Base Cleavage of β,γ-Unsaturated Bicyclic Cyclobutanones

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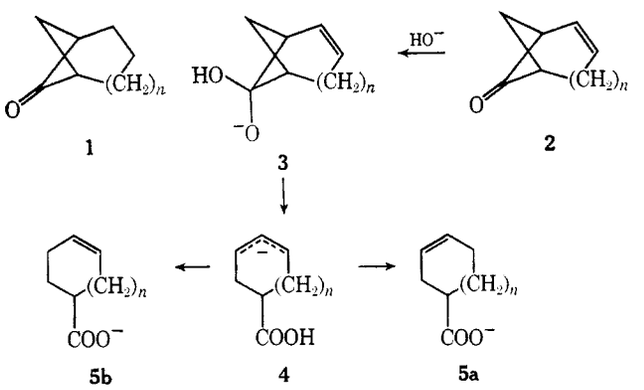
Treatment of chrysanthenone (**13**) with hydroxide ion under a variety of conditions produced as the major product acid **15a** and a smaller but significant quantity of acid **17a**. The ratio of **15a**:**17a** varied from 91:9 to 76:24 depending upon reaction conditions. Treatment of the isomeric ketone **20** with hydroxide ion under the same conditions produced relatively greater quantities of acid **17a**: *i.e.*, the ratio of **15a** to **17a** varied from 72:28 to 43:57. Cleavage of **13** or **20** with potassium methoxide afforded the corresponding esters in approximately the same ratios: 60:40 *vs.* 56:44, respectively. Cleavage of the ketone **14** with hydroxide provided both acids **16a** and **22a** in ratios which again varied with reaction conditions, *i.e.*, 72:28 to 56:44. The mechanistic implications of these contrasting results are discussed.

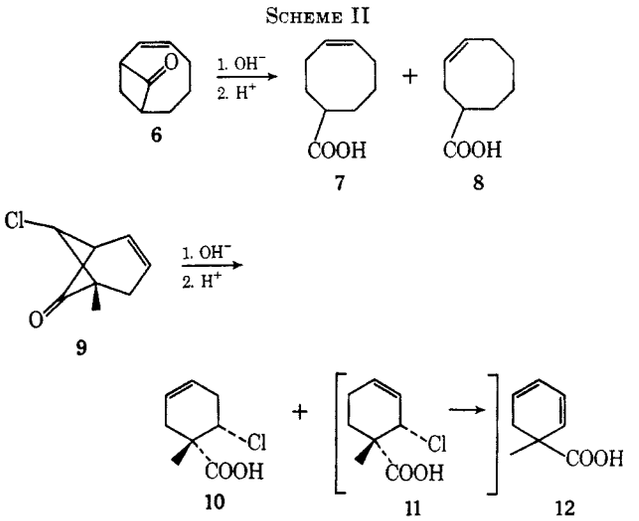
Whereas saturated four-membered ring ketones contained in a bicyclic ring structure of the type **1** are stable to refluxing methanolic potassium hydroxide, the corresponding β,γ-unsaturated ketones **2** are relatively labile under these conditions.[3-6] The driving force for the cleavage of these ketones results from a combination of ring strain and the stabilization rendered by the π orbitals of the double bond to an incipient carbanion developing in the transition state. Since protonation can occur at either of two sites of the developing allyl anion **4**, cleavage of ketones of type **2** would be expected to yield both possible olefinic carboxylates **5a** and **5b** (Scheme I).

SCHEME I

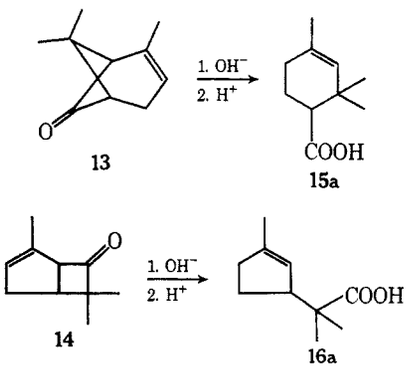


Indeed, bicyclo[5.1.1]non-2-en-8-one (**6**) on treatment with 20% methanolic potassium hydroxide is transformed (after acidification) to a mixture of approximately equimolar quantities of *cis*-4-cyclooctene-1-carboxylic acid (**7**) and *cis*-3-cyclooctene-1-carboxylic acid (**8**)[3] (Scheme II). Similarly the chloro ketone **9** is cleaved to a mixture of 1-methyl-2-*cis*-chloro-4-cyclohexene-1-carboxylic acid (**10**) and 1-methyl-2,4-cyclohexadiene-1-carboxylic acid (**12**) (presumably *via* the intermediate **11**).[6b,c]

SCHEME II



In contrast to the above anticipated reactions, hydroxide ion cleavages of chrysanthenone (**13**) and 2,6,6-trimethylbicyclo[3.2.0]hept-2-en-7-one (**14**) are reputed to yield the single isomeric products 2,2,4-trimethyl-3-cyclohexene-1-carboxylic acid (**15a**)[4] and 2,2-dimethyl-2-(3-methyl-2-cyclopentenyl)acetic acid (**16a**),[7] respectively. A reinvestigation of the base cleavage of these and related cyclobutanones was initiated in order to understand better the mechanism of the cleavage process and explain the exclusive formation of isomers **15a** and **16a**.



Results

Cleavage of Chrysanthenone. Initially, the exact procedure of de Pascual Teresa, *et al.*,[4] was followed for the cleavage of chrysanthenone with aqueous meth-

(1) The Procter & Gamble Co.

(2) Indiana University. E. W. and P. W. J. acknowledge gratefully support by the National Science Foundation.

(3) W. F. Erman and H. C. Kretschmar, *J. Amer. Chem. Soc.*, **89**, 3842 (1967).

(4) J. de Pascual Teresa, H. Sanchez Bellido, and I. Sanchez Bellido, *Anales Real Soc. Espan. Fis. Quim.* (Madrid), **B58**, 339 (1962).

(5) A. R. Penfold, G. R. Ramage, and J. L. Simonsen, *J. Chem. Soc.*, 1496 (1939).

(6) (a) R. M. Dodson, J. R. Lewis, W. P. Webb, E. Wenkert, and R. D. Youssefyeh, *J. Amer. Chem. Soc.*, **83**, 938 (1961); (b) C. L. Leicht, Ph.D. Dissertation, Indiana University, 1964; (c) although **10** is slowly converted to **12** under the same conditions, the rate of formation of **12** from **10** is too low to account for the yield of **12** obtained in the base cleavage of **9**: E. Wenkert and P. Bakuzis, unpublished observations.

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

Table I

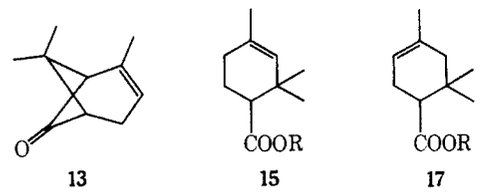
Base Cleavage of Cyclobutanones 13 and 20

Run	Ketone	Base	Base source	Solvent	Base concn, M	Temp, °C	% yield[a] 15b	% yield[a] 17b	% of recd starting ketone	Ratio[b] 15:17	
1	13	KOH	Reagent pellets	Anhy CH_3OH	2	78	41	6		87	13
2	13	KOH	Reagent pellets	Anhy CH_3OH	4	78	32	6	16	85	15
3	13	KOH	Reagent pellets	95% aq CH_3OH	4	78	49	8	17	86	14
4	13	KOH	$KH-H_2O$ (3:1)	THF	c	26–27	28	3		91	9
5	13	KOH	$(CH_3)_3CO^-K^+-H_2O$ (3:1)	THF	c	26–27	49	15	11	76	24
6	13	KOH	$(CH_3)_3CO^-K^+-H_2O$ (1:1.4)	THF	c	26–27	45	14	11	76	24
7	13	$CH_3O^-K^+$	CH_3OH, K	CH_3OH	1	78	16	11	9	60	40
8	13	$CH_3O^-K^+$	CH_3OH, K	CH_3OH	4	78	39[d]	24[d]	0	61	39
9	13	$(CH_3)_3CO^-K^+$	$(CH_3)_3COH$, K	$(CH_3)_3COH$	1	82	39[e]	24[e]	0	63	37[f]
10	20	KOH	Reagent pellets	CH_3OH	2	78	20	27		43	57
11	20	KOH	Reagent pellets	CH_3OH	4	78	21	28	20	42	58
12	20	KOH	$(CH_3)_3CO^-K^+-H_2O$ (10:3)	THF	c	78	31	16	1	66	34
13	20	$CH_3O^-K^+$	CH_3OH, K	CH_3OH	1	26–27	29	22	0	56	44

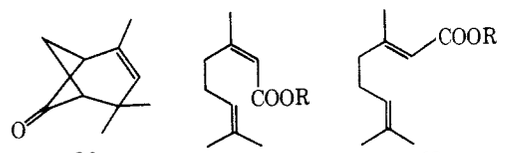
[a] Based upon distilled methyl ester derivatives. [b] Based upon gas chromatographic analysis of the methyl ester derivatives before and after distillation. The product ratios of all runs were duplicated within 3%. [c] Heterogeneous mixture. [d] Based upon combined yield of methyl ester produced directly from the reaction and the methyl ester produced from treatment of the acidic products with diazomethane. [e] Based upon combined yield of *t*-butyl ester produced directly from the reaction and the methyl ester produced from treatment of the acidic products with diazomethane. [f] Based upon the ratio of *t*-butyl esters only.

anolic potassium hydroxide (run 3, Table I). Although both acids **15a** and **17a** were produced under these conditions,[8] the former greatly predominated regardless of the concentration of base or water present in the reaction mixture (compare runs 1–3, Table I). At lower concentrations of base small quantities of neric acid (**18a**) and geranic acid (**19a**) are produced by a competitive thermally induced process[9–12] (see Experimental Section, run 1). When the ketone **13** was treated with a dispersion of anhydrous potassium hydroxide (prepared by adding water to excess potassium hydride)[13] the two acids **15a** and **17a** were produced in a ratio of 91:9. Surprisingly, the ratio of **15a**:**17a** dropped to 76:24 when the hydroxide was generated from potassium *t*-butoxide–water using the general cleavage procedure of Gassman, *et al.*[13] Scission of **13** with potassium methoxide in methanol showed only a slight preference for the production of ester **15b** (runs 7 and 8, Table I).

In contrast to the case of chrysanthenone the isomeric ketone 2,4,4-trimethylbicyclo[3.1.1]hept-2-en-6-one (**20**), when cleaved with methanolic potassium hydroxide, afforded the two acids **15a** and **17a** in almost equimolar quantities with the acid **17a** slightly predominating (runs 10, 11, Table I). However, when potassium hydride–water[13] (run 13, Table I) or potassium butoxide–water[13] (run 12, Table I) was employed for cleavage of **20** the acid **15a** predominated once again. The ratio of **15b** to **17b** from cleavage of **20** with methoxide compared favorably with that obtained from the cleavage of **13** with methoxide (compare run 13 to runs 7 and 8, Table I).



13 15 17



20 18 19

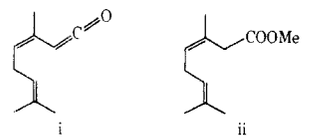
a, R = H; b, R = Me; c, R = *t*-Bu; d, R = Et

The acids **15a**, **17a**, **18a**, and **19a** were identified by comparison of the infrared and nmr spectra and gas chromatography retention times of the corresponding methyl ester derivatives of each with authentic specimens. An authentic specimen of **15b** prepared by diazomethane methylation of the known 2,2,4-trimethyl-3-cyclohexene-1-carboxylic acid,[14a] was converted to the isomer **17b** by heating with boron trifluoride etherate in dichloroethane. That skeletal rearrangement or further migration of the olefin did not occur during the acid treatment was clearly shown by examination of the nmr spectrum of **17b**. Thus, the *gem*-dimethyl protons were apparent as uncoupled superimposed singlets at τ 9.06, the C-4 methyl peak persisted at 8.40, and the single olefinic proton appeared at 4.75.

In view of the possibility of equilibration of **15a** and

(8) The free acids are produced from the carboxylate salt only after acidification of the alkaline solution with hydrochloric acid during work-up.

(9) Conversely, in refluxing 5% aqueous potassium hydroxide the ketone **13** is converted exclusively to geranic acid instead of the acids **15a** and **17a**.[4,5,10] This latter reaction undoubtedly is thermally initiated, however, and probably proceeds *via* the ketene i.[11] In an analogous manner, chrysanthenone undergoes slow cleavage to methyl 3,7-dimethyl-*seq-cis*-3,6-octadienoate (ii) in refluxing methanol in the absence of hydroxide ion.[12]



i ii

(10) M. Kotake and H. Nonaka, *Ann.*, **607**, 153 (1957).

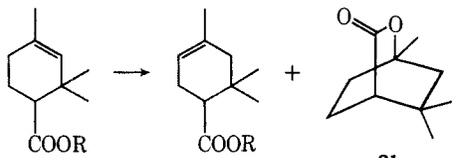
(11) E. P. Blanchard, Jr., *Chem. Ind.* (London), 293 (1958).

(12) W. F. Erman, *J. Amer. Chem. Soc.*, **90**, 779 (1969).

(13) P. G. Gassman, J. T. Lumb, and F. V. Zalar, *ibid.*, **89**, 946 (1967). We should emphasize that maximum yields of acid cleavage products were obtained when the Gassman method was employed. Since ring opening occurs at low temperatures (25–26°) under these conditions, competitive thermal scission is avoided. In contrast to the conditions required for fragmentation of larger ring ketones, the exact 3:1 ratio of potassium *t*-butoxide to water was not required for cleavage of the cyclobutanones. In fact water could be used in excess (*e.g.*, see run 6) without variation in results.

17a during work-up of the product mixtures from each of the above reactions further comment about the acid-catalyzed isomerization of **15a** to **17a** is necessary. The acid **15a** is isomerized slowly to **17a** on storage, but undergoes more rapid conversion to **17a** in ethereal hydrogen chloride Thus treatment of **15a** for 3 hr at room temperature with ethereal hydrogen chloride produced **15a** and **17a** and the lactone **21** in 47, 9, and 3% yields, respectively. Prolonged treatment (16 hr) with ethereal hydrogen chloride afforded the same materials in yields of 33, 16, and 18%, respectively. However, isomerization during work-up of the base cleavage products of **13** and **20** was negligible when they were methylated with diazomethane immediately after acidification and extraction with ether. Thus, the product distribution observed was that resulting directly from base cleavage of the ketones and not from subsequent acid-catalyzed rearrangement.

Product distribution of the free acids at equilibrium was not determined since under more drastic conditions the acids were transformed exclusively to the lactone **21** (see, for example, isomerization with boron trifluoride etherate, Experimental Section). However, acid isomerization of the ester **15b** indicated a thermodynamic preference for the ester **17b** at equilibrium. The ratio of **17b**:**15b** reached a maximum of 70:30 after a 30-min reflux with 10% boron trifluoride etherate in dichloroethane and this ratio did not change on further treatment with acid.

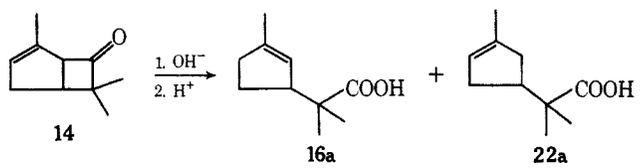


15 17 21

a, R = H; b, R = Me; c, R = *t*-butyl; d, R = Et

Isomerization of an isolated double bond normally requires a base stronger than hydroxide ion.[14b] However, in order to gain some assurance that the initially produced acids **15a** and **17a** are not isomerized under the basic conditions employed for cleavage, the one isomer **15a** was treated with hydroxide ion under the conditions described for base cleavage runs 3 and 5. The acid was recovered unchanged in each instance.

Cleavage of 2,6,6-Trimethylbicyclo[3.2.0]hept-2-en-7-one (14).—Cleavage of the cyclobutanone **14** with base produced both possible isomeric olefinic acids **16a** and **22a** regardless of the conditions employed



14 16a 22a

(see Table II). When the exact conditions of Beereboom[7] were used (run 2, Table II) the isomer **16a** reached a maximum, but, even under these conditions, **22a** was produced in significant quantities. Almost equimolar quantities of the two acids were isolated when the cleavage was performed employing the conditions of Gassman, *et al.*[13]

(14) (a) O. N. Jitkow and M. T. Bogert, *J. Amer. Chem. Soc.*, **68**, 1979 (1941); (b) see A. Schriesheim and C. A. Rowe, Jr., *ibid.*, **84**, 3160 (1962), for a review.

The structure of the acid **16a** was confirmed by comparison of the spectral properties of its methyl ester derivative with those of methyl 2,2-dimethyl-2-(3-methyl-2-cyclopentenyl)acetate (**16b**) reported by Beereboom.[7] The spectral properties of the isomeric ester **22b** are strikingly similar to those of **16b**. However, an exhaustive comparison of the nmr spectra of **16b** and **22b** clearly distinguished the two structures. As expected of an allyl proton the ring C-1 proton in **16b** occurred at 0.48 ppm lower field than the nonallylic C-1 proton in **22b** (see the Experimental Section for details of the nmr spectrum).

Discussion

The cleavage of β,γ-unsaturated cyclobutanones may be envisioned as a three-step process: (1) attack of base on the carbonyl function to produce the intermediate anion **3**, (2) bond scission, and (3) protonation of the resulting allyl anion **4** at either of two possible sites. The exact mode of protonation, however, is a point of speculation. Thus, protonation may occur either by an inter- or intramolecular process at a point in the bond scission which resembles more closely the initially produced anion **3** or at a point which approximates the fully developed allyl anion **4**. In the subsequent discussion we propose that protonation is concerted with bond scission but that the mode and timing of the process is dependent upon reaction conditions and structure variations in the cyclobutanones.

The diverse nature of the protonation process may be developed by considering first the cleavage of chrysanthenone with hydroxide ion. Attack of hydroxide on **13** yields the initial anion **23** which would collapse to the allyl anion **25**.

We will consider first that protonation occurs at a point in the bond-scission process which closely resembles the fully developed anion **25**.[15a] It is at once tempting to suggest that production of **15** as the major product is the consequence of inter- or intramolecular protonation at the less hindered C-5 position of the anion **25** (see Scheme III). The relatively small differences in product distribution observed from cleavage of **13** under different solvent conditions could be interpreted as differences in susceptibility of the specific proton source to steric factors.[15b]

Such an argument, however, seems untenable in light of the striking difference in product distribution from cleavage of ketones **13** and **20** in methanolic potassium hydroxide (compare runs 1 and 2 with 10 and 11). Scission of these ketones would lead to the same allyl ion **25** and, consequently, under identical conditions of

(15) (a) Such a mechanism was originally proposed by Cristol for the base cleavage of dehydronorcamphor to 3-cyclopentenyl acetic acid.[15b] Recently, however, Paasivirta has shown that base cleavage of this ketone yields a 1:1 mixture of the 2- and 3-cyclopentylacetic acids.[15c] (b) S. J. Cristol and P. K. Freeman, *ibid.*, **83**, 4427 (1961); (c) J. Paasivirta, *Tetrahedron Letters*, 2867 (1968); *Suomen Kemistilehti*, **B41**, 335 (1968). (d) It is assumed, without qualification, that protonation of the anion occurs before the dianion iii is produced. Cleavages with potassium *t*-butoxide–water or potassium hydride–water, in fact, could proceed *via* the dianion iii. Intermolecular protonation of the dianion iii, however, should proceed with the same stereoselectivity as for the anion **25**.

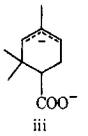


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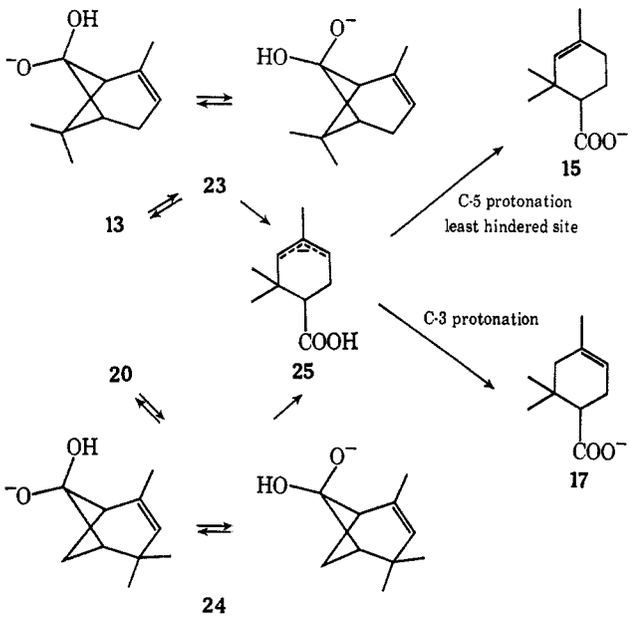
Table II

Base Cleavage of Cyclobutanone 14

Run	Ketone	Base	Base source	Solvent	Base concn, M	Temp, °C	% yield[a] 16b	% yield[a] 22b	% of recd starting material	Ratio[b] 16b	Ratio[b] 22b
1	14	KOH	Reagent pellets	CH_3OH	4	78	4	3	14	62	38
2	14	KOH	Reagent pellets	95% aq CH_3OH	4	78	5	2	9	72	28
3	14	KOH	$(CH_3)_3CO^-K^+$–H_2O (3:1)	THF	c	26–27	28	22	6	56	44

[a] Based upon distilled methyl ester derivatives. [b] Based upon gas chromatography of the corresponding methyl ester derivatives before and after distillation. The product ratios were reproduced within 3%. [c] Heterogeneous mixture.

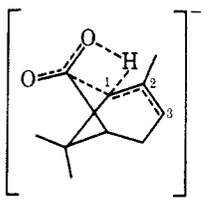
Scheme III



cleavage, should yield products of the same composition regardless of whether protonation is intramolecular or intermolecular. When **13** and **20** are cleaved in methanolic potassium hydroxide, protonation must occur before the completely developed anion **25** is produced, *i.e.*, protonation must occur concerted with ring rupture at a point in the transition state which more closely resembles the anions **23** and **24**, below.[16]

Logical arguments can be presented to explain the observed results if it is assumed that protonation in the presence of an aprotic solvent occurs exclusively by an intramolecular process and in the presence of a protic solvent by competing inter- and intramolecular processes.

Again considering first the cleavage of chrysanthenone (**13**), intramolecular protonation at the C-1 site by what can be envisaged as a 1,3-proton transfer (see structure **26**) would produce **17**; intramolecular protonation at C-3 by a 1,5-proton transfer (see structure **27**) would produce **15**.[17] Examination of a Dreiding model of **23** reveals that the hydroxyl proton is ideally disposed to interact with the π orbitals of the olefin. It is reasonable, therefore, to expect predominant protonation of the C-3 site of **23** if intramolecular protonation is the principal course of reaction. The formation of maximum yields of acid **15a** with hydroxide in the presence of an aprotic solvent (run 4, Table I) is consistent with this proposal. The C-4 *gem*-dimethyl group in **24**, however, might be expected to retard intramolecular protonation (depicted by **29**) at the C-3 site in this isomer and allow competitive intramolecular (depicted by **28**) and intermolecular protonation at C-1. This would explain the fact that significant quantities of both acids **15a** and **17a** are produced from **20** regardless of cleavage conditions. The differences in relative proportions of **15a** and **17a** produced from **20** in the absence and presence of a protic solvent could be explained by the relative contributions of intramolecular and intermolecular protonation with this isomer.



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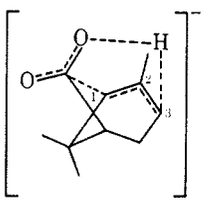

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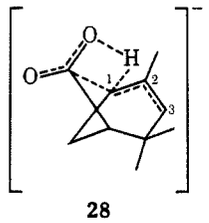

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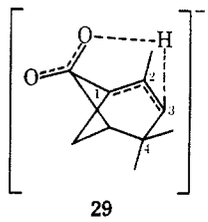

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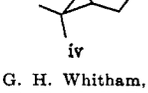
If methoxide ion (or butoxide ion) replaces hydroxide as the attacking nucleophile, intramolecular protonation of the expected intermediate anion **30**[18,19] and **31** (from **13** and **20**, respectively) is impossible and only intermolecular protonation can occur. Approximately equimolar quantities of the two isomeric acids should be, and are, produced from both ketones **13** and **20** under these conditions.

(16) We have already eliminated the possibility that the isomer of greater thermodynamic stability is produced from cleavage of **13** on grounds that the Δ^4 isomer (**17b**) is favored over the Δ^3 isomer (**15b**) on acid equilibration by a factor of at least 7:3. Isolation of different quantities of the two acids **15a** and **17a** from methanolic potassium hydroxide scission of **13** and **20** also precludes the possibility that protonation occurs in such a manner as to produce the most stable olefin.

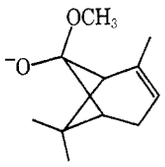
(17) For other examples of base-catalyzed 1,3- and 1,5-hydrogen transfers involving allylic anion systems see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, Chapter V, pp 175–210.

(18) Lithium aluminum hydride reduction of chrysanthenone (**13**) leads exclusively to the alcohol iv.[19] In analogy, solvated methoxide should approach from the least hindered side of the molecule to produce the intermediate **30** in exclusion of its epimer.



iv

(19) (a) J. J. Hurst and G. H. Whitham, *J. Chem. Soc.*, 2864 (1960); (b) P. Demarco, E. Farkas, D. Doddrell, B. L. Mylari, and E. Wenkert, *J. Amer. Chem. Soc.*, **90**, 5480 (1968).



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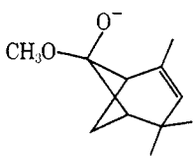

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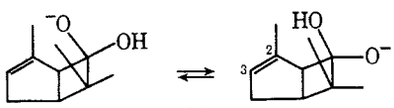
Thus far in our discussion we have ignored the results obtained from cleavage of ketone **13** and **20** using the potassium *t*-butoxide–H_2O–THF system of Gassman. At least 1 equiv of *t*-butyl alcohol is present in the system but whether the *t*-butyl alcohol is complexed with hydroxide ion or whether a heterogeneous or homogeneous system is present is uncertain. Speculation about these runs therefore must be withheld until the characteristics of this system are better understood. Nonetheless, the results of these cleavages are included to emphasize the synthetic value of Gassman's procedure (see ref 13).

In the case of the cleavage of the five/four fused ketone **14**, regardless of cleavage conditions, both isomeric acids are produced in significant quantities. Examination of molecular models indicates that the hydroxyl proton of the initially produced anion **32** is not ideally suited for a 1,5-proton transfer. In this instance protonation may occur by one of the several other mentioned inter- or intramolecular processes.



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Experimental Section

General.—Melting points were determined on a Thomas–Hoover capillary melting point apparatus or on a micro hot stage and are corrected; boiling points are uncorrected. Infrared spectra were recorded on Perkin-Elmer Model 137 or Model 257 spectrophotometers. Nuclear magnetic resonance spectra were run as 10% solutions in carbon tetrachloride on a Varian HA-100 spectrometer using tetramethylsilane as an internal reference. Chemical shifts are recorded as parts per million on the τ scale, coupling constants as hertz. Nuclear magnetic resonance data are recorded in the order: chemical shift (multiplicity, where s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet; coupling constant, interpretation). Gas chromatographic separations were made on one of two columns: column 1, a 10 ft × 0.25 in. stainless steel column packed with 20% GE-SF-96 silicon oil on 70–80 mesh Anakrom ABS; column 2, a 10 ft × 0.25 in. stainless steel column packed with 20% Reoplex 400 on 60–80 mesh Anakrom 300. Microanalyses were performed by T. Atanovich and associates of these laboratories and by Spang Microanalytical Laboratories, Ann Arbor, Mich. Gas chromatographic retention times are recorded relative to air.

Preparation of Chrysanthenone (13).—Chrysanthenone[20] was prepared by a variation[21] of the procedure of Hurst and Whitman.[19a] A solution of 13.332 g of verbenone[22] ($[\alpha]^{26}D$ −256°) in 400 ml of glacial acetic acid was irradiated as previously described[21] with a 450-W Hanovia mercury arc lamp for a period of 2 hr and 35 min. The reaction mixture was diluted with 400 ml of water and extracted with 1 l. of ether. The ethereal layer was separated, washed with three 250-ml portions of water, four 150-ml portions of saturated sodium carbonate, two 250-ml portions of water, and 100 ml of saturated sodium chloride solution, and dried over magnesium sulfate. Evaporation of ether under reduced pressure afforded 13.38 g of yellow liquid. The combined product from two runs was distilled from an 18-in. spinning band column to afford 1.742 g of a mixture of chrysanthenone (**13**) and ketone **20**, bp 70–80° (10.0 mm), 11.864 g of ketone **13**, bp 80–81° (11.2 mm), $[\alpha]^{26}D$ −12.2°, and 3.753 g of a mixture of isopiperitenone and 1,2-dimethyltricyclo[3.3.0.$0^{2,7}$]-octan-6-one, bp 70–80° (7.0–5.25 mm). The ketone **13**, bp 80–81° (11.2 mm), $[\alpha]^{26}D$ −12.2°, was used for the cleavage reactions described below.

Preparation of 2,4,4-Trimethylbicyclo[3.1.1]hept-2-en-6-one (20).—A solution of 7.923 g of chrysanthenone (**13**), $[\alpha]^{26}D$ −12.2°, in 450 ml of cyclohexane was irradiated as previously described[21] for a period of 130 min. Removal of solvent and flash distillation afforded 0.2588 g of liquid, bp 92–106° (44–72 mm), consisting of 2,4,4-trimethylbicyclo[3.1.0]hex-2-ene and 2,6,6-trimethylbicyclo[3.1.0]hex-2-ene and 3.193 g (40%) of liquid, bp 87–89° (10.0 mm), comprised of ketone **13** (39%) and ketone **20** (61%). The two isomers were separated by preparative glpc on an F & M Model 770 instrument using an 8 ft × 0.75 in. stainless steel column packed with 15% Carbowax 20M on 60–70 mesh Anakrom ABS at 100° and 150 ml/min helium flow. There was isolated 997 mg of ketone **20**, bp 89° (10.0 mm), the spectral data of which were consistent with those reported previously.[21] The material as prepared above from several combined runs was employed in the base cleavage reactions.

2,6,6-Trimethylbicyclo[3.2.0]hept-2-en-7-one (14) was prepared by the method of Beereboom[7,23] except that the pure ketone was isolated by fractional distillation as described by Erman.[21] After fractionation there was isolated from 200.0 g of geranic acid 25.78 g of ketone **14**, bp 81° (11.0 mm), containing only traces of *p*-methyl-α-methylstyrene. Redistillation afforded 18.80 g of ketone **14**, bp 88–89° (12.2 mm). Gas chromatographic analysis on column 2 at 100° and 60 ml/min helium flow showed a single peak. The spectral properties (nmr, uv, ir) were consistent with those reported by Beereboom.[7]

Alkaline Cleavage of Chrysanthenone (13). A. With 4.0 *M* 95% Methanolic Potassium Hydroxide (Run 3, Table I).—Essentially the method of de Pascual Teresa, *et al.*,[4] was employed for the cleavage of chrysanthenone with 95% methanolic potassium hydroxide. A solution of 504 mg (0.003 mol) of chrysanthenone, $[\alpha]^{26}D$ −12.2°, in 5 ml of 4.0 *M* 95% methanolic potassium hydroxide solution maintained under a nitrogen atmosphere was heated at reflux for a period of 16 hr. The bulk of the solvent was removed under reduced pressure; the mixture was diluted with 20 ml of water and was washed with 100 ml of ether. The ethereal layer was evaporated to yield 176 mg of residual liquid. Analysis of the liquid by glpc indicated the presence of 50% ketone **13** (17% yield). The aqueous layer was acidified with 9 ml of 2 *N* hydrochloric acid. The precipitated oil was extracted with 100 ml of ether; the ethereal layer was washed with two 10-ml portions of water, dried by swirling over magnesium sulfate for a period of 10 min, and evaporated to afford 519 mg of colorless crystals. The crystalline residue was immediately dissolved in 50 ml of ether and treated with 100 ml of a 2–3% ethereal diazomethane solution. The mixture was stored at 0–5° for 30 min, washed with 6 ml of dilute hydrochloric acid, water, 5 ml of saturated sodium bicarbonate, and water, and dried over magnesium sulfate. Evaporation of ether under reduced pressure and short-path distillation of the residual liquid afforded 343 mg of colorless liquid, bp 80–85° (4.0 mm), which was comprised of methyl 2,2,4-trimethyl-4-cyclohexene-1-carboxylate (**17b**), retention time 75.5 min (14%, 8% yield), and methyl 2,2,4-trimethyl-3-cyclohexene-1-carboxylate (**15b**), retention time 80.8 min (86%, 49% yield) (analyzed by gas chromatography on column 1 at 100° and 60 ml/min helium flow).

Each of the esters **15b** and **17b** was collected by preparative gas chromatography on the same column above. The gas chromatographic retention time and the infrared and nmr spectra of the ester **15b** were identical with the sample of methyl 2,2,4-trimethyl-3-cyclohexene-1-carboxylate (**15b**) prepared by Diels–Alder condensation of acrylic acid and 2,4-dimethyl-2,4-pentadiene and subsequent methylation, below.

The nmr and infrared spectral properties and gas chromatography retention time of the ester **17b** were identical with the ester **17b** obtained by acid-catalyzed rearrangement of the ester **15b**, below.

B. With 4 *M* Methanolic Potassium Hydroxide (Run 2, Table I).—Essentially the same procedure as described above for

(20) A sample of chrysanthenone was kindly furnished by Dr. Sanchez Bellido for initial experiments.

(21) W. F. Erman, *J. Amer. Chem. Soc.*, **89**, 3828 (1967).

(22) We are grateful to The Organic Chemicals Group, Glidden-Durkee Division, SCM Corp., Jacksonville, Fla., for a generous supply of verbenone.

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

cleavage of **13** in 95% methanol was employed. Treatment of 500 mg (0.003 mol) of ketone **13** with 5 ml of 4.0 *M* methanolic potassium hydroxide solution maintained at reflux for 16 hr afforded, after work-up, methylation, and distillation, 230 mg of a mixture of ester **15b** (85%, 32% yield) and **17b** (15%, 6% yield), bp 85–100° (4.25–4.5 mm). The products were isolated and identified as above. From the ethereal washings there was recovered 161 mg of residual liquid. Analysis of the residue by glpc indicated the presence of 48% ketone **13** (16% yield).

C. With 2 *M* Methanolic Potassium Hydroxide (Run 1, Table I).—From 383 mg (2.5×10^{-3} mol) of ketone **13** in 5 ml of 2.0 *M* methanolic potassium hydroxide solution there was isolated after methylation and distillation 234 mg of a mixture, bp 70–80° (2.5 mm), comprised of **17b**, retention time 75.5 min (12%, 6% yield), **15b**, retention time 80.8 min (82%, 41% yield), methyl nerate (**18b**), retention time 111.8 min (2%, 1% yield), and methyl geranate (**19b**), retention time 148 min (4%, 2% yield) (analyzed by glpc as in A).

The esters **15b** and **17b** were isolated and identified as before. The esters **18b** and **19b** were similarly isolated by preparative glpc. Comparison of the glpc retention time and the infrared and nmr spectral properties of the esters **18b** and **19b** with those of authentic specimens of methyl nerate and methyl geranate, prepared below, proved the identity of these two materials.

D. With Potassium Hydride–Water (Run 4, Table I).—Essentially the procedure of Gassman, *et al.*,[13] was followed. To a rapidly stirred suspension of 10.0 g of 40% potassium hydride (4.0 g, 0.10 mol, of potassium hydride in mineral oil) in 12.5 ml of anhydrous tetrahydrofuran maintained under a nitrogen atmosphere at 0–5° was added 540 mg of water. The mixture was allowed to warm to room temperature, 26–27°, when 499 mg (0.003 mol) of chrysanthenone (**13**) in 12.5 ml of tetrahydrofuran was added. The mixture was stirred at 26–27° for 24 hr and cooled to 0–5° and 10 ml of water was added cautiously. The mixture was immediately washed with ether; the water layer was partitioned and acidified with 31 ml of 2 *N* hydrochloric acid. The precipitated acid was extracted with 100 ml of ether; the ethereal layer was washed with water and dried. The solvent was evaporated to yield 742 mg of residual liquid. Esterification with diazomethane afforded 189 mg of distilled liquid, bp 90–100° (4.0–9.0 mm), consisting of **15b** (91%, 28% yield) and **17b** (9%, 3% yield). Products were isolated and identified as above.

E. With Potassium *t*-Butoxide–Water (3:1) (Run 5, Table I).—Essentially the procedure of Gassman, *et al.*,[13] was employed except that tetrahydrofuran was utilized as solvent. To a solution of 4.001 g (0.036 mol) of potassium *t*-butoxide in 12.5 ml of tetrahydrofuran maintained at 26–27° under an atmosphere of argon was added 200 mg of water. To this mixture was added 507 mg (0.003 mol) of **13** in 12.5 ml of tetrahydrofuran. The mixture was stirred at room temperature for 24 hr and worked up as above for the potassium hydride run. Esterification afforded 391 mg of distilled liquid, bp 94–100° (4.2 mm), consisting of **15b** (76%, 49% yield) and **17b** (24%, 15% yield). From the ethereal washings there was isolated 59 mg (11%) of recovered ketone **13**.

F. With Potassium *t*-Butoxide–Water (1:1.4) (Run 6, Table I).—The procedure was the same as above except for the ratio of potassium *t*-butoxide to water.

G. With 4 *M* Methanolic Potassium Methoxide (Run 8, Table I).—A solution of 505 mg (0.003 mol) of **13** in 5.0 ml of 4.0 *M* methanolic potassium methoxide (prepared by addition of 1.55 g of potassium to 10 ml of dry methanol) was heated at reflux under a nitrogen atmosphere for 16 hr. The bulk of the methanol was removed under reduced pressure, and the mixture was diluted with 10 ml of water and extracted with 100 ml of ether. The ethereal layer was washed with five 10-ml portions of water, dried, and distilled to yield 228 mg of a mixture of **15b** (61%, 23% yield) and **17b** (39%, 14% yield). The water layer was acidified and the acid fraction was esterified as in A above to yield 159 mg of ester mixture, bp 68–75° (3.0 mm), consisting of **15b** (61%, 16% yield) and **17b** (39%, 10% yield).[24]

H. With 1 *M* Methanolic Potassium Methoxide (Run 7, Table I).—A solution of 250 mg (1.7×10^{-3} mol) of chrysanthenone (**13**) in 5.0 ml of 1.0 *M* anhydrous methanolic potassium methoxide was heated at reflux under a nitrogen atmosphere for a period of 16 hr. The bulk of the methanol was removed under reduced pressure, and the residue was diluted with 5.0 ml of water and extracted with 50 ml of ether. The ethereal layer was washed with four 10-ml portions of water and dried over magnesium sulfate for 4 hr; the solvent was evaporated and the product was subjected to short-path distillation to afford 157 mg of colorless liquid, bp 70–80° (2.5 mm). Gas chromatography as described in A, above, indicated the presence of five compounds: chrysanthenone (**13**) (14%, 9% yield), ester **17b** (21%, 11% yield), ester **15b** (31%, 16% yield), methyl nerate (**18b**) (12%, 6% yield), and methyl geranate (**19b**) (22%, 12%, yield).

Each of the compounds **1–5** was collected by preparative gas chromatography as described above. The nmr and infrared spectra and gas chromatography retention times of each of the compounds **15b**, **17b**, **18b**, and **19b** were identical with authentic specimens as described above.

I. With Potassium *t*-Butoxide in *t*-Butyl Alcohol (Run 9, Table I).—A solution of 204 mg (1.7×10^{-3} mol) of chrysanthenone (**13**) in 5.0 ml of a solution of 1.0 *M* potassium *t*-butoxide in *t*-butyl alcohol was heated at reflux (80°) under a nitrogen atmosphere for a period of 16 hr. The mixture was cooled to 40° and the bulk of the *t*-butyl alcohol was removed under reduced pressure. The residue was diluted with 10 ml of water and extracted with 100 ml of ether. The ethereal layer was washed with four 10-ml portions of water and dried over magnesium sulfate. Evaporation of solvent and short-path distillation afforded 43 mg of liquid, bp 141° (10.5 mm), comprised of *t*-butyl 2,2,4-trimethyl-4-cyclohexene-1-carboxylate (**17c**) (37%, 5% yield) and *t*-butyl 2,2,4-trimethyl-3-cyclohexene-1-carboxylate (**15c**) (63%, 8% yield) (analyzed on column 1 at 135° and 60 ml/min helium flow). The two peaks were isolated by preparative gas chromatography on the same column and identified by comparison of the infrared and nmr spectrum of each with the authentic specimens prepared below.

The combined water layers from above were acidified by dropwise addition of concentrated hydrochloric acid; the product was extracted with 100 ml of ether; the ethereal layer was washed with two 10-ml portions of water and dried over magnesium sulfate. Evaporation of solvent afforded 150 mg of residual carboxylic acid, infrared λ 3.5–3.9, 5.85–5.9 μ, which was dissolved in 50 ml of ether and treated with 50 ml of 2% diazomethane solution. After storage at 0–5° for 2 hr the excess diazomethane was destroyed by cautious addition of 12 ml of 10% hydrochloric acid; the ethereal solution was washed with three 20-ml portions of water and dried over magnesium sulfate. Evaporation of solvent and short-path distillation afforded 125 mg of colorless liquid, bp 70–75° (2.5 mm), which consisted of methyl ester **17b** (38%, 19% yield) and methyl ester **15b** (62%, 31% yield). Methyl nerate and methyl geranate were not observed in the reaction mixture. The two esters (**17b** and **15b**) were collected and their identities revealed by nmr and infrared spectral comparisons with authentic specimens.

Base Cleavages of 2,4,4-Trimethylbicyclo[3.1.1]hept-2-en-6-one (20) (Runs 10–14, Table I).—Cleavages of the ketone **20** were performed in the same manner as the cleavages of ketone **13**. In each instance 500 ± 5 mg of ketone was treated with base. Yields are based upon distilled ester product. Results are recorded in Table I.

Base Cleavages of 2,6,6-Trimethylbicyclo[3.2.0]hept-2-en-7-one (14).—Alkaline cleavages of ketone **14** were performed as above for ketone **13** using 500 ± 4 mg of ketone **14**. Results are recorded in Table II. Best yields of esters **16b** and **22b** were obtained under conditions of run 3, Table II. Isolation of products from a 1.0-g scale run is described below.

Preparation of Methyl 2-(3-methyl-2-cyclopentenyl-2,2-dimethylacetate (16b) and Methyl 2-(3-methyl-3-cyclopentenyl)-2,2-dimethylacetate (22b).—A solution of 1.005 g (6.8×10^{-3} mol) of ketone **14** was treated as described in E above with potassium *t*-butoxide–water except that double the quantities of reagents were used. After work-up, esterification, and distillation of product, there was isolated 470 mg of colorless liquid, bp 120–126° (4.0–4.5 mm), which was comprised of ester **16b** (56%, 22% yield) and ester **22b** (44%, 17% yield). The two esters were isolated by preparative glpc on column 2 at 100° and 120 ml/min helium flow. Final purification was made by short-path distillation.

The ester **16b**, retention time 26.5 min, was isolated as a colorless liquid: ir (CCl_4) 5.77 (carbonyl), 6.02 μ (olefin); nmr (CCl_4)

(24) The acid products undoubtedly arise *via* an S_N2 displacement by methoxide on the methyl ester carbon: see, for example, J. F. Bunnett, M. M. Robison, and F. C. Pennington, *J. Amer. Chem. Soc.*, **72**, 2378 (1950); R. A. Sneen and A. M. Rosenberg, *J. Org. Chem.*, **26**, 2099 (1961); and W. von E. Doering and L. H. Knox, *J. Amer. Chem. Soc.*, **74**, 5683 (1952).

τ 4.91 (m, olefinic proton), 6.46 (s, ester methyl), 7.10 (broad m, C-1), 7.8–8.4 (m, C-4, C-5 protons), 8.31 (m, C-3 methyl protons), 8.98, 9.01 (singlets, *gem*-dimethyls). The nmr spectrum of **16b** in $CDCl_3$ was identical with that reported by Beereboom.[7]

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.50; H, 9.85.

The ester **22b**, retention time 39.5 min, was isolated as a colorless liquid: ir (CCl_4) 5.77, 9.01 μ; nmr (CCl_4) τ 4.90 (m, C-4 proton), 6.46 (s, ester methyl protons), 7.52 (quintet with fine splitting, C-1 proton), 7.8–8.1 (m, C-2 and C-5 protons), 8.39 (s, C-2 methyl protons), 8.96 (s, *gem*-dimethyl protons).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.47; H, 9.90.

Preparation of Methyl Nerate (18b) and Methyl Geranate (19b).—Treatment of 10.00 g (0.06 mol) of commercial geranic acid (Fritzsche Bros., Inc.) with excess diazomethane afforded 7.346 g (68%) of the corresponding methyl ester mixture, bp 95–96° (2.5 mm) [lit.[25] bp 90–92° (3 mm)], comprised of 28% methyl nerate and 72% methyl geranate. The two isomers **18b**, relative retention time 12.3 min, and **19b**, relative retention time 15.0 min, were separated by gas chromatography on column 1 at 150° and 60 ml/min helium flow or on an 8 ft × 0.75 in. column packed with 15% Carbowax 20 M on 60–70 mesh Anakrom ABS at 150° and 100 ml/min helium flow.

Methyl nerate was isolated as a colorless liquid: ir (neat) 5.79 (conj C=O), 6.05 (olefin) 8.58 μ (ester); nmr (CCl_4) τ 4.42 (s, C-2 proton), 4.95 (t with fine splitting, C-6 proton), 6.40 (s, ester methyl), 7.3–7.6 (m, C-4 protons), 7.8–8.1 (m, C-5 protons), 8.15 (s, C-3 methyl), 8.35, 8.40 (s, C-7 methyls).

Methyl geranate was isolated as a colorless liquid: ir (neat) 5.79 (C=O), 6.03 (olefin), 8.1–8.2, 8.63 μ (ester); nmr (CCl_4) τ 4.38 (s, C-2 proton), 4.96 (m, C-6 proton), 6.37 (s, ester methyl), 7.83 (s, with fine splitting, C-3 methyl), 8.32, 8.40 (s, C-7 methyls).

Preparation of 2,2,4-Trimethyl-3-cyclohexene-1-carboxylic Acid (15a).—Essentially the procedure of Jitkow and Bogert[14] was employed with the following exceptions. A mixture of 65.60 g (0.68 mol) of 2,4-dimethyl-1,3-pentadiene and 73.90 g (1.03 mol) of acrylic acid was heated in a glass-lined autoclave under a back pressure of 1500 psi nitrogen at 155–160° for 16 hr. After work-up and distillation from a 12-in. Vigreux column there was isolated 58.118 g (51%) of **15a**, bp 125° (3.1 mm), mp 79–81°. One recrystallization from acetic acid–water afforded **15a** as colorless plates: mp 84.0–85.1° (59% recovery); ir (CCl_4) 3.0–4.0 (carboxyl OH), 5.90 μ (C=O); nmr (CCl_4) τ 4.90 (m, C-3 proton), 7.6–7.8 (m, C-5 proton), 7.8–8.3 (m, C-1 and C-6 protons), 8.32 (broad s, C-4 methyl), 8.82, 9.01 (C-2 *gem*-dimethyls).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.46; H, 9.72.

Methyl 2,2,4-Trimethyl-3-cyclohexene-1-carboxylate (15b) was prepared either by treatment of the acid **15a** with excess diazomethane or by treatment of the corresponding acid chloride with methanol.

From 342 mg (2.2×10^{-3} mol) of acid **15a**, mp 84.0–85.1°, in 50 ml of ether treated with 20 ml of 2% ethereal diazomethane for a period of 1 hr, there was obtained 289 mg (78%) of the ester **15b**: bp 127° (7.5 mm); ir (neat) 5.75 (C=O), 8.25, 8.65, 9.63 μ; nmr (CCl_4) τ 5.00 (s, C-3 proton), 6.45 (s, ester methyl), 7.7–8.0 (m, C-5 allyl), 8.0–8.5 (m, C-1 and C-6 protons), 8.42 (s, C-4 methyl), 8.97, 9.15 (C-2 *gem*-dimethyls).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.51; H, 9.73.

Isomerization of 2,2,4-Trimethyl-3-cyclohexene-1-carboxylic Acid (15a). A. With Ethereal Hydrogen Chloride.—A solution of 158 mg (9.4×10^{-4} mol) of the acid **15a**, mp 84–85°, in 100 ml of anhydrous ether saturated with dry hydrogen chloride was stored at 26–27° for a period of 16 hr. The mixture was washed cautiously with three 20-ml portions of water, dried, and evaporated to afford 149 mg of colorless oil: ir (neat) 3–4 (carboxyl OH), 5.7–5.9 μ broad (lactone C=O and carboxylic acid C=O). The oil was dissolved in 10 ml of ether and treated with 20 ml of 2–3% ethereal diazomethane and this mixture was stored at 0–5° for 20 min. Excess diazomethane was destroyed by addition of 5 ml of 10% hydrochloric acid. The ethereal layer was washed with 10 ml of 10% hydrochloric acid, 5 ml of saturated sodium bicarbonate, and two 10-ml portions of water and dried over magnesium sulfate. Evaporation of solvent and short-path distillation afforded 140 mg of distillate, bp 120–144° (7.75–8.50 mm). Analysis by temperature-programmed gas chromatography on column 2 at 100–150° indicated the presence of three components: ester **17b**, 20% (16% yield); ester **15b**, 40% (33% yield); and lactone **21**, 20% (18% yield).

The two esters **17b** and **15b** were collected by preparative gas chromatography on column 2 at 100° and 60 ml/min helium flow as liquids and identified by spectral comparisons, respectively, with the authentic ester **15b** prepared from the acid **15a** above, and the ester **17b**, prepared by rearrangement of the ester **15b** with boron trifluoride etherate, below.

The lactone **21** was collected on the same column at 150° as colorless crystals, mp 58.5–61.5°, identical with the lactone prepared below, procedure B.

Treatment of 96.2 mg of the acid **15a** in a similar manner with ethereal hydrogen chloride for a period of 3 hr afforded 61 mg of a mixture of **17b**, 16% (9% yield); **15b**, 80% (47% yield); and **21**, 5% (3% yield).

B. With Boron Trifluoride Etherate in 1,2-Dichloroethane. Preparation of 2,2,4-Trimethyl-4-*cis*-hydroxy-3-cyclohexene-1-carboxylic Acid Lactone (21).—A solution of 1.008 g (0.006 mol) of the acid **15a**, mp 81.0–83.1°, in 23 ml of 1,2-dichloroethane containing 8.0 ml of boron trifluoride etherate was heated at reflux for 75 min. The bulk of the dichloroethane was removed under reduced pressure; the residue was dissolved in 100 ml of ether, and the ethereal layer was washed with 25 ml of water, 10 ml of 10% sodium hydroxide, and four 20-ml portions of water and dried over magnesium sulfate. Evaporation of solvent afforded 679 g (70%) of residual oil which, on analysis by gas chromatography as above, indicated the presence only of lactone **21**. Short-path distillation gave 412 mg (42%) of colorless oil, bp 120–130° (4.5 mm). The oil crystallized from petroleum ether afforded 205 mg (21%) of the lactone **21** as colorless prisms: mp 66.8–67.8°; ir (CCl_4) 5.70 μ (bicyclic lactone[26]); nmr (CCl_4) τ 7.91–8.60 (m, methylene and methyne protons), 8.70 (s, C-4 methyl), 8.90, 8.96 (s, C-2 *gem*-dimethyl).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.4; H, 9.6. Found: C, 71.5; H, 9.5.

Isomerization of Methyl 2,2,4-Trimethyl-3-cyclohexene-1-carboxylate (15b).—A solution of 964 mg (5.3×10^{-4} mol) of the ester **15b**, bp 122° (7.25 mm), in 20 ml of 1,2-dichloroethane containing 6.0 ml of boron trifluoride etherate was heated at reflux for 30 min. The mixture was cooled to room temperature, diluted with 50 ml of ether, and washed with two 15-ml portions of water, 15 ml of saturated sodium bicarbonate, and two 15-ml portions of water, dried, and evaporated to yield 844 mg of colorless liquid. Distillation from a modified Hickman still afforded 425 mg of colorless liquid, bp 120–144° (7.75–8.50 mm), consisting of ester **17b**, 70% (31% yield), and ester **15b**, 30% (13% yield), as analyzed by programmed-temperature gas chromatography on colunm 2 at 100–150°.

The two esters were isolated by gas chromatography on column 2 at 100° and 60 ml/min helium flow. The ester **15b** was identical in every respect with the ester **15b** prepared directly from acid **15a** above. The ester **17b** was isolated as a colorless liquid: ir (neat) 5.75 (C=O), 8.1–8.9, 8.96, 8.75 μ; nmr (CCl_4) τ 4.75 (m, C-5 proton), 6.46 (s, ester methyl), 7.75–8.3 (m, C-1, C-3, C-6 protons), 8.40 (broad s, C-4 methyl), 9.06 (s, *gem*-dimethyl protons).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.48; H, 9.82.

Treatment of 436 mg (2.4×10^{-4} mol) of the ester **15b**, bp 85–88° (5.25–6.25 mm), in 10.0 ml of dichloroethane containing 3.0 ml (3.357 g) of boron trifluoride etherate at reflux for 1.0 hr afforded 233 mg of liquid, bp 125–140° (7.5 mm), containing ester **17b**, 14% (8% yield); ester **15b**, 6% (2% yield); lactone **21**, 50% (29% yield); and a mixture of ethyl 2,2,4-trimethyl-3-cyclohexene-1-carboxylate (**15d**) and ethyl 2,2,4-trimethyl-4-cyclohexene-1-carboxylate (**17d**), 30% (16% yield).

Preparative gas chromatography on column 2 at 150° and 60 ml/min helium flow separated the esters **17b** and **15b** (relative retention time 9.0 min) from the esters **15d** and **17d** (relative retention time 14.2 min) and the lactone **21** (relative retention time 16.5 min). The two isomers **17b** and **15b** were separated

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and collected on the same column at 100° and 60 ml/min helium flow. The lactone was recollected at 150° for final purification.

The ester mixture **15d–17d** could not be separated by glpc. That the latter mixture was indeed composed of **17d** and **15d** was shown by the infrared [5.76 μ (ester C=O)] and nmr spectra. The nmr spectrum indicated the presence of ~70% **17d** and 30% **15d**. Principal peaks of the nmr spectrum of **15d** were assigned as follows: τ 5.0 (s, C-3 proton), 7.9 (q, ester methylene), 7.9–8.3 (m, C-1, C-4, C-5 protons), 8.38 (s, C-4 methyl), 8.75 (t, ester methyl), 8.91, 9.11 (s, C-2 *gem*-dimethyls). Nmr signals of isomer **17d** were assigned as follows: τ 4.72 (m, C-5 proton), 7.9 (q, ester methylene), 7.9–8.3 (m, C-1, C-4, C-5 protons), 8.38 (s, C-4 methyl), 8.75 (t, ester methyl), 9.02, 9.03 (s, C-2 *gem*-dimethyls).

Preparation of *t*-Butyl 2,2,4-Trimethyl-3-cyclohexene-1-carboxylate (15c).—To a solution of 5.587 g (0.050 mol) of potassium *t*-butoxide in 45 ml of *t*-butyl alcohol (freshly distilled over sodium) was added 4.00 g of the acid chloride of **15a** prepared in the same manner as described for preparation of ester **15b** and this mixture was stirred at room temperature under a nitrogen atmosphere for a period of 45 min. After removal of the bulk of the *t*-butyl alcohol under reduced pressure the mixture was diluted with 25 ml of water and extracted with 150 ml of ether. The ethereal layer was washed with four 25-ml portions of water and dried over magnesium sulfate. Evaporation of solvent afforded 1.699 g of residual liquid which on short-path distillation afforded 862 mg (18%) of **15c** as a colorless liquid: bp 141° (10.5 mm); ir (neat) 5.76 μ; nmr (CCl_4) τ 5.12 (broad s, C-3), 8.0 (t, J = 6.1 Hz, C-1), 8.2–8.4 (m, C-5, C-6), 8.5 (s, fine splitting, C-4 olefinic methyl), 8.69 (s, *t*-butyl methyls), 9.02, 9.20 (s, C-2 *gem*-dimethyls).

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.09; H, 10.79.

Treatment of 2,2,4-Trimethyl-3-cyclohexene-1-carboxylic Acid (15a) with Base. A. With Potassium *t*-Butoxide–Water (3:1)–THF.—To a solution of 4.011 g (0.036 mol) of potassium *t*-butoxide in 12.5 ml of tetrahydrofuran was added 200 mg of water followed by 500 mg of the acid **15a**, mp 84–85°, as described in cleavage reaction E, above. The mixture was stirred at 26–27° for 24 hr when the bulk of the THF was removed under reduced pressure. The residue was dissolved in 25 ml of water and the water layer was washed with ether. The cold aqueous layer was acidified with 23 ml of 2 N hydrochloric acid and the acid was extracted in the usual fashion to furnish 347 mg (70%) of crystalline acid. Esterification with diazomethane afforded 300 mg of ester, bp 80–105° (0.5–1.0 mm), which on analysis by glpc on two different columns (0.25 in. × 10 ft columns packed with 20% SE-30 silicon oil and with 20% Carbowax 20M TMPA on 60–80 mesh AW DMCS-300) showed a single peak of retention time identical with ester **15b**. (The isomeric ester **17b** was separated cleanly from **15b** under these conditions.) The infrared spectrum of the collected material was identical in every major respect with ester **15b** prepared above.

B. With 4 *M* 95% Methanolic Potassium Hydroxide.—A solution of 503 mg of acid **15a** in 5 ml of 4.0 M 95% methanolic potassium hydroxide solution was heated at reflux for 16 hr as in cleavage run 3 above. Removal of solvent, dilution with 20 ml of water, acidification, and ether extraction afforded 419 mg (84%) of recovered acid, mp 79–81°. Esterification with diazomethane afforded 347 mg of ester, bp 90–100° (1.0 mm). Analysis by glpc as described above for the attempted base isomerization with potassium *t*-butoxide–water indicated only ester **15b**.

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Registry No.—**15a**, 13746-43-5; **15b**, 19766-10-0; **15c**, 19766-11-1; **15d**, 19766-12-2; **16b**, 19766-13-3; **17b**, 19766-14-4; **17d**, 19766-15-5; **18b**, 1862-61-9; **19b**, 1189-09-9; **21**, 19766-16-6; **22b**, 19766-17-7.

Syntheses, Spectra, and Identification of Isomeric, Fused-Ring Paracyclophane Derivatives

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We report the stereoselective syntheses and chemical structure proof of the *exo* (**1a**) and *endo* (**1b**) isomers of 17-hydroxymethyl-4,5-tetramethylene[2.2]paracyclophane. We have also examined the spectral properties of these and related isomeric, fused-ring paracyclophanes, and have discovered an interesting nmr correlation which is indicative of *exo* or *endo* substitution in these systems.

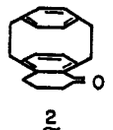
The acetolysis of 2-([2.2]paracyclophenyl)ethyl *p*-toluenesulfonate involves intermediate formation of a phenonium ion.[1] Because of the presence of two aromatic rings in paracyclophanes, several questions arise concerning the stereochemistry of this acetolysis reaction. To examine the stereochemical details of solvolysis reactions of [2.2]paracyclophane derivatives,[2] we have synthesized the *exo* (**1a**) and *endo* (**1b**) isomers of 17-hydroxymethyl-4,5-tetramethylene[2.2]paracyclophane. In this paper we discuss the details of the stereoselective syntheses. We also report an interesting nmr correlation that may be a general method for determining the *exo* or *endo* stereochemistry at the 17 position of 4,5-tetramethylene[2.2]paracyclophanes that have an oxygen atom in the substituent group.

1a, Y = CH_2OH, X = H

1b, Y = H, X = CH_2OH

Results

Synthetic.—The starting material for the syntheses of alcohols **1a** and **1b** is 4,5-tetramethylene-17-oxo-[2.2]paracyclophane (**2**).[3] We were not consistently



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