A. Moore for technical assistance.

Registry No. **2**, 66478-66-8; (±)-**8a**, 124175-46-8; (±)-**8b**, 124175-74-2; **9a**, 124175-47-9; **9b**, 124175-75-3; **10a**, 124175-48-0; **10b**, 124175-76-4; (±)-**11a**, 124175-49-1; (±)-**11b**, 124175-77-5; **12a**, 124175-50-4; **12b**, 124175-78-6; **13a**, 124175-51-5; **13b**, 124175-79-7; **14a**, 124175-52-6; **14b**, 124175-80-0; (±)-**15**, 124175-53-7; **16**, 124175-54-8; **17**, 124175-55-9; (±)-**18**, 124175-56-0; **19**, 124175-57-1; **20**, 124175-58-2; **21**, 74237-20-0; **22**, 124175-59-3; **23**, 102631-99-2; **24**, 124175-60-6; **25**, 124175-61-7; **26**, 124175-62-8; (±)-**27a**, 124175-63-9; (±)-**27b**, 124175-81-1; (±)-**27c**, 124175-82-2; **28a**, 124175-64-0; **28b**, 124175-83-3; (±)-**28b** epoxide, 124175-73-1; **28c**, 124175-84-4; (±)-**29**, 124175-65-1; (±)-**30**, 15255-24-0; **31**, 124175-66-2; (±)-**32**, 124175-67-3; **33**, 124175-68-4; (±)-**34**, 124175-69-5; (±)-**35**, 98719-19-8; **36**, 124175-70-8; (±)-**37**, 124175-71-9; (±)-**38**, 124175-72-0; HC≡CBu-*n*, 693-02-7; HC≡CCH$_2$C$_6$H$_5$, 10147-11-2; CH$_2$=C(Li)Bu-*n*, 124156-74-7; 4-ClC$_6$H$_4$Li, 14774-78-8; HC≡CH, 74-86-2; HC≡CSi(CH$_3$)$_3$, 1066-54-2; (U)-CH$_3$CHCl(CH$_2$)$_2$CH=C(CH$_3$)$_2$, 72055-86-8; CH$_2$=C(Br)CH$_3$, 557-93-7; HC≡CCH$_3$, 74-99-7.

Synthesis of α-(Halomethyl)cycloalkanones†

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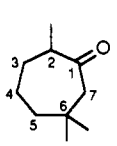
Received March 9, 1989

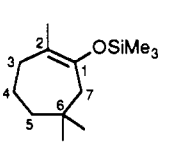
Cyclopropane unravelling of cyclopropanes and halocyclopropanes, prepared by cyclopropanation of 2,6,6-trimethyl-1-((trimethylsilyl)oxy)cycloheptene and 2-methyl-5-isopropyl-1-((trimethylsilyl)oxy)cyclohexene, is described. Solvolysis, halogenolysis, and protolysis of the cyclopropanes are discussed, and methods of facile synthesis of α-(halomethyl)cycloalkanones are introduced.

α-Alkyl-α-(halomethyl)cyclohexanones have served as useful intermediates in diterpene,[1] alkaloid[2], and sesquiterpene[3] syntheses. The preparation of the ketones has depended heretofore largely on the formation of cyclohexadienones in Reimer–Tiemann reactions as, for example, the construction of dienone products of the reactions of carvacrol (1) with chloroform[4] and bromoform en route to bicyclic ketones depicted in Scheme I (see the Experimental Section). Unfortunately several factors work against the frequent use of the Reimer–Tiemann reaction in this connection: (a) low yield of cyclohexadienone product, (b) the dienone being constrained to a six-membered ring, and (c) the halomethyl substituent being always a dichloromethyl or dibromomethyl group. Hence an alternate, more flexible route of synthesis of α-(halomethyl)cycloalkanones was in demand and a study of its development was initiated.

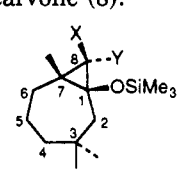
In principle, halogenolysis of cyclopropanol derivatives or protolysis of halocyclopropanol derivatives could be envisaged to yield ready access to α-(halomethyl)cycloalkanones.[5] Whereas especially the latter reaction has been assumed to take an alternate path (i.e. an electrocyclic process induced by halide solvolysis furnishing a conjugated enone product),[6] there were some indications that even in this case the desired ring opening could be accomplished.[7] Hence various ring cleavages of cyclopropanol derivatives were undertaken, all starting compounds being based on tetrahydroeucarvone (8).[8]



8



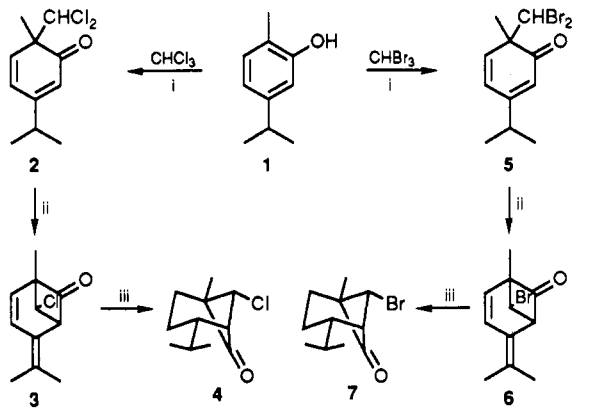
9



10a: X = Y = H
b: X = Y = Cl
c: X = Y = Br
d: X = Cl; Y = Br
e: X = Br; Y = Cl
f: X = Cl; Y = H

Bicyclo[5.1.0]octan-1-ol derivatives **10**, needed for the present study, were prepared in the following manner.

Scheme I[a]



[a] (i) 50% NaOH–H_2O, C_6H_6, 80 °C; (ii) Na_2CO_3, DMSO, 80 °C; (iii) H_2, 10% Pd/C, EtOAc.

Exposure of ketone **8** to trimethylsilyl chloride, sodium iodide, and triethylamine in acetonitrile afforded silyl enol ether **9** (91% yield),[9] whose cyclopropanation with methylene iodide and zinc–copper couple in ether gave bicycle

† Dedicated to the memory of Professor Edgar Lederer.

(1) (a) Wenkert, E.; Stevens, T. E. *J. Am. Chem. Soc.* **1956**, *78*, 5627. (b) Wenkert, E.; Afonso, A.; Bredenberg, J. B-son; Kaneko, C.; Tahara, A. *J. Am. Chem. Soc.* **1964**, *86*, 2038.
(2) Bartlett, M. F.; Taylor, W. I. *J. Am. Chem. Soc.* **1960**, *82*, 5941.
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(6) (a) Amice, P.; Blanco, L.; Conia, J. M. *Synthesis* **1976**, 196. (b) Weyerstahl, P. Dihalocyclopropanes In *The Chemistry of Functional Groups, Supplement D, The Chemistry of Halides, Pseudo-halides and Azides*; Patai, S., Rappoport, Z., Eds.; John Wiley and Sons, Inc.: New York, 1983; Part 2, Chapter 27, pp 1451–1497.
(7) Fried, J. J.; U.S. Pat. 3,376,291, 2 April 1968; *Chem. Abstr.* **1968**, *69*, 87368x. U.S. Pat. 3,376,323, 2 April 1968; *Chem. Abstr.* **1969**, *70*, 4416h.
(8) (a) Naves, Y.; Ardizio, P. *Helv. Chem. Acta* **1949**, *32*, 329. (b) Campbell, J. R. B.; Islam, A. M.; Raphael, R. A. *J. Chem. Soc.* **1956**, 4096. (c) Welch, S. C.; Walters, R. L. *J. Org. Chem.* **1974**, *39*, 2665.
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0022-3263/90/1955-1185$02.50/0

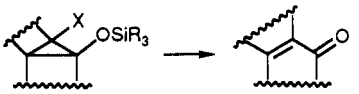
Table I. ^{13}C NMR Shifts of Bicyclo[5.1.0]octanes 10 and 14[a,b]

carbon	10a	10b	10c	10f	14a	14b	14c
1	62.2	66.3	66.2	62.5	60.8	58.5	63.1
2	50.6	45.2	47.1	50.5	50.5	50.1	44.8[c]
3	34.4	35.9	36.1	35.1	34.4	35.0	36.1
4	44.9	45.9	46.2	46.1	45.4	45.4	44.9[c]
5	21.6	21.5	21.7	21.9	21.6	22.0	21.5
6	38.5	34.2	37.3	39.5	39.1	39.1	34.2
7	24.2	34.4	34.3	28.4	24.5	28.2	34.2
8	30.6	77.2	60.2	50.8	31.0	50.5	76.9
7-Me	18.2	15.2	18.3	13.7	17.9	13.2	15.1

[a] The δ values are in parts per million downfield from Me_4Si: $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm. [b] *gem*-Dimethyl function δ(Me) = 25.7 ± 0.8 and 33.4 ± 0.4 ppm; trimethylsilyl group δ(Me) = 1.5 ± 0.6 ppm. [c] Signals may be interchanged.

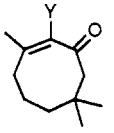
10a (80%). Treatment of the enol ether with ethyl trichloroacetate and sodium methoxide in pentane yielded dichloride **10b** (88%), and reaction with bromoform and potassium *tert*-butoxide in pentane resulted in the formation of dibromide **10c** (ca. 75%), whose lability required its immediate use in subsequent reactions. Cyclopropanation of enol ether **9** with chlorodibromomethane and potassium *tert*-butoxide furnished a mixture of bicycles **10d** and **10e**. Reduction of dichloride **10b** with tri-*n*-butyltin hydride and azobisisobutyronitrile in benzene[10] led to exo chloride **10f** (71%). The stereochemistry of the latter substance was determined by comparison of its ^{13}C NMR spectrum with that of unhalogenated bicycle **10a** and dichloro compound **10b** (Table I). The chlorines exert a γ effect on the vicinally cis carbon sites, e.g. in dichloride **10b** the endo chlorine on carbons 2 and 6 and the exo chlorine on the angular methyl group. In view of only the methyl group of the monochloro bicycle being shielded (vis-à-vis compound **10a**), this substance must possess the configuration depicted in formula **10f**.[11]

The first investigation, forming the background of the subsequent study, involved the undesired, but heretofore common, ring opening of halocyclopropyl silyl ethers of type **10b–f** via halide solvolysis, cyclopropane bond scission at the bridgehead carbon sites, and cycloalkenone formation (eq 1). This reaction sequence has been reported to occur on thermolysis in hydrocarbon solvents and under acid or base catalysis in protic media.[16] In like fashion, the following base-induced reactions on halides **10b–f** yielded cyclooctenones as solvolysis products.

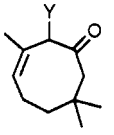


(1)

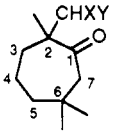
Treatment of chlorides **10f** and **10b** with methanolic sodium methoxide afforded cyclooctenones **11a** (90%) and **11b** (87%), respectively. Exposure of dichloride **10b** to



11a: Y = H
b: Y = Cl
c: Y = Br



12a: Y = Cl
b: Y = Br

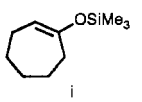


13a: X = Y = H
b: X = Cl; Y = H
c: X = Br; Y = H
d: X = Y = Cl
e: X = Y = Br
f: X = Cl; Y = Br

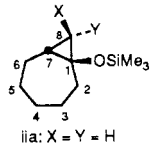
tetra-*n*-butylammonium fluoride in tetrahydrofuran, containing <5% water, led to cyclooctenone **11b** (43%), its isomer **12a** (11%), and the (dichloromethyl)cycloheptanone **13d** (32%). The same reaction with dibromide **10c** furnished cyclooctenone **11c** (65%) and (dibromomethyl)cycloheptanone **13e** (15%), while the reaction with the chlorobromide mixture **10d** and **10e** produced cyclooctenone **11b** (74%) and a ca. 2:1 mixture (10%) of stereoisomeric (bromochloromethyl)cycloheptanones **13f**.[17]

(10) Cf.: Groves, J. T.; Kittisopikul, S. *Tetrahedron Lett.* **1977**, 4291.

(11) Since this stereochemistry implies hydrogen delivery from the trialkylstannane to the intermediate cyclopropyl radical[12] from the concave side of the bicycle and opposite to that of the bridgehead substituents, it became of interest to study the reduction of a structurally related dichloride less sterically encumbered at its bridgeheads and bicycle iib was chosen for this purpose. Cycloheptanone was converted into its trimethylsilyl enol ether i[13] (90%), whose exposure to the Simmons–Smith reaction yielded bicycle iia[14] (77%) [^1H NMR δ 0.38 (dd, 1, *J* = 5, 5 Hz, endo H-8), 0.82 (ddd, 1, *J* = 15, 14, 11 Hz, endo H-6), 0.91 (dd, 1, *J* = 10, 5 Hz, exo H-8), 1.02 (dddd, 1, *J* = 15, 10, 6, 5 Hz, H-7), 1.1–1.9 (m, 6, C-3, C-4, C-5 Hs), 1.30 (dd, 1, *J* = 15, 11 Hz, endo H-2), 2.11 (ddd, 1, *J* = 14, 7, 6 Hz, exo H-6), 2.24 (dd, 1, *J* = 15, 7 Hz, exo H-2); ^{13}C NMR δ 1.3 (methyls), 22.1 (C-8), 24.9 (C-7), 25.4 (C-4), 28.6 (C-5), 31.2 (C-6 or C-3), 31.9 (C-3 or C-6), 37.6 (C-2), 61.0 (C-1); *m/e* 198 (M^+, 17%), 183 (22), 155 (28), 75 (45), 73 (base)]. Treatment of ether i with chloroform and potassium *tert*-butoxide in pentane gave dichloride iib (65%)[15] [liquid: ^1H NMR δ 0.23 (s, 9, methyls), 1.1–1.6 (m, 4, methylenes), 1.7–2.0 (m, 5, methine, methylenes), 2.1–2.2 (m, 2, CH_2); ^{13}C NMR δ 0.8 (methyls), 25.4 (C-4), 26.9 (C-3), 27.4 (C-5), 31.5 (C-2), 33.0 (C-6), 40.8 (C-7), 67.7 (C-1), 71.8 (C-8)], whose reduction with tri-*n*-butyltin hydride and azobisisobutyronitrile in benzene produced a 1.3:1 mixture of chlorides iic [liquid: ^{13}C NMR δ 1.0 (methyls), 25.5 (C-4), 27.5 (C-5), 29.9 (C-6), 31.6 (C-3), 34.2 (C-7), 37.1 (C-2), 46.4 (C-8), 62.7 (C-1)] and iid [liquid: ^{13}C NMR δ 0.9 (methyls), 23.0 (C-7), 24.5 (C-6), 25.5 (C-4), 27.8 (C-5), 28.3 (C-2), 31.6 (C-3), 44.0 (C-8), 63.3 (C-1)].



i



iia: X = Y = H
b: X = Y = Cl
c: X = Cl; Y = H
d: X = H; Y = Cl

It thus appears that the angular methyl group of dichloride **10b** offers some, albeit minor steric resistance to exo hydrogen transfer in the tin hydride reduction.

(12) Cf.: Applequist, D. E.; Peterson, A. H. *J. Am. Chem. Soc.* **1960**, *82*, 2372.

(13) Friedrich, E.; Kalinowski, H. O.; Lutz, W. *Tetrahedron* **1980**, *36*, 1051.

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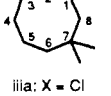
(16) (a) Stork, G.; Macdonald, T. L. *J. Am. Chem. Soc.* **1975**, *97*, 1264. (b) Reference 6a. (c) Blanco, L.; Amice, P.; Conia, J.-M. *Synthesis* **1981**, 289.

(17) A minor, labile product, which isomerized readily into cyclooctenone **11b**, was 2-chloro-6,6-dimethyl-3-methylenecyclooctanone iiia [^1H NMR δ 0.99, 1.02 (s, 3 each, methyls), 1.2–1.6 (m, 4, methylenes), 2.1–2.2 (m, 1, H-4), 2.25 (d, 1, *J* = 12 Hz, H-8), 2.52 (d, 1, *J* = 12 Hz, H-8), 2.5–2.7 (m, 1, H-4), 4.79 (s, 1, H-2), 5.24 (s, 1, olefinic *E*-H), 5.41 (s, 1, olefinic *Z*-H)].



iiia: X = Cl
b: X = Br

Table II. ^{13}C NMR Shifts of Cycloheptanones 13 and 15–17[a]

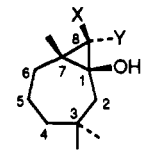
carbon	13a	13b	13c	13d	13e	16	17	15
1	216.2	213.6	213.1	211.7	210.9	211.0	211.2	206.4
2	47.2	51.5	50.9	57.8	57.3	57.7	57.6	65.2
3	39.6	34.0	35.1	31.0	33.4	32.6	32.0	32.9
4	20.6	20.1	20.2	20.0	20.1	20.0	20.0	21.2
5	44.4	44.2	44.2	44.4	44.5	44.5	44.4	44.0
6	32.9	33.2	33.2	33.4	33.4	33.4	33.4	33.8
7	51.9	53.7	53.6	55.8	55.8	55.5	56.0	56.2
X-C	25.7	51.3	41.5	79.8	55.0	67.9	69.0	89.1
2-Me	25.7	22.4	23.3	21.2	22.1	20.9	22.3	20.6
6-Me	29.3	29.2	29.0	26.2	25.8	25.9	26.1	25.0
	29.3	29.3	29.6	32.3	32.9	32.9	32.5	34.7

[a] The δ values are in parts per million downfield from Me_4Si: $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm.

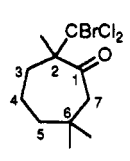
The unstable dibromide **10c**, when kept in chloroform solution for several hours, underwent transformation into a mixture of cyclooctenone **11c** and its isomer **12b**.[18]

It is noteworthy that the unravelling of halocyclopropanes **10b–e** constitutes the first examples of the use of fluoride ion in such ring openings and that the halide solvolysis products consist not only of conjugated enones, but also of β,γ-unsaturated cycloalkenones (unobserved heretofore). Furthermore, it was of major importance that the fluoride-induced reactions gave not only halide solvolysis products, but also protolysis products, i.e. halomethylcycloheptanones.

One reaction known to transform unhalogenated cyclopropanol derivatives into α-(halomethyl)cycloalkanones was the halogenative cyclopropane scission.[5,19] Hence it now was used in the bicyclo[5.1.0]octane series (**10**). Interaction of cyclopropyl ether **10a** with *tert*-butyl hypochlorite in carbon tetrachloride and, separately, with bromine in methylene chloride furnished 2-(chloromethyl)-2,6,6-trimethylcycloheptanone (**13b**) (78%) and its bromo equivalent **13c** (89%), respectively. Exposure of chlorocyclopropyl ether **10f** to *N*-bromosuccinimide in moist ether yielded ketone **13f** (61%) and cyclopropanol **14b** (26%). Apparently the steric interference of the cyclopropyl chlorine reduced the rate of ring opening, while the hydrobromic acid liberated in the solution caused hydrolysis of the silyl ether moiety. When dichlorocyclopropyl ether **10b** was made to react with *N*-bromosuccinimide, it produced only cyclopropanol **14c**. But reaction with bromine in methylene chloride afforded ketone **15** (52%) and cyclopropanol **14c** (36%).



14a: X = Y = H
b: X = Cl; Y = H
c: X = Y = Cl



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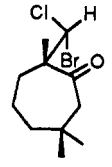

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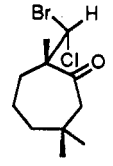
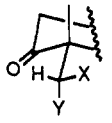


17

The above brominative ring opening of cyclopropane **10f** had led to a single **13f** stereoisomer, whose structure was identical with the major dihalocycloheptanone component of the **10d/10e → 11b/13f** reaction. In view of the known inversion of configuration at the halogenation site in brominative ring cleavages of cyclopropanols[19] the product of the **10f → 13f** transformation possesses the stereochemistry illustrated in formula **16** and hence the minor dihalocycloheptanone product of the **10d/10e → 11b/13f** conversion can be portrayed by stereostructure **17**. These formulations are in accord with the ^{13}C NMR spectral analysis of the two **13f** stereoisomers in the light of spectral data on all cycloheptanones **13** and **15** (Table II) and on the assumption of the halomethyl groups being equatorially disposed to the ketonic ring in preferred rotamer populations of such nature as to minimize ketone–halogen interactions, i.e. the carbon–oxygen double bond being trans, antiparallel to the carbon–halogen linkage in the monohalides **13b** and **13c** (conformations **18a** and **18b**, respectively) and the carbon–hydrogen bond of the dihalomethyl group being gauche to the carbonyl and 2-methyl carbons in the dihalo compounds **13d–f** (conformations **18c–f**, respectively).



18a: X = Cl; Y = H
b: X = Br; Y = H
c: X = Y = Cl
d: X = Y = Br
e: X = Cl; Y = Br
f: X = Br; Y = Cl

Finally and perhaps most importantly, an investigation of the protolytic cleavage of cyclopropyl silyl ethers **10** was undertaken. Whereas the unhalogenated, three-membered ring system **10a** could btransformed into 2,2,6,6-tetramethylcycloheptanone (**13a**) (88%) on treatment with methanolic potassium hydroxide and was en route to the same compound on interaction with methanolic acid (early quenching yielding cyclopropanol **14a** (81%) and ketone **13a** (12%)), unravelling halocyclopropyl ethers without chloride solvolysis proved difficult. However, the following procedure gave the desired result. Exposure of cyclopropyl ethers **10f**, **10b**, and **10c** to ethereal hydrogen bromide furnished ketones **13b** (82%), **13d** (68%), and **13e** (43%), respectively. *Thus two procedures for the synthesis of α-(halomethyl)cycloalkanones, by means other than the Reimer–Tiemann reaction, now were on hand—cyclopropanation of cycloalkanone silyl enol ethers, followed by halogenolytic or protolytic three-membered ring opening.*

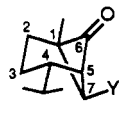
Some time ago it had been demonstrated that treatment of α-(halomethyl)cyclohexanones of type tetrahydro-**2** with base leads to their conversion into cyclobutanones of type **4** or **19a**.[4,20] It now became of interest to learn whether

(18) A minor, unstable product, which isomerized easily into cyclooctenone **11c**, proved to be bromide iiib [^1H NMR δ 1.00, 1.02 (s, 3 each, methyls), 1.2–1.6 (m, 4, methylenes), 2.1–2.3 (m, 1, H-4), 2.48 (s, 2, 2 H-8), 2.6–2.7 (m, 1, H-4), 4.97 (s, 1, H-2), 5.24 (s, 1, olefinic *E*-H), 5.43 (s, 1, olefinic *Z*-H); ^{13}C NMR δ 21.6 (C-5), 27.3 (Me), 31.3 (Me), 32.8 (C-7), 36.1 (C-6), 37.9 (C-4), 47.8 (C-8), 63.4 (C-2), 120.7 (olefinic CH_2), 143.0 (C-3), 201.6 (C-1)].

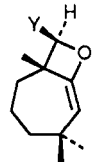
(19) DePuy, C. H.; Armey, W. C., Jr.; Gibson, D. H. *J. Am. Chem. Soc.* **1968**, *90*, 1830.

(20) Wenkert, E.; Bakuzis, P.; Baumgarten, R. J.; Leicht, C. L.; Schenk, P. *J. Am. Chem. Soc.* **1971**, *93*, 3208.

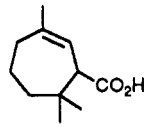
some of the α-(halomethyl)cycloheptanones (**13**) could be induced to undergo a similar reaction. When ketones **13b** as well as **13c** were exposed to potassium *tert*-butoxide in *tert*-butyl alcohol solution, they were transformed into oxetane **20a** (65 and 67%, respectively), i.e. an O- instead of C-alkylation product.[21,22] Treatment of the dihalo ketones **13d-f** with base under the same conditions also led to an unexpected result—the formation of acid **21**,[23] thus thwarting an approach to the bicyclo[4.1.1]octan-7-one system.



19a: Y = Cl
b: Y = Br
c: Y = CO_2Et
d: Y = CO_2H



20a: Y = H
b: Y = Cl

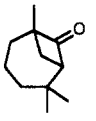


21

Application. The first utilization of the above α-(halomethyl)cycloalkanone synthesis method involved the production of enantiomerically pure α-(dichloromethyl)-cyclohexanones of the tetrahydro-**2** type as well as bromocyclobutanones **7** and **19b**, needed for the construction of copaenic sesquiterpenes[25] or as intermediates for a potential ylangene synthesis.[4]

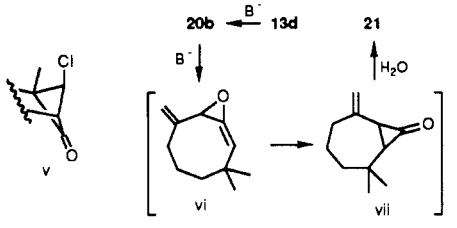
(21) Cf.: Discussions on related products in footnote 13 of ref 4 and in ref 20.

(22) The minor sideproduct was the expected 1,5,5-trimethylbicyclo-[4.1.1]octan-7-one (iv) [^{1}H NMR δ 0.92, 0.96, 1.03 (s, 3 each, methyls), 1.4-1.8 (m, 6, methylenes), 1.65 (dd, 1, J = 12, 9 Hz, c-butanone ax H-8), 1.94 (dd, 1, J = 12, 3 Hz, cyclobutanone eq H-8), 2.77 (dd, 1, J = 9, 3 Hz, H-6); ^{13}C NMR δ 21.3 (Me), 21.5 (Me), 26.7 (C-8), 27.7 (5-Me), 27.8 (5-Me), 35.2 (C-2), 38.8 (C-4), 67.4 (C-6)].



iv

(23) The mechanism of this reaction remains obscure. Whereas the simplest explanation of the **13d** → **21** transformation involves base-induced β-chlorocyclobutanone formation followed by hydroxide-induced 1,3-elimination of chloride ion (with ring opening),[20] it is not acceptable in view of (a) the known stability of β-halocyclobutanones of type **4** or **7** toward base,[20] (b) the alternate stereostructure v, i.e. the proper stereochemistry required for the 1,3-elimination process, having never been observed as a product of the dehydrohalogenation of β-(dihalomethyl)-cycloalkanones,[4,20] (c) the solvent having been kept meticulously dry, and (d) *tert*-butoxide being too bulky a nucleophile to participate in the 1,3-elimination and, had it taken part in the cyclobutanone scission, a *tert*-butyl ester would have been formed and have remained intact during workup.

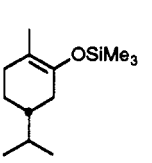


The following represents a tentative portrayal of the reaction path in the formation of acid **21**. In analogy with the **13b** → **20a** conversion dichloro ketone **13d** is transformed firstly into oxetane **20b**. The second dehydrochlorination involves chloride solvolysis of the latter. Rearrangement of the resultant, metastable allene epoxide (vi) (presumably via an oxyallyl system) into a cyclopropanone (vii)[24] and hydration thereof on work-up leads to acid **21**.

(24) (a) Crandall, J. K.; Machleder, W. H. *J. Am. Chem. Soc.* **1968**, *90*, 7347. (b) Camp, R. L.; Greene, F. D. *Ibid.* **1968**, *90*, 7349.

(25) Wenkert, E.; Bookser, B., unpublished observations. Bookser, B. C. Ph.D. Dissertation, University of California—San Diego, La Jolla, CA 92093, 1988.

A carvomenthone–isocarvomenthone mixture, prepared by hydrogenation of *l*-carvone,[26] was converted into enol ether **22** (97%) (vide supra for comparable preparation of enol ether **9**),[9] whose treatment with chloroform and potassium *tert*-butoxide in hexane produced cyclopropyl ethers **23a** (87%). Exposure of the latter stereoisomer mixture to an ethereal, saturated hydrogen bromide solution led to cyclohexanones **26a** (34%) and **26b** (28%) as well as, to a minor extent (8%), to cycloheptenone **24a**.



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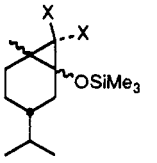
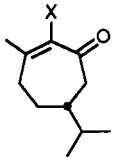
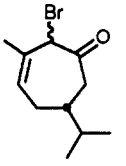


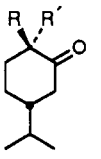
23



a: X = Cl **24**
b: X = Br



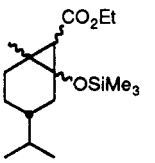
25



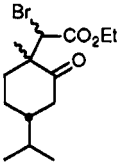
26a: R = Me; R′ = $CHCl_2$
b: R = $CHCl_2$; R′ = Me
c: R = Me; R′ = $CHBr_2$
d: R = $CHBr_2$; R′ = Me

Interaction of enol derivative **22** with bromoform and potassium *tert*-butoxide in pentane furnished dibromocyclopropanes **23b**, whose fragility prevented their isolation in pure form and caused their conversion into cycloheptenones **24b** (27%) and **25** (7%) and a mixture (4%) of cyclohexanones **26c** and **26d**. The instability of the cyclopropanes **23b** led to the exploration of an alternate route to the desired bicyclic ketones.

Decomposition of ethyl diazoacetate under copper acetylacetonate catalysis in a benzene solution of enol ether **22** and subsequent interaction of the resultant ester mixture **27** with *N*-bromosuccinimide in moist ether furnished esters **28** in 64% overall yield. Treatment of the latter with potassium *tert*-butoxide in *tert*-butyl alcohol solution afforded keto esters **19c** (30%) and **29a** (14%). Finally, as tie-up of these esters with the bromocyclobutanones, the following experiment was carried out. Alkaline hydrolysis of the keto esters as a mixture, conversion of the resultant acids **19d** and **29b** (as a mixture) into their acid halides with oxalyl chloride, and replacement of the chlorocarbonyl moiety by bromine under the influence of α-mercaptopyridine *N*-oxide, γ-(dimethylamino)pyridine, and bromotrichloromethane[27] produced bromo ketones **7** (12%) and **19b** (22%).



27



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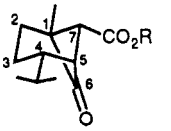


29a: R = Et
b: R = H

Experimental Section

Melting points were taken on a Reichert microhotstage and are uncorrected. Infrared spectra of chloroform solutions were observed on a Perkin-Elmer 1330 spectrophotometer. ^{1}H NMR spectra of deuteriochloroform solutions (Me_4Si as internal

(26) Rothman, E. S.; Day, A. R. *J. Am. Chem. Soc.* **1954**, *76*, 111.

(27) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901.

standard) were measured on Varian EM-390 and Nicolet QE-300 spectrometers and ^{13}C NMR spectra of deuteriochloroform solutions on the latter instrument, operating at 75.5 MHz in the Fourier transform mode. The carbon shifts are in parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm. Most reactions were carried out under nitrogen. The extracts of all crude products were washed with brine, dried over anhydrous Na_2SO_4, and evaporated. Chromatographic separations were performed on Davison silica (60–200 mesh commercial grade H) and by medium-pressure liquid chromatography (MPLC) on Merck Lobar silica gel columns with the aid of a Fluid Metering, Inc., pump.

(1α,4β,5α,7R*)-(±)-7-Chloro-4-isopropyl-1-methylbicyclo[3.1.1]heptan-6-one (4). The earlier preparation[4] of ketone **4** was improved in the following manner.

A 50% sodium hydroxide solution (320 mL, 4.0 mol) was added dropwise to a solution of 100.0 g (0.67 mol) of carvacrol and 320 mL (4.0 mol) of chloroform in 660 mL of benzene, and the mixture then refluxed for 2.5 h. The cooled mixture was diluted with 1 L of ice water, and the aqueous layer was extracted twice with 200 mL of chloroform each. The combined nonaqueous layer and extracts were washed twice with 500 mL of water each and once with 500 mL of brine and evaporated. A solution of the residual, brown oil in 400 mL of petroleum ether was washed twice with 500 mL of 10% sodium hydroxide solution, twice with 500 mL of a 20% solution, four times with 500 mL of Claisen's alkali (252 g of potassium hydroxide in 180 mL of water and 220 mL of methanol), twice with 500 mL of water, and once with 500 mL of brine. (Emulsions and precipitates were removed with the aqueous washings.) The solution then was dried and evaporated. Chromatography of the residual, red oil (50 g), ca. 18 g at a time, and elution with 25:1 petroleum ether–ethyl acetate, followed by Kugelrohr distillation (81 °C (0.1 Torr)) of the orange oil (25 g), gave 18.4 g (12%) of pale yellow, liquid 6-(dichloromethyl)-3-isopropyl-6-methyl-2,4-cyclohexadienone (**2**):[4] ^{13}C NMR δ 20.5 (Me), 20.6 (Me), 24.1 (6-Me), 34.3 (CH), 56.8 (C-6), 76.9 (Cl_2CH), 119.6 (C-2), 125.7 (C-4), 139.1 (C-5), 163.4 (C-3), 200.2 (C=O).

A solution of 18.4 g (78.7 mmol) of ketone **2** and 38.7 g (256 mmol) of sodium carbonate in 450 mL of dry dimethyl sulfoxide was stirred at 85 °C for 48 h. It was cooled, poured into 1 L of ice water, and neutralized with a solution of 60 mL of concentrated hydrochloric acid in 100 mL of water. The aqueous layer was washed exhaustively with petroleum ether and the combined nonaqueous layer and extracts with 10% sodium bicarbonate solution, water, and brine. The latter solution was dried and evaporated. Chromatography of the residual, red oil (15 g) and elution with 25:1 petroleum ether–ethyl acetate afforded 11.4 g of orange oil and 2 g of impure material, Kugelrohr distillation (80 °C (0.05 Torr)) of the former of which provided 10.3 g of pale yellow, liquid product. MPLC of the impure oil and elution with 50:1 petroleum ether–ethyl acetate led to 0.9 g of more product; hence a total of 11.2 g (72%) of liquid (1α,5α,7R*)-(±)-7-chloro-2,3-dehydro-4-isopropylidene-1-methylbicyclo[3.1.1]heptan-6-one (**3**):[4] ^{13}C NMR δ 12.8 (1-Me), 20.5 (Me), 20.6 (Me), 60.6 (C-7), 68.7 (C-1), 72.1 (C-5), 126.6 (C-3), 128.0 (*i*-Pr C), 132.5 (C-4), 134.5 (C-2), 202.3 (C=O). The compound was used immediately in the next reaction.

Hydrogenation of diene **3** followed the earlier procedure,[4] except for the necessity of subjecting the product to a second hydrogenation (although this in ethyl acetate). Kugelrohr distillation (60 °C (0.1 Torr)) of the chromatographed material led to an 80% yield of colorless, liquid ketone **4**:[4] ^{13}C NMR δ 14.8 (1-Me), 19.4 (Me), 19.5 (Me), 22.8 (C-3), 32.3 (CH), 39.7 (C-2), 53.4 (C-4), 61.3 (C-7), 67.8 (C-1), 69.4 (C-5), 209.2 (C=O).

(1α,4β,5α,7R*)-(±)-7-Bromo-4-isopropyl-1-methylbicyclo[3.1.1]heptan-6-one (7). A 50% sodium hydroxide solution (270 mL, 3.4 mol) was added dropwise over a 2-h period to a solution of 200.0 g (1.3 mol) of carvacrol and 300 mL (3.4 mol) of bromoform in 1.34 L of benzene, and the resultant pink emulsion was stirred at room temperature for 12 h and then, while refluxing, for 3 h. The mixture was poured into 2 L of ice water and worked up as in the preparation of ketone **2**. Chromatography of the red oil (110 g), ca. 40 g at a time, and elution with 25:1 petroleum ether–ethyl acetate yielded 47 g of an orange oil and 7.5 g of a red mixture. The former was subjected to Kugelrohr distillation (95 °C (0.1 Torr)), furnishing 36.9 g of pale yellow liquid, and MPLC of the latter (elution with 25:1 petroleum ether–ethyl acetate) produced 2.2 g of the same oil, totalling 39.1 g (9%) of 6-(dibromomethyl)-3-isopropyl-6-methyl-2,4-cyclohexadienone (**5**): IR (CCl_4) (C=O) 1664 (s), 1642 (m), (C=C) 1574 (w) cm^{-1}; ^1H NMR δ 1.18 (d, 6, J = 6 Hz, *i*-Pr methyls), 1.30 (s, 3, 6-Me), 2.59 (septet, 1, J = 6 Hz, *i*-Pr CH), 5.92 (s, 1, H-2), 5.96 (s, 1, BrCH), 6.44 (d, 1, J = 10 Hz, H-4), 6.67 (d, 1, J = 10 Hz, H-5); ^{13}C NMR δ 20.5 (Me), 20.6 (Me), 25.6 (6-Me), 34.2 (CH), 50.4 (BrCH), 56.3 (C-6), 119.7 (C-2), 125.4 (C-4), 140.7 (C-5), 163.4 (C-3), 199.9 (C=O).

A solution of 39.1 g (121 mmol) of ketone **5** and 51.3 g (484 mmol) of sodium carbonate in 600 mL of dry dimethyl sulfoxide was stirred at 85 °C for 72 h. Workup and chromatography as in the preparation of ketone **3** led to the recovery of 3.3 g of starting material (**5**) and to 22.1 g of product, whose Kugelrohr distillation (75 °C (0.05 Torr)) gave 20.7 g (78%, based on consumed **5**) of colorless, liquid (1α,5α,7R*)-(±)-7-bromo-2,3-dehydro-4-isopropylidene-1-methylbicyclo[3.1.1]heptan-6-one (**6**): IR (CCl_4) (C=O) 1796 (s), (C=C) 1665 (w) cm^{-1}; ^1H NMR δ 1.30 (s, 3, 1-Me), 1.75, 1.78 (s, 3 each, *i*-Pr methyls), 4.27 (s, 1 H-7), 4.34 (s, 1, H-5), 5.85 (d, 1, J = 8 Hz, H-2), 6.46 (d, 1, J = 8 Hz, H-3); ^{13}C NMR δ 15.0 (1-Me), 20.6 (Me), 20.7 (Me), 52.9 (C-7), 68.6 (C-1), 72.5 (C-5), 126.6 (C-3), 128.0 (*i*-Pr C), 132.9 (C-4), 134.7 (C-2), 202.2 (C=O). The compound was used immediately in the next reaction.

A mixture of 20.7 g (86 mmol) of ketone **6** and 2 g of 10% palladium–charcoal in 125 mL of ethyl acetate was hydrogenated under 45 psi of pressure in a Parr apparatus. Upon cessation of hydrogen uptake it was filtered, another 2 g of catalyst was added, and the hydrogenation was continued. This procedure was repeated twice more, the mixture was filtered, and the filtrate was evaporated. Chromatography of the residue and elution with 35:1 petroleum ether–ethyl acetate afforded 15.8 g of a colorless oil, whose Kugelrohr distillation (70 °C (0.03 Torr)) provided 15.4 g (74%) of colorless, liquid ketone **7**: IR (CCl_4) (C=O) 1788 (s) cm^{-1}; ^1H NMR δ 0.89, 0.90 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.19 (s, 3, 1-Me), 1.3–2.5 (m, 6, methylenes, methines), 3.28 (s, 1, H-5), 3.96 (s, 1 H-7); ^{13}C NMR δ 17.3 (1-Me), 19.6 (Me), 19.7 (Me), 22.8 (C-3), 32.3 (*i*-Pr CH), 39.9 (C-2), 53.1 (C-7), 54.2 (C-4), 67.8 (C-1), 70.1 (C-5), 208.9 (C=O).

Anal. Calcd for $C_{11}H_{17}OBr$: C, 53.89; H, 6.99 Found: C, 53.73; H, 7.15.

3,3,7-Trimethyl-1-((trimethylsilyl)oxy)bicyclo[5.1.0]octane (10a). The conversion of eucarvone [^{13}C NMR δ 19.6 (2-Me), 26.5 (C-6 methyls), 32.7 (C-6), 53.6 (C-7), 121.7 (C-4), 133.4 (C-3), 137.9 (C-2), 148.3 (C-5), 199.6 (C=O)] into tetrahydroeucarvone (**8**) [^{13}C NMR δ 17.9 (2-Me), 22.6 (C-4), 27.5 (ax 6-Me), 31.2 (eq 6-Me), 32.5 (C-6), 32.9 (C-3), 44.1 (C-5), 47.5 (C-2), 53.4 (C-7), 215.1 (C=O)] followed a known procedure.[8]

A solution of 12.2 g (81.2 mmol) of sodium iodide in 85 mL of dry acetonitrile was added in one portion to a mixture of 10.0 g (64.9 mmol) of ketone **8**, 8.85 g (8.12 mmol) of trimethylsilyl chloride, and 8.20 g (81.2 mmol) of triethylamine, and the mixture was stirred at room temperature for 1 h. It was extracted exhaustively with pentane, and the extract was washed with cold water, dried ($MgSO_4$), and evaporated, yielding 13.2 g (91%) of liquid 2,6,6-trimethyl-1-((trimethylsilyl)oxy)cycloheptene (**9**): IR (C=C) 1670 (m), CMe_2 1380 (m), 1360 (m) cm^{-1}; ^1H NMR δ 0.15 (s, 9, $SiMe_3$), 0.91 (s, 6, C-6 methyls), 1.3–2.1 (m, 6, methylenes), 1.60 (s, 3, 2-Me), 2.10 (s, 2, C-7 Hs); ^{13}C NMR δ 0.7 ($SiMe_3$), 18.3 (2-Me), 22.4 (C-4), 28.8 (C-6 methyls), 30.5 (C-6), 33.0 (C-3), 45.7 (C-5), 47.9 (C-7), 115.9 (C-2), 144.8 (C-1). The substance was used in the next reactions without further purification.

A mixture of 16 mmol of zinc–copper couple,[28] 2.00 g (8.9 mmol) of enol ether **9**, and 3.80 g (14.2 mmol) of methylene iodide was refluxed for 40 h and then filtered.[29] The filtrate was washed consecutively with cold ammonium chloride solution, sodium bicarbonate solution, and water, dried ($MgSO_4$), and evaporated. MPLC of the residue and elution with 60:1 petroleum ether–ethyl acetate furnished 1.91 g (90%) of colorless, liquid, bicyclic ether **10a**: IR CMe_2 1388 (w), 1365 (w) cm^{-1}; ^1H NMR δ 0.11 (s, 9, $SiMe_3$), 0.32 (d, 1, J = 5 Hz, H-8), 0.47 (d, 1, J = 5 Hz, H-8), 0.7–0.9 (m, 1 H-6), 0.86, 1.04, 1.11 (s, 3 each, methyls), 1.32 (d, 1, J = 15

(28) Rawson, R. J.; Harrison, I. T. *J. Org. Chem.* **1970**, *35*, 2057.
(29) Cf. Murai, S.; Aya, T.; Sonoda, N. *J. Org. Chem.* **1973**, *38*, 4354.

Hz, H-2), 1.4–1.8 (m, 4, methylenes), 1.9–2.0 (m, 1, H-6), 2.00 (d, 1, J = 15 Hz, H-2); exact mass m/e 240.1902 (calcd for $C_{14}H_{28}OSi$ m/e 240.1909).

8,8-Dichloro-3,3,7-trimethyl-1-((trimethylsilyl)oxy)bicyclo[5.1.0]octane (10b). Ethyl trichloroacetate (1.65 g, 8.6 mmol) was added in one portion to a stirring mixture of 1.50 g (6.6 mmol) of enol ether **9** and 0.54 g (10.0 mmol) of freshly prepared sodium methoxide in 40 mL of anhydrous pentane at 0 °C, and the stirring continued at this temperature for 6 h.[30] After being allowed to stir at room temperature for 15 h, the mixture was filtered and the precipitate was washed with pentane. The combined filtrate and washings were evaporated to dryness, and the residue was chromatographed. Elution with 60:1 petroleum ether–ethyl acetate led to the recovery of 230 mg of starting ether **9** and 1.53 g (88%, based on consumed ether **9**) of colorless, liquid ether **10b**: IR CMe_2 1385 (w), 1365 (w) cm^{-1}; ^1H NMR δ 0.25 (s, 9, $SiMe_3$), 0.94, 1.02, 1.20 (s, 3 each, methyls), 1.4–1.6 (m, 1, H-6), 1.7–1.9 (m, 1, H-6), 1.4–1.9 (m, 4, methylenes), 1.82, 1.96 (d, 1 each, J = 15 Hz, C-2 Hs); exact mass (M – Cl) m/e 273.1446 (calcd for $C_{14}H_{26}OClSi$ m/e 274.1442).

8-*exo*-Chloro-3,3,7-trimethyl-1-((trimethylsilyl)oxy)bicyclo[5.1.0]octane (10f). A mixture of 1.00 g (3.2 mmol) of dichloride **10b**, 709 mg (3.2 mmol) of tri-*n*-butyltin hydride, and 100 mg of azobisisobutyronitrile (AIBN) in 15 mL of anhydrous benzene was refluxed for 3.5 h and then evaporated. Chromatography of the residue and elution with 60:1 petroleum ether–ethyl acetate yielded 631 mg (71%) of colorless, liquid chloride **10f**: IR CMe_2 1388 (w), 1366 (w) cm^{-1}; ^1H NMR δ 0.21 (s, 9, $SiMe_3$), 0.7–0.9 (m, 1, H-6), 0.90, 1.05, 1.08 (s, 3 each, methyls), 1.0–1.7 (m, 4, methylenes), 1.36 (d, 1, J = 15 Hz, H-2), 2.0–2.1 (m, 1, H-6), 2.07 (d, 1, J = 15 Hz, H-2), 2.63 (s, 1, H-8); exact mass (M – Cl) m/e 239.1824 (calcd for $C_{14}H_{27}OSi$ m/e 239.1831).

Cyclooctenones 11. A solution of 149 mg (0.54 mmol) of chloride **10f** and 32 mg (0.60 mmol) of sodium methoxide in 2.5 mL of a 50:1 methanol–water mixture was kept at room temperature for 1 h. Water was added, and the mixture was extracted with petroleum ether. The extract was washed, dried, and evaporated. MPLC of the residue and elution with 40:1 petroleum ether–ethyl acetate gave 80 mg (90%) of colorless, liquid 3,7,7-trimethyl-2-cyclooctenone (**11a**): IR (C=O) 1635 (s) cm^{-1}; ^1H NMR δ 0.99 (s, 6, *gem*-methyls), 1.3–1.4 (m, 2, C-6 Hs), 1.6–1.8 (m, 2, C-5 Hs), 1.97 (d, 3, J = 3 Hz, 3-Me), 2.6–2.7 (m, 2, C-4 Hs), 2.61 (s, 2, C-8 Hs), 6.12 (s, 1, H-2); ^{13}C NMR δ 19.8 (C-5), 27.8 (3-Me), 29.1 (7-methyls), 31.3 (C-4), 31.4 (C-7), 34.7 (C-6), 53.8 (C-8), 132.0 (C-2), 153.6 (C-3), 199.7 (C=O); exact mass m/e 166.1355 (calcd for $C_{11}H_{18}O$ m/e 166.1358).

A solution of 150 mg (0.49 mmol) of dichloride **10b** and 29 mg (0.53 mmol) of sodium methoxide in 2.5 mL of a 50:1 methanol–water mixture was kept at room temperature for 1.2 h. Workup as above furnished 84 mg (87%) of colorless, liquid 2-chloro-3,7,7-trimethyl-2-cyclooctenone (**11b**): mp 26–27 °C; IR (C=O) 1658 (s), (C=C) 1586 (m), CMe_2 1391 (w), 1370 (m) cm^{-1}; ^1H NMR δ 0.93 (s, 6, *gem*-methyls), 1.2–1.4 (m, 2, C-6 Hs), 1.6–1.8 (m, 2, C-5 Hs), 2.17 (s, 3, 3-Me), 2.7–2.9 (m, 2, C-4 Hs), 2.73 (s, 2, C-8 Hs); ^{13}C NMR δ 20.1 (C-5), 26.9 (3-Me), 29.1 (7-methyls), 32.1 (C-7), 34.0 (C-4 or C-6), 34.5 (C-6 or C-4), 54.4 (C-8), 133.9 (C-2), 149.5 (C-3), 191.8 (C=O); exact mass m/e 200.0962 (calcd for $C_{11}H_{17}OCl$ m/e 200.0968).

A mixture of 750 mg (2.4 mmol) of dichlorocyclopropane **10b** and a 1 M tetrahydrofuran solution (containing <5% of water) of tetra-*n*-butylammonium fluoride (2.5 equiv) was kept at 0 °C for 0.5 h and then at room temperature for 1 h. Water was added, and the mixture was extracted with ether. The extract was washed with water and brine, dried, and evaporated. MPLC of the residue and elution with 30:1 petroleum ether–ethyl acetate led to 184 mg (32%) of colorless, crystalline 2-(dichloromethyl)-2,6,6-trimethylcycloheptanone (**13d**): mp 54–56 °C; IR (C=O) 1692 (s), (CMe_2) 1391 (w), 1379 (m), 1369 (w) cm^{-1}; ^1H NMR δ 0.81, 0.95, 1.19 (s, 3 each, methyls), 1.4–2.2 (m, 6, methylenes), 2.22 (dd, 1, J = 12, 1 Hz, H-7), 2.73 (d, 1, J = 12 Hz, H-7), 5.78 (s, 1, ClCH); exact mass m/e 236.0745 (calcd for $C_{11}H_{18}OCl_2$ m/e 236.0736).

Further elution afforded 53 mg (11%) of colorless, liquid 2-chloro-3,7,7-trimethyl-3-cyclooctenone (**12a**) [^1H NMR δ 1.01 (s, 3, 7-Me), 1.08 (s, 3, 7-Me), 1.93 (s, 3, 3-Me), 1.2–2.1 (m, 4, methylenes), 2.19 (d, 1, J = 12 Hz, H-8), 2.66 (d, 1, J = 12 Hz, H-8), 4.63 (s, 1, H-2), 5.69 (t, 1, J = 9 Hz, H-4); ^{13}C NMR δ 23.3 (C-5), 23.5 (ax 7-Me), 27.6 (3-Me), 31.6 (eq 7-Me), 36.6 (C-7), 39.4 (C-6), 48.6 (C-8), 67.8 (C-2), 130.6 (C-3), 132.2 (C-4), 202.1 (C=O)] and 209 mg (43%) of colorless, liquid ketone **11b** (vide supra). Ketone **12a** underwent quantitative isomerization in chloroform into ketone **11b** after a few hours.

Dibromochloromethane (1.38 g, 6.6 mmol) was added dropwise over a 45-min period to a stirring mixture of 1.00 g (4.4 mmol) of enol ether **9** and 880 mg (0.79 mmol) of potassium *tert*-butoxide in 25 mL of anhydrous pentane at 0 °C. The stirring at this temperature was maintained for 6 h and then continued at room temperature for 12 h. The mixture was filtered, the precipitate was washed with pentane, and the combined filtrate and washings were evaporated to dryness. A mixture of the residue (1.43 g of crude cyclopropanes **10d** and **10e**) and a 1 M tetrahydrofuran solution (containing <5% of water) of tetra-*n*-butylammonium fluoride (2.5 equiv, based on a theoretically quantitative **9** → **10d** + **10e** conversion) was kept at 0 °C for 1 h and then worked up as in the above, related reaction of cyclopropane **10b**. The products consisted of 132 mg (10%) of a colorless, liquid, ca. 2:1 **13f** mixture [IR (C=O) 1693 (s), CMe_2 1391 (w), 1379 (m), 1370 (m) cm^{-1}] of ketone **16** (vide infra) [^1H NMR δ 0.81, 0.96, 1.23 (s, 3 each, methyls), 1.4–2.4 (m, 6, methylenes), 2.19 (d, 1, J = 12 Hz, H-7), 2.81 (d, 1, J = 12 Hz, H-7), 5.80 (s, 1, BrCH)] and 2-(bromochloromethyl)-2,6,6-trimethylcycloheptanone **17** [^1H NMR δ 0.81, 0.95, 1.19 (s, 3 each, methyls), 1.4–2.4 (m, 6, methylenes), 2.23 (d, 1, J = 12 Hz, H-7), 2.75 (d, 1, J = 12 Hz, H-7), 5.83 (s, 1, BrCH)] and 665 mg (74%) of colorless ketone **11b** (vide supra).

Bromoform (1.43 g, 5.7 mmol) was added dropwise over a 1-h period to a stirring mixture of 800 mg (3.5 mmol) of enol ether **9** and 793 mg (7.1 mmol) of potassium *tert*-butoxide in 20 mL of anhydrous pentane at 0 °C, and stirring continued at this temperature for 6 h and then at room temperature for 12 h. Workup as in the above preparation of the **10d–e** cyclopropanes led to 1.92 g of crude 8,8-dibromo-3,3,7-trimethyl-1-((trimethylsilyl)oxy)bicyclo[5.1.0]octane (**10c**) [^1H NMR δ 0.23 (s, 9, $SiMe_3$), 0.88, 0.95, 1.16 (s, 3 each, methyls), 1.3–2.1 (m, 6, methylenes), 1.87 (dd, 1, J = 15, 2 Hz, H-2), 2.00 (d, 1, J = 15 Hz, H-2)]. Fluoride-induced cyclopropane cleavage of the latter followed the procedure and workup of the above **10d–e** scission, leading to the recovery of 46 mg of enol ether **9**, to 162 mg (15%, based on consumed ether **9**) of colorless, crystalline 2-(dibromomethyl)-2,6,6-trimethylheptanone (**13e**) [mp 58–59 °C; IR (C=O) 1703 (s), CMe_2 1392 (w), 1377 (m), 1360 (m) cm^{-1}; ^1H NMR δ 0.88, 1.03, 1.28 (s, 3 each, methyls), 1.4–2.1 (m, 6, methylenes), 2.26 (d, 1, J = 12 Hz, H-7), 2.88 (d, 1, J = 12 Hz, H-7), 5.82 (s, 1, BrCH); exact mass (M – Br) m/e 245.0537 (calcd for $C_{11}H_{18}OBr$ m/e 245.0542)], and to 529 mg (65%, based on consumed ether **9**) of colorless, crystalline 2-bromo-3,7,7-trimethyl-2-cyclooctenone (**11c**): mp 30–31 °C; IR (C=O) 1655 (s), (C=C) 1582 (s), CMe_2 1390 (m), 1370 (m) cm^{-1}; ^1H NMR δ 1.00 (s, 6, 7-methyls), 1.3–1.4, 1.7–1.8, 2.8–2.9 (m, 2 each, methylenes), 2.30 (s, 3, 3-Me), 2.82 (s, 2, C-8 Hs); ^{13}C NMR δ 20.4 (C-5), 29.3 (7-methyls), 30.6 (3-Me), 32.5 (C-7), 34.7 (C-6 or C-4), 34.9 (C-4 or C-6), 53.4 (C-8), 128.4 (C-2), 152.1 (C-3), 192.1 (C=O); exact mass m/e 244.0458 (calcd for $C_{11}H_{17}OBr$ m/e 244.0463).

The unstable dibromocyclopropane **10c** undergoes bromide solvolysis in chloroform in a few hours, partitioning into mostly ketone **11c** and some 2-bromo-3,7,7-trimethyl-3-cyclooctenone (**12b**) [^1H NMR δ 1.01, 1.08 (s, 3 each, 7-methyls), 1.2–2.1 (m, 4, methylenes), 1.95 (s, 3, 3-Me), 2.18 (d, 1, J = 12 Hz, H-8), 2.74 (d, 1, J = 12 Hz, H-8), 4.78 (s, 1, H-2), 5.69 (t, 1, J = 9 Hz, H-4)]. When the solution was kept somewhat longer, the latter ketone isomerized quantitatively into the former.

2-(Halomethyl)tetrahydroeucarvones (13). *tert*-Butyl hypochlorite (226 mg, 2.1 mmol) was added dropwise to a solution of 250 mg (1.0 mmol) of cyclopropyl ether **10a** in 5 mL of dry carbon tetrachloride at 0 °C, and the mixture was stirred at this temperature for 4 h. Upon evaporation of the solvent, MPLC of the residue, and elution with 40:1 petroleum ether–ethyl acetate there was obtained 165 mg (78%) of colorless, liquid (solid at 0 °C) 2-(chloromethyl)-2,6,6-trimethylcycloheptanone (**13b**): IR (C=O) 1693 (s), (CMe_2) 1392 (w), 1376 (m), 1369 (m) cm^{-1}; ^1H

(30) Cf. Parham, W. E.; Soeder, R. W.; Throckmorton, J. R.; Kuncl, K.; Dodson, R. M. *J. Am. Chem. Soc.* **1965**, *87*, 321.

NMR δ 0.93 (s, 6, Me_2), 1.14 (s, 3, 2-Me), 1.4–2.2 (m, 6, methylenes), 2.45 (d, 1, J = 11 Hz, H-7), 2.50 (d, 1, J = 11 Hz, H-7), 3.56 (d, 1, J = 11 Hz, ClCH), 3.60 (d, 1, J = 11 Hz, ClCH); exact mass m/e 202.1108 (calcd for $C_{11}H_{19}OCl$ m/e 202.1125).

A solution of 167 mg (1.0 mmol) of bromine in 0.5 mL of dry methylene chloride was added dropwise to a solution of 250 mg (1.0 mmol) of ether **10a** in 2 mL of dry methylene chloride at −78 °C. The solution then was stirred at room temperature for 0.5 h and evaporated under vacuum. MPLC of the residue and elution with 40:1 petroleum ether–ethyl acetate yielded 229 mg (89%) of colorless, liquid (solid at 0 °C) 2-(bromomethyl)-2,6,6-trimethylcycloheptanone (**13c**): IR (C=O) 1692 (s), (CMe_2) 1390 (w), 1374 (m), 1368 (m) cm^{-1}; ^1H NMR δ 0.87 (s, 6, Me_2), 1.10 (s, 3, 2-Me), 1.4–2.1 (m, 6, methylenes), 2.44 (s, 2, C-7 Hs), 3.40 (d, 1, J = 10 Hz, BrCH), 3.45 (d, 1, J = 10 Hz, BrCH); exact mass m/e 246.0622 (calcd for $C_{11}H_{19}OBr$ m/e 246.0620).

A solution of 250 mg (0.91 mmol) of cyclopropyl ether **10f** and 195 mg (1.1 mmol) of *N*-bromosuccinimide in 30 mL of moist ether was refluxed for 3.5 h, whereupon the mixture was filtered. The filtrate was washed with water and brine, dried, and evaporated. MPLC of the residue and elution with 30:1 petroleum ether–ethyl acetate furnished 156 mg (61%) of colorless, crystalline 2-(bromochloromethyl)-2,6,6-trimethylcycloheptanone (**13f, 16**): mp 64–65 °C; IR (C=O) 1693 (s), CMe_2 1392 (w), 1377 (m), 1368 (w) cm^{-1}; exact mass m/e 280.0222 (calcd for $C_{11}H_{18}OBrCl$ m/e 280.0231).

Further elution afforded 48 mg (26%) of colorless, liquid cyclopropanol **14b**: ^1H NMR δ 0.91, 1.08, 1.13 (s, 3 each, methyls), 0.8–1.0 (m, 1, H-6), 1.1–1.9 (m, 4, methylenes), 1.40 (d, 1, J = 15 Hz, H-2), 2.0–2.2 (m, 1, H-6), 2.06 (dd, 1, J = 15, 1 Hz, H-2), 2.74 (s, 1, ClCH); exact mass (M − HCl) m/e 166.1368 (calcd for $C_{11}H_{18}O$ m/e 166.1358).

Interaction of cyclopropyl ether **10b** with *N*-bromosuccinimide under the conditions and workup identical with those of ether **10f** (vide supra) led in 95% yield to colorless, liquid cyclopropanol **14c**: IR (OH) 3560 (m), 3400 (br w), CMe_2 1388 (w), 1366 (m), 1362 (w) cm^{-1}; ^1H NMR δ 0.96, 1.06, 1.27 (s, 3 each, methyls), 1.1–1.8 (m, 4, methylenes), 1.5–1.7 (m, 1, H-6), 1.8–1.9 (m, 1, H-6), 1.86 (dd, 1, J = 15, 1 Hz, H-2), 2.00 (d, 1, J = 15 Hz, H-2); exact mass m/e 236.0736 (calcd for $C_{11}H_{18}OCl_2$ m/e 236.0736).

A reaction between 280 mg (0.91 mmol) of cyclopropyl ether **10b** and 174 mg (1.1 mmol) of bromine followed the above **10a**–Br_2 reaction and workup procedure, leading to 155 mg (52%) of colorless, crystalline 2-(bromodichloromethyl)-2,6,6-trimethylcycloheptanone (**15**): mp 49–51 °C; IR (C=O) 1695 (s), 1391 (w), 1378 (m), 1369 (w) cm^{-1}; ^1H NMR δ 0.77, 0.99, 1.45 (s, 3 each, methyls), 1.2–2.4 (m, 6, methylenes), 2.16 (d, 1, J = 11 Hz, H-7), 3.25 (d, 1, J = 11 Hz, H-7); exact mass (M − Br) m/e (calcd for $C_{11}H_{17}OCl_2$ m/e 235.0657). Further chromatographic elution led to 80 mg (36%) of cyclopropanol **14c** (vide supra).

Protolyses of Cyclopropyl Ethers 10a and 10b. A 1% methanolic potassium hydroxide solution (15 mL) of cyclopropyl ether **10a** (294 mg, 1.2 mmol) was heated at 85 °C for 6 h. Water was added, and the mixture was extracted with petroleum ether. The extract was washed with water and brine, dried, and evaporated. Chromatography of the residue and elution with 30:1 petroleum ether–ethyl acetate gave 181 mg (88%) of colorless, liquid 2,2,6,6-tetramethylcycloheptanone (**13a**): IR (C=O) 1690 (s), (CMe_2) 1390 (w), 1385 (m), 1364 (w) cm^{-1}; ^1H NMR δ 0.93, 1.06 (s, 6 each, methyls), 1.3–1.6 (m, 6, methylenes), 2.43 (s, 2, C-7 Hs); exact mass m/e 168.1507 (calcd for $C_{11}H_{20}O$ m/e 168.1514).

A solution of 200 mg (0.83 mmol) of cyclopropyl ether **10a** and 0.1 mL of 5% hydrochloric acid in 5 mL of dry methanol was refluxed for 0.5 h and then diluted with water and extracted with ether. The extract was washed with water and brine, dried, and evaporated. Chromatography of the residue and elution with 30:1 petroleum ether–ethyl acetate afforded 17 mg (12%) of ketone **13a** (vide supra) and then 138 mg (81%) of colorless, liquid 3,3,7-trimethyl-1-bicyclo[5.1.0]octanol (**14a**): IR (OH) 3596 (m), 3415 (br w), (CMe_2) 1389 (w), 1376 (m), 1364 (m) cm^{-1}; ^1H NMR δ 0.38 (d, 1, J = 5 Hz, H-8), 0.53 (d, 1, J = 5 Hz, H-8), 0.90, 1.08, 1.21 (s, 3 each, methyls), 1.0–1.8 (m, 5, H-6), methylenes), 1.48 (d, 1, J = 15 Hz, H-2), 1.99 (dd, 1, J = 15, 6 Hz, H-6), 2.10 (dd, 1, J = 15, 1 Hz, H-2); exact mass m/e 168.1526 (calcd for $C_{11}H_{20}O$ m/e 168.1514).

A solution of 100 mg (0.36 mmol) of cyclopropyl ether **10f** in 3 mL of anhydrous ether, saturated with hydrogen bromide, was refluxed for 20 h. Petroleum ether was added, and the mixture was washed with water, dried, and evaporated. MPLC of the residue and elution with 30:1 petroleum ether–ethyl acetate produced 61 mg (82%) of ketone **13b** (vide supra).

A solution of 74 mg (0.24 mmol) of cyclopropyl ether **10b** in 2 mL of anhydrous ether, saturated with hydrogen bromide, was refluxed for 84 h (hydrogen bromide being replenished every 24 h). Workup as above gave 40 mg (68%) of ketone **13d** (vide supra), 5 mg (8%) of cyclopropanol **14c** (vide supra), and 7 mg (14%) of ketone **11b** (vide supra).

A solution of 250 mg (0.63 mmol) of crude cyclopropyl ether **10c** in 5 mL of dry ether, saturated with hydrogen bromide, was refluxed for 1 h. Workup as above led sequentially to 88 mg (43%) of ketone **13e** (vide supra) and 28 mg (18%) of ketone **11c** (vide supra).

9-Oxa-3,3,7-trimethylbicyclo[5.2.0]non-1-ene (20a). A solution of 150 mg (0.74 mmol) of ketone **13b** and potassium *tert*-butoxide (from 43 mg (1.1 mmol) of potassium) in 1.5 mL of dry *tert*-butyl alcohol was kept at 35 °C for 24 h. After the addition of water the mixture was extracted with petroleum ether. The extract was washed with water and brine, dried, and evaporated. MPLC of the residue and elution with 30:1 petroleum ether–ethyl acetate led to 80 mg (65%) of colorless, liquid oxetane **20a**: IR (C=C) 1711 (m), (CMe_2) 1386 (w), 1378 (m), 1362 (w) cm^{-1}; ^1H NMR δ 1.00, 1.08, 1.55 (s, 3 each, methyls), 1.4–1.9 (m, 6, methylenes), 4.10 (d, 1, J = 4 Hz, OCH_2 H), 4.36 (d, 1, J = 4 Hz, OCH_2H), 4.60 (s, 1, H-2); ^{13}C NMR δ 21.7 (C-5), 23.3 (7-Me), 29.6 (3-Me), 33.4 (3-Me), 35.7 (C-6), 43.7 (C-4), 46.7 (C-3), 62.8 (C-7), 80.9 (C-8), 106.0 (C-2), 165.2 (C-1); exact mass m/e 166.1357 (calcd for $C_{11}H_{18}O$ m/e 166.1358). The side product[22] (<10%) was difficult to purify.

A solution of 400 mg (1.6 mmol) of ketone **13c** in 1 mL of dry *tert*-butyl alcohol was added dropwise over a 2.5-h period into a solution of 82 mg (2.1 mmol) of potassium in 3 mL of dry *tert*-butyl alcohol at 65 °C, and the mixture was stirred at this temperature for 2 h. Workup as above gave 180 mg (67%) of oxetane **20a**.

1,4,4-Trimethylcycloheptene-3-carboxylic Acid (21). A solution of 1.00 equiv of (dihalomethyl)cycloheptanone **13d, 13e**, or **13f** in 1.5 mL of dry *tert*-butyl alcohol was added dropwise over a 2.5-h period to a stirring solution of 2.00 equiv of potassium *tert*-butoxide in 3 mL of *tert*-butyl alcohol at 65 °C, and the stirring was continued at this temperature for 3 h (the same result for reactions at room temperature for 48 h). The cooled mixture was poured into 5% sodium hydroxide solution and extracted with petroleum ether. The extract was washed with water and brine, dried, and evaporated, leaving 25–30% of starting halide (**13d, 13e**, or **13f**). The basic, aqueous solution was acidified with 5% hydrochloric acid and extracted with ether. The extract was washed with water and brine, dried, and evaporated, leaving colorless, oily acid **21** (35–40%): IR (OH) 3100–3600 (m), (C=O) 1700 (s), (C=C) 1630 (m) cm^{-1}; ^1H NMR δ 1.06 (s, 6 methyls), 1.4–2.3 (m, 6, methylenes), 1.78 (s, 3, 1-Me), 3.23 (d, 1, J = 6 Hz, H-3), 5.39 (d, 1, J = 6 Hz, H-2); ^{13}C NMR δ 21.4 (C-6), 21.9 (4-Me), 25.7 (1-Me), 29.9 (4-Me), 33.1 (C-7), 34.0 (C-4), 46.7 (C-5), 54.3 (C-3), 121.2 (C-2), 144.7 (C-1), 180.6 (C=O); exact mass m/e 182.1312 (calcd for $C_{11}H_{18}O_2$ m/e 182.1307).

7,7-Dichloro-3(*R*)-isopropyl-6-methyl-1-((trimethylsilyl)oxy)bicyclo[4.1.0]heptanes (23a). A solution of 6.70 g (44.6 mmol) of sodium iodide in 44 mL of dry acetonitrile was added in one portion to a stirring solution of 5.50 g (35.7 mmol) of a mixture of carvomenthone and isocarvomenthone, 6.2 mL (44.6 mmol) of dry triethylamine, and 5.65 mL (44.6 mmol) of dry trimethylsilyl chloride, and the stirring was continued for 45 min. The mixture was extracted exhaustively with petroleum ether. The extract was washed with ice-cold water and brine, dried, and evaporated, providing 7.83 g (97%) of colorless, liquid 5(*R*)-isopropyl-2-methyl-1-((trimethylsilyl)oxy)-1-cyclohexene (**22**): IR (CCl_4) (C=C) 1690 (m) cm^{-1}; ^1H NMR δ 0.20 (s, 9, $SiMe_3$), 0.95 (d, 6, J = 6 Hz, *i*-Pr methyls), 1.1–2.2 (m, 8, methylenes, methines), 1.53 (s, 3, 2-Me).

Dry chloroform (0.36 mL, 4.46 mmol) was added dropwise to a stirring mixture of 337 mg (1.49 mmol) of enol ether **22** and 460 mg (4.46 mmol) of potassium *tert*-butoxide in 3 mL of dry hexane

at 0 °C, and the stirring was continued at this temperature for 3 h and at room temperature for 2 h. The mixture was filtered, the filtrate was evaporated, and the residue was inspected by ^{1}H NMR spectroscopy, revealing only ca. 80% completion of the reaction. Hence, the residue was treated once again with potassium *tert*-butoxide (307 mg, 2.98 mmol) and chloroform (0.24 mL, 2.98 mmol) as above. Chromatography of the crude product on neutral alumina (activity III) and elution with petroleum ether gave 401 mg (87%) of colorless, liquid cyclopropanes **23a**: ^{1}H NMR δ 0.25 (s, 9, $SiMe_3$), 0.86 (d, 6, J = 6 Hz, *i*-Pr methyls), 1.0–2.5 (m, 8, methylenes, methines), 1.20, 1.22 (s, 3 total, angular Me); exact mass (M – Me_3SiCl) m/e 200.0957 (calcd for $C_{11}H_{17}OCl$ m/e 200.0966).

Protolysis of Cyclopropane 23a. Hydrogen bromide gas was bubbled rapidly into a solution of 179 mg (0.58 mmol) of cyclopropyl ethers **23a** in 5 mL of dry ether, the reaction flask was capped, and the solution was stirred at room temperature for 144 h. Ether was added, and the mixture was washed with water, dried, and evaporated. MPLC of the residue and elution with 40:1 petroleum ether–ethyl acetate provided 47 mg (34%) of colorless, crystalline (+)-2(*S*)-(dichloromethyl)-5(*R*)-isopropyl-2-methylcyclohexanone (**26a**):[4,31] mp 95–97 °C (MeOH); $[\alpha]^{23}_D$ +132.9° ($CHCl_3$, c = 1.00); CD_{max} $[\theta]^{19}_{298}$ +16 044° ($CHCl_3$, c = 5 × 10^{-2}); IR (CCl_4) (C=O) 1720 (s) cm^{-1}; ^{1}H NMR δ 0.92, 0.93 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.26 (s, 3, 2-Me), 1.5–1.8 (m, 5, methylenes, methines), 2.2–2.4 (m, 2, H-3, H-6), 2.46 (dm, 1, J = 14 Hz, eq H-6), 6.31 (s, 1, ClCH); ^{13}C NMR δ 17.2 (2-Me), 19.3 (*i*-Pr Me), 1.95 (*i*-Pr Me), 23.5 (C-4), 32.1 (*i*-Pr CH), 34.8 (C-3), 42.3 (C-6), 45.5 (C-5), 56.2 (C-2), 76.5 (ClCH), 209.0 (C=O).

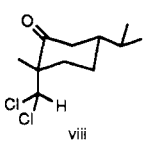
Further elution led to 38 mg (28%) of colorless, liquid (+)-2-(*R*)-(dichloromethyl)-5(*R*)-isopropyl-2-methylcyclohexanone (**26b**):[4,31] $[\alpha]^{23}_D$ +42.6° ($CHCl_3$, c = 1.00); CD_{max} $[\theta]^{19}_{296}$ +6062° ($CHCl_3$, c = 5 × 10^{-2}); IR (CCl_4) (C=O) 1710 (s) cm^{-1}; ^{1}H NMR δ 0.91, 0.92 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.32 (s, 3, 2-Me), 1.4–2.0 (m, 4, methines, C-4 Hs), 2.01 (ddd, 1, J = 13, 3, 3 Hz, eq H-3), 2.15 (ddd, 1, J = 13, 13, 4 Hz, ax H-3), 2.22 (dd, 1, J = 15, 12 Hz, ax H-6), 2.39 (ddd, 1, J = 15, 3, 3 Hz, eq H-6), 6.19 (s, 1, ClCH); ^{13}C NMR δ 19.1 (*i*-Pr Me), 19.3 (*i*-Pr Me), 22.0 (2-Me), 23.9 (C-4), 30.2 (C-3), 32.1 (*i*-Pr CH), 42.0 (C-6), 43.5 (C-5), 55.3 (C-2), 78.9 (ClCH), 210.6 (C=O).

Further elution afforded 9 mg (8%) of colorless, liquid 2-chloro-6(*R*)-isopropyl-3-methyl-2-cycloheptenone (**24a**): IR (CCl_4) (C=O) 1683 (s), (C=C) 1607 (m) cm^{-1}; ^{1}H NMR δ 0.88, 0.92 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.4–2.8 (m, 8, methylenes, methines), 2.18 (s, 3, 3-Me); exact mass m/e 200.0956 (calcd for $C_{11}H_{17}OCl$ m/e 200.0967).

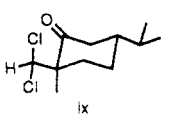
Cycloheptenones 24b and 25. Dry bromoform (0.36 mL, 4.10 mmol) was added dropwise over a 20-min period to a stirring mixture of 686 mg (3.03 mmol) of enol ether **22** and 510 mg (4.54 mmol) of potassium *tert*-butoxide in 3 mL of pentane at 0 °C, and the stirring was continued at this temperature for 4 h and at room temperature for 14 h. The mixture was filtered, and the filtrate was evaporated. MPLC of the residue and elution with 40:1 petroleum ether–ethyl acetate provided 51 mg (7%) of colorless, liquid 2-bromo-6-isopropyl-3-methyl-3-cycloheptenone (**25**): IR (CCl_4) (C=O) 1707 (s), (C=C) 1660 (w) cm^{-1}; ^{1}H NMR δ 0.90, 0.93 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.4–2.6 (m, 6, methylenes, methines), 1.90 (s, 3, 3-Me), 5.75 (t, 1, J = 6 Hz, H-4); exact mass m/e 244.0464 (calcd for $C_{11}H_{17}OBr$ m/e 244.0461).

Further elution yielded 40 mg (4%) of a mixture of cyclohexanones **26c** and **26d** (vide infra) and subsequently 204 mg (27%) of colorless, liquid 2-bromo-6-isopropyl-3-methyl-2-cycloheptenone (**24b**): IR (CCl_4) (C=O) 1680 (s), (C=C) 1603 (m) cm^{-1}; ^{1}H NMR δ 0.90, 0.93 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.3–2.8 (m, 8, methylenes, methines), 2.20 (s, 3, 3-Me); exact mass m/e 244.0484 (calcd for $C_{11}H_{17}OBr$ m/e 244.0461).

(31) The NMR spectroscopy and CD data of ketones **26a** and **26b** show the compounds to possess preferred, solution conformations viii and ix, respectively.



viii



ix

Crystallization of the **26c–d** cyclohexanone mixture from petroleum ether and MPLC of the mother liquor permitted the separation of the ketones and led to colorless, crystalline 2(*S*)-(dibromomethyl)-5(*R*)-isopropyl-2-methylcyclohexanone (**26c**): mp 97–99 °C (MeOH); IR (CCl_4) (C=O) 1720 (s) cm^{-1}, ^{1}H NMR δ 0.92, 0.93 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.31 (s, 3, 2-Me), 1.4–2.4 (m, 7, methylenes, methines), 2.45 (dm, 1, J = 14 Hz, eq H-6), 6.26 (s, 1, BrCH); ^{13}C NMR δ 19.2, 19.4, 19.5 (methyls), 23.6 (C-4), 32.4 (*i*-Pr CH), 36.7 (C-3), 42.2 (C-6), 46.0 (C-5), 51.6 (BrC), 56.4 (C-2), 208.6 (C=O).

Anal. Calcd for $C_{11}H_{18}OBr_2$: C, 40.52; H, 5.56. Found: C, 40.79; H, 5.61.

The chromatographed compound was colorless, liquid isomer **26d**: IR (CCl_4) (C=O) 1710 (s) cm^{-1}; ^{1}H NMR δ 0.91, 0.92 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.32 (s, 1, 2-Me), 1.4–2.0 (m, 4, CH_2, methines), 2.07 (ddd, 1, J = 13, 3, 3 Hz, eq H-3), 2.19 (ddd, 1, J = 13, 13, 4 Hz, ax H-3), 2.21 (dd, 1, J = 16, 12 Hz, ax H-6), 2.39 (ddd, 1, J = 16, 4, 3 Hz, eq H-6), 6.15 (s, 1, BrCH); ^{13}C NMR δ 19.1, 19.3 (*i*-Pr methyls), 23.5 (2-Me), 24.2 (C-4), 32.1 (*i*-Pr CH), 32.3 (C-3), 42.1 (C-6), 43.3 (C-5), 54.8 (C-2), 55.1 (BrC), 210.2 (C=O); exact mass (M – Br) m/e 245.0542 (calcd for $C_{11}H_{18}OBr$ m/e 245.0539).

Ethyl [1*S*-(1α,4α,5α,6α)]-4-Isopropyl-1-methyl-6-oxobicyclo[3.1.1]heptane-7-carboxylate (29a) and Ethyl [1*R*-(1α,4α,5α,6α)]-4-Isopropyl-1-methyl-6-oxobicyclo[3.1.1]heptane-7-carboxylate (19c). A solution of 4.40 mL (42 mmol) of ethyl diazoacetate in 166 mL of dry benzene was added dropwise over a 3-h period to a stirring mixture of 7.83 g (35 mmol) of enol ether **22** and 390 mg of cupric acetylacetonate[32] at 90 °C, and the stirring was continued at this temperature for 0.5 h. The mixture was evaporated, and a petroleum ether suspension of the residue was filtered through alumina. Evaporation of the filtrate afforded 9.91 g of colorless, oily, crude cyclopropane esters **27**. A solution of the latter and 7.85 g (44 mmol) of *N*-bromosuccinimide in 720 mL of moist ether was refluxed for 1 h, and the mixture then filtered. The colorless filtrate was washed with water and brine, dried, and evaporated. MPLC of the residue and elution with 20:1 petroleum ether–ethyl acetate gave 7.06 g (64%) of colorless, liquid ethyl (4(*R*)-isopropyl-1-methyl-2-oxocyclohexyl)bromoacetates (**28**).

A potassium *tert*-butoxide solution (from 250 mg (6.5 mmol) of potassium in 13 mL of dry *tert*-butyl alcohol) was poured in one portion into a solution of 1.36 g (4.3 mmol) of keto esters **28** in 25 mL of dry *tert*-butyl alcohol. The mixture was stirred at room temperature for 5 min and then poured into cold water. The mixture was extracted with ether, and the extract was washed with 5% sodium hydroxide solution, water, and brine, dried, and evaporated. MPLC of the residue and elution with 20:1 petroleum ether–ethyl acetate led to 142 mg (14%) of colorless, liquid keto ester **29a**: $[\alpha]^{23}_D$ +59.8° ($CHCl_3$, c = 1.00); CD_{max} $[\theta]^{21}_{290}$ +2591° ($CHCl_3$, c = 0.10); IR (CCl_4) (C=O) 1785 (s), 1730 (s) cm^{-1}; ^{1}H NMR δ 0.90, 0.92 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.08 (s, 3, 1-Me), 1.27 (t, 3, J = 7 Hz, Me of Et), 1.3–2.4 (m, 6, methylenes, methines), 2.53 (s, 1, H-7), 3.26 (s, 1, H-5), 4.18 (q, 2, J = 7 Hz, OCH_2); ^{13}C NMR δ 14.1 (ethyl Me), 15.0 (1-Me), 19.5, 19.6 (*i*-Pr methyls), 22.8 (C-3), 32.3 (*i*-Pr CH), 40.4 (C-2), 49.4 (C-4), 52.6 (C-7), 60.6 (OCH_2), 61.3 (C-5), 66.6 (C-1), 172.4 (ester C=O), 209.5 (C=O).

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.27; H, 9.48.

Further elution yielded 302 mg (30%) of colorless, liquid keto ester **19c**: $[\alpha]^{23}_D$ –8.8° ($CHCl_3$, c = 1.00); CD_{max} $[\theta]^{21}_{294}$ 2425 ($CHCl_3$, c = 0.10); IR (CCl_4) (C=O) 1788 (s), 1730 (s) cm^{-1}; ^{1}H NMR δ 0.90, 0.92 (d, 3 each, J = 6 Hz, *i*-Pr methyls), 1.06 (s, 3, 1-Me), 1.27 (t, 3, J = 7 Hz, Me of Et), 1.5–2.3 (m, 6, methylenes, methines), 3.01 (s, 1, H-7), 3.20 (s, 1, H-5), 4.17 (q, 2, J = 7 Hz, OCH_2); ^{13}C NMR δ 13.8 (ethyl Me), 14.5 (1-Me), 19.5, 19.5 (*i*-Pr methyls), 20.5 (C-3), 32.2 (*i*-Pr CH), 38.6 (C-2), 39.7 (C-4), 49.9 (C-7), 60.4 (C-5), 60.4 (OCH_2), 65.6 (C-1), 172.9 (ester C=O), 212.5 (C=O).

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.25; H, 9.48.

Keto ester **19c** semicarbazone: mp 189–191 °C (EtOH).

(32) Cf.: Reissig, H.-U.; Hirsch, E. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 813.

[1*R*-(1α,4β,5α,7*R)]-7-Bromo-4-isopropyl-1-methylbicyclo[3.1.1]heptan-6-one [(+)-7] and [1*S*-(1α,4β,5α,7*R**)]-7-Bromo-4-isopropyl-1-methylbicyclo[3.1.1]heptan-6-one [(+)-19b].** A solution of 293 mg of a crude **19c–29a** keto ester mixture (from a cyclization of 478 mg (1.5 mmol) and esters **28**) and 1 N potassium hydroxide in 15 mL of methanol and 5 mL of water was refluxed for 2 h. It was poured into 5% sodium hydroxide solution and extracted with ether. The aqueous solution was acidified with 6 N hydrochloric acid and extracted exhaustively with ether. The extract was washed with brine, dried, and evaporated. The residual mixture (247 mg) of acids **19d** and **29b** [IR (CCl_4) (OH) 3100–3400 (m), (C=O) 1787 (s), 1701 (s) cm^{-1}] and 0.05 mL of dimethylformamide were dissolved in 1 mL of dry benzene, and 0.5 mL (5.9 mmol) of oxalyl chloride was added dropwise at 0 °C. The solution was stirred at room temperature for 1 h and then evaporated. A solution of the residue in 5 mL of dry bromotrichloromethane was added dropwise over a 15-min period to a refluxing mixture of 209 mg (1.4 mmol) of sodium 1-oxypyridine-2-thiolate and 13 mg (0.12 mmol) of γ-(dimethylamino)pyridine in 10 mL of dry bromotrichloromethane. Refluxing was continued for 2 h, and the resultant, light orange suspension was filtered through Celite. The filtrate was evaporated, and the residual oil was dissolved in ether. The solution was washed with water and brine, dried, and evaporated. MPLC of the residue and elution with 40:1 petroleum ether–ethyl acetate provided 44 mg (12%) of liquid bromo ketone **7**: $[\alpha]^{23}_D$ +59.9° ($CHCl_3$, c = 0.60); CD_{max} $[\theta]^{21}_{293}$ +3212° ($CHCl_3$, c = 0.10); IR and ^1H NMR spectrally identical with the above sample of racemic ketone **7**.

Anal. Calcd for $C_{11}H_{17}OBr$: C, 53.89; H, 6.99. Found: C, 54.24; H, 7.07.

Further elution afforded 81 mg (22%) of colorless, liquid bromo ketone **19b**: $[\alpha]^{23}_D$ +7.1 ($CHCl_3$, c = 0.70); CD_{max} $[\theta]^{21}_{298}$ +2444 ($CHCl_3$, c = 0.10); IR (CCl_4) (C=O) 1790 (s) cm^{-1}; ^1H NMR δ 0.93, 0.94 (d, 3 each, *i*-Pr methyls), 1.17 (s, 3, 1-Me), 1.5–2.3 (m, 6, methylenes, methines), 3.28 (s, 1, H-5), 4.41 (s, 1, H-7); ^{13}C NMR δ 16.9 (1-Me), 19.6, 19.8 (*i*-Pr methyls), 20.3 (C-3), 32.2 (*i*-Pr CH), 39.2 (C-2), 47.3 (C-4), 52.0 (C-7), 67.1 (C-1), 69.4 (C-5), 212.1 (C=O).

Anal. Calcd for $C_{11}H_{17}OBr$: C, 53.89; H, 6.99 Found: C, 53.99; H, 7.11.

Bromo ketone **19b** semicarbazone: mp 201–202 °C (EtOH).

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Registry No. **1**, 499-75-2; (±)-**2**, 124355-77-7; (±)-**3**, 124439-20-9; (±)-**4**, 124355-78-8; (±)-**5**, 124355-79-9; (±)-**6**, 124355-80-2; **7** (isomer 2), 124379-63-1; (±)-**7**, 124508-22-1; (±)-**8**, 124355-81-3; **9**, 124355-82-4; (±)-**10a**, 124355-83-5; (±)-**10b**, 124355-98-2; (±)-**10c**, 124355-99-3; (±)-**10d**, 124356-00-9; (±)-**10e**, 124439-22-1; (±)-**10f**, 124356-01-0; **11a**, 124379-64-2; **11b**, 124379-66-4; **11c**, 124379-67-5; (±)-**12a**, 124379-65-3; (±)-**12b**, 124379-68-6; **13a**, 2862-86-4; (±)-**13b**, 124356-02-1; (±)-**13c**, 124356-03-2; (±)-**13d**, 124356-04-3; (±)-**13e**, 124356-05-4; (±)-**14a**, 124355-84-6; (±)-**14b**, 124356-06-5; (±)-**14c**, 124356-07-6; (±)-**15**, 124355-85-7; (±)-**16**, 124355-86-8; (±)-**17**, 124355-87-9; **19b**, 124355-88-0; **19b** semicarbazone, 124356-12-3; **19c**, 124356-08-7; **19c** semicarbazone, 124356-17-8; **19d**, 124356-09-8; (±)-**20a**, 124355-89-1; (±)-**21**, 124355-90-4; **22**, 124355-91-5; **23a** (isomer 1), 124355-92-6; **23a** (isomer 2), 124356-18-9; **24a**, 124355-93-7; **24b**, 104857-78-5; **25** (isomer 1), 124355-94-8; **25** (isomer 2), 124439-26-5; **26a**, 124439-21-0; **26b**, 124439-23-2; **26c**, 124356-10-1; **26d**, 124439-24-3; **27**, 124355-95-9; **28**, 124355-96-0; **29a**, 124355-97-1; **29b**, 124356-11-2; i, 22081-48-7; (±)-iia, 124356-13-4; (±)-iib, 124356-14-5; (±)-iic, 124356-15-6; (±)-iid, 124439-25-4; (±)-iiia, 124379-69-7; (±)-iiib, 124379-69-7; (±)-iv, 124356-16-7; ethyl trichloroacetate, 515-84-4; carvomenthone, 5206-83-7; isocarvomenthone, 7065-48-7.

Synthesis of 2,3-Dihydro-8-(3-hydroxy-3-methylbut-1-enyl)-7-methoxy-2-phenyl-4*H*-1-benzopyran-4-one: A Novel Structure for Falciformin

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Synthesis of 2,3-dihydro-8-(3-hydroxy-3-methylbut-1-enyl)-7-methoxy-2-phenyl-4*H*-1-benzopyran-4-one (1) has been achieved in order to verify the proposed structure of falciformin, a new constituent of *Tephrosia falciformis*. The melting point and spectral characteristics of synthetic 1 are not consistent with those reported for the natural sample, thereby showing that the proposed structure is erroneous. Based on the data reported for the natural product, the new structure 2,3-dihydro-5-(1,1-dimethyl-2-hydroxyprop-2-enyl)-6-methoxy-2-phenyl-4*H*-1-benzopyran-4-one (4) is tentatively proposed for falciformin. The mass spectral fragmentation patterns of 1 and 4 are discussed in detail in support of their structures.

2,3-Dihydro-2-phenyl-4*H*-1-benzopyran-4-ones occur abundantly in plants and exhibit different biological activities, e.g. spasmolytic,[1] cytotoxic,[2] antihepatotoxic,[3] and antidiabetic (antigalactosemic cataract).[4] Among acyclic isopentenylated flavonoids, those possessing 3-methyl-

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