1062 (s), 998, 973 (s), 956 (s), and 902 (s) cm^{-1}; nmr ($CHCl_3$) δ 3.9 (br s, 2 H), 3.5 (br unresolved m, 2 H), 2.0 (m, 5 H), and 1.61 (br s, 7 H). A sample of **10** was prepared according to the directions of Appleton, *et al.*,[9] and spectral comparison showed it to be identical with the 5% diol above.

The 2% component (11) was not isolated in pure form, being contaminated with stopcock grease and traces of alumina. This crude material (84 mg) was stirred at 25° with 75 ml of 0.0125 *M* potassium periodate solution and 7.5 ml of 2.0 *N* sulfuric acid for 24 hr. Titration according to the directions given by Jackson[24] showed that periodate equivalent to 17.4 mg of diol was consumed.

The 46% component (9) was isolated as a crystalline solid and was purified by sublimation: mp 118–121°; ir (KBr) 3320, 1150 (w), 1074, 1052 (s), 1034, 1008 (s), 996, 906, and 720 cm^{-1}; ir (CCl_4) 2930, 2872, 2856, 1468, and 1466 cm^{-1}; nmr ($CHCl_3$) δ 4.05 (br s, 2 H), 3.49 (m, 2 H), 2.16 (m), 1.93 (br s), 1.58 (br s), and 1.0–2.4 (12 H).

Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.48; H, 10.38.

A sample (118 mg, 0.76 mmol) of this diol was oxidized with periodate as described above. In 24 hr at 25°, 113% of the theoretical amount of periodate was consumed. The reaction mixture was concentrated *in vacuo*, saturated with sodium chloride, and extracted with chloroform. The extracts were dried ($MgSO_4$) and the solvent was evaporated to give 130 mg of solid, mp 154–156°, which reacted with dinitrophenylhydrazine and showed bands in the infrared at 2710 and 2810 cm^{-1}. Treatment of the crude material with 30% hydrogen peroxide gave a crystalline acid, mp 153–155° (lit.[15] mp 150–152°).

Enol Fraction.—Glpc examination of the enol fraction showed three components. The major component (23% of the solvolysis product or 50% of the enol fraction) was shown by glpc comparison (12 ft × 0.125 in. 5% FFAP column at 145°) to be identical with the main component of the trifluoroacetolysis, *i.e.*, **3** + **4**. The minor component (3% of the solvolysis product or 6% of the enol fraction) was not isolated, but was shown by glpc comparison to be different from the hydride reduction products of either **5** or **6**.

A sample of the enol fraction (110 mg) was hydrogenated over palladium on charcoal in methanol solution. The main product was collected from a preparative gas chromatographic run: mp 176–178°; ir 3400, 2980, 1480, 1040, 982, 963, and 910 cm^{-1}. The spectral data and melting point identify this as **2**.

Partial separation of the two main enol components was achieved in a preparative scale gas chromatography run on 5 ft × 0.25 in. 20% SE-30 on Chromosorb W column at 90°. A crude sample enriched in component **7** (21% of the solvolysis mixture) was obtained: mp 127–131°; ir (CCl_4) 3620, 3360 (br), 3020, 2920, 1458, 1446, 1250, 1220, 1067 (w), 1045 (m), and 985 cm^{-1} (s); nmr (CCl_4) δ 5.5–6.0 (m, 2 H), 3.82 (unresolved, 1 H), 2.23 (m), 2.08 (s, 1 H), 2.0 (m), 1.5 (br s), and 1.2–2.4 (11 H). Compound **7** is reported[11] to melt at 103–103.5°, but the overlap between the peaks for enols **3** + **4** and **7**, even on an analytical level, prevented isolation of pure **7** on a preparative scale.

A portion of this enol (125 mg) was treated with 200 mg of chromium trioxide in 5 ml of pyridine at 25° for 14 hr. The solution was diluted with ether and an excess of water was added. The ether layer was separated and passed through an activity IV alumina column. The ether eluate was concentrated and the ketonic products were separated by preparative gas chromatography (10% SF-96 on silanized Chromosorb at 114°). The main product was isolated as a white solid: mp 98–100° (lit.[11] mp 97.5–98.5°); ir (CCl_4) 1675 cm^{-1}; uv λ_{max} 235 nm; nmr (CCl_4) δ 6.89, 6.12 (modified AB, 2 H, J_{AB} = 9.8 Hz), and 1.5–2.8 (m, 10 H).

(24) E. L. Jackson, *Org. Reactions*, **2**, 341 (1944).

Registry No.—**1**, 13366-99-9; **9**, 22485-96-7.

The Lactonization of Camphene-8-carboxylic Acid

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Whereas lactonization of camphene-8-carboxylic acid with formic acid has been reported to give β lactone **2**, the initial product has been identified as the γ lactone **3**. The structure and configuration of bornane-1-carbo-2-*exo*-lactone (**3**) have been established by conversion with excess phenyllithium into the same glycol **10** as obtained from 10-benzoyl-2-*exo*-bornanol (**9**) with excess phenylmagnesium bromide. The configuration of **8**, previously reported as the *endo* alcohol, was proven by degradation to isoborneol (2-*exo*-bornanol). A second lactone, *exo*-2,3-dimethyl-*endo*-3-hydroxynorbornane-*endo*-2-acetic acid lactone (**4**), is produced from **1** and **3** on longer heating with formic acid or prolonged standing with trifluoroacetic acid. A third lactone, *endo*-2,3-dimethyl-*exo*-3-hydroxynorbornanane-*exo*-2-acetic acid lactone (**5**), is also formed in small quantity. Lactone **5** is the major or exclusive product when **1**, **3**, or **4** are treated with 10% sulfuric acid–formic acid for 6.5 hr, 50% sulfuric acid, or concentrated sulfuric acid, respectively. The structure and configuration of lactone **5** have been unequivocally established by degradation to 9-methylcamphene, which has been synthesized by a stereospecific reaction sequence. Convenient syntheses of optically active **1** from nopol (10-hydroxymethyl-α-pinene) and camphene *via* camphene-8-methanol are described, and it is noted that lactonization of optically active **1** is accompanied by complete racemization. Deuterium exchange reactions involving **1** and the lactones **3**, **4**, and **5** are described and a probable mechanistic pathway from **1** to the lactones is suggested. Finally, hydrochlorination of **1**, previously described by Langlois, is shown to produce *exo*-2-chlorocamphane-10-carboxylic acid rather than the reported 2-chloro-3,3-dimethylbornane-2-acetic acid.

For a number of years, studies in one of these laboratories have been concerned with the various types of rearrangements encountered in the camphane–isocamphane systems[3–5] with particular attention to camphene racemization,[4,5] while studies in the other laboratory have been concerned with devising simple synthetic routes to certain terpene intermediates.[6] In the course of these studies the attention of both groups of investigators was attracted independently to a paper

(1) Work supported in part by Public Health Service Grants CA 05406 and 10202 from the National Cancer Institute and a Faculty Research Grant from the Horace H. Rackham School of Graduate Studies, The University of Michigan. Inquiries should be addressed to W. R. Vaughan, The University of Connecticut or J. Wolinsky, Purdue University.

(2) Abstracted in part from Ph.D. dissertations The University of Michigan, by F. S. Seichter, 1959, and R. R. Dueltgen, 1967, and by S. Grey, 1968, Purdue University.

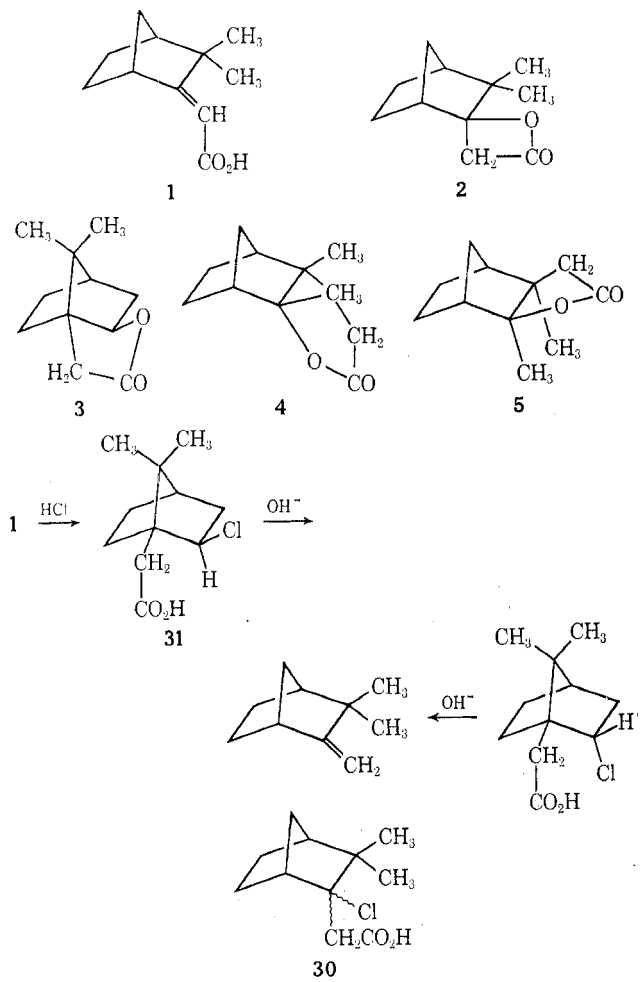
(3) W. R. Vaughan and R. Perry, Jr., *J. Amer. Chem. Soc.*, **74**, 5355 (1952).

(4) W. R. Vaughan and R. Perry, Jr., *ibid.*, **75**, 3168 (1953).

(5) W. R. Vaughan, C. T. Goetschel, M. H. Goodrow, and C. L. Warren, *ibid.*, **85**, 2282 (1963).

(6) J. Wolinsky, D. R. Dimmel, and T. W. Gibson, *J. Org. Chem.*, **32**, 2087 (1967).

by Langlois[7] in which camphene-8-carboxylic acid (**1**) was converted by treatment with formic acid or formic–sulfuric acids into a substance with unspecified optical properties alleged to be β lactone **2**. In view of the unusual stability of this lactone, both groups were prompted to reexamine the lactonization of camphene-8-carboxylic acid, and it may now be jointly reported that, depending upon conditions, one or more of three different lactones, **3**–**5**, are produced. In this paper the structures of these lactones will be delineated and probable pathways for their formation will be considered.



The conditions described by Langlois[7] for the lactonization of acid **1** were followed explicitly and solids were obtained whose melting points corresponded exactly with those reported. When acid **1** was heated for 1–2 hr in 90% formic acid[7] or allowed to stand at ambient temperature in trifluoroacetic acid for 3 days, a lactone mixture was produced from which pure lactone **3**, mp 198.5–199.5°, could be obtained by recrystallization. Examination of the nmr spectrum of the mother liquors from the formic acid lactonization demonstrated the presence of lactone **4**. As shown in Table I, optimum conditions for the production of lactone **3** involve heating acid **1** for 1–2 hr in formic acid or allowing it to stand in trifluoroacetic acid for 2–3 days. Optically active acid **1** gave optically inactive **3** using these methods.

(7) G. Langlois, *Bull. Soc. Chim. Fr.*, **41**, 384 (1927).

Conditions which favor the production of lactone **4** as the major lactonic product (see Table I) include allowing acid **1** to stand in trifluoroacetic acid for any length of time in excess of 9 days, heating it with formic acid or trifluoroacetic acid for longer than 3–4 days, or heating it with 10% sulfuric acid in 90% formic acid[7] for 30–90 min. Lactone **4** is readily isolated in pure form by recrystallization from pentane.

TABLE I
LACTONIZATION OF CAMPHENE-8-CARBOXYLIC ACID (1)

Conditions	Time	Lactone 3, %	Lactone 4, %	Lactone 5, %
90% formic acid	1 hr	28.2	18.8	
at 100°	2 hr	31.1	25.2	
	6 hr[a]	20.5	41.9	?
	4 days	9.9	73.1	?
	10 days	6.5	81.0	?
	14 days		84.5	15.5
CF_3CO_2H at 25°	2 hr	9.0		
	6 hr	12.3	1.7	
	16 hr	23.8	3.2	
	2 days	50	9.4	
	6 days	46.4	42.8	
	9 days	41.7	54	
	15 days	26.4	73.6	
	25 days		100	Trace
CF_3CO_2H at 72°	3.5 days		79.4	21.6
10% H_2SO_4 in	0.5 hr		92	9
formic acid	1.0 hr		82.5	17.5
	3.0 hr		57	43
	6.5 hr		37	63
50% H_2SO_4	0.5 hr		47	53
	1.0 hr		45	55
	2.0 hr		25.6	74.4
95% H_2SO_4 at 0°	6 hr		11	89

[a] An unknown product with a methyl resonance at δ 0.8 ppm builds up to a maximum of 25% at 6 hr and disappears slowly thereafter.

Prolonged heating of acid **1** with 10% sulfuric acid–90% formic acid, heating it at 150° with 50% sulfuric acid, or allowing it to stand at 0° with 95% sulfuric acid for 6 hr gives lactone **5** as the major product.

Finally, it was observed that treatment of α-pinene-10-carboxylic acid with trifluoroacetic acid for 4 months gave a poor yield of a lactone mixture which appeared to be predominantly lactone **4**.

The three lactones, whose properties are listed in Table II, are isomeric and presumably arise as a consequence of rearrangements common to the extremely labile bicyclic systems from which they are necessarily derived. We turn next to explicit proofs of structure for each of the lactones.

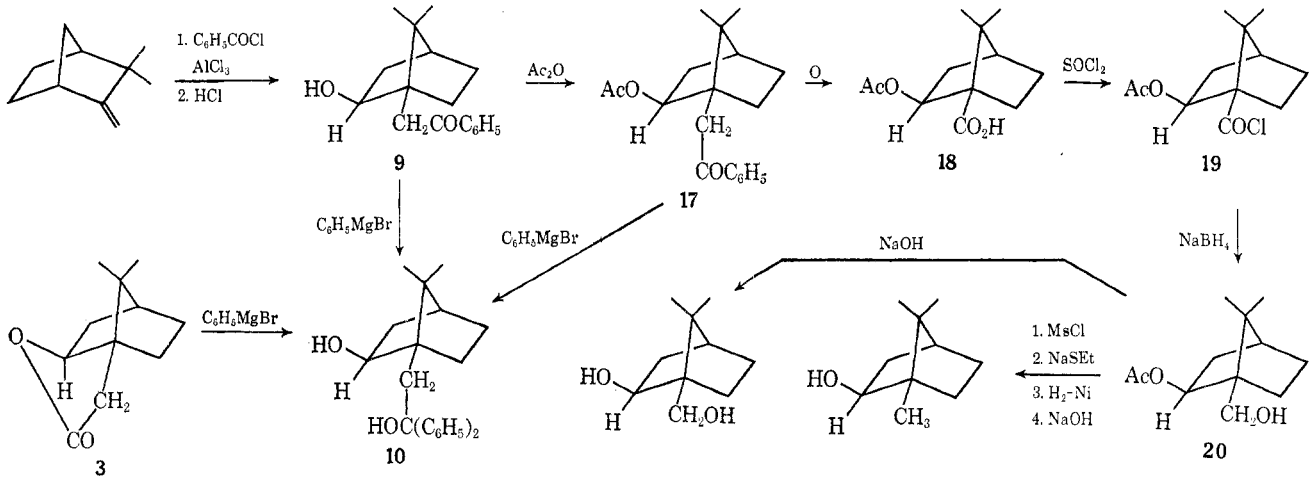
TABLE II
PROPERTIES OF LACTONES 3–5

Lactone	Mp, °C	Ir carbonyl stretch, μ	Glpc[a] retention time, min	Nmr[b] CH_3CCH_3	Nmr[b] HCO
3	198.5–199.5	5.65	19.8	0.94	4.19
				0.98	
4	170–171	5.65	20.6	1.16	
				1.32	
5	157–161	5.65	27.6	1.12	
				1.32	

[a] DEGS at 175°, 12 psi, 10-ft column. [b] δ in parts per million (60 Mc, internal TMS).

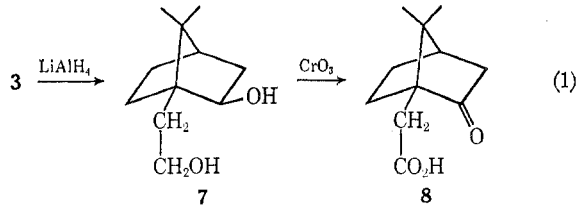
SCHEME I

CONFIGURATION PROOF FOR 3 AND 9



Examination of the infrared spectrum of **3** immediately disposed of Langlois' β-lactone hypothesis, since the carbonyl absorption corresponds to that characteristic of a typical γ lactone. If **1** experiences a rearrangement typical of the camphene system, it seemed likely that **3** should be identical, except for its lack of optical activity, with a lactone obtained by Bain[8] as a minor product of treatment of *endo*-2-chlorocamphane-10-carboxylic acid (**6**) with base. Comparison of infrared spectra of optically inactive **3** and optically active lactone kindly furnished by Dr. Bain established the identity of the two lactones, and consequently provided a strong inference as to the structure of **3**.

Further inferences regarding the structure of **3** are possible. The skeletal arrangement is confirmed by lithium aluminum hydride reduction to 10-hydroxymethylisoborneol (**7**), which was oxidized according to the Jones procedure[9] to the known camphor-10-carboxylic acid (**8**) (eq 1), and the *exo* configuration



(1)

of the oxygen at C-2 in 3 is suggested by the nmr spectrum of diol **7**, in which the multiplicity of the C-2 proton is characteristic of an *endo* 2 proton and the substantial nonequivalence of the geminal methyl groups is typical of bornane derivatives with an *exo* hydroxyl group.[10]

The configuration of **3** was definitively established *via* the following correlation. The reaction product of camphene with benzoyl chloride in the presence of aluminum chloride upon hydrolysis, had been reported as 10-benzoylborneol,[11] whereas its degradation to isoborneol (Scheme I) requires that it be 10-benzoylisoborneol (**9**). Originally, it was planned to degrade **3** *via* the Barbier–Wieland procedure, and to this end it was converted by treatment with excess phenylmagnesium bromide into 10-(diphenylhydroxymethyl)isoborneol (**10**), which could also be obtained by treatment of **9** or its acetate with excess phenyllithium, thereby establishing both structural and configurational relationships between **3** and **9**. Unfortunately the attractive prospect of such a degradation could not be realized directly. Thus simple dehydration of **10** afforded a cyclic ether **11**, and acetylation of the secondary hydroxyl yielded the glycol monoacetate **12**, which upon dehydration afforded 10-benzhydrylideneisobornyl acetate (**13**), which failed to react with ozone, as did its hydrolysis product, 10-benzhydrilideneisoborneol (**14**). Nor was it possible to oxidize the double bond in **13** or **14** with any other reagent. On the other hand, **14** could be oxidized to 10-benzhydrilidenecamphor (**15**) by Jones reagent,[9] and sodium borohydride reduction of **15** regenerated **14**. The only reaction affecting the double bond in this system was catalytic hydrogenation of **13** to give 10-benzhydrylisobornyl acetate (**16**).

However, **9** was readily acetylated to a 10-benzoylisobornyl acetate (**17**), and **17** could be oxidized, albeit in poor yield, to *exo*-2-acetoxyapocamphane-1-carboxylic acid (**18**).[12] Conversion of the carboxyl group into methyl involved acid chloride (**19**) formation, reduction by sodium borohydride to the carbinol **20** (which upon hydrolysis of the acetate afforded the known 10-hydroxyisoborneol[13,14]), and an adaptation of Stork's conversion of hydroxymethyl groups in the cantharidine synthesis[15] into the present system. Identification of the final product as isoborneol was accomplished by comparison of infrared spectra, melting points, and mixture melting points and preparation and comparison of *p*-nitrobenzoates. This degradation (see Scheme I) explicitly defines the configuration of the lactone **3** as well as that of 10-benzoylisoborneol (**9**).

We turn next to the gross structures of lactones **4** and **5**. Both lactones displayed the characterististic

(8) J. P. Bain, A. H. Best, B. L. Hampton, G. A. Hawkins, and J. L. Kitchen, *J. Amer. Chem. Soc.*, **72**, 3124 (1950).

(9) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, **39** (1946).

(10) J. Musher, *Mol. Phys.*, **6**, 93 (1963).

(11) P. Lipp, P. Küppers, and H. Holl, *Chem. Ber.*, **60**, 1575 (1927).

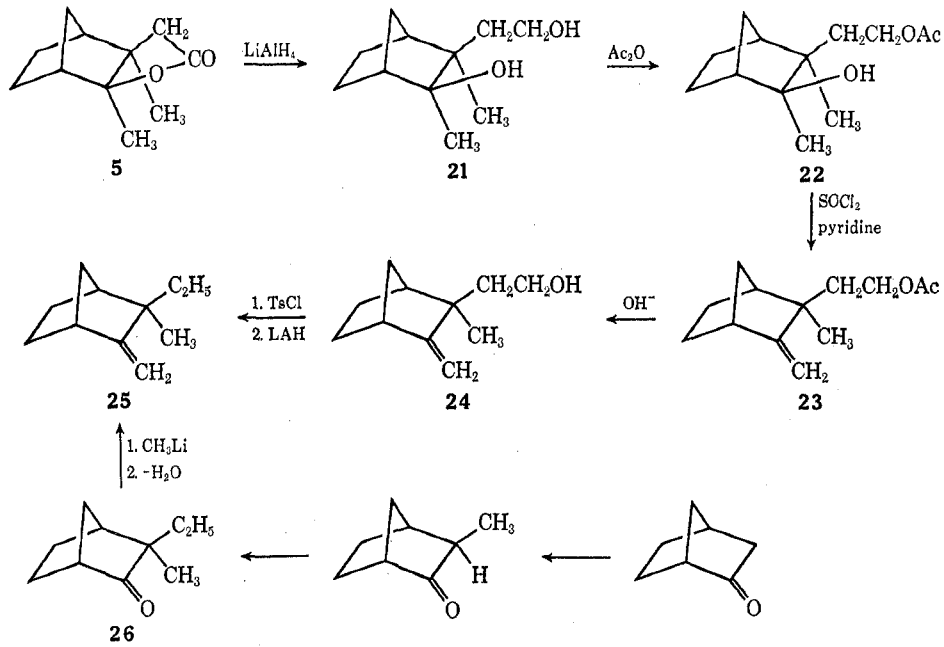
(12) P. Lipp, H. Bräucker, and H. Sauer, *ibid.*, **73**, 1146 (1940).

(13) B. A. Arbuzov and Z. G. Iseva, *Zh. Obshch. Khim.*, **21**, 1250 (1954).

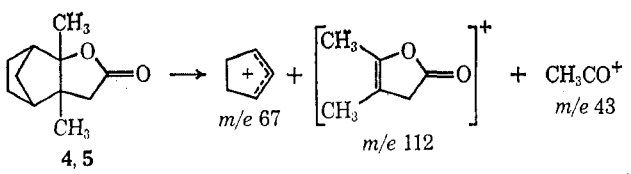
(14) T. Kuusinen, *Suomen Kemistilehti, B*, **31**, 179 (1958).

(15) G. Stork, E. E. Van Tamelen, L. J. Friedman, and A. W. Burgstahler, *J. Amer. Chem. Soc.*, **75**, 384 (1953).

SCHEME II
STRUCTURE PROOF FOR 5



γ-lactone absorption of 5.65 μ, which eliminates possible formulations involving a δ-lactone ring. The nmr spectra of lactones **4** and **5** exhibit two distinctive singlet methyl resonances (see Table II) and wholly lack a signal for a proton on an oxygen-bearing carbon atom. The mass spectra of **4** and **5** are almost identical and show abundant ions at *m/e* 43, 67, and 112 which correlate[16] with the breakdown pattern shown in eq 2. Taken together, these observations establish



(2)

the gross structures for both compounds, and, since a *trans* ring junction is extremely unlikely, it is reasonable to infer that one isomer is the *endo,cis* lactone **4** while the other is the *exo,cis* lactone **5**.

The structure and configuration of lactone **5** are definitively established by the following transformations (Scheme II). Lithium aluminum hydride reduction of **5** afforded the crystalline diol **21**, which was converted into the monoacetate **22** by reaction with acetic anhydride and a catalytic amount of pyridine. Dehydration of **22** with thionyl chloride in pyridine gave 9-acetoxymethylcamphene (**23**). This was converted *via* 9-hydroxymethylcamphene (**24**) into the tosylate, which was then reduced with lithium aluminum hydride to 9-methylcamphene (**25**), identical with an authentic sample obtained from *exo*-3-ethyl-*endo*-3-methylnorbornan-2-one (**26**).[6,17] This series of reactions unambiguously establishes the *exo* ring fusion of lactone **5** and by inference establishes an *endo* ring fusion for lactone **4**.

(16) D. R. Dimmel and J. Wolinsky, *J. Org. Chem.*, **32**, 2735 (1967).
(17) E. J. Corey, R. Hartmann, and P. A. Vatakencherry, *J. Amer. Chem. Soc.*, **84**, 2611 (1962).

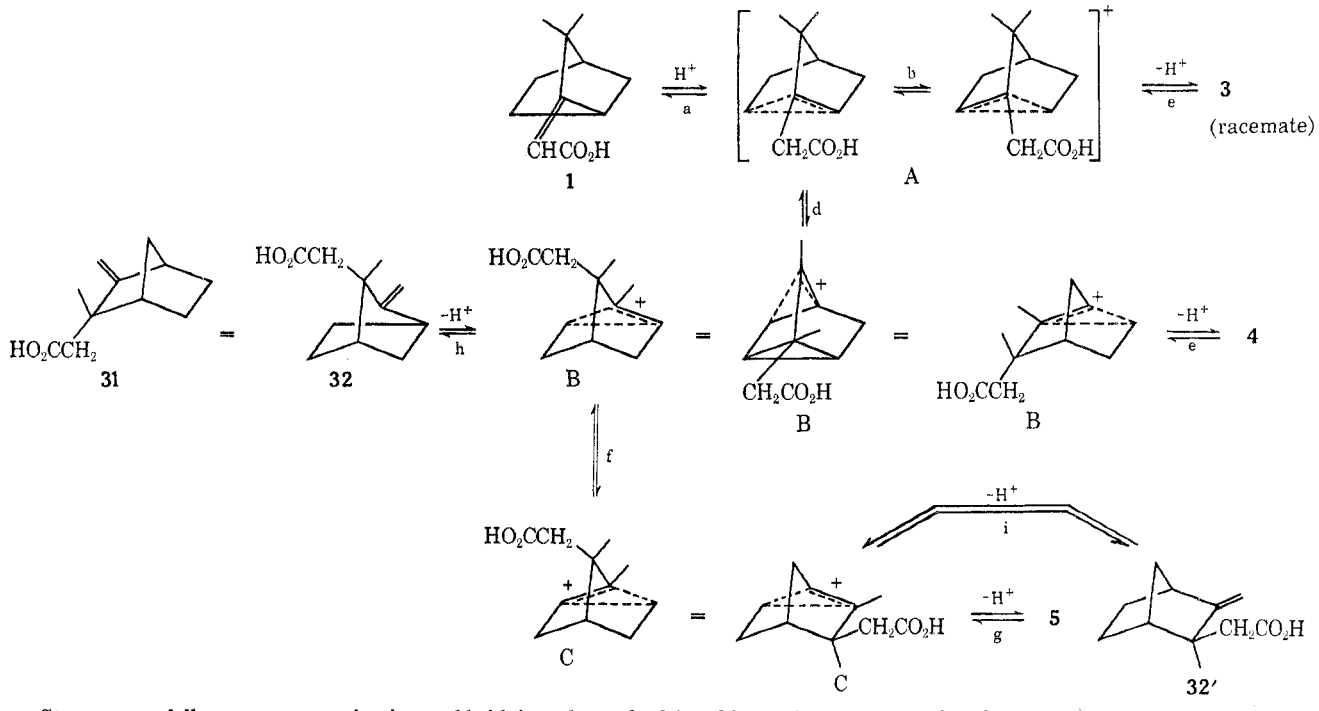
Prior to the availability of nmr and mass spectrometric data, it was thought that **4** might possibly be the *endo* isomer of **3**. Samples of **4** prepared from α-pinene[18-20] or from nopol (10-hydroxymethyl-α-pinene) resisted crystallization. However, it was possible to treat the impure **4** with excess phenylmagnesium bromide and obtain the same glycol (**27**) as could be similarly prepared from pure samples of **4**, thus confirming the product identity of isomerizations of **1** and α-pinene-10-carboxylic acid. Attempts to monoacetylate this glycol (**27**) were for the most part unproductive, cyclization to an ether **28** occurring readily. However, in one attempt a very small amount of glycol monoacetate **12** was isolated. It is possible that this arose from slight contamination of the original lactone **4** with lactone **3**, but it is just conceivable that a retro rearrangement occurred. Experimentally most significant is the fact that 10-benzhydrilidenecamphor (**15**) can be reduced under equilibrating conditions with aluminum isopropoxide to 10-benzhydrilideneborneol (**29**), whose nmr spectrum, as expected, exhibits a signal for a proton on oxygen-bearing carbon, whereas no such signal is present in the nmr spectrum of either **4** or **27**. Thus the original hypothesis had to be abandoned, and structural and configurational proofs for **4** depend upon its relationship to **5** as suggested by the nmr and mass spectrometric data cited above.

Langlois[7] claimed that the addition of hydrogen chloride to camphene-8-carboxylic acid (**1**) gave chloro acid **30**. The nmr spectrum of this compound (see Experimental Section) demonstrates that it should be reformulated as the *exo*-chloro acid **31**. Like the *endo*-chloro acid **6**,[8] the *exo* isomer **31** is largely transformed

(18) V. N. Ipatieff, C. J. Czajkowski, and H. Pines, *ibid.*, **73**, 4098 (1951).
(19) H. Rupe and H. Hertier, *Justus Liebigs Ann. Chem.*, **459**, 171 (1927).
(20) D. Tishchenko, N. Persiantseva, and V. Foliadov, *J. Gen. Chem. USSR*, **22**, 1829 (1952).

SCHEME III[a,b]

LACTONIZATION–REARRANGEMENTS



[a] Steps are as follows: a, protonization and bridging; b, 2,6-hydride shift (+A → − A); c, ring closure and deprotonizaton (A → **3**); d, *exo*-methyl shift (A → B); e, ring closure and deprotonization (B → **4**); f, 2,6-hydride shift (B → C); g, ring closure and deprotonization (C → **5**); h and i, deprotonization. [b] Note that the lower case letters apply to the forward reactions (*e.g.*, A → B). The lettered ions are pictured as nonclassical ions for convenience only.

TABLE III

THE ACTION OF ACIDS ON LACTONES **3–5**

Lactone	Conditions	Time	Lactone 3, %	Lactone 4, %	Lactone 5, %
3	10% H_2SO_4 in HCO_2H at 100°	0.5 hr	...	90.8	9.2
		1.0 hr	...	82.5	17.5
		2.0 hr	...	71.8	28.2
		3.0 hr	...	56.9	41.8
		6.5 hr	...	37.4	62.6
	50% H_2SO_4 at 150°	2.5 hr	...	21.0	79.0
4	50% H_2SO_4 at 150°	2.5 hr	...	23.8	76.2
5	90% HCO_2H at 100°	3.0 days	...	...	100.0
5	Refluxing CF_3CO_2H	3.0 days	...	...	100.0
5	10% H_2SO_4 in HCO_2H at 100°	3.0 hr	...	...	100.0
5	50% H_2SO_4 at 150°	2.0 hr	...	...	100.0

into camphene when treated with sodium carbonate in water.

Possible Reaction Paths.—Examination of Table I demonstrates that camphene-8-carboxylic acid (**1**) is first converted into lactone **3**, which is then transformed into lactone **4** with passage of time. Lactone **5** only appears much later in the reaction sequence and is only an important product when sulfuric acid is present or the mixture in trifluoroacetic acid is heated for some time. Control experiments (Table III) confirm the reaction sequence **1** → **3** → **4** → **5**. Thus, bearing in mind that starting with optically active **1** only racemic products are obtained, it becomes possible to delineate the sequence of mechanistic steps (Scheme III).

The lactonization of acid **1** in deuteriotrifluoroacetic acid was followed by nmr spectroscopy and the resulting lactone **4** was isolated and analyzed by mass spectroscopy. Little, if any, deuterium exchange of the olefinic proton in acid **1** was noted, suggesting that protonation of acid **1** is a rate-determining step which triggers the Wagner–Meerwein rearrangement and accompanying 6,2-hydride shift which culminate in the formation of lactone **3**. The slower rate of lactonization in the deuterated acid ($k_H/k_D \cong 2$) is in accord with this assumption. Mass spectrometric analysis of lactone **4**, which eventually is produced, demonstrated it to be a mixture of d_1–d_5 isomers with the d_2 and d_3 compounds accounting for *ca.* 60% of the mixture. At least two deuterium atoms were located at the carbon atom α to the carbonyl group, and the presence of ions in the region of *m/e* 43–46 placed the remaining deuterium atoms in the CH_3CO group. This is supported by the integrated values for the methyl groups in the nmr spectra (see Experimental Section). This conclusion was confirmed by the examination of the mass spectrum of lactone **4**-d_2, prepared by the exchange of the hydrogens α to the carbonyl group using sodium methoxide in CH_3OD. Incorporation of deuterium into the methyl group most likely proceeds by way of unsaturated acid **32**.

Extensive exchange of CH_3CO and CH_2CO_2 hydro-

gens occurred when lactone **3** was heated for 3 days in deuteriotrifluoroacetic acid. This observation suggests the existence of an equilbrium between lactone **4**, ion B, and unsaturated acid **32** in this solvent. Deuterium exchange also took place with lactone **5** under the same conditions, but to a much lesser extent in the CH_3CO group. This is in accord with the greater thermodynamic stability of lactone **5** and its lesser tendency to revert to ion C.

Since only racemic products (lactones) are obtained, and since rate control appears to be vested in protonation of **1**, it can be assumed that reaction b is a relatively rapid one, reaction c being slower than b but faster than a; *i.e.*, that lactone **3** is the primary kinetically controlled product.

Lactone **4** appears later in the course of reaction and, given the proper conditions, can be isolated essentially free of **3** or **5**; it can be formed (without isolation of **3**) from **1** or from **3**. Therefore, one may postulate that, under the reaction conditions used, **4** is thermodynamically more stable than **3**, while the energy barrier in reactions d and e is higher than that in reactions a–c. Otherwise, **4** would be formed more readily than **3**.

Finally, since **5** does not revert into other members of the series, it must be assumed that, under conditions leading to its formation, **5** is the most stable lactone and that the energy barrier in reactions f and g is still higher than that in reactions d and e. In other words, the thermodynamic stabilities of the acid **1** and lactones **3**–**5** are in the order **1** < **3** < **4** < **5** and the energy barriers for the conversions are in the order **1** → **3** < **3** → **4** < **4** → **5**. Racemization of A (reaction b) is probably the fastest reaction, and the principal energy barriers are probably to be associated with reactions a, d, and f, since there is no *a priori* reason why the ring-closure deprotonation reactions (c, e, and g) should have markedly different energy requirements or even be involved until actual work-up. Thus bridging (*i.e.*, Wagner–Meerwein rearrangement) appears to be easier than an *exo*-methyl shift (Nametkin rearrangement), which in turn is easier than a 2,6-hydride shift. If these inferences are valid, then the most notable situation is the implied large difference in ease of accomplishment between the two 2,6-hydride shifts (b and f), one being the fastest reaction (interconversion of enantiomers) and the other the slowest reaction (interconversion of epimers) in the sequence.

There are, of course, four additional lactones which could form in these transformations; one, a δ lactone, could be produced from ion C (Scheme III), and three, bornane-8-carbo-3-*exo*-lactone, 1,2-dimethylnorbornane-2-*exo*-acetic acid 3-*exo*-lactone, and 1,2-dimethylnorbornane-2-*endo*-acetic acid 3-*endo*-lactone, could be produced from an ion, not shown, formed from ion C by a 3,2-hydride shift. However, lack of signals for a proton on a carbon atom bearing an oxygen atom (except those exhibited by lactone **3**) in all nmr spectra rules out these lactones, as it does the C-2 epimer of lactone **3**.

Failure to obtain a δ lactone is consistent with the greater thermodynamic stability of γ lactones relative to δ lactones and is paralleled by the formation of γ lactones in the lactonization of teresantalic acid,[21] 2,3-dimethyl-3-hydroxynorbornane-2-carboxylic acid,[22] tricycloekasantalic acid,[23,24] and the isomeric bicycloekasantalic acids.[24]

In summary, the lactonization of camphene-8-carboxylic acid (**1**) involves a rapid, reversible Wagner–Meerwein rearrangement accompanied or followed by a 6,2-hydride shift, followed by a slower exclusive *exo*-methyl Nametkin migration. The *exo* lactone **5** would appear to be most readily accessible by an *endo*-methyl shift in ion A or related classical counterparts. However, there is to date no compelling evidence in support of an *endo*-methyl migration in the norbornane series, whereas *exo*-methyl migration is well documented.[25] Lactone **5** is most likely produced from ion B *via* ion C or classical counterparts.

Experimental Section

Camphene-8-carboxylic Acid (**1**).—The racemic acid was prepared most conveniently by the oxidation of camphene-8-methanol obtained by the reaction of camphene with formaldehyde. Compound (−)-**1**, of high optical purity, was obtained from nopol utilizing a modification of Bain's procedure.[8]

A.[26]—A solution of 200 g (1.47 mol) of camphene, 47 g (1.56 mol) of paraformaldehyde, 20 ml of acetic anhydride, and 300 ml of glacial acetic acid was heated at reflux for 48 hr. Most of the acetic acid was distilled at atmospheric pressure and the residue was distilled under diminished pressure to give 170.0 g of β-acetoxymethylcamphene, bp 90–104° (1.5 mm), and 30.0 g of a mixture of 10-acetoxymethylisobornyl acetate and another unidentified acetate, bp 135–141° (1.5 mm).

From 8.0 g of (+)-camphene, $[\alpha]^{29}D$ +35.8°, there was obtained 5.5 g of 8-acetoxymethylcamphene, $[\alpha]^{29}D$ +29.4° {lit.[27] $[\alpha]^{25}D$ +18.9° from (+)-camphene, $[\alpha]^{25}D$ + 25.5°}.

Alkaline hydrolysis of (±)-8-acetoxymethylcamphene gave 39.4 g (82%) of (±)-camphene-8-methanol: bp 85–93° (1.8 mm); $n^{23}D$ 1.5028; ir 3.0 and 6.01 μ; nmr δ 1.02 and 1.04 (s, 6, CH_3CCH_3), 0.85–1.97 (complex m), 2.87 (s, 1, C-1 H), 3.45 (s, 1, OH), 4.0 (d, 2, J = 7 Hz, CH_2OAc), and 5.1 ppm (t, 1, J = 7 Hz, HC=C).

To an ice-cooled solution of 20.0 g of camphene-8-methanol in 50.0 ml of pure acetone was added 60 ml of 8 *N* chromium trioxide in sulfuric acid–water. After the solution was stirred for 30 min, the excess oxidant was destroyed with isopropyl alcohol. After the usual work-up, distillation gave 16.5 g of (±)-8-formylcamphene: bp 128–130° (12 mm) [lit.[28] bp 130° (12 mm)]; ir 5.95 and 6.01 μ; λ_{max} 235 mμ (ϵ 11,200).

The 2,4-dinitrophenylhydrazone of this aldehyde was crystallized from ethanol–ethyl acetate, mp 201–203°.

8-Formylcamphene, 16.5 g, was placed in a large beaker and kept in contact with air for 5 days. The partially solidified mixture was taken up in ether and extracted with 5% sodium carbonate solution. The basic solution was acidified and extracted with ether. The ether was removed and the residue was recrystallized from hexane to give 11.0 g of (±)-camphene-8-carboxylic acid: mp 122–124°; nmr 1.10 (s, 2-CH_3), 4.04 (s, C-1 H), 5.44 (s, HC=C), and 11.86 ppm (s, CO_2H). The acid **1** obtained from partially active (±)-8-acetoxymethylcamphene exhibited $[\alpha]^{29}D$ −49.8°.

B.[29]—The direct addition of hydrogen chloride to nopol (instead of to the acetate of nopol[8]) and molecular distillation proved the most convenient route to 2-*endo*-chlorocamphane-10-methanol.[8] A 20.3-g (0.100 mol) sample of this material was refluxed in 100 ml of glacial acetic acid for 2 hr with 16.7 g (0.100 mol) of silver

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(29) Work was done at The University of Michigan and The University of Connecticut. Microanalyses were done by Spang Microanalytical Laboratory, Ann Arbor, Mich.

acetate. The mixture was then filtered and the filtrate was made slightly basic with 5% sodium bicarbonate solution, after which the aqueous mixture was continuously extracted with ether for several hours and dried over magnesium sulfate. The ether was removed and the residue was distilled and then twice redistilled to give 18.7 g (90%) of (+)-8-acetoxymethylcamphene: bp 75° (0.03 mm); sp gr 0.996 (27°); $n^{27}D$ 1.4843; $[\alpha]^{27}D$ +93.72°. The infrared spectrum is identical with that of a racemic sample.[28]

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.95; H, 9.68. Found: C, 74.83; H, 9.47.

Hydrolysis of the ester using 50% aqueous ethanol and potassium hydroxide afforded 24 g (85%) of (+)-camphene-8-methanol, whose infrared spectrum is identical with that of a racemic sample:[28] bp 76° (0.40 mm); sp gr 0.9705 (30°); $n^{28}D$ 1.5015; $[\alpha]^{30}D$ +92.42° {lit. bp 125–126° (8 mm); sp gr 0.987 (15°); $[\alpha]D$ +45°[8]}.

Oxidation to (−)-camphene-8-carboxylic acid was carried out according to the directions of LoCicero.[30] The product was recrystallized from low-boiling petroleum ether, mp 119.5–121° $[\alpha]^{26}D$ −260° (chloroform). The infrared spectrum is indistinguishable from those of the racemic samples.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.22; H, 8.90.

(+)-α-Pinene-10-carboxylic Acid.[29] **A.**—(+)-α-Pinene was converted into (+)-myrtenol: bp 100–101° (10 mm); d^{27} 0.9809; $n^{26}D$ 1.4966; $[\alpha]^{27}D$ +25.4° {lit.[31] bp 105° (9 mm); nD 1.4966; $[\alpha]D$ +49.7°}. Oxidation with selenium dioxide followed by reduction with lithium aluminohydride was used.

(+)-α-Pinene-10-carboxylic acid was prepared from (+)-myrtenol *via* the bromide (phosphorus tribromide)[19] and nitrile,[20] $[\alpha]^{27}D$ +10 ± 2°. A 4.0-g sample of the nitrile was converted into the amide by mixing it with 8.4 g of 30% hydrogen peroxide, and enough absolute ethanol was added to provide homogeneity. The pH was adjusted to 9.0 by addition of dilute sodium hydroxide and the solution was refluxed for 4 hr. The pH was adjusted to 5.0 and the solution was extracted with chloroform. Removal of the solvent and recrystallization from ethanol–water afforded white crystals, mp 98.5–101°, yield 95%.

Anal. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56. Found: C, 73.51; H, 9.52.

The nitrile was hydrolyzed in aqueous alcoholic potassium hydroxide to the free acid as described by Arnold and Danzig,[32] with similar results.

B.—A hot solution of 5.10 g of nopyl tosylate[32] in dry dimethyl sulfoxide was added as fast as possible, with due regard for the possibility of the reaction getting out of hand, to a solution of 445 g of sodium bicarbonate in 2 l. of dimethyl sulfoxide held at 150°. After complete addition, the reaction was held at 145–150° for 15 min and the stirred solution was cooled to room temperature and filtered. The filtrate was diluted with an equal volume of water, and the combined extracts were dried over anhydrous magnesium sulfate and distilled, yield 319 g of colorless distillate, bp 72–79° (0.25 mm). Analysis by glpc showed this material to be a 1:1 mixture of the desired aldehyde and nopol.

This mixture was dissolved in 1750 ml of absolute ethanol containing a solution of 204 g (1.2 mol) of silver nitrate in 300 ml of water, and, with rapid stirring, there was added a solution of 144 g (3.6 mol) of sodium hydroxide in 2 l. of water at a rate sufficient to maintain ambient temperature. After complete addition, stirring was continued for 24 hr and the mixture was filtered the residue being thoroughly washed with water and ethanol. The filtrate was extracted with *ca.* 3 l. of ether, and the aqueous alcoholic basic phase was acidified to pH 2 and extracted with 2 l. of ether in 250-ml portions. The ethereal extracts were combined, dried over magnesium sulfate, and distilled to yield 18.85 g of light yellow oil, bp 122–129° (0.45 mm) [lit.[32] bp 95° (0.05 mm)], which solidified on cooling, mp 50–60°. Recrystallization from aqueous ethanol afforded white crystals, mp 73.0–74.5°.

The infrared spectrum of this acid shows a strong olefinic absorption at 6.14 μ and a carbonyl absorption at 5.92 μ, comparable with that of the amide reported above (6.14 μ, carbonyl 5.99 μ). These data strongly suggest conjugation; but, as reported,[32] the acid can be reduced to nopol by treatment with lithium aluminum hydride.

10-Carboxyisoborneol Lactone (3).[26]—A solution of 3.0 g of (±)-camphene-8-carboxylic acid (1) in 10 g of 90% formic acid was heated at reflux for 1 hr. The dark solution was poured into water and extracted with ether. The ether was washed repeatedly with 5% sodium carbonate solution, and water and dried. Evaporation of the solvent left a reddish solid which displayed a carbonyl peak at 5.65 μ. One half of this solid was sublimed *in vacuo* and the other half was recrystallized from hexane. The sublimed material showed a melting point of 149–165°, and its infrared spectrum indicated that it was contaminated with a trace of acid 1. Vpc analysis showed only one major peak; however, the nmr of this solid displayed, in addition to the methyl resonances at 0.9 ppm characteristic of lactone **3**, singlets at 1.12 and 1.32 ppm which are characteristic of lactone **4**. It was estimated that the solid contained 64% **3** and 36% **4**.

The recrystallized portion exhibited a melting point of 190–195° and displayed an infrared spectrum identical with that of Bain's lactone **3**: nmr δ 0.94 and 0.98 (s, 6, CH_3CCH_3), 2.32 (CH_2CO), 4.19 (m, 1, CHO), and 1.02–1.90 ppm (complex m); mass spectrum *m/e* 180 (parent peak) and abundant ions at *m/e* 152, 137, 122, 108, 93, 80, 67, 55, and 43.

When[29] a solution of 3.3 g of (−)-1 in 15 ml of trifluoracetic acid was kept at room temperature for *ca.* 3 days, there was obtained 3.2 g of crude lactone. The crude lactone was first recrystallized from ethanol–water and then repeatedly from petroleum ether (bp 60–75°) to give a solid, mp 198.5–199.5° (lit.[7] mp 198–199°). The lactone **3** is optically inactive, and its infrared spectrum is superimposable upon that of the lactone **3** kindly supplied by Dr. J. P. Bain.[8]

***exo*-2,3-Dimethylbicyclo[2.2.1]heptane-*endo*-3-hydroxy-*endo*-2-acetic Acid Lactone (4). A. Formic–Sulfuric Acid Lactonization of Camphene-8-carboxylic Acid (1).**[26]—A solution of 8.0 g of camphene-8-carboxylic acid (1), 6.95 g of concentrated sulfuric acid, and 46.5 g of 88% formic acid was allowed to stand for 6.25 days at 25°. The solution was diluted to *ca.* 350 ml with water and extracted with ether. The ether solution was washed with 10% bicarbonate and water and dried over anhydrous magnesium sulfate. The solvent was removed to leave 7.0 g of crude product, mp 155°. Recrystallization from petroleum ether (bp 30–60°) and chromatography on a short Florisil column (chloroform eluent) gave pure lactone **4**: mp 170–171°; ir 5.55 μ; nmr, two methyl singlets at δ 1.32 and 1.16 ppm and no signals below δ 2.45 ppm; mass spectrum *m/e* 180 (parent ion) and abundant ions at *m/e* 112, 97, 67, and 43.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.31; H, 8.95. Found: C, 73.11; H, 8.79.

B. Trifluoroacetic Acid Lactonization of 1.[26,29]—A solution of 2.0 g of acid **1** in 15 ml of trifluoroacetic acid was allowed to stand for 7 days at room temperature. Work-up gave 1.94 g of crude lactone, which was recrystallized from petroleum ether (bp 30–60°) to yield **4**, mp 170°.

C.[29]—A solution of 40 g of α-pinene-10-carboxylic acid in 100 ml of trifluoroacetic acid was kept for 4 months. Work-up in the usual manner gave 2.0 g (10%) of an optically inactive oil whose infrared spectrum was nearly identical with that of lactone **4**. Reaction with phenylmagnesium bromide gave diol **27**, mp 167–168°, which was dehydrated to ether **28**, mp 118–119°. Identity of these samples was established by comparison of nmr spectra of authentic materials (see below).

***endo*-2,3-Dimethyl-*exo*-3-hydroxybicyclo[2.2.1]heptane-*exo*-2-acetic Acid Lactone (5).**[26]—A mixture of 8.0 g of camphene-8-carboxylic acid (1) and 50 ml of 50% sulfuric acid was heated at 160–165° for 2 hr. The resulting dark brown solution was washed thoroughly with 5% sodium carbonate and dried, and the ether was removed to give a dark brown oil which on recrystallization from hexane afforded 5.5 g of lactone **5**: mp 155–159° (sublimation *in vacuo* raised the melting point to 157–161°); ir 5.65 μ; nmr, prominent methyl signals at δ 1.32 and 1.12 ppm and no signals below δ 2.45 ppm; mass spectrum *m/e* 180 (parent ion) and abundant ions at *m/e* 112, 92, 67, and 43.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.24; H, 8.95. Found: C, 73.30; H, 9.02.

Vpc analysis of the crude lactone mixture using a DEGS column at 170° indicated the presence of lactones **5** and **4** in a 4:1 ratio. The minor component with a shorter retention time was collected, mp 155–164°, and shown to be identical with lactone **4** by infrared and nmr comparison.

Alternatively, a solution of 4.0 g of acid **1** and 5.0 g of concentrated sulfuric acid in 30 ml of 90% formic acid was heated at

(30) J. C. LoCicero and R. T. Johnson, *J. Amer. Chem. Soc.*, **74**, 2094 (1952).

(31) A. R. Penfold, G. R. Ramage, and J. L. Simonsen, *J. Proc. Roy. Soc. N. S. Wales*, **68**, 36 (1934).

(32) R. T. Arnold and M. J. Danzig, *J. Amer. Chem. Soc.*, **79**, 892 (1957).

reflux for 3.5 hr. Work-up gave 3.2 of crude lactone. Recrystallization from hexane afforded 3.0 g of white solid, mp 163 167°. Vpc analysis indicated the presence of lactones **5** and **4** in a ratio of 5:1.

10-Hydroxymethylisoborneol (7).[26]—To a stirred slurry of 0.5 g of lithium aluminum hydride in 20 ml of ether was added slowly a solution of 2.0 g of lactone **3** in ether. The mixture was stirred overnight and then decomposed with saturated sodium sulfate solution. The ether layer was separated, dried, and concentrated to give 1.7 g of solid. Recrystallization from hexane afforded 1.5 g of white crystals, mp 84–87°, which displayed two singlet methyl resonances at δ 0.82 and 1.03 ppm, complex multiplets at δ 1.10–1.92 ppm owing to nine protons, a three-proton multiplet at δ 3.72 ppm, and a broad two-proton multiplet at δ 4.52 ppm.

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.77; H, 10.89.

The diacetate derivative of 10-hydroxymethylisoborneol showed carbonyl absorption at 5.77 μ and nmr signals at δ 0.85 and 1.0 (s, 2-CH_3), 2.1 [s, 2 $CH_3(C{=}O)O$], 4.0 (m, CH_2O), and 4.72 ppm (m, CHO).

Camphor-10-carboxylic Acid (8).[26]—To a stirred and ice-cooled solution of 1.0 g of 10-hydroxymethylisoborneol (**7**) in 20 ml of acetone was added 5.5 ml of 8 *N* chromium trioxide solution. After 5 min the excess oxidant was destroyed with isopropyl alcohol and the mixture was worked up in the usual manner to give, after two recrystallizations from hexane, 0.77 g of camphor-10-carboxylic acid: mp 95–97° (lit.[9] mp 92–93°); nmr singlets at δ 0.90 and 1.02 ppm for two methyl groups, two-proton multiplets at δ 2.11 and 2.2–2.33 ppm, and a carboxyl proton at 11.14 ppm.

The semicarbazone derivative of the keto acid was recrystallized from aqueous ethanol, mp 196–199° (lit.[8] mp 199–200°).

10-(Dimethylhydroxymethyl)isoborneol.[29]—Treatment of **3** with 2 equiv of methylmagnesium iodide afforded an 80% yield of product, white needles from ethyl acetate–petroleum ether (bp 60–75°), mp 143–145°.

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.79; H, 11.36.

10-(Diphenylhydroxymethyl)isoborneol (10).[29]—Treatment of **3** with 2 equiv of phenylmagnesium bromide (ammonium chloride work-up) afforded a 98% yield of **10**, recrystallized from ethyl acetate–petroleum ether (bp 60–75°) and benzene–petroleum ether (bp 60–75°), mp 158–159°.

Anal. Calcd for $C_{23}H_{26}O_2$: C, 82.10; H, 8.39. Found: C, 82.26; H, 8.45.

This substance was also prepared from 10-benzoylisoborneol (**9**)[11] and 10-benzoylisobornyl acetate (**17**)[11] (both originally assigned the bornyl configuration[11]) using phenyllithium in appropriate amounts. The infrared spectra are superimposable and mixture melting points show no depression.

10a,10a-Diphenyl-2-*exo*-10a-epoxy-10-homobornane (11).[29]—This ether was most readily prepared from **9** by refluxing in benzene with a catalytic amount of iodine, using 0.33 g of **10**, 0.03 g of iodine, and 25 ml of benzene, for 24 hr. The iodine was removed with 5% sodium thiosulfate and the product was obtained as an oil on evaporation. Recrystallization from petroleum ether (bp 60–75°) affords a 90% yield of product, mp 141.0–142.5°. The infrared spectrum lacks absorption in the hydroxyl region.

Anal. Calcd for $C_{23}H_{26}O$: C, 86.74; H, 8.23. Found: C, 86.54; H, 8.19.

10-(Diphenylhydroxymethyl)isobornyl Acetate (12).[29]—This acetate may be prepared from **10** in acetic anhydride alone by gently refluxing for 18 hr, or in benzene solution containing acetic anhydride and a catalytic amount of sodium acetate by refluxing, using 0.45 g of **10**, 13 g of acetic anhydride, and 0.10 g of sodium acetate in 12 ml of dry benzene, for 2.5 days. In either case an essentially quantitative yield may be obtained. Recrystallization from benzene–petroleum ether (bp 60–75°) affords analytically pure material, but there appear to be several different crystal forms, as indicated by different melting points on different batches of product with superimposable infrared spectra, mp 134.0–134.5°, remelted at 144–145° and 150–153°.

Anal. Calcd for $C_{25}H_{30}O_3$: C, 79.33; H, 7.99. Found: C, 79.53; H, 8.16.

10-Benzhydrylideneisobornyl Acetate (13).[29]—A 5.0-g sample of **12** and 50 mg of iodine in 50 ml of dry benzene were refluxed for 15 hr, after which the iodine was removed by washing with 5% sodium thiosulfate. Evaporation after drying afforded an oil, which was recrystallized from petroleum ether (bp 60–75°) or ethanol–water (98%), mp 108–109°.

Anal. Calcd for $C_{25}H_{28}O_2$: C, 83.29; H, 7.83. Found: C, 83.21; H, 7.57.

The product gave a negative test with bromine in carbon tetrachloride but produced a color with tetranitromethane

10-Benzhydrylideneisoborneol (14).[29]—Hydrolysis of **13** was achieved with sodium hydroxide in 50% aqueous ethanol by refluxing, using 1.1 g of **13** and 2.5 g of sodium hydroxide in 50 ml, for 3 hr. The ethanol was removed by distillation and the product was extracted into 1:1 ether–benzene and dried. After removal of solvent there remained 0.96 g (93%) of an oil which was recrystallized from petroleum ether (bp 60–75°), mp 108–109°.

Anal. Calcd for $C_{23}H_{26}O$: C, 86.74; H, 8.23. Found: C, 87.53; H, 8.39.

10-Benzhydrylidenecamphor (15).[29]—A 1.0-g sample of **14** in 30 ml of acetone was titrated at room temperature with Jones reagent[9] and then the reaction mixture was diluted with ice–water and extracted several times with ether. The ether extracts were combined and washed free of acid, dried over magnesium sulfate, and evaporated to dryness, leaving 1 g of solid product which was twice recrystallized from petroleum ether (bp 60–75°), mp 110–111°.

Anal. Calcd for $C_{23}H_{24}O$: C, 87.30; H, 7.65. Found: C, 87.27; H, 7.80.

10-Benzhydrylisobornyl Acetate (16).[29]—A 1.0-g sample of **13** in 50 ml of glacial acetic acid was hydrogenated for 1.5 hr at 1-atm pressure over 0.021 g of Adams catalyst. Removal of the solvent and recrystallization from petroleum ether (bp 30–40°), ethanol–water, and finally ethanol afforded the product, mp 78–84°.

Anal. Calcd for $C_{25}H_{30}O_2$: C, 82.83; H, 8.34. Found: C, 83.00; H, 8.11.

***exo*-2-Acetoxyapocamphane-1-carboxylic Acid (18).**[29]—A mixture of 12 g (0.040 mol) of 10-benzoylisobornyl acetate (**17**)[11] and 8.0 g (0.80 mol) of chromic anhydride in 200 ml of glacial acetic acid and 40 ml of water was refluxed for 12 hr with stirring, and then the greater portion of the acetic acid was removed by evaporation in an air stream. The residual oil was dissolved by shaking with equal volumes of 10% sodium carbonate and ether. From the ether layer there was recovered 8 g of **17** (infrared spectrum). Acidification of the aqueous layer with concentrated hydrochloric acid, extraction with ether–benzene, washing of the extract with water, drying (magnesium sulfate), and evaporation afforded a mixture of benzoic acid and **18**. These were finally separated on a Florosil column by eluting the benzoic acid with carbon tetrachloride, yield 2.0 g of **18**, mp 117–119° (lit.[12] 121–122°), neut equiv 228 ± 2.

The acid chloride **19** was prepared by means of thionyl chloride, bp 94–96° (0.75 mm). [The previous report, bp 111–113° (0.30 mm),[2] is probably in error, 3.0 mm being more likely for the pressure used.] A Rosenmund reduction on this material failed. On a larger scale, chromatography of the oxidation products is better omitted and separation achieved by fractional distillation of the acid chlorides.

10-Hydroxyisobornyl Acetate (20).[29]—To a well-stirred suspension of 10 g (0.26 mol) of sodium borohydride in 150 ml of dioxane (dried over calcium hydride and distilled from lithium aluminum hydride) was added 31 g (0.13 mol) of **19** in 50 ml of dioxane (similarly dried) at room temperature. The heterogeneous mixture was heated on the steam bath for 1 hr with stirring, cooled, hydrolyzed with a small amount of ice–water, and evaporated in an air stream to *ca.* one-fourth its volume. The gelatinous residue was stirred with equal volumes of water and ether, which were then separated, the ether layer being washed well with water, dried, and evaporated to give a dense oil, yield (24 g). Distillation afforded a single liquid fraction, bp 130–135° (0.10 mm), yield 15 g (54%), and a solid residue, yield 9.0 g (40%). A portion of the distillate was hydrolyzed with sodium hydroxide, and the hydrolysate and solid residue were each recrystallized from petroleum ether (bp 60–75°), mp 246–248°, no depression of mixture melting point, identical infrared spectra. The reported melting point for 10-hydroxyisoborneol is 241–243°.[13] *Ca.* 4% of the original **18** was recovered from the initial alkaline solution.

Conversion of 10-Hydroxyisobornyl Acetate (20) into Isoborneol.[29]—A solution of 2.4 g of **20** in a mixture of 10 ml of pyridine and 10 ml of benzene was cooled to 5°, and a solution of 1.8 g of methanesulfonyl chloride in 4 ml of pyridine was added

with stirring. After standing for 14 hr at 5°, the mixture (containing a precipitate) was poured into ice–water and the new mixture was acidified with concentrated hydrochloric acid. The resultant solution was extracted with ether, and the ethereal extract was washed well with 5% sodium hydroxide and then with water, dried over magnesium sulfate, and evaporated to give a light yellow oil (10-methanesulfonoxyisobornyl acetate) which could not be distilled owing to extensive decomposition above 80°.

A solution of 1.40 g (0.0048 mol) of the preceding mesylate in 20 ml of dry benzene was added to a solution of 0.022 mol (0.85 g potassium metal) of potassium *t*-butoxide in 18 ml of *t*-butyl alcohol at room temperature to which had been added 1.78 g (2.0 ml) of ethyl mercaptan. The mixture was refluxed with mechanical stirring for 15 hr, during which time it became a thick, viscous gel. Next it was carefully diluted with a large volume of water, extracted with ether, and dried. After removal of the solvent, the residual oil, 10-ethylthioisobornyl acetate, was obtained, yield 1.1 g (90%), bp 102–104° (0.25 mm).

This distillate was added to *ca.* 20 g of freshly prepared Raney nickel[33] in 80 ml of reagent grade methanol. The mixture was refluxed for 3 hr, cooled, and filtered, and on evaporation the semisolid residue was dissolved in 200 ml of 50% aqueous ethanol containing 10 g of sodium hydroxide. After this solution was stirred for 8 hr at 40°, the ethanol was distilled and the residual alkaline solution was cooled, extracted with ether, and dried. The ether was evaporated, leaving 0.5 g (80%) of isoborneol, mp 211–212°, with no depression on mixture with an authentic sample. The infrared spectrum was identical with that of an authentic sample, and the *p*-nitrobenzoate, mp 127–128° (with no depression on mixture with an authentic sample), has an infrared spectrum identical with that of an authentic sample

Diol 21.[26]—A solution of 2.5 g of lactone **5** in ether was added to a suspension of 1.5 g of lithium aluminum hydride in ether. The mixture was stirred at room temperature overnight and then decomposed with sodium sulfate solution. The salts and solvent were removed, leaving 2.2 g of a waxy solid. Recrystallization from hexane afforded 2.0 g of diol **21**: mp 97–100°; nmr δ 0.87 and 1.14 (ss, 6, CH_3CCH_3), 3.54 (m, 2, CH_2O), 5.52 (m, 2, OH), and 1.19–2.2 ppm (complex m, 10).

Unsaturated Acetate 23.[26]—A solution of 2.0 g of diol **21** in 30 ml of acetic anhydride containing a trace of pyridine was heated at reflux for 2 hr. Work-up gave an oil which showed infrared absorption at 2.9 and 5.76 μ (OH and $OCOCH_3$).

The crude hydroxy acetate **22** was dissolved in 15 ml of methylene chloride, and to the cooled solution was added 10 ml of thionyl chloride and 10 ml of pyridine. The stirred mixture was poured into cold water after 30 min and extracted with ether. The ether solution was washed with 5% hydrochloric acid and water, dried, and the ether removed to leave 1.6 g of an oil which on vpc analysis showed only one major peak. A vpc purified sample showed infrared peaks at 5.76, 6.01, and 11.25 μ and prominent nmr signals at δ 2.1 (CH_3CO) and 4.52 and 4.82 ($C{=}CH_2$) ppm.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.67. Found: C, 74.90; H, 9.63.

9-Hydroxymethylcamphene (24).[26]—Unsaturated ester **23** (1.5 g) was saponified with 10% potassium hydroxide in ethanol to give 1.1 g of a colorless liquid, bp 93–96° (1.5 mm), which showed infrared absorption at 3.0, 6.01, and 11.25 μ and prominent nmr signals at δ 1.01 (s, CH), 3.74 (OH), and 4.48 and 4.71 (s, CH_2) ppm.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.41; H, 10.85. Found: C, 79.66; H, 11.15.

9-Methylcamphene (25).[26]—A mixture of 0.57 g of *p*-toluene sulfonic acid, 0.5 g of 9-hydroxymethylcamphene (**24**), and 5 g of pyridine was stirred overnight and then poured into ice. The mixture was extracted with ether and the ether solution was washed with dilute hydrochloric acid, 5% sodium carbonate, and water and dried. The ether was evaporated, leaving an oil which could not be induced to crystallize.

A hexane solution of the crude tosylate derivative was added to a stirred solution of 0.8 g of lithium aluminum hydride in ether. The excess hydride was decomposed after 16 hr. The salts and solvent were carefully removed and the residue was purified by vpc to give a liquid whose infrared spectrum showed peaks at 6.02 and 11.30 μ, characteristic of a terminal methylene group. The mass spectrum had a parent ion at *m/e* 150 and abundant ions at *m/e* 122, 121, 94, 93, 79, 67, and 41. The nmr spectrum displayed signals at 1.00 (s, CH_3), 2.62 (m, C-1 H), and 4.42 and 4.72 (s, $C{=}CH_2$) ppm

Anal. Calcd for $C_{11}H_{18}$: C, 87.92; H, 12.05. Found: C, 87.75; H, 11.97.

3-*endo*-Methyl-3-*exo*-ethyl-2-norbornanone (26).[26]—To a stirred solution of 5.0 g (0.042 mol) of 3-methyl-2-norbornanone in 15 ml of anhydrous ether was added an ethereal solution of tritylsodium until the red color persisted. Ethyl iodide, 70.0 g (0.57 mol), was added and the solution was stirred at room temperature for 24 hr. Water was added, and the ether solution was separated, washed with water, and dried, and the ether was evaporated. Distillation of the residue gave 3.82 g of **26**, bp 50–55° (1.5 mm), which was shown to be about 95% pure by vpc. The infrared spectrum of **26** showed a strong carbonyl band at 5.73 μ. The nmr spectrum showed prominent signals at δ 2.42 ppm for a two-proton multiplet, a singlet methyl group at δ 0.92 ppm, and a triplet methyl at δ 1.01 ppm. The mass spectrum showed a parent ion at *m/e* 152 and abundant ions at *m/e* 124, 83, 67, 55, and 41.

9-Methylcamphene from Ketone 26.[26]—To an ether solution containing 0.092 mol of methyllithium was added an ether solution of 3.5 g (0.023 mol) of 3-*endo*-methyl-3-*exo*-ethyl-2-norbornanone (**26**). The resulting solution was heated and stirred for 2 days. The reaction mixture was poured into-ice water and the ether solution was separated. Distillation gave 2.8 g (80%) of tertiary alcohol, bp 65–73° (1.5 mm), which showed strong hydroxyl absorption but no carbonyl absorption.

The alcohol was dissolved in 30 ml of methylene chloride and treated at −5° with 15 ml of thionyl chloride and 15 ml of pyridine, and the mixture was stirred for 40 min. Pentane was added and the reaction mixture was poured into ice–water. The organic layer was separated, washed with dilute hydrochloric acid and water, and dried over anhydrous magnesium sulfate. Distillation gave 1.2 g of liquid, bp 58–62° (1.7 mm), whose infrared spectrum showed the presence of terminal methylene at 11.31 μ. Vpc analysis using a SF-96 column at 140° indicated the presence of a minor component (*ca.* 5–10%) with lower retention. The major component was collected and displayed terminal olefin absorption at 6.02 and 11.30 μ and two olefin protons as singlets at δ 4.71 and 4.42 ppm. The infrared, nmr, and mass spectrum of this sample of 9-methylcamphene were identical with those of the methylcamphene obtained by degradation of lactone **5**.

***cis*-2,3-Dimethyl-*endo*-3-hydroxy-2-(2,2-diphenyl-2-hydroxyethyl)bicyclo[2.2.1]heptane (17).**[29]—The Grignard reagent from 2.24 g (14.0 mmol) of bromobenzene and 0.292 g (12.5 mg-atoms) of magnesium turnings was prepared in a total of 35 ml of dry ether. To this was added 0.75 g (4.16 mmol) of lactone **4** in a solution of 10 ml of dry ether and 10 ml of dry benzene. After addition, the mixture was stirred and refluxed for 30 min and poured into 50 ml of saturated ammonium chloride solution containing 10 drops of concentrated hydrochloric acid. The organic layer was separated, dried over magnesium sulfate, and evaporated. The resulting crude solid was triturated with cold petroleum ether (bp 30–60°) to give a white solid, mp 148–149°, yield 0.73 g (52.5%). Recrystallization from petroleum ether (bp 30–60°) gave an analytical sample, mp 163.0–163.5°.

Anal. Calcd for $C_{23}H_{26}O_2$: C, 82.17; H, 8.39. Found: C, 82.00; H, 8.23.

Dehydration of Diphenyl Glycol 27. Formation of Ether 28.[29]—Several attempts were made to obtain a monoacetate from the glycol **27**. These met with uniform failure, the products being either unchanged diol or the derived ether **28**. In all cases an excellent material balance was realized.

The ether, *endo,cis*-3a,7a-dimethyl-2,2-diphenyl-4,7-methanooctahydrobenzofuran, was obtained as white crystals, mp 115–116°, from aqueous ethanol.

Anal. Calcd for $C_{23}H_{26}O$: C, 86.74; H, 8.23. Found: C, 86.89; H, 8.31.

Possible Retrorearrangement.[29]—In one attempted acetylation, 6 mmol of **27**, 6 mmol of previously reacted acetyl chloride, and 7 mmol of pyridine in 10 ml of dry benzene were refluxed for 5 days. Extensive chromatography on Florisil finally yielded 50 mg of monoacetylated glycol, which was recrystallized from petroleum ether (bp 60–70°) to give 43 mg of **12**, mp 142.5–143.5°.

Anal. Calcd for $C_{25}H_{30}O_3$: C, 79.33; H, 7.99. Found: C, 79.42; H, 8.06.

The nmr and infrared spectra correspond with those for **12**. Further confirmation is provided by iodine dehydration to **13**,

(33) R. Mozingo, D. E. Wolf, S. A. Harris, and K. Folkers, *J. Amer. Chem. Soc.*, **65**, 1013 (1943).

TABLE IV

Time, days	Lactone 3, %	Lactone 4, %
1	21.1	...
2	27.6	4.6
8	33.5	9.1
14	68.0	12.4
21	70.2	14.3

phene-8-carboxylic acid (1) in 0.9 ml of deuterated trifluoroacetic acid was placed in an nmr tube and the progress of the reaction at ambient temperature (Table IV) was followed by periodically examining the nmr spectrum of the solution.

endo **Lactone 4-d_2.**[26]—To a stirred solution prepared by adding 600 mg of sodium to 5 ml of CH_3OD was added 600 mg of *endo* lactone **4**. The solution was kept at room temperature for 3 days, concentrated, and diluted with deuterium oxide. The solution was extracted with ether. The ether solution was dried over anhydrous magnesium sulfate, the ether was removed, and the resulting solid was recrystallized from hexane and sublimed to give 106 mg of lactone **4**-d_2. The mass spectrum showed a parent ion at *m/e* 182 and abundant ions at *m/e* 139, 114, 113, 93, 67, and 43.

TABLE V

DEUTERIUM EXCHANGE AT ROOM TEMPERATURE IN DEUTERIOTRIFLUOROACETIC ACID

Starting compd	Lactone 4						$OCCH_3$			
	d_0, %	d_1,[a] %	d_2, %	d_3, %	d_4, %	d_5	*m/e* 43; d_0, %	*m/e* 44;[a] d_1, %	*m/e* 45; d_2, %	*m/e* 46; d_3, %
1	9.7	27.7	33.2	19.1	7.3	2.9	61.7	28.9	8.5	0.9
4	7.5	15.6	35.1	18.5	12.0	7.4	32.1	36.8	24.5	6.6
5	54.8	34	11.2	...	...	...	88	7.5	3.9	...

[a] Corrected for natural contribution of M + 1.

mp 106–108°, no depression on mixture with authentic **13**. The ultraviolet, infrared, and nmr spectra correspond with those of **13**. In view of the very small amount of **12** isolated from 2.0 g of **27**, it is possible that **27** was contaminated with a trace of **10**, arising from **4** having been contaminated with a trace of **3**.

10-Benzhydrilideneborneol (29).[29]—A 4.95-g (0.015 mol) sample of **15** was sealed in a glass tube with 12.24 g (0.060 mol) of aluminum isopropoxide (excess to permit complete equilibration to the more stable epimer[34]) and 40 ml of isopropyl alcohol (a preliminary experiment using the toluene solvent recommended afforded very little product). The tube was heated at 135° for 10.5 days, cooled, and opened, and the contents were poured into 100 ml of cold 10% hydrochloric acid. After four 50-ml ether extractions were performed, the extracts were combined, washed with saturated sodium chloride solution until neutral, and dried over anhydrous magnesium sulfate. Evaporation of the solvent (oil pump at end) left a gum whose infrared spectrum showed some residual **15**. The gum was chromatographed on Florisil, and, after elution with pure petroleum ether (bp 60–70°) and benzene–petroleum ether (bp 60–70°) mixtures up to 50%, pure benzene afforded a crystalline eluate, mp 103–113°. Several recrystallizations from aqueous ethanol gave **29**, mp 118–119° no carbonyl in the infrared. The nmr spectrum showed a singlet for one vinyl proton at δ 5.98 ppm and a multiplet (two closely spaced quartets) at δ 5.04 ppm, characteristic for the borneol system in these compounds.

Anal. Calcd for $C_{23}H_{26}O$: C, 86.74; H, 8.23. Found: C, 86.67; H, 8.25.

The melting point of the acetate, 74–76°, clearly differs from that of the epimer **13**.

Anal. Calcd for $C_{25}H_{28}O_2$: C, 83.29; H, 7.83. Found: C, 83.18; H, 7.72.

Addition of Hydrogen Chloride to Camphene-8-carboxylic Acid to Give 31.[26]—A solution of 5.0 g of **1** in 35 ml of acetic acid was saturated with hydrogen chloride gas and stirred for 2 days. The solvent was removed under diminished pressure, leaving 3.6 g of a dark brown solid. Recrystallization from hexane followed by sublimation *in vacuo* gave a white solid: mp 150–156° (lit.[7] mp 150–156°); nmr 0.90 and 1.14 (s, 6, CH_3CCH_3), 2.41 and 2.70 (CH_2CO_2), 4.42 (m, 1, HCCl), and 11.42 ppm (s, 1, CO_2H).

The recrystallized chloro acid **31** was washed several times with 5% sodium carbonate solution. The aqueous solution was extracted with ether. The ether solution was dried and the ether was removed to leave a semisolid. Vpc analysis of this material showed one component, which was collected and spectrally identified as camphene.

Lactonization of Camphene-8-carboxylic Acid (1) with Deuterated Trifluoroacetic Acid.[26]—A solution of 250 mg of camphene-8-carboxylic acid (1) in 0.9 ml of deuterated trifluoroacetic acid was placed in an nmr tube and the progress of the reaction at ambient temperature (Table IV) was followed by periodically examining the nmr spectrum of the solution.

Treatment of Acid 1 and Lactones 3–5 with Deuterated Trifluoroacetic Acid.[26]—Samples of *ca.* 500 mg of camphene-8-carboxylic acid (1), lactone **3**, and lactone **4** in *ca.* 0.5 ml of deuterated trifluoroacetic acid were heated at reflux for 3 days. The solution was worked up in the usual manner and the resulting deuterated lactone **4** was analyzed by mass spectroscopy. Lactone **5** was treated in a similar manner and the recovered lactone **5** was analyzed by mass spectroscopy.

The integrated areas of the methyl resonances at δ 1.34 and 1.16 ppm in lactone **4** are in a ratio of 23:29, supporting the mass spectrometric assignment of deuterium incorporation into the CCH_3 group (*cf.* Table V above).

Registry No.—(±)-**1**, 22485-76-3; (−)-**1**, 22485-80-9; **3**, 22485-77-4; **4**, 22485-78-5; **5**, 22485-79-6; **7**, 22528-22-9; **10**, 22479-79-4; **11**, 22479-80-7; **12**, 22479-81-8; **13**, 22479-82-9; **14**, 22482-99-1; **15**, 22483-00-7; **16**, 22528-23-0; **21**, 22483-01-8; **23**, 22528-24-1; **24**, 22483-02-9; **25**, 22483-03-0; **26**, 22485-68-3; **27**, 22485-69-4; **28**, 22485-70-7; **29**, 22528-25-2; **29** acetate, 22485-71-8; (±)-camphene-8-methanol, 22485-72-9; (+)-8-acetoxymethylcamphene, 22485-73-0; (+)-α-pinene-10-carboxamide, 22485-74-1; 10-(dimethylhydroxymethyl)isoborneol, 22485-75-2.

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(34) C. F. Wilcox, Jr., M. Sexton, and M. F. Wilcox, *J. Org. Chem.*, **28**, 1079 (1963).