The Chemistry of Methylnorbornyl Cations. II. Sources and Identification of Sixteen of the Methylnorbornanols[1]

Jerome A. Berson,[2a,b] Arthur W. McRowe,[2b] Robert G. Bergman,[2b,3] and Donald Houston[2c]

Contribution from the Departments of Chemistry, University of Wisconsin, Madison, Wisconsin, and the University of Southern California, Los Angeles, California.
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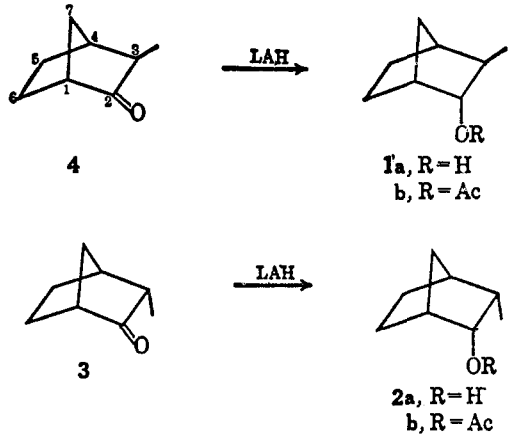
Abstract: Structures are assigned to 16 of the methylnorbornanols by a variety of methods including independent syntheses, structural interconversions, and proton magnetic resonance spectroscopy. The substances involved are the four 3-methyl-2-norbornanols, the four 5- and 6-methyl-2-*exo*-norbornanols, the two 7-methyl-2-*exo*-norbornanols, the two 1-methyl-2-norbornanols, the two 1-methyl-3-norbornanols, and the two 2-methyl-2-norbornanols.

In connection with studies of methyl-labeled norbornyl cations,[4] it was necessary to be able to identify 16 of the methylnorbornanols. Since some of these compounds were unknown when this work was begun, and the literature did not provide strong assignments of structure or unambiguous methods of synthesis for some of the others, we set out to acquire the needed information. This paper presents the results.

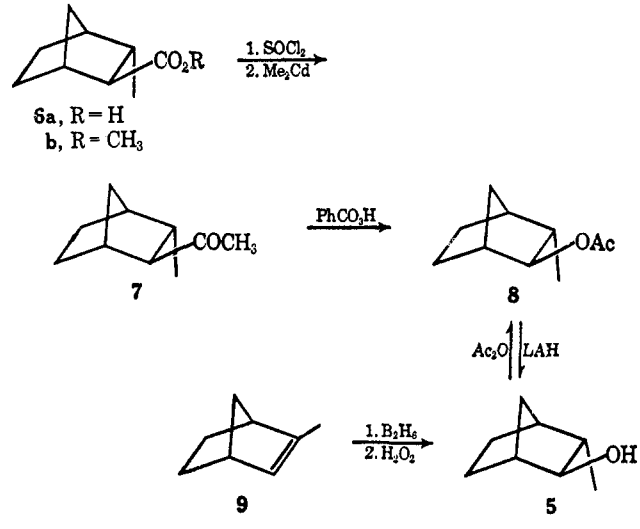
The Four 3-Methyl-2-norbornanols. Both of the previously known stereoisomers of 3-methyl-2-norbornanol, **1a** and **2a**, have an *endo* hydroxyl and differ only in the configuration of the methyl group. The configurations were assigned[5,6] on the following grounds. The *cis-endo* compound **2a** and the 3-*exo*-methyl isomer **1a** were the major products of the lithium aluminum hydride reduction of 3-*endo*- and 3-*exo*-methyl-2-norbornanone (**3** and **4**), respectively.[6] We confirm this in the case of ketone **4**, which gives 86.6% **1a** and 13.4% *cis-exo* isomer (**10**). Analogy[5,6] to other examples of such reactions with *syn*-7-unsubstituted norbornanones[7] suggested that attack from the *exo* direction would be preferred. Further, of the two alcohols then known, the one derived from **4** showed the larger cryoscopic molecular weight exaltation and was thus the less hindered, as would be expected for the *trans* member of a *cis–trans-endo* pair.[5,6]



4 → **1a**, R = H; **b**, R = Ac

3 → **2a**, R = H; **b**, R = Ac

Syntheses of the two remaining members of the series provide confirmation of the assignments. The other *trans* isomer **5** is obtained by two routes, first by the "acid → acetate" sequence from the known[6,8a] 3-*endo*-methyl-2-*exo*-norbornanecarboxylic acid (**6a**), and also by hydroboration–oxidation[8b] of 2-methyl-2-norbornene (**9**).[9] The second procedure is more easily



6a, R = H; **b**, R = CH_3

7 → **8**

8 ⇄ **9** → **5**

adapted to the preparation of substantial quantities of alcohol **5**, since the requisite olefin **9** is readily available, and the hydroboration–oxidation step, in accord with previous experience,[8b] proceeds quite cleanly in an *exo-cis* anti-Markovnikov manner. The crude product is 94% **5** and is readily purified to the level of 99% or better by a single pass through an automatic preparative gas chromatograph.

The *cis-exo* acetate **10** is obtained as a side product in the Baeyer–Villiger oxidation of 3-*exo*-methyl-2-*endo*-acetylnorbornane (**11**), which in turn is preparable

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(2) (a) To whom inquiries should be directed; (b) University of Wisconsin; (c) University of Southern California.

(3) National Institutes of Health Predoctoral Fellow, 1964–1966.

(4) Paper I of this series: J. A. Berson, J. H. Hammons, A. W. McRowe, R. G. Bergman, A. Remanick, and D. Houston, *J. Am. Chem. Soc.*, **89**, 2561 (1967), and following papers.

(5) S. Beckmann, A. Dürkop, R. Bamberger, and R. Mezger, *Ann.*, **594**, 199 (1955).

(6) S. Beckmann and R. Mezger, *Chem. Ber.*, **90**, 1559, 1564 (1957).

(7) For a review and summary of references, see J. A. Berson in "Molecular Rearrangements," Part 3, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963.

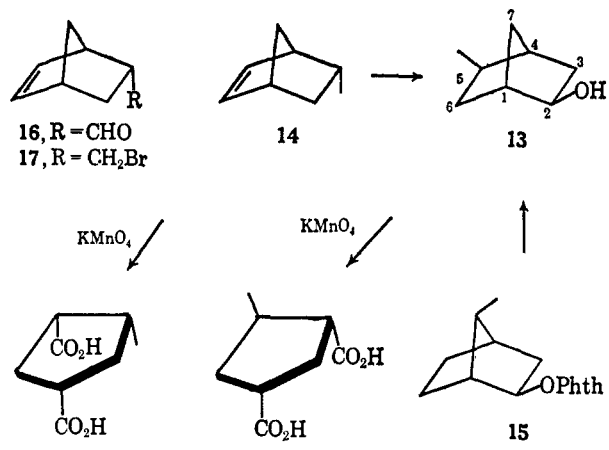
(8) (a) Syntheses of several methyl esters and carboxylic acids needed as reference compounds in the 3-methyl-2-norbornane and 3-methyl-5-norbornene-2-carboxylic acid series are described in the Experimental Section. (b) *Cf.* H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

(9) K. Alder and H. J. Ache, *Chem. Ber.*, **95**, 503, 511 (1962).

from the known[6] 3-*exo*-methyl-2-*endo*-carboxylic acid (**12**). Oxidation with perbenzoic acid is slow, but no epimerization occurs, and 3-*exo*-methyl-2-*endo*-norbornyl acetate (**1b**) is obtained free of **10**. Although oxidation with peroxytrifluoroacetic acid is faster, epimerization now becomes noticeable, and isolable quantities of the *cis-exo* acetate **10** are formed. This substance is also the minor component of the mixture obtained by acetylation of the lithium aluminum hydride reduction product from 3-*exo*-methyl-2-norbornanone (**4**).

The configurational assignments are confirmed by the nuclear magnetic resonance (nmr) spectra. In the acetates, the C-2 proton resonance occurs in a readily identifiable region about 4.5 ppm downfield from tetramethylsilane. The spectrum of the *cis-endo* acetate **2a** shows this resonance as a doublet of doublets with $J \cong 5$, 4 cps; that of the *cis-exo* acetate **10** shows a broadened doublet, $J = 7$ cps. The pattern in the **2a** spectrum is consistent with moderately strong coupling between the C-2 proton and *both* the C-3 and C-1 protons, as has been observed with many other C-2 *exo* protons in analogous systems.[10] In **10**, however, the C-2 *endo* proton is strongly coupled only to the *cis-endo* proton at C-3 and weakly or not at all to the bridgehead C-1 proton, again in accord with experience.[10] Although we have made no real attempt to identify it, the additional weak coupling that produces the slight broadening of the components of the C-2 multiplet (3.5 cps width at half-height) probably is attributable to long-range splitting, perhaps with the *anti*-7 proton.[10] This interpretation is supported by the absence of such broadening in 7-*anti*-methyl-2-*exo*-norbornyl acetate, the C-2 spectrum of which shows a doublet of doublets with widths at half-height of <1 cps for each component. The spectrum of the *trans* compound **1a**, with a C-2 *exo* proton, shows a doublet of doublets, $J \cong 3.5$, 3.5 cps. These splittings are about the same as those previously observed for C-1 to *exo* C-2 and *trans* C-2 to C-3 couplings,[10] in agreement with the assigned stereochemistry. In the spectrum of *trans*-acetate **8**, with a C-2 *endo* proton, one sees a poorly resolved doublet of doublets, in accord with the expected relatively weak long-range and *trans*-vicinal couplings.[10]

The 5- and 6-Methyl-2-*exo*-norbornanols. Esters of an alcohol assigned the structure 5-*exo*-methyl-2-*exo*-norbornanol (**13**) were isolated from formic acid or acetic–sulfuric acid treatment of a hydrocarbon assigned the structure 5-*endo*-methylnorbornene (**14**)[11] and from formolysis of *syn*-7-methyl-2-*exo*-norbornyl acid phthalate (**15**).[12] Oxidation of **13** and **14** gave two different 4-methylcyclopentane-*cis*-1,3-dicarboxylic acids.[12] The possibility that the alcohol was a 6-methyl derivative was excluded on the grounds that its formation from **15** would require a vicinal secondary–secondary hydride shift, which had been sought for and not found in the parent norbornyl system.[13] The *exo* configuration for the hydroxyl group was assigned[12] on the basis of the observed facile further rearrangement of the alcohol in formic acid. These arguments,



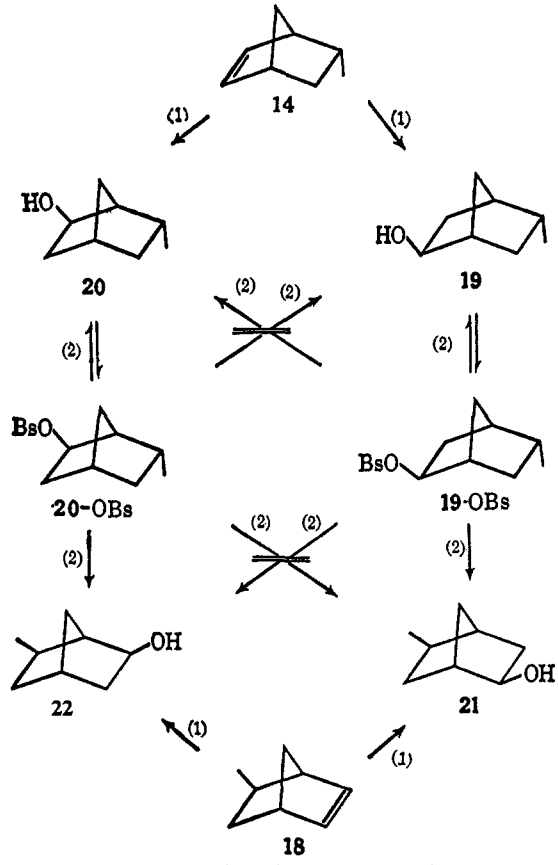
while plausible, are not completely convincing. The exclusion of the 6-methyl possibility seems less than absolute, since it now is quite probable[14] that vicinal secondary–secondary shift, although slow, does occur in formic acid, especially under equilibrating conditions. The assignment of the *exo* stereochemistry to the methyl group of **13** depends critically on the assignment of the *endo* stereochemistry to the hydrocarbon **14**. Otherwise, the argument is circular, for internally, the oxidation–hydration scheme merely demonstrates that the alkene and the alcohol are Wagner–Meerwein related and would apply equally well to the *exo*-methylnorbornene–*endo*-methyl alcohol pair. The assignment of stereochemistry to the hydrocarbon **14** rests entirely on the application of the Alder rule of *endo* addition to the precursors (the cyclopentadiene adducts **16** and **17**) used for its preparation.[11] Since the rule is frequently violated,[15] independent evidence for the assignments of stereochemistry seems desirable.

Stereochemically homogeneous *endo*- and *exo*-2-methyl-5-norbornenes (**14** and **18**) can be prepared from the corresponding known[16,17a] carboxylic acids by a reduction–arenesulfonylation–reduction sequence.[17b] Hydroboration of each leads to a pair of alcohols. Although the pair from 2-*exo*-methyl-5-norbornene (**18**) can be analyzed by capillary gas chromatography, preparative separation is difficult. However, the two alcohols from the *endo* olefin **14** are readily separable by preparative gas chromatography. In this way, 5-*endo*-methyl-2-*exo*-norbornanol (**19**) and 6-*endo*-methyl-2-*exo*-norbornanol (**20**) are obtained in pure form. Conversion of **19** and **20** to *p*-bromobenzenesulfonates (**19**-OBs and **20**-OBs) and solvolyses of the latter[18] under nonequilibrating conditions establish the identities of the entire series. Thus, **19**-OBs gives **19**, **21**, and the characteristic products derived from the complex series of transannular hydride shifts and Wagner–Meerwein rearrangements summarized in the scheme given elsewhere,[19] but does not give any **20** or

(10) J. C. Davis, Jr., and T. V. Van Auken, *J. Am. Chem. Soc.*, **87**, 3900 (1965), and references cited therein.
(11) S. Beckmann and R. Schaber, *Chem. Ber.*, **88**, 1703 (1955).
(12) S. Beckmann and G. Eder, *ibid.*, **91**, 2878 (1958).
(13) J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **76**, 4501 (1954).
(14) C. C. Lee and L. K. M. Lam, *ibid.*, **88**, 5355 (1966), and references cited therein.
(15) J. A. Berson, Z. Hamlet, and W. A. Mueller, *ibid.*, **84**, 297 (1962).
(16) C. D. Ver Nooy and C. S. Rondestvedt, Jr., *ibid.*, 77, 3583 (1955).
(17) (a) *Cf.* J. A. Berson and D. A. Ben-Efraim, *ibid.*, **81**, 4083 (1959); (b) J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *ibid.*, **83**, 3986 (1961).
(18) Paper IV of this series: J. A. Berson, A. W. McRowe, and R. G. Bergman, *ibid.*, **89**, 2573 (1967).
(19) Paper I of this series.[4]

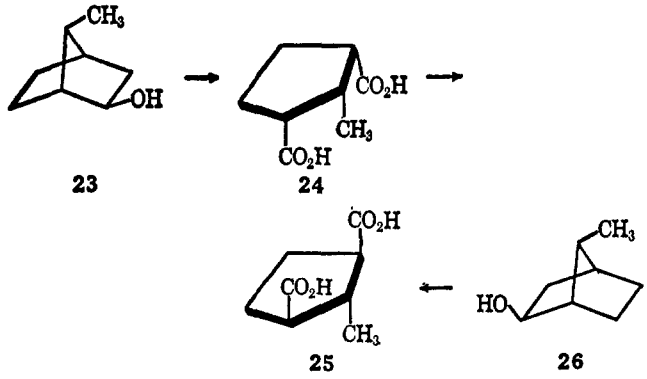
22, whereas 20-OBs, being blocked from that maelstrom by the barrier to secondary–secondary vicinal hydride shift, merely regenerates 20 and the Wagner–Meerwein related 22 in addition to tertiary product from 6,2 shift.[18] The data combined with the reasonable assumption that these kinetically controlled solvolyses give *exo* products[7] are consistent with only one formulation, which is shown in Scheme I.

Scheme I



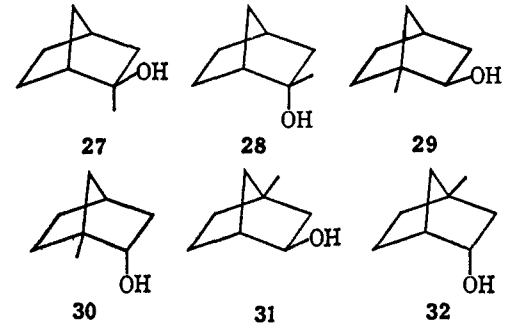
(1) hydroboration, (2) solvolysis

The 7-Methyl-2-*exo*-norbornanols. Deaminative nitrosation of 3-*exo*-methyl-2-*endo*-norbornylamine was reported to give a complex mixture of products. Fractional crystallization of the acid phthalate and saponification gave an alcohol "isoaposantenol," which was assigned the structure *syn*-7-methyl-2-*exo*-norbornanol (**23**).[20] The location and stereochemistry of the methyl



group at C-7 were established by oxidation to "isoaposantenic acid" (**24**), which was not identical with but was epimerizable to an acid "*cis*-aposantenic acid," **25**, prepared by structurally unquestionable synthesis and shown to have *cis*-carboxyl groups. If the less stable of the two acids is the "all-*cis*" form **24**, then "isoaposantenol" is **23**. The *anti* isomer **26** was never isolated pure,[20] but its presence in the deamination mixture from 3-*endo*- and/or -*exo*-methyl-2-*endo*- and/or -*exo*-norbornylamine was inferred from the isolation of "*cis*-aposantenic acid" (**25**) from the oxidation of a fraction of the mixed alcohols obtained by combining reaction products from both amines. Although a detailed reexamination of the deaminations is reported elsewhere,[18] we note here merely that alcohol **26** is formed in substantial quantity from the 3-*endo*-methyl-2-*exo* amine and also (as the acetate) from acetolysis of the corresponding arenesulfonates. It can readily be isolated in pure form by preparative vapor chromatography.[18] The structure assigned is supported on the circumstantial grounds that **26** formed by carbonium ion process is invariably accompanied by an approximately equal amount of its Wagner–Meerwein relative 3-*endo*-methyl-2-*exo*-norbornanol (**5**).[18] Also, the nmr spectrum of the acetate of **26** shows a sharp doublet (J = 7 cps) at δ 0.9 (superimposed on diffuse absorption), attributable to the C-7 methyl group, and a clean doublet of doublets centered around δ 4.5, attributable to the *endo*-C-2 proton coupled with the appropriate[10] coupling constants ($J_{2,3\ trans}$ = 3 cps, $J_{2,3\ cis}$ = 7 cps) to the C-3 *exo* and *endo* protons, respectively. The absence of further splitting ($J \cong 1$ cps)[10] of this multiplet is consistent with the absence of a 7-*anti* proton. Further, chemical evidence for the structure is provided by a number of transformations.[21]

1- and 2-Methyl-2-norbornanols and 1-Methyl-3-norbornanols. The 2-methyl-2-norbornanols **27** and **28** and the 1-methyl-2-norbornanols **29** and **30** are well known,[6,12,22] and require no further comment. 1-



Methyl-3-*exo*-norbornanol (**31**) is formed together with 1-methyl-2-*exo*-norbornanol (**29**) in the hydroboration of 1-methyl-2-bornornene. The epimer 1-methyl-3-*endo*-norborneol (**32**) is obtained in a mixture with **31** by oxidation of **31** and hydride reduction of the derived ketone.

Experimental Section[23]

Vapor chromatographic (vpc) analyses were performed with capillary columns on Barber–Colman gas chromatographs,

(20) G. Komppa and S. Beckmann, *Ann.*, **523**, 68 (1936).

(21) Paper III: J. A. Berson and R. G. Bergman, *J. Am. Chem. Soc.*, **89**, 2569 (1967).

(22) N. J. Toivonen, E. Siltanen, and K. Ojala, *Ann. Acad. Sci. Fennicae, Ser. AII*, No. 64 (1955).

(23) Microanalyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich.

Models 61-C and 5000, using argon carrier gas and radium or tritium ionization detectors. Column stationary phases were TCEP (tri-β-cyanoethoxypropane, 250 ft) (column L) and two polypropylene glycol columns (Ucon 50-HB-2000, 100 and 250 ft) (columns M and N). Preparative vpc separations were accomplished with Wilkens (now Varian) Aerograph Models A-90-P and A-700 Autoprep instruments equipped with thermal conductivity detectors and using helium carrier gas. Tricyanoethoxypropane (TCEP) stationary phase as obtained commercially always contained impurities which showed infrared absorption at 2.7–3.1 and 5.9–6.3 μ. Although good packed columns could be prepared with this material, it was unsuitable for capillary work, since columns prepared from it bled excessively and had short useful lifetimes. The TCEP was purified by percolation (as a solution in pure methylene chloride) through Woelm alumina, basic, activity grade III. The material so prepared gave relatively durable capillary columns. Table I lists the packed and capillary columns used in this work.

Table I. Vapor Chromatographic Columns

Column	Substrate	Dimensions, mm × m	Substrate, %	Chromosorb[f] Type	Mesh
		Packed columns			
A	TCEP[a]	9.5 × 6	20	P	45–60
B	TCEP	6.5 × 3	25	P	60–80
C	TCEP	22.5 × 5	25	P	60–80
D	Ucon[b]	9.5 × 6	30	W	60–80
D-1	Ucon	6.5 × 4	20	P	60–80
E	Carbowax[c]	9.5 × 6	20	P	60–80
F	Carbowax	9.5 × 3.5	30	W	60–80
G	Carbowax	6.5 × 2	20	P	45–60
G-1	Carbowax	9.5 × 6	25	P	60–80
G-2	Carbowax	6.5 × 9	20	P	60–80
H	DC-200[d]	9.5 × 6	25	P	60–80
H-1	SF-96[d]	6.5 × 0.8	20	P	60–80
J	FFAP[e]	9.5 × 6	30	W	60–80
K	FFAP	6.5 × 2	20	W	60–80
		Capillary columns			
L	TCEP	0.25 × 80	..	..	...
M	Ucon	0.25 × 30	..	..	...
N	Ucon	0.25 × 80	..	..	...
N-1	Ucon	0.25 × 90	..	..	...
O	DC-200	0.25 × 50	..	..	...

[a] Tri-β-cyanoethoxypropane. [b] Union Carbide polypropylene glycol. [c] Union Carbide polyethylene glycol. [d] Dow-Corning silicone oil. [e] Wilkens Aerograph "free fatty acid phase." [f] Johns-Manville diatomaceous silica.

Proton magnetic resonance spectra (nmr) were obtained with a Varian Associates A-60 instrument. Samples of about 50 mg were dissolved in 250 μl of carbon tetrachloride containing tetramethylsilane as internal standard, and resonance positions are reported in parts per million downfield from tetramethylsilane (δ units). The *J* values reported are approximate multiplet spacings which in some but not all cases are the same as true coupling constants.

Infrared spectra of neat films (unless otherwise indicated) were taken with the Perkin-Elmer Model 137 or Beckman Model IR-8 instruments.

A number of carboxylic acids and the corresponding methyl esters were prepared for use as reference compounds in this work. Some of the acids but none of the esters had been previously reported. Analytical data for the esters and a new acid **35** are given in Table II. The table also lists melting points for the previously known acids, which were prepared by literature procedures. The methyl esters were prepared by the action of ethereal diazomethane on the acids followed by bulb-to-bulb distillation. They were homogeneous by capillary vpc.

3-*endo*-Methyl-2-*endo*-carbomethoxy-5-norbornene (35, R = CH_3) was obtained in the following manner. A crude acidic fraction was derived from mother liquors from the preparation of 3-*exo*-methyl-5-norbornene-2-*endo*-carboxylic acid (**33**, R = H) by zinc reduction of the corresponding iodolactone.[5] This material was treated with diazomethane to give a mixture of **33**, **34**, and **35** (R = CH_3) in proportions that varied with the purity of the iodolactone starting material and the amount of **33** (R = H) removed in the crystallization. Preparative vpc on column H, afforded pure **35** (R = CH_3), homogeneous by capillary vpc under conditions where **33** and **34** where cleanly detectable. The retention times on both capillary columns were identical with those of the minor component of the 96:4 two-component mixture produced by epimerization of **34** (R = CH_3) in boiling methanol–sodium methoxide for 3 hr. The nmr spectrum showed a methyl doublet (*J* = 7 cps) at δ 0.75, a methoxyl singlet at 3.55, a complex series of multiplets between 1.3 and 2.9 (6-proton intensity), and a 2-proton signal in the olefinic region centered near 6.15 as a pair of four-line multiplets separated by 17 cps, *J* = 3 cps. The corresponding acid, **35** (R = H), was obtained in small yield by saponifying the ester with aqueous methanolic sodium hydroxide and recrystallizing the resulting product from acetonitrile. The corresponding saturated ester, **37** (R = CH_3), was isolated by preparative vpc on column H.

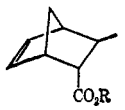
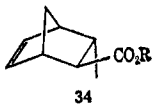
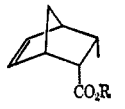
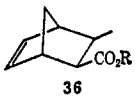
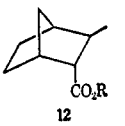
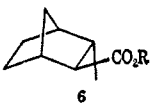
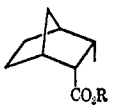
The *exo-cis* unsaturated ester **36** (R = CH_3) was obtained only in admixture with the *trans* form **33** by epimerization of the latter.

The TCEP capillary column separated the four unsaturated esters in the following order of elution: **34**, **33**, **35**, **36**.

3-*exo*-Methyl-2-*endo*-acetylnorbornane (11). Pure, racemic 3-*exo*-methyl-2-*endo*-norbornanecarboxylic acid (**12**), 27.0 g (0.24 mole), was treated with 35 ml of freshly distilled thionyl chloride for 10 hr at room temperature. The excess reagent was distilled off and the acid chloride distilled at 86–87° (20 mm) to yield 39.6 g of product (96%).

Dimethylcadmium reagent was prepared by adding 60 g (0.63 mole) of dry methyl bromide to 13.5 g (0.55 g-atom) of magnesium turnings in 400 ml of ether, letting the Grignard reagent stand 3 hr, and then adding with cooling 58 g (0.32 mole) of anhydrous cadmium chloride and allowing the mixture to stir for 2 hr at room temperature.

Table II. Properties of Some Acids and Esters

	Mp, °C — Acid, R = H	Lit.[a]	Me ester, R = CH_3, Found,[b] % C	H
 **33**	91–93	95	72.05	8.57
 **34**	59–61	61–62	71.96	8.42
 **35**	120.5–121[d]	...	72.26	8.44
 **36**	...	...	*c*	
 **12**	67.5–69	68–69	71.36	9.64
 **6**	44–45	40–41	71.59	9.77
 **37**	...	...	71.33	9.75

[a] References 6 and 20. [b] *Anal.* Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. [c] Identified by retention time; not isolated. [d] *Anal.* Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 70.91; H, 7.96.

The cadmium reagent was cooled to −5°, and the acid chloride in 200 ml of ether was slowly added dropwise with efficient stirring to maintain a temperature below +5°. After 2 hr at room temperature, the mixture was poured onto dilute hydrochloric acid and ice. The separated ether layer was washed successively with water, saturated sodium bicarbonate solution, and saturated brine, dried over sodium sulfate, and carefully concentrated through a short fractionation column. The residue distilled at 92.0–92.5° (22 mm) to give 27.9 g (80%) of clear, colorless liquid. The product was homogeneous on both capillary columns.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 79.01; H, 10.60.

The **semicarbazone** was recrystallized from 95% ethanol; it had mp 177–178°.

Anal. Calcd for $C_{11}H_{19}N_3O$: C, 63.13; H, 9.15. Found: C, 63.08; H, 9.11.

The **2,4-dinitrophenylhydrazone** was recrystallized from aqueous methanol to give orange-yellow plates, mp 114–115°.

Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.95; H, 6.09; N, 16.87.

3-*exo*-Methyl-2-*endo*-acetoxynorbornane (1b). Method A. A chloroform solution of peroxybenzoic acid was prepared in the usual manner,[24] with the exception that the suggestion of Vilkas[25] was utilized. This modification involved addition of the basic solution of the peracid *to* the aqueous acid prior to the chloroform extraction. In this manner, there was always excess acid present, and the rapid decomposition of the half-neutralized solution was avoided. Titrimetric assay indicated yields greater than 95% were typical.

To 4.46 g (29.3 mmoles) of pure ketone **11** was added 6.1 g (50% excess) of peroxybenzoic acid in 130 ml of chloroform. The solution was stoppered and stored in darkness at room temperature for 21 days. Assay of an aliquot indicated that 10% of the original peracid activity remained. Enough 10% sodium bisulfite solution was added to give a negative starch–iodide test. The organic layer was washed with 50 ml of 1 *N* sodium hydroxide solution, twice with 50 ml of saturated sodium bicarbonate solution, and twice with saturated brine; it was dried twice over sodium sulfate. The solvent was fractionated off, and the pale yellow residue was distilled at 75.0–75.5° (7 mm). Another fraction distilled over at *ca.* 70° (1 mm). Both were clear and colorless. The first fraction was 3.7 g (74%) of a mixture analyzing on the Ucon capillary column as 94% of the desired acetate (**1b**) and 6% of the starting ketone **11**. The second component, 1.0 g, contained only 3% of the desired acetate, the remainder being condensation products.

Some of the fraction contaminated with 6% of the ketone was purified on column C and distilled bulb to bulb at reduced pressure to yield pure **1b** homogeneous on the Ucon capillary. The nmr spectrum showed $COCH_3$, δ 1.96, singlet; $CHCH_3$, δ 1.03, doublet, J = 6 cps; C-2-*exo*-H, δ 4.31, doublet of doublets, $J \simeq 3$ cps, 8 cps wide at half-height.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58. Found: C, 71.34; H, 9.59.

The methyl ester **12** (R = OCH_3) that would have resulted from methyl migration instead of the observed ring migration was cleanly separated on columns L and N and was shown to be completely absent from the reaction mixture. Likewise, the presence of the epimeric *cis-exo* acetate **10** could have been detected, but was not noted.

Method B. Methyl ketone **12**, 38.0 g (0.25 mole), with less than 1% epimeric contamination was dissolved in 780 ml of methylene chloride and 147 g (1.04 mole) of sodium monohydrogen phosphate was added. Peroxytrifluoroacetic acid prepared[26] from 10.9 ml (0.4 mole) of 90% hydrogen peroxide, 99 ml (0.46 mole) of trifluoroacetic anhydride, and 130 ml of methylene chloride was slowly added to the ketone mixture with stirring at a rate sufficient to maintain a modest reflux rate. There was considerable evolution of gases, and the odor of ozone was prominent. Stirring and reflux were maintained for 6 hr after the stiff foam and gas evolution subsided, a total of 24 hr. The mixture was then cooled, and 450 ml of water was added to completely dissolve the buffer salts.

The organic layer was drawn off and the aqueous phase was washed twice with more solvent. The combined organic layers were twice washed with saturated brine and dried over two successive portions of sodium sulfate. The solution was carefully concentrated and the residue distilled through a 300 × 7 mm tantalum wire spiral column at 16 mm. The main fraction distilled at 95–97° and amounted to 34.8 g (82.8%). The second fraction, 10.4 g, boiled over a considerable temperature range. This material was not investigated further; it contained less than 5% of the desired product as determined by capillary vpc. The major fraction consisted mainly of the acetate **1b** contaminated with several impurities; 1.5% starting ketone, *ca.* 0.5% of material presumed to be trifluoroacetate (infrared absorption 5.57 μ), and smaller amounts of three other acetates. This material was not further purified but directly converted to the alcohol.

When a large-scale run of the oxidation of ketone **11** was carried out by method B in the optically active series,[27] the distilled acetate product contained 10% of a compound which was isolated by preparative vpc on column D. It emerged shortly after acetate **1b** and was repassed to achieve purification to capillary vpc homogeneity. The new material was assigned the structure **3-*exo*-methyl-2-*exo*-norbornyl acetate (10)** on the grounds given in the Discussion.

3-*exo*-Methyl-2-*endo*-norbornanol (1a). Acetate **1b**, prepared by method A (after chromatographic purification), gave pure alcohol **1a** in high yields on reduction with lithium aluminum hydride. No contamination was noted on either capillary column. Pure alcohol **1a** from the acetate could be obtained more quickly by reduction of the product mixture and separation of the alcohol mixture, utilizing the greater separation of the alcohols for larger injections on columns C or A. Alcohol obtained similarly from acetate of method B contained about 2% of several impurities on column N and was most easily purified in the racemic series by conversion to the acid phthalate, mp 126.5–128.0° (lit.[6] mp 131–132°).

The ***p*-toluenesulfonate** of alcohol **1a**, recrystallized from absolute methanol, yielded white needles, mp 43–44°.

Anal. Calcd for $C_{15}H_{20}O_3S$: C, 64.27; H, 7.19. Found: C, 64.15; H, 7.17.

The ***p*-bromobenzenesulfonate**, recrystallized from absolute methanol or hexane, melted at 101–102°.

Anal. Calcd for $C_{14}H_{17}O_3BrS$: C, 48.70; H, 4.96; Br, 23.14. Found: C, 48.71; H, 4.95; Br, 23.25.

The ***p*-nitrobenzenesulfonate**, prepared from alcohol **1a** of low optical activity, gave light yellow crystals on recrystallization from absolute ethanol, mp 104–106°.

Anal. Calcd for $C_{14}H_{17}O_5NS$: C, 54.01; H, 5.50; N, 4.50. Found: C, 54.03; H, 5.66; N, 4.52.

3-*endo*-Methyl-2-*exo*-acetylnorbornane (7). Pure, racemic acid **6a** was converted to its acid chloride and the acid chloride to the ketone **7** *via* the dimethylcadmium reagent as in the *endo* series. The distilled acid chloride, bp 95–96° (17 mm), was prepared in 97% yield from thionyl chloride. The ketone **7** isolated in 75% yield from the acid chloride contained several small impurities as detected on capillary column L. The higher boiling residue, amounting to about 20% of the expected yield, distilled readily at 120° (3 mm) to give a mixture of material which, to judge by its infrared spectrum, contained aldol condensation products (ketol and α,β-unsaturated ketone).

The **semicarbazone** was recrystallized from 95% ethanol, mp 184–185° dec.

Anal. Calcd for $C_{11}H_{19}ON_3$: C, 63.13; H, 9.15. Found: C, 63.27; H, 9.24.

Ketone **7** was obtained homogeneous on capillary vpc (columns L and N) from the semicarbazone by hydrolysis in warm 20% aqueous sulfuric acid, immediate steam distillation, pentane extraction, drying over calcium sulfate, and concentration. Distillation through a short Vigreux column yielded solvent-free material, bp 94.5–95.0° (22 mm). This material was identical in every respect with a small sample of material purified by preparative vpc on column A.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.88; H, 10.57.

The **2,4-dinitrophenylhydrazone**, mp 119.5–120.0° from methanol, had mp 103–106° when admixed with that of ketone **11**.

Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.88; H, 6.05; N, 16.95.

3-*endo*-Methyl-2-*exo*-norbornyl Acetate (8). Pure, racemic ketone **7**, 6.0 g (39.4 mmoles), was oxidized with two portions of excess perbenzoic acid in chloroform over 5 days at room temperature.

(24) G. Braun, "Organic Syntheses," Coll. Vol. I, 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1941, p 431.

(25) M. Vilkas, *Bull. Soc. Chim. France*, 1401 (1959).

(26) M. F. Hawthorne, W. D. Emmons, and K. S. McCallum, *J. Am. Chem. Soc.*, 80, 6393 (1958).

(27) *Cf.* paper VI: J. A. Berson, J. H. Hammons, A. W. McRowe, R. G. Bergman, A. Remanick, and D. Houston, *ibid.*, 89, 2590 (1967).

The oxidation also was achieved with *m*-chloroperbenzoic acid in methylene chloride. The material was worked up as in the *endo* series (method A). The crude residue contained no starting ketone. The acetate was distilled at 76–77° (7 mm) to give a colorless liquid, homogeneous by capillary vpc (column L), in 79% yield. Infrared spectrum and vpc retention times were identical with the material obtained by hydroboration of 2-methyl-2-norbornene, oxidation, and acetylation. The latter is the more convenient method for obtaining either racemic or optically active acetate **8**. The nmr spectrum showed bands for $COCH_3$, δ 1.93, singlet; $CHCH_3$, δ 1.04, doublet, J = 7 cps; C-2-*endo*-H, δ 3.96, doublet of doublets, $J \sim 2.5, 2.5$ cps.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.17; H, 9.44.

From Hydroboration of 2-Methyl-2-norbornene (9). A three-necked round-bottomed flask equipped with a magnetic stirring apparatus was charged with 22.5 g of 2-methyl-2-norbornene,[9] 3.70 g of sodium borohydride, and 150 ml of tetrahydrofuran (THF), distilled from $LiAlH_4$ before use. A solution of 16.7 ml of boron trifluoride etherate (freshly distilled) dissolved in 50 ml of THF was then added dropwise to the flask, with rapid stirring. A white precipitate formed during the addition. After the resulting mixture had been stirred overnight, it was cooled to −5° in an ice–salt bath, and 5 ml of water was slowly added, followed by 50 ml of a 10% aqueous solution of sodium hydroxide. The flask was then allowed to warm to room temperature while 55 ml of a 30% aqueous solution of hydrogen peroxide was added dropwise with stirring.

After the resulting two-phase mixture had been stirred for 3 hr, the phases were separated, and the aqueous layer extracted twice with pentane. The combined organic phases were washed three times with a 10% aqueous solution of sodium hydroxide and once with a solution of saturated NaCl, and dried overnight over solid sodium sulfate. The liquid was then decanted and the pentane carefully removed by distillation through a Vigreux column on a steam bath, leaving 25.1 g (96%) of alcohol as a slightly greenish oil which slowly solidified into a gummy mass. The alcohol was converted to 3-*endo*-methyl-2-*exo*-norbornyl acetate in the usual way and the acetate distilled bulb to bulb to give a water-white, sweet-smelling oil which had an infrared spectrum and vpc retention time identical with those of the acetate obtained as above from 3-*endo*-methyl-2-*exo*-acetylnorbornane. The acetate obtained from the hydroboration route was contaminated with about 6% of presumably isomeric materials. It could be purified by automatic chromatography (Wilkens A-700 "Autoprep" instrument) on column E; by this procedure it was obtained 99.0% pure after one pass, as determined by analysis on capillary columns L and N-1.

3-*endo*-Methyl-2-*exo*-norbornanol (5). The purified 3-*endo*-methyl-2-*exo*-norbornyl acetate (**8**) described above was reduced to the corresponding alcohol (**5**) with lithium aluminum hydride in the standard way. The alcohol was again obtained as a semisolid which was sublimed at 120° (15 mm) to give fine, white crystals, mp 95.5–97.0°.

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.14; H, 11.25.

3-*endo*-Methyl-2-*exo*-norbornyl acid phthalate was obtained after two recrystallizations from heptane as a white powder, mp 89.5–90.0°.

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 70.20; H, 6.57.

3-*endo*-Methyl-2-*exo*-norbornyl *p*-toluenesulfonate was formed when 0.79 g of the alcohol in 3 ml of pyridine was stirred at 0° and treated portionwise with 1.20 g of solid *p*-toluenesufonyl chloride (freshly recrystallized from carbon tetrachloride). After 4 days at 5°, the mixture was poured onto cracked ice and extracted with ether. The ether solution, after thorough washing with water and brine, was dried over sodium sulfate, decanted, and evaporated. The residue was dried *in vacuo* (0.1 mm for 3 hr) to give 1.50 g (84%) of a solid which, after four recrystallizations from heptane, had mp 58.8–59.8°.

Anal. Calcd for $C_{15}H_{19}O_2S$: C, 64.26; H, 7.19; S, 11.44. Found: C, 63.98; H, 7.06; S, 11.31.

The corresponding ***p*-bromobenzenesulfonate** was obtained by a procedure which differed only in that the reaction mixture was stored in the cold for only 36 hr. The compound was obtained as white crystals, mp 71–72°, from heptane; it was moderately stable at −5° but decomposed to a black, intractable semisolid on standing overnight at room temperature.

Anal. Calcd for $C_{14}H_{16}O_2SBr$: C, 48.68; H, 4.96; S, 9.29; Br, 23.15. Found: C, 48.56; H, 4.96; S, 9.34; Br, 23.21.

5- and 6-*endo*-Methyl-2-*exo*-norbornyl Acetates (Acetates of 19 and 20). Pure, racemic 5-norbornene-2-*endo*-carboxylic acid was converted to 5-*endo*-methyl-2-norbornene (**14**) *via* the methanol and its *p*-bromobenzenesulfonate according to the method previously reported.[17b] To a slurry of 35 ml of purified tetrahydrofuran (distilled from lithium aluminum hydride after reflux over potassium hydroxide), 4.68 g (43.3 mmoles) of the pure hydrocarbon, and 0.85 g (22.4 mmoles) of sodium borohydride was slowly added 3.7 ml of boron trifluoride etherate in 10 ml of solvent with vigorous stirring. The hydroboration mixture was allowed to stir for 18 hr. With cautious dropwise addition of 10 ml of 10% sodium hydroxide solution and 10 ml of 30% hydrogen peroxide solution, the very exothermic oxidation was achieved within a 1-hr period. The addition of water and extraction with ether four times, back washing the combined organic layers three times with saturated brine, drying over sodium sulfate, and careful concentration yielded the crude alcohol mixture which was inseparable on capillary columns L or N. Acetylation gave a mixture of acetates, which showed on capillary vpc on column L two main peaks contaminated by less than 2% unidentified olefins and 1% isomeric acetates. The acetates of **20** and **19** were present in the ratio of 56.3:43.7 (average over two separate hydroborations and work-ups, standard deviation = ±0.3% absolute) in order of increasing retention time on column L.

The two major acetate components could be preparatively separated with relative ease on columns A or E.

6-*endo*-Methyl-2-*exo*-norbornyl acetate, the first main fraction of the preceding hydroboration mixture, was repassed once again on column E to give colorless liquid acetate, pure by capillary vpc. This compound was not present in the products resulting from the acetolysis of arenesulfonates of 3-*exo*-methyl-2-*endo*-norbornanol (**1a**) or 5-*endo*-methyl-2-*exo*-norbornanol (**19**).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.24; H, 9.69.

6-*endo*-Methyl-2-*exo*-norbornanol (20) was obtained from its acetate by reduction with lithium aluminum hydride in the usual manner. Bulb-to-bulb distillation at reduced pressure produced a low melting solid, not completely liquified at room temperature.

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 75.92; H, 11.06.

The ***p*-nitrobenzoate,** after two recrystallizations from absolute methanol, melted at 108.5–109.0°.

Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22. Found: C, 65.29; H, 6.34.

The ***p*-toluenesulfonate 20-OTs** was isolated as an oil which began to crystallize after 2 months standing at −20°. Recrystallization from pentane–ethyl acetate at about −50° gave white plates, mp 37.5–38.5°, which were not stable for more than 1 day at room temperature.

The ***p*-bromobenzenesulfonate 20-OBs** was isolated as white needles while wet with pyridine. Recrystallization from pentane or vacuum suction to remove the pyridine resulted in the spontaneous decomposition of the *p*-bromobenzenesulfonate within 5 min at 0°.

6-*endo*-Methyl-2-norbornanone. A small amount of the alcohol **20** was oxidized with Jones reagent in acetone to yield the ketone contaminated with about 5–8% alcohol. The ketone was purified by preparative vpc on column G to yield a low melting, waxy solid.

Anal. Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.51; H, 9.84.

The **2,4-dinitrophenylhydrazone** was obtained as orange crystals, mp 129.4–130.0°.

Anal. Calcd for $C_{14}H_{16}N_4O_4$: C, 55.26; H, 5.30; N, 18.41. Found: C, 55.12; H, 5.37; N, 18.35.

5-*endo*-Methyl-2-*exo*-norbornyl acetate, the component of longer retention time from the hydroboration of 5-*endo*-methylnorbornene, was repassed once again on column E to give a liquid acetate pure by capillary vpc. This material had a retention time (column L) identical with that of one of the products of the acetolysis of 3-*exo*-methyl-2-*endo*-norbornyl *p*-bromobenzenesulfonate.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.36; H, 9.50.

5-*endo*-Methyl-2-*exo*-norbornanol (19) was obtained from the acetate by reduction with lithium aluminum hydride. After bulb-to-bulb distillation it was a viscous mass.

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.29; H, 11.12.

The *p*-**nitrobenzoate** had mp 56.5–57.0° (from absolute methanol).

Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22. Found: C, 65.22; H, 6.17.

The *p*-**toluenesulfonate** of this alcohol remained a liquid in our hands. The *p*-bromobenzenesulfonate, **19**-OBs, decomposed in a similar manner to that of **20**.

5-*endo*-Methyl-2-norbornanone. A small sample of alcohol **19** was converted to the ketone with Jones reagent in acetone and the product purified on column G to yield a clear liquid which crystallized just below room temperature.

Anal. Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.20; H, 9.92.

The **2,4-dinitrophenylhydrazone** of the ketone was obtained as orange platelets, mp 151.0–151.5° (absolute methanol).

Anal. Calcd for $C_{14}H_{16}N_4O_4$: C, 55.26; H, 5.30; N, 18.41. Found: C, 55.22; H, 5.36; N, 18.25.

5- and 6-*exo*-Methyl-2-*exo*-norbornyl acetates (acetates of 21 and 22) were obtained from pure 5-norbornene-2-*exo*-carboxylic acid by the same procedure used for the 5- and 6-*endo*-methyl compounds. Analysis with capillary column L showed two main peaks to be present in a ratio of 1:1 and two smaller peaks, each of intensity about 3% of the total. Presumably the latter peaks represent a small amount of *endo*-hydroboration product. The first emerging of the two major peaks, the 6-*exo*-methyl-2-*exo* isomer (acetate of **22**), was completely absent from the acetolysis products of **19**-OBs or the arenesulfonates of **1a**. Its retention time was identical with that of one of the two products from acetolysis of **20**-OBs, the second product being the acetate of **20**.[18]

The other major peak (acetate of **21**) had a retention time identical with that of one of the products from the acetolysis of **19**-OBs and **1a**.[18]

1-Methyl-3-*exo*-norbornanol (31) was formed by alkaline hydrogen peroxide oxidation of the residues from partial asymmetric hydroboration[9b] of 1-methyl-2-norbornene,[9] a reaction that had been carried out in another study.[28] The resulting mixture of 1-methyl-2-*exo*- and 1-methyl-3-*exo*-norbornanols (**29** and **31**) was separated by vpc on column D (**31** emerged second) and then on column F. Alcohol **31** was obtained as a waxy solid.

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 75.97; H, 11.29.

The *p*-**nitrobenzoate** was recrystallized from methanol and had mp 93–94°.

Anal. Calcd for $C_{15}H_{17}O_4N$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.35; H, 6.12; N, 5.06.

The **acetate** was a liquid.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.53; H, 9.62.

The *p*-**toluenesulfonate** was a liquid that could not be induced to crystallize at −65° in pentane. It was homogeneous by thin layer chromatography.

Jones oxidation of **31** followed by lithium aluminum hydride reduction of the resulting ketone gave a two-component mixture of **31** and a much larger amount of another alcohol, presumably 1-methyl-3-*endo*-norbornanol (**32**), which emerged just before **31** on column L.

(28) S. Fanega, unpublished work.

The Chemistry of Methylnorbornyl Cations. III. Configurational Correlation of 2,3- and 2,7-Substituted Norbornyl Derivatives by Way of 3-Substituted Nortricyclenes[1]

Jerome A. Berson and Robert G. Bergman[2]

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin. *Received October 31, 1966*

Abstract: The relative configurations and optical rotations of *anti*-7-methyl-2-*exo*- and -3-*endo*-methyl-2-*exo*-norbornyl acetates are established by two independent correlations. Both correlations involve 3-nortricyclene derivatives as relay compounds, and the transformations provide absolute configurations and rotations of these substances also.

Although a network of absolute and relative configurational correlations among 1- and 2-substituted bridged bicycloheptane and bicyclooctane derivatives has been constructed,[3] only a few correlations between 2- and 7-substituted norbornanes are available. In studying one aspect of the mechanism of carbonium ion rearrangements of methyl-labeled norbornyl cations,[4] we found the need to establish such correlations. Since the methods adopted to achieve this involve nortricyclenic relay compounds, the present results also provide the first determinations of absolute configuration of nortricyclenes.

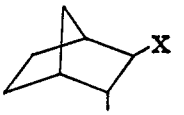
(1) The support of part of this work by the National Institutes of Arthritis and Metabolic Diseases through Grant No. AM-07505 is gratefully acknowledged.

(2) National Institutes of Health Predoctoral Fellow, 1964–1966.

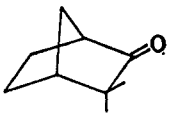
(3) (a) *Cf.*, *inter alia*, J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *J. Am. Chem. Soc.*, **83**, 3986 (1961), and references cited therein; (b) K. Mislow and J. G. Berger, *ibid.*, **84**, 1956 (1962); (c) J. A. Berson and A. Remanick, *ibid.*, **86**, 1749 (1964).

(4) Paper V of this series: J. A. Berson, R. G. Bergman, J. H. Hammons, and A. W. McRowe, *ibid.*, **89**, 2581 (1967).

Acetolysis of the *p*-bromobenzenesulfonate (**1b**) of optically active 3-*endo*-methyl-2-*exo*-norborneol (**1a**) gives a mixture of products[4] from which are isolated (−)-3-*endo*-methyl-2-*exo*-norbornyl acetate (**1c**), identical in sign and magnitude of rotation with **1c** obtained by direct acetylation of **1a**, and (−)-7-*anti*-methyl-2-*exo*-norbornyl acetate (**2b**). (The rotatons refer to the sodium D line.) The absolute configuration of (−)-**1c** is established by oxidation and methylation to (+)-camphenilone (**3**).[4] For reasons discussed elsewhere,[4] a correlation of **1b** and **2b** is mechanistically significant but cannot be based on the assumption that (−)-**1c** and (−)-**2b** are related as simple Wagner–Meerwein



1a, X = OH
b, X = OBs
(−)-**c**, X = OAc



(+)-**3**