collected by preparative glc as before. The compounds **4**, **5**, and **6** were identified by comparison of spectral parameters and glc retention times with authentic specimens. Ketone **8** showed $[\alpha]^{25}D$ +10.2° (*c* 0.69, $CHCl_3$). The phenol **7**, mp 46–47°, was identified by comparison of spectral properties (ir, nmr) with an authentic specimen of thymol.

The ketone **8** was isolated as a colorless liquid: $[\alpha]^{25}D$ −16.4° (*c* 0.196, $CHCl_3$); ir (CCl_4) 5.63 (C=O), 9.5 (characteristic strong absorption), 12.30 μ (trisubstituted olefin); nmr ($CDCl_3$) τ 4.60 (m, 1), 6.13 (sextet, 1, $J_1 = J_2 = 8.0 \pm 0.5$, $J_3 = 3.0$ Hz), 7.05 (broadened d, 1, $J = 8.0 \pm 0.5$ Hz), 7.3–7.7 (m, 2), 8.24 (broad s, 3), 8.71 (s, 3), 8.95 (s, 3) (see the Results for interpretation of spectrum); mass spectrum (70 eV) *m/e* (relative intensity) 150 (10), 135 (4), 122 (27), 107 (33), 91 (18), 80 (100), 79 (79), 78 (16), 77 (30), 70 (46). For data on ultraviolet, ORD, and CD curves see Table I.

Treatment of 2,6,6-Trimethylbicyclo[3.2.0]hept-2-en-7-one (4) with Acetic Acid. A solution of 506 mg of (±)-**4**[7] in 15 ml of glacial acetic acid was heated at 60° as above for chrysanthenone (**3**) for a period of 76 hr. After work-up and removal of solvent there was isolated 396 mg of recovered **4**. Not even trace quantities of ketones **5**, **6**, or **8** were observed on glc analysis of the crude product.

Treatment of Ketone 4 with Boron Trifluoride Etherate. A. At 25–26°. A solution of 2.005 g of **4** and 6.0 ml of boron trifluoride etherate in 60 ml of 1,2-dichloroethane was stored at 25–26° for a period of 2 hr 25 min. Work-up as above afforded a residual liquid consisting of **4** (26%), **8** (6%), **5** (57%), **6** (6%), and **7** (5%). Short-path distillation afforded 1.177 g (59%) of liquid, bp 100–155° (6.0–11.0 mm), consisting of **4** (10%; 6% yield), **8** (3%; 2% yield), **5** (65%; 38% yield), **6** (19%; 11% yield), and **7** (3%; 2% yield).

In separate runs starting with 500 mg of **4** there was isolated **4**, **8**, **5**, **6**, and **7** in yields of 2–4, 0.8–1, 20–29, 6–11, and 0–1%, respectively.

B. At 110–111°. A solution of 203 mg of **4** in 10 ml of toluene containing 1.0 ml of boron trifluoride etherate was maintained at reflux for a period of 24 hr. The cooled reaction mixture was poured into 10 ml of cold water and the product was extracted with 100 ml of ether. The ethereal layer was washed with sodium bicarbonate and water and dried, and the solvent was evaporated to yield 189 mg of residual liquid. Gas-chromatographic analysis on a 10 ft × 0.25 in. column packed with 20% FFAP on 60–80 mesh Chromosorb AW-DMCS at 200° and a flow rate of 75 ml/min of helium indicated the presence of piperitenone (65%), thymol (17%), and seven other unidentified peaks (18%). No evidence could be found for the presence of starting ketone **4**, isopiperitenone (**5**), or the two bicyclo[2.2.1]heptenones: 3,3,6-trimethyl-6-methylenebicyclo[2.2.1]-heptan-2-one[7] and 3,3,6-trimethylbicyclo[2.2.1]hept-5-en-2-one.[7]

Treatment of 2,4,4-Trimethylbicyclo[3.1.1]hept-2-en-6-one (11) with Boron Trifluoride Etherate. Treatment of 455 mg of ketone **11**, $[\alpha]^{25}D$ +29.1° (*c* 0.258, $CDCl_3$), with boron trifluoride etherate as above for a period of 30 min afforded 235 mg (52%) of 2,4,4-trimethylbicyclo[3.2.0]hept-2-en-7-one (**12**) as a colorless liquid, bp 100–118° (11–12 mm). The liquid showed one peak on gas chromatographic analysis on column 1 at 100 and 150°. The nmr and infrared spectra of **12** were identical with those of a sample of **12** prepared previously.[5] A sample of **12** collected by glc showed $[\alpha]^{25}D$ −328° (*c* 0.204, $CHCl_3$). The ultraviolet spectrum is discussed in the section on absolute configurations.

Acid-Catalyzed Isomerization of Isopiperitenone (5). A solution of 250 mg of isopiperitenone (**5**) and 0.8 ml of boron trifluoride etherate in 8 ml of dichloroethane was stored at 25–26° for a period of 24 hr. Work-up in the usual manner afforded 247 mg of residual liquid. Analysis of the liquid by glc on a 10 ft × 0.25 in. column packed with 20% FFAP on 60–80 mesh Chromosorb AW-DMCS indicated the presence of **5** (52%), **6** (48%), and **7** (trace).

Acid-Catalyzed Isomerization of Piperitenone (6). A solution of 511 mg of piperitenone (**6**) and 1.5 ml of boron trifluoride etherate in 15 ml of 1,2-dichloroethane was stored at 25–26° for a period of 24 hr. Work-up in the usual manner afforded 490 mg of residual liquid. Analysis of the liquid by glc indicated the presence only of ketone **6** and traces of thymol (**7**). Flash distillation afforded 269 mg of liquid consisting of **6** (99%) and **7** (<1%).

Thermal Racemization of Chrysanthenone (3) in Cyclohexane (81°). A solution of 500 mg of **3**, $[\alpha]^{26}D$ −24.0° (*c* 0.242, $CHCl_3$), in 15 ml of spectroquality cyclohexane was heated at reflux under a nitrogen atmosphere for a period of 77 hr. The bulk of the cyclohexane was removed under reduced pressure and the residual liquid dissolved in 10 ml of petroleum ether and filtered through a column containing 2.86 g of a 1:1 mixture of carbon–Celite. Removal of solvent yielded 438 mg (88%) of recovered **3**. Short-path distillation gave 255 mg (51%) of **3**, $[\alpha]^{25}D$ −7.0° (*c* 0.228, $CHCl_3$) (75% racemization). When a solution of 503 mg of **3**, $[\alpha]^{25}D$ −36.4° (*c* 1.24, $CHCl_3$) in cyclohexane was refluxed for a period of 25 hr and worked up as above, 496 mg (98%) of recovered **3** was obtained. Distillation yielded 397 mg (79%) of **3**, $[\alpha]^{25}D$ −26.0° (*c* 2.12, $CHCl_3$) (29% racemization).

Thermolysis of Chrysanthenone (3). A. In Methanol (65°). A solution of 506 mg of chrysanthenone (**3**) in 15 ml of methanol was heated at reflux for a period of 16 hr. Evaporation of solvent under reduced pressure and short-path distillation of the residual liquid afforded 447 mg of colorless liquid, bp 100–127° (6.0–7.0 mm). Analysis of the liquid by glc on column 1 at 60 ml/min helium flow and at temperatures of 100 and 150° indicated the presence of recovered **3** (50%; 43% recovery) and the ester **22** (50%; 37% yield).

The compounds **3** and **22** were collected by preparative glc on the same column as above and identified by comparison of the nmr and ir spectra of each with those of authentic specimens of **3** and **22**.[5]

B. Neat (235–260°). A 509-mg sample of chrysanthenone (**3**) ($[\alpha]^{25}D$ −12.2°) was placed in a 5-ml pear-shaped flask fitted with reflux condenser and nitrogen system. The flask was lowered into a Woods-metal bath preheated to 242° and the mixture was heated at 242–250° for a period of 20 min. Analysis of the crude product on column 3 at 100 and 150° and 70 ml/min helium flow indicated the presence of ketone **4** (33%), ketone **5** (6%), ketone **6** (46%), and a mixture of small quantities of at least ten other components (15%).

Distillation of the crude product afforded 90.5 mg of ketone **4** (90% purity; 16% yield), bp 115–126° (10.0 mm), and 114 mg of

a mixture of ketone **5** (11%; 3% yield), ketone **6** (81%; 18% yield), and unidentified peaks (8%), bp 125–150° (2.75 mm).

Each of the ketones **4**, **5**, and **6** was collected by preparative glc on column 1 at 150° and 70 ml/min helium flow. Final purification of ketone **3** was made by preparative glc on column 1 at 100°. The identity of products was made by comparison of glc retention times and nmr and ir spectra with those of the authentic specimens previously mentioned. The purified ketone **4** showed $[\alpha]^{25}D$ +1.8° (*c* 1.11, $CHCl_3$).

C. Sealed Tube (240–260°). A 502-mg sample of **3** was heated at 240–260° in a 110 × 8 mm evacuated sealed tube for a period of 20 min. Analysis of the crude product as above indicated the presence of ketone **4** (17%), ketone **5** (8%), ketone **6** (56%), and a mixture of small quantities of at least ten other components (18%).

Attempted Thermolysis of 2,6,6-Trimethylbicyclo[3.2.0]hept-2-en-7-one (4) in Methanol. A solution of 504 mg of (±)-ketone **4** in 15 ml of absolute methanol was heated at reflux for a period of 16 hr. Removal of methanol under reduced pressure afforded 462 mg of residual liquid which showed only the presence of **4** on glc analysis on column 1 at 125° and 120 ml/min helium flow. Distillation afforded 355 mg of pure **4**, bp 100–105° (10 mm). The glc retention time and spectral properties (nmr, ir) of recovered **4** were identical with those of starting ketone **4**.

Attempted Racemization of Ketone 4 in Cyclohexane. A 206-mg sample of **4**, $[\alpha]^{25}D$ +22° (*c* 0.156, $CHCl_3$), was heated at reflux as above for ketone **3** for a period of 16 hr. The bulk of the cyclohexane was removed under reduced pressure to yield 370 mg of residue consisting only of cyclohexane and ketone **4** (analysis on column 3 at 110° and 60 ml/min helium flow). Flash distillation afforded 81 mg of ketone **4** whose spectral properties were consistent with a sample of pure **4** prepared above, $[\alpha]^{25}D$ +22° (*c* 0.250, $CHCl_3$).

Acid-Catalyzed Rearrangement of 7-*exo*-Chloro-5-methylbicyclo[3.1.1]hept-2-en-6-one (13). To a refluxing solution of 1.50 g of ketone **13**[16] in 25 ml of 1,2-dichloroethane, dried over 4-Å molecular sieves, was added 0.2 g of boron trifluoride etherate. After stirring 5 min, the hot solution was poured immediately into 150 ml of ice water. The organic layer was separated, washed twice with water, and dried over magnesium sulfate. Distillation of the solvent gave 1.46 g of a mixture of compounds, shown by nmr to contain two components. The minor component was an unidentified aromatic compound (yields of this component increased with increasing reaction time). The major component was a mixture of 85% of 6-*exo*-chloro-5-methylbicyclo[3.2.0]hept-2-en-7-one (**14**) and 15% of starting material. [The ratio of the two cyclobutanones was invariant on longer reaction time. Glc separation was not successful, since a third cyclobutanone appeared in the collected fractions, shown by nmr to be formed at the expense of the bicyclo[3.2.0]heptanone (**14**).] Separation of the two cyclobutanones was accomplished on 100 g of 60–200 mesh silica gel packed in 2% ether–98% petroleum ether (30–60°). Elution with 800 ml of this mixture gave nothing. Continued elution with 600 ml of solvent gave 955 mg of **14**. Further elution with 300 ml of the solvent mixture provided 90 mg of a mixture of 4 parts of cyclobutanone **14** mixed with 1 part of a compound that might be its *endo*-chloro epimer. Starting material **13** (133 mg) was eluted with an additional 400 ml of solvent mixture. An analytical sample of 6-*exo*-chloro-5-methylbicyclo[3.2.0]hept-2-en-7-one (**14**) was prepared by two distillations at 65° (1.3 mm): ir (neat) 5.58 (C=O), 6.23 μ (C=C); nmr ($CDCl_3$) τ 4.0–4.5 (m, 2, olefinic hydrogens), 5.14 (d, 1, *J* = 3.5 Hz, chloromethine), 6.0–6.3 (m, 1, bridgehead hydrogen), 7.1–7.4 (m, 2, allylic hydrogen), 8.64 (s, 3, methyl).

Anal. Calcd for C_8H_9ClO: C, 61.35; H, 5.79. Found: C, 61.41; H, 5.80.

Acid-Catalyzed Rearrangement of 6-*exo*-Chloro-5-methylbicyclo[3.2.0]hept-2-en-7-one (14). To a refluxing solution of 58 mg of ketone **14** in 1 ml of 1,2-dichloroethane was added 2 drops of boron trifluoride etherate. The mixture was stirred for 5 min and the hot solution was poured into 50 ml of ice water and extracted twice with ether. The organic layer was washed twice with water and dried over magnesium sulfate, and the solvent removed to give 55 mg of a mixture, shown by nmr to be 85% of 6-*exo*-chloro-5-methylbicyclo[3.2.0]hept-2-en-7-one (**14**) and 15% of 7-exo-chloro-5-methylbicyclo[3.1.1.]hept-2-en-6-one (**13**).

Hydrogenation of 6-*exo*-Chloro-5-methylbicyclo[3.2.0]hept-2-en-7-one (14). A mixture of 340 mg of ketone **14** and 40 mg of 10% Pd/C in 5 ml of ethanol was hydrogenated at atmospheric pressure. After an uptake of 1.1 mol of hydrogen, the mixture was filtered, washed with water, and dried over magnesium sulfate, the solvent removed, and the residue distilled at 83° (1.8 mm) to give 307 mg of product containing some starting material. A 100-mg sample of this mixture was adsorbed on 5 g of silica gel (50–200 mesh) and eluted with 5% ether–95% petroleum ether (30–60°). Elution with 80 ml of the above solvent gave 15 mg of a mixture of starting material and reduced ketone **15**. Continued elution with 60 ml of the solvent gave 87 mg of 7-*exo*-chloro-1-methylbicyclo[3.2.0]heptan-6-one (**15**). An analytical sample was prepared by bulb-to-bulb distillation at 55° (3.75 mm): ir (neat) 5.60 μ (C=O); nmr ($CDCl_3$) τ 5.46 (d, 1, *J* = 3.0 Hz, chloromethine), 6.65–7.0 (m, 1, C-5 hydrogen), 7.8–8.5 (m, 6, C-2, C-3, C-4 hydrogens), 8.62 (s, 3, methyl).

Anal. Calcd for $C_8H_{11}ClO$: C, 60.58; H, 6.99. Found: C, 60.62; H, 6.87.

Zinc–Acetic Acid Reduction of 7-*exo*-Chloro-1-methylbicyclo[3.2.0]heptan-6-one (15). A mixture of 100 mg of chloro ketone **15** and 800 mg of zinc dust in 5 ml of acetic acid was stirred at room temperature for 3 hr. The mixture was decanted into 50 ml of water and extracted twice with petroleum ether. The extract was washed with water and dried over magnesium sulfate, and the solvent removed to give 74 mg of 1-methylbicyclo[3.2.0]heptan-6-one (**16**).[17]

Acid-Catalyzed Rearrangements of 7-*exo*-Chloro-1-methylbicyclo[3.1.1]heptan-6-one (17). A. A mixture of 1.00 g of bicycloheptanone **17**[19] and 1.5 g of boron trifluoride etherate in 50 ml of 1,2-dichloroethane was refluxed under nitrogen for 22.5 hr. (Aliquots, analyzed by glc at 15 min and 1.75 hr, showed essentially the same results as were obtained by work-up after 22.5 hr.) The mixture was poured into 100 ml of water. The organic layer was washed four times with water and dried over magnesium sulfate, and the solvent removed by atmospheric distillation through an 8-in. vacuum-jacketed column. Distillation of the residue at 74° (4 mm) gave 836 mg of a mixture, shown by glc and nmr to consist of three components: 86% of 7-*exo*-chloro-5-methylbicyclo[3.2.0]heptan-6-one (**18**), 4% of 7-*endo*-chloro-5-methylbicyclo[3.2.0]heptan-6-one (**19**), and 10% of starting material **17**.

B. A mixture of 1.00 g of bicycloheptanone **17** and 16 ml of 97% formic acid was refluxed for 108 hr. The solution was poured into water and extracted three times with petroleum ether (30–60°). The organic layer was washed three times with water and dried over sodium sulfate. Analysis of this solution on column 4 at 175° using an internal standard and correcting for differences in molar response to the detector gave the following yields: 39% of the exo ketone **18** (retention time 3.0 min), 35% of the endo ketone **19** (retention time 3.7 min), and 9% of starting material **17** (retention time 4.7 min). (A similar run worked up after 18 hr gave 73% of the exo ketone **18**, 10% of the endo ketone **19**, and 18% of starting material **17**.) The ketones were separated on a 10 ft × 0.375 in. 30% SF-96 column at 120° (170 ml/min helium flow): the exo ketone **18** appeared at 60–78 min, the endo ketone **19** at 80–86 min, and starting material at 90–97 min. The total yield of collected products was 50%. Analytical samples were prepared by a second preparative glc collection followed by bulb-to-bulb distillation at a bath temperature of 60° (3.5 mm).

The 7-*exo*-chloro-5-methylbicyclo[3.2.0]heptan-6-one (**18**) had the following spectral properties: ir (neat) 5.60 μ (C=O); nmr ($CDCl_3$) τ 5.72 (d, 1, *J* = 4.0 Hz, chloromethine), 7.3–7.7 (m, 1, bridgehead hydrogen), 7.7–8.6 (m, 6, C-2, C-3, C-4 hydrogens), 8.62 (s, 3, methyl).

Anal. Calcd for $C_8H_{11}ClO$: C, 60.58; H, 6.99. Found: C, 60.41; H, 7.05.

The 7-*endo*-chloro-5-methylbicyclo[3.2.0]heptan-6-one (**19**) showed these spectral parameters: ir (neat) 5.59 μ; nmr ($CDCl_3$) τ 4.90 (d, 1, *J* = 9.5 Hz, chloromethine), 6.9–7.3 (m, 1, bridgehead hydrogen), 7.7–8.5 (m, 6, C-2, C-3, C-4 hydrogens), 8.64 (s, 3, methyl).

Anal. Calcd for $C_8H_{11}ClO$: C, 60.58; H, 6.99. Found: C, 60.51; H, 6.85.

Acid-Catalyzed Rearrangement of 7-*exo*-Chloro-5-methylbicyclo[3.2.0]heptan-6-one (18). A solution of 77 mg of bicycloheptanone **18** in 3 ml of 97% formic acid was refluxed for 120 hr. Work-up as above gave 68 mg of a mixture, shown by nmr and glc to be 62% of 7-*endo*-chloro-5-methylbicyclo[3.2.0]heptan-6-one (**19**), 33% of 7-*exo*-chloro-5-methylbicyclo[3.2.0]heptan-6-one (**18**), and 5% of 7-*exo*-chloro-1-methylbicyclo[3.1.1]heptan-6-one (**17**). (A fourth, unknown compound, formed in less than 2% overall yield, appeared 0.4 min before the *exo*-bicycloheptanone **18**.)

Acid-Catalyzed Rearrangement of 7-*endo*-Chloro-5-methylbicyclo[3.2.0]heptan-6-one (19). A solution of 45 mg of bicycloheptanone **19** in 2 ml of 97% formic acid was refluxed for 9 days. Work-up as above gave 41 mg of a mixture, shown by glc to be 66% of 7-*endo*-chloro-5-methylbicyclo[3.2.0]heptan-6-one (**19**), 29% of 7-*exo*-chloro-5-methylbicyclo[3.2.0]heptan-6-one (**18**),

and 5% of 7-*exo*-chloro-1-methylbicyclo[3.1.1]heptan-6-one (**17**). (The fourth unknown compound mentioned above appeared again in about 2% overall yield.)

Zinc–Acetic Acid Reduction of 7-*exo*-Chloro-5-methylbicyclo-[3.2.0]heptan-6-one (18). A mixture of 53 mg of bicycloheptanone **18** and 400 mg of zinc dust in 3 ml of acetic acid was stirred at room temperature for 3 hr. The solution was decanted into 100 ml of water and extracted with petroleum ether (30–60°). The extract was washed five times with water and dried over magnesium sulfate. Removal of the solvent gave 31 mg of 5-methylbicyclo-[3.2.0]heptan-6-one (**21**), identical in all major respects with an authentic sample.[20]

Zinc–Acetic Acid Reduction of 7-*endo*-Chloro-5-methylbicyclo-[3.2.0]heptan-6-one (19). A mixture of 38 mg of bicycloheptanone (**19**) and 250 mg of zinc dust in 2 ml of acetic acid was stirred at 60° for 2 hr. Work-up as above gave 21 mg of 5-methylbicyclo-[3.2.0]heptan-6-one (**21**) containing traces of starting material.

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The Stereochemistry of Cyclopropylcarbinyl Rearrangements. Synthesis and Solvolysis of Cyclopropylcarbinyl-*1,1',1'-trans*-*2,3,3*-d_6 Methanesulfonate[1]

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Abstract: The stereochemistry of the three different rearrangement processes involving the cyclopropylcarbinyl cation was investigated under solvolysis conditions. The substrate employed, cyclopropylcarbinyl-*1,1',1'-trans*-*2,3,3*-d_6 mesylate (**1b**), contained only a single hydrogen atom as label, to facilitate pmr analysis of the solvolysis products (60% aqueous acetone, $CaCO_3$): cyclopropylcarbinol-d_6 (**2**), cyclobutanol-d_6 (**3**), and 1-buten-4-ol-d_6 (**4**). The cis-2 hydrogen of **1b** was distributed in these products as follows: in **2**, 77% at the cis-2 (and cis-3) and 23% at the carbinyl (1') positions; in **3**, 60% at the cis-2 (and cis-4) and 40% at the cis-3 positions; and in **4**, *ca.* 32% at the cis-1, *ca.* 30% at the 3, and *ca.* 38% at the 4 positions. Within experimental error all three rearrangement processes, the cyclopropylcarbinyl → cyclopropylcarbinyl, the cyclopropylcarbinyl → cyclobutyl, and the cyclopropylcarbinyl → allylcarbinyl, were completely stereospecific.

Not only is the cyclopropylcarbinyl cation unusually stable, it is also particularly rearrangement prone.[3–10] Three types of rearrangements are possible: ring expansion to give cyclobutyl products, ring opening to give allylcarbinyl products, and a degenerate cyclopropylcarbinyl–cyclopropylcarbinyl isomerization which can be detected by use of isotopic labels. Such labeling experiments further reveal that extensive methylene group scrambling occurs during formation of the cyclobutyl and allylcarbinyl products.[3–5] Very recently it has been possible to demonstrate the degenerate cyclopropylcarbinyl–cyclopropylcarbinyl rearrangement by direct nmr observation of the stable cyclopropylcarbinyl cation in SbF_5–SO_2ClF solution at −80°.[8] On the nmr time scale, equilibration of the three methylene groups is so rapid that only a single signal (consisting of a pair of doublets, one for the three cis and one for the three trans protons) is observed.

Our paper is concerned with the stereochemistry of these three rearrangement processes with the parent cyclopropylcarbinyl cation. When our work was commenced in 1968 very little pertinent information was available. Subsequently, results from a number of laboratories on substituted cyclopropylcarbinyl and cyclobutyl derivatives have indicated all three types of rearrangements to be at least highly stereoselective.[4c,6,7,11] Experimental work on the parent cyclo-

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(3) Reviews: Chapters by H. G. Richey, Jr., and by K. B. Wiberg, B. A. Andes, Jr., and A. J. Ashe in "Carbonium Ions," G. A. Olah and P. v. R. Schleyer, Ed., Vol. III, Interscience, New York, N. Y., in press.

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