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Synthesis and Chemistry of Some Tricyclo[4.2.1.0^{2,5}]nonane Derivatives[1]

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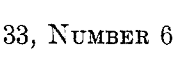
Syntheses of *exo*- and *endo*-tricyclo[4.2.1.0^{2,5}]nonanes (**1** and **2**) and several of their derivatives are described. The key intermediates were *exo*- and *endo*-tricyclo[4.2.1.0^{2,5}]non-7-enes (**23** and **24**) which were prepared by cyclization of diiodides **25** and **26** with phenyllithium. Reactions involving carbonium ions generated at C-7 invariably produced derivatives of alcohol **35** as the major product.

Our continuing interests in the synthesis and chemistry of tricyclic ring systems prompted a survey of reactions designed to lead to the *exo*- and *endo*-tricyclo[4.2.1.0^{2,5}]nonane systems **1** and **2**. Although numerous reports dealing with derivatives of these systems have appeared in the recent literature,[2] the parent hydrocarbons **1** and **2** have not yet been described. Furthermore, the syntheses of related systems are either not readily adaptable to large-scale work or to systematic derivitization.



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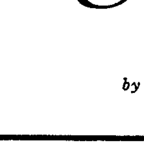

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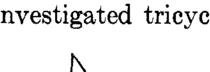
The systems in question are of importance in that they bridge the gap between the relatively well-known tetrahydrodicyclopentadiene[3] (**3**) and the more recently investigated tricyclo[3.2.1.0^{2,4}]octyl systems[4] **4**. Thus, a study of the chemistry of suitable derivatives of **1** and **2** is clearly of importance before complete analysis of the behavior of these substituted norbornyl systems can be made.[5] This paper enumerates some synthetic studies in this area as well as the results of some carbonium ion reactions in this series.



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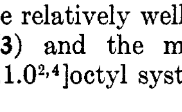

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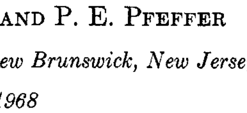
Results and Discussion

Synthetic Studies.—Initial studies involved reactions of derivatives of tricyclo[3.2.1.0^{2,4}]octylcarbinyl systems (**5**) which by ring expansion would be expected to lead to tricyclo[4.2.1.0^{2,5}]nonyl systems (*e.g.*, **6**). This method was appealing owing to the availability of the precursors *via* the reaction of ethyl diazoacetate with norbornene.[6]



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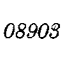

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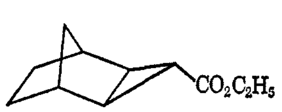
Amine **9** was readily obtained by reduction of amide **8** with lithium aluminum hydride. Deamination of **9**



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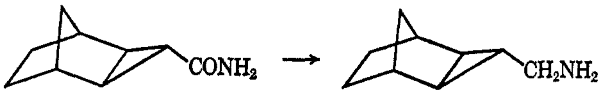

8 **9**

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[1] Presented in part at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965, Abstracts, p 38S.

[2] For some other recent syntheses of these ring systems, see (a) L. G. Cannell, *Tetrahedron Lett.*, 5967 (1966); (b) L. Watts, J. D. Fitzpatrick, and R. Pettit, *J. Amer. Chem. Soc.*, **88**, 623 (1966); (c) C. D. Smith, *ibid.*, **88**, 4273 (1966); (d) G. N. Schrauzer and P. Glockner, *Chem. Ber.*, **97**, 2451 (1964); (e) R. L. Cargill and M. R. Willcott, III, *J. Org. Chem.*, **31**, 3938 (1966); (f) D. Scharf and F. Korte, *Tetrahedron Lett.*, 821 (1963).

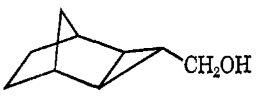
[3] (a) S. J. Cristol, W. K. Seifert, D. W. Johnson, and J. B. Jurale, *J. Amer. Chem. Soc.*, **84**, 3918 (1962); (b) K. Takeuchi, T. Oshika, and Y. Koga, *Bull. Chem. Soc. Jap.*, **38**, 1318 (1965); (c) P. D. Bartlett, Abstracts, 12th National Organic Chemistry Symposium, June 1951, p 1.

[4] (a) R. R. Sauers, J. A. Beisler, and H. Feilich, *J. Org. Chem.*, **32**, 569 (1967); (b) K. B. Wiberg and G. Wenzinger, *ibid.*, **30**, 2278 (1965); (c) A. K. Colter and R. C. Musso, *ibid.*, **30**, 2462 (1965); (d) K. B. Wiberg and W. J. Bartley, *J. Amer. Chem. Soc.*, **82**, 6375 (1960); (e) H. E. Simmons and R. D. Smith, *ibid.*, **81**, 4256 (1959).

[5] For other data on these and related systems, see G. D. Sargent, *Quart. Rev.* (London), **20**, 319 (1966).

[6] R. R. Sauers and P. E. Sonnet, *Tetrahedron*, **20**, 1029 (1964). In the present work variable amounts (12–18%) of an isomer of the *exo-anti* adduct **7** were obtained. That this material was the *exo-syn* adduct was shown by ethoxide-catalyzed epimerization.

with nitrous acid led to a complex mixture of products. The major constituent (44%) was shown to be identical with the carbinol (**10**) obtained by reduction of **7**. The



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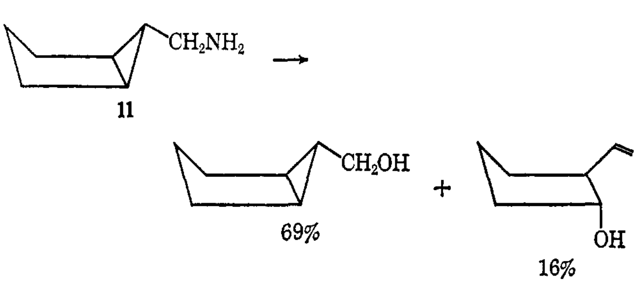
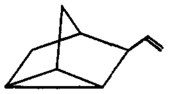
other two important products were present in nearly equal amounts and were characterized as vinyl alcohols as shown by the presence of appropriate infrared and nmr absorptions.[7]

These results are not surprising in view of the recent findings of Bond and Scerbo with the closely related bicyclic system **11**.[8] These workers found no cyclobutyl product in a similar reaction sequence.



In a subsequent experiment, amine **9** was subjected to deamination under poorly solvating conditions.[9] The hydrocarbon fraction (34%) from this reaction was isolated and shown to consist of two isomers in a 7:1 ratio. The major product proved to be 3-vinylnortricyclene (**12**) as shown by degradation to the known acid **13**. The minor constituent was most likely *anti*- or *syn*-7-vinylnorbornene (**14**) as evidenced by the appearance of typical vinyl absorptions superimposed on norbornene absorptions in the infrared and nmr spectra.



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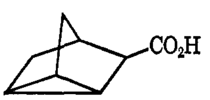

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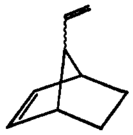

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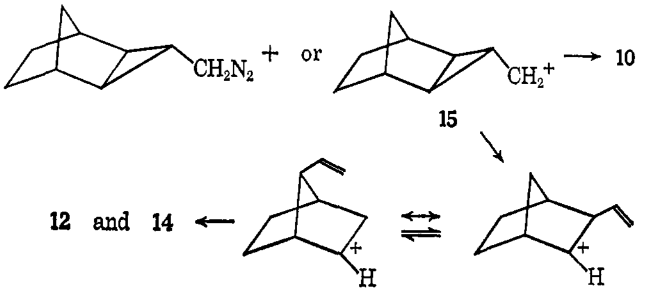
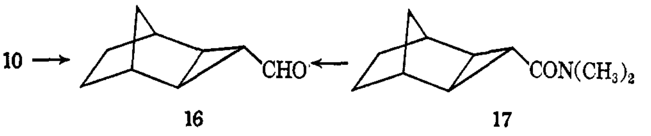
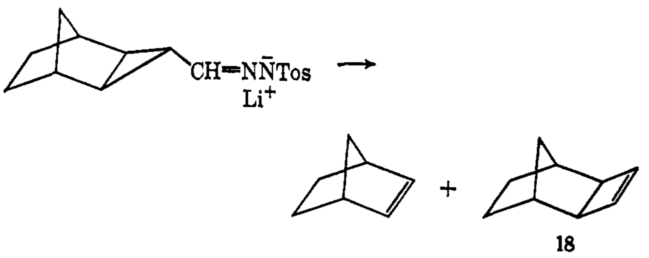
These rearrangements seem best rationalized by competitive ring opening of the cation **15** or the corresponding diazonium ion with the formation of a substituted norbornyl ion. Subsequent loss of a proton or reaction with solvent would lead to the observed products[10] **12** and **14**.



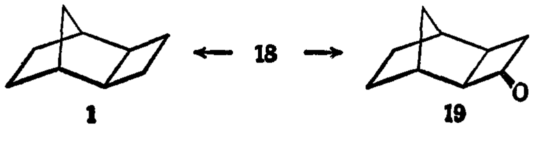
Attention was next turned to the possibility of utilizing carbenic routes. A relatively high degree of success has been attained in the preparation of cyclobutenes from cyclopropylcarbinyl derivatives in this way.[11] In the case at hand, it was necessary to prepare the aldehyde **16** for conversion into the tosylhydrazone. Mild oxidation of alcohol **10** with manganese dioxide[12] or partial reduction[13] of the amide **17** with a mixed hydride both served to produce the aldehyde **16** in modest yields.



Pyrolysis of the lithium salt of the tosylhydrazone of **16** led[14] to a mixture of two hydrocarbons in a 1:3:4 ratio.



The minor product proved to be norbornene. The major product was a C_9H_{12} hydrocarbon which showed a strong absorption at 14.30 μ in the infrared spectrum and two protons as a sharp singlet at 5.85 ppm in the nmr spectrum.[15] Chemical evidence in support of structure **18** was provided by quantitative catalytic reduction to *exo*-tricyclo[4.2.1.$0^{2,5}$]nonane (**1**) which was identical with the sample prepared independently below. In addition, hydroboration of **18** followed by chromic acid oxidation gave a ketone **19** with a carbonyl



absorption band at 5.62 μ in agreement with the cyclobutanone structure.

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(7) The complete structure proofs of these products have not been completed. Evidence for the presence of *syn*-7-vinyl-*exo*-norbornanol is presented in the Ph.D. Thesis of P. E. Sonnet, Rutgers, The State University, 1963. That the other product is not a 3-vinylnorboranol has been shown by P. E. Pfeffer (Ph.D. Thesis, Rutgers, The State University, 1966).

(8) F. T. Bond and L. Scerbo, *Tetrahedron Lett.*, 4255 (1965). For a detailed discussion of the intermediates in these reactions, see K. B. Wiberg and A. J. Ashe, III, *J. Amer. Chem. Soc.*, **90**, 63 (1968), and P. von R. Schleyer and G. W. Van Dine, *ibid.*, **88**, 2321 (1966).

(9) J. Bayless, L. Friedman, J. A. Smith, F. B. Cook, and H. Shechter, *ibid.*, **87**, 661 (1965).

(10) The hydrocarbon fraction from the solvolysis of norbornyl brosylate has been shown to consist of 98% nortricyclene and 2% norbornene. *Cf.* S. Winstein, E. Clippinger, R. Howe, and E. Vogelfanger, *ibid.*, **87**, 376 (1965).

(11) L. Friedman and H. Shechter, *ibid.*, **82**, 1002 (1960); W. Kirmse and K. H. Pook, *Chem. Ber.*, **98**, 4022 (1965).

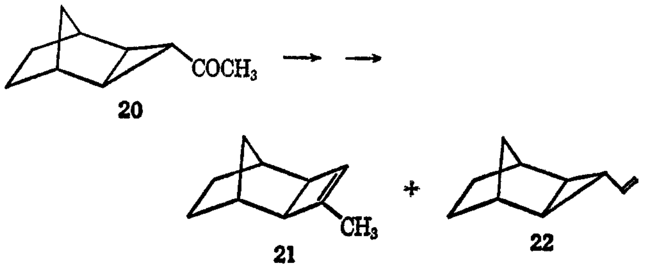
(12) L. Crombie and J. Crossley, *J. Chem. Soc.*, 4983 (1963).

(13) H. C. Brown and A. Tsukamoto, *J. Amer. Chem. Soc.*, **81**, 502 (1959).

(14) G. M. Kaufman, J. A. Smith, G. G. Van der Stouw, and H. Shechter, *ibid.*, **87**, 935 (1965).

(15) Cyclobutene displays a singlet at 5.95 ppm; see S. Borčič and J. D. Roberts, *ibid.*, **87**, 1057 (1965). A compound assigned this structure by M. Hara, Y. Odiara, and S. Tsutsumi [*Tetrahedron*, **22**, 95 (1966)] showed peaks of unspecified multiplicity at 5.87, 2.87, and 2.22 ppm. Our material is apparently *not* the same substance.

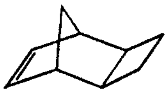
This synthetic method was also extended to the methyl homolog (**21**) *via* a sequence starting with the methyl ketone **20**. A small amount (12%) of a second product was also obtained. Infrared and nmr absorptions characteristic of vinyl groups appeared in the spectra of this product. These findings and analogy[14] support **22** as a reasonable structure for this product.



20

21 **22**

The second phase of the synthetic studies dealt with possible methods for construction of the two tricyclo$[4.2.1.0^{2,5}]$non-7-enes **23** and **24**. These olefins were considered key intermediates for the completion of the mechanistic studies already mentioned.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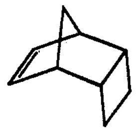
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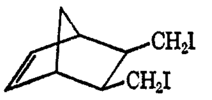

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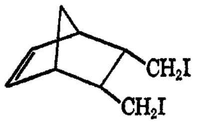

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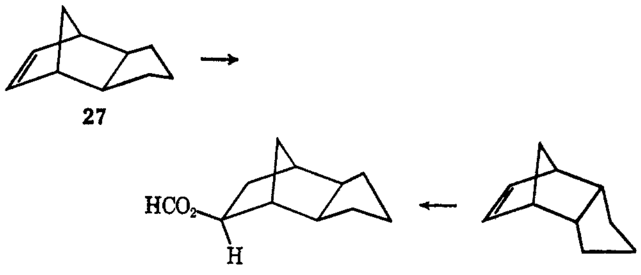
The availability of the two isomeric diiodides **25** and **26**[16] prompted a study of possible ring-closure reactions. Smooth cyclization was effected with phenyllithium in a synthesis patterned after that developed for bicyclo[4.2.0]octane.[17] The nature of the cyclized products was revealed by the presence of absorptions in both the infrared and nmr spectra attributable to norbornene-type double bonds.[18] Quantitative catalytic hydrogenation led to the saturated hydrocarbons **1** and **2** with the absorption of 1 mol of hydrogen in both cases. The identity of the reduction product of **23** with that of **18** firmly establishes the structure and stereochemistry of these compounds.

Addition and Solvolysis Reactions.—In this section product studies of reactions involving carbonium-ion intermediates at C-7 will be discussed. By way of comparison, the homologous series **3** and **4** do not present a completely consistent picture. For example, addition of formic acid to either olefin **27** or **28** produced the formate **29**.[3a] Likewise, acetolysis of any of the four tosylates with gross structure **30** produced the *exo-exo* system **31** as the major product.



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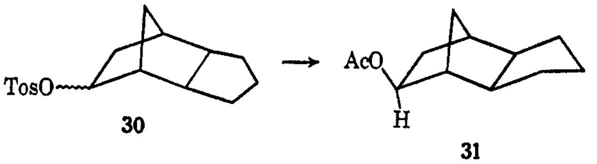
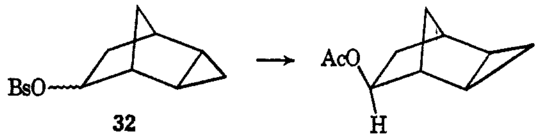
29 **28**

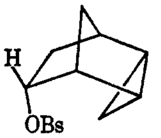


30 **31**

An interesting observation was that only three of the four isomeric tricyclo$[3.2.1.0^{2,4}]$octyl brosylates (**32**) reacted analogously to **27** yielding **33**. The *endo-endo* system **34** apparently underwent a more complex rearrangement.[4b]



32 **33**



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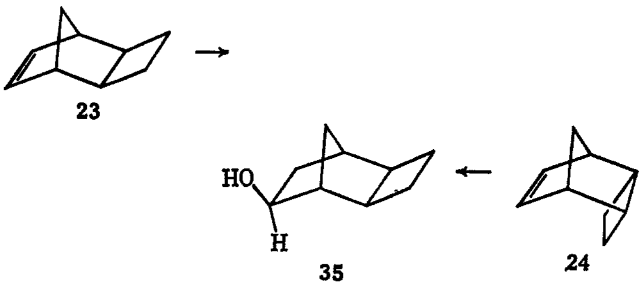
With this background it was not surprising that addition of formic acid to either **23** or **24** yielded essentially the same mixtures of formates in the ratio 98:2. After conversion into alcohols, the major product was isolated and shown to be identical with the hydroboration–oxidation product (**35**) of the *exo* olefin **23**. The reaction sequence clearly produces the product (**35**) with *exo* stereochemistry by analogy with norbornene and **27**.[19] The minor alcohol formed in the addition was assumed to be the *endo* derivative **36** based on retention time comparisons with a sample prepared by hydroboration–oxidation of **24**.[20]



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35 **24**

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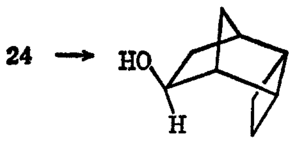
(16) K. Alder and W. Roth, *Chem. Ber.*, **87**, 161 (1954).

(17) K. Alder and H. A. Dortman, *ibid.*, **87**, 1492 (1954).

(18) The chemical shifts of the olefinic protons are sensitive to the stereochemistry of the attached rings. The downfield shift in the absorption of the olefinic protons in **24** relative to **23** of *ca.* 0.5 ppm has also been noted in various norbornadiene dimers by D. R. Arnold, D. J. Trecker, and E. B. Whipple [*J. Amer. Chem. Soc.*, **87**, 2596 (1965)] and attributed to van der Waals interactions.

(19) H. C. Brown and G. Zweifel, *ibid.*, **83**, 2544 (1961); S. J. Cristol, W. K. Seifert, and S. B. Soloway, *ibid.*, **82**, 2351 (1960).

(20) The chemical shifts of the carbinol protons in **35** and **36** provide a clear example of steric deshielding.[18] Whereas the carbinol proton of **35** and *exo*-norbornanol have similar chemical shifts (3.55 and 3.52 ppm, respectively), the analogous proton in **36** appears at 4.37 ppm. For other examples, see S. Winstein, P. Carter, F. A. L. Anet, and A. J. F. Bourn, *ibid.*, **87**, 5247 (1965).



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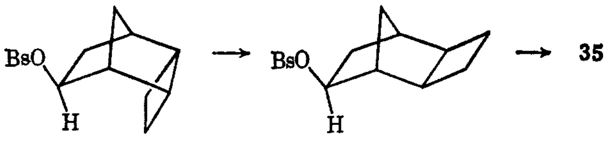
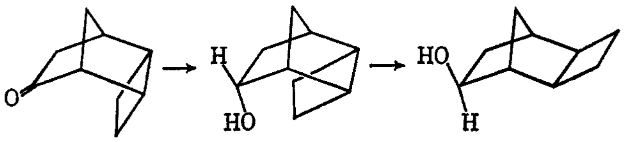
The availability of alcohols **35** and **36** prompted studies of the behavior of their bromobenzenesulfonate esters in buffered acetic acid. Analogous[3b,4b] to the behavior of the higher and lower homologs, **37** underwent a rapid rearrangement at 25° to form the *exo* isomer **38**. At elevated temperatures, acetolysis ensued and the product isolated proved to be the *exo-exo* alcohol **35**.



37 38

Finally, the *endo-endo* brosylate **41** was synthesized *via* the ketone **39** and the alcohol **40**. Acetolysis of **41**, in contrast to the lower homolog produced the *exo-exo* system **35** in 95.5% yield.



39 40 35

Thus, the outcome of the product-forming steps in all but one[4b] of these solvolysis reactions of fused norbornyl derivatives follows a general pattern; namely, predominant *exo* substitution and *exo*-ring junctures.[21] The latter result is most likely a reflection of the greater stability of *exo*-fused bridges.[22] Interpretation of the high degree of stereoselectivity toward *exo* substitution is complex since the exact structure of the intermediate ions is not known with certainty.[23]

Experimental Section

Microanalyses were performed by G. Manser, Herliberg Switzerland; G. Robertson, Florham Park, N. J.; and Micro-Tech Laboratories, Skokie, Ill. Infrared spectra were recorded from carbon tetrachloride solutions or as noted on a Perkin-Elmer Model 21 spectrophotometer. Nuclear magnetic resonance spectra were obtained in carbon tetrachloride solutions with tetramethylsilane as an internal standard on a Varian Model A-60 spectrophotometer. Gas chromatograms were determined on an Aerograph Model A-90 P instrument in the preparative and analytical runs. All columns were 0.25 in. (o.d.) and Chromosorb G was the solid phase. The abbreviations used refer to the following columns: C, Carbowax 20M, 9–15 ft; A, Apiezon L, 9 ft. Capillary gas chromatograms were determined on a Barber-Colman flame ionization system (Model 5000). The column (0.01 in.) was U (Ucon, 50 ft).

Ethyl *exo*-Tricyclo[3.2.1.0^{2,4}]octane-3-*syn*- and -*anti*-carboxylates (7).—The addition of ethyl diazoacetate was carried out as previously described.[6] Gas chromatographic analysis on a 9-ft Apiezon L (190°) column revealed the presence of 12–18% of a second product. The two isomers were separated by gas chromatography and examined separately. The most significant difference in the nmr spectra was the position of the bridgehead protons. The *anti* isomer showed these protons as a singlet at 2.37, whereas in the *syn* epimer they appeared at 2.45 ppm. These two peaks could be seen in the initial mixture of the two. The infrared spectrum of the *anti* isomer showed maxima at 5.77 (s), 6.83, 7.10, 7.63 (s), 7.95 (s), 8.56 (s), 8.80, 9.13, 9.50, and 9.75 μ. The *syn* isomer showed maxima at 5.77 (s), 6.83, 7.12, 7.46, 7.57, 7.72, 8.42 (s), 8.72 (s), 8.85, 8.98, and 9.17 μ.

Epimerization Experiment.—The separated esters were placed in nmr tubes containing ethanol and a small piece of sodium. The spectrum of the substance assigned the *anti* structure remained unchanged over a 40-day period. The other isomer gradually became converted into the *anti* system during this period. Gas chromatographic analysis at the end of the period indicated complete absence of the *syn* isomer and the presence of only the *anti* isomer **7** in both tubes.

***exo*-Tricyclo[3.2.1.0^{2,4}]octane-3-carbinol (10).**—The tricyclic esters (65.5 g, 0.37 mol) were dissolved in 60 ml of ether and the solution was added to a stirred suspension of 15 g (0.39 mol) of lithium aluminum hydride in 600 ml of ether. The resulting mixture was heated at reflux for 4 hr at which time water was added to hydrolyze the salts and to destroy excess hydride. The precipitate was removed and washed with methylene chloride. The combined organic phases were distilled under vacuum, whereupon a residue, bp 85–90° (0.9 mm), was obtained. The yield was 43.8 g (86%).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.20. Found: C, 78.23; H, 10.14.

The nmr spectrum displayed two doublets (J = 7 cps) in the region expected for H–C–O protons at 3.20 and 3.68 ppm. The area ratios were 10:1, respectively. The minor component (presumably) is the *syn*-carbinol. The bridgehead protons appeared at 2.25 ppm.

The 3,5-dinitrobenzoate of **10** was prepared in pyridine and had mp 92–94° after crystallization from methanol.

Anal. Calcd for $C_{16}H_{16}N_2O_6$: C, 57.83; H, 4.85; N, 8.43. Found: C, 57.82; H, 4.91; N, 8.44.

***exo*-Tricyclo[3.2.1.0^{2,4}]octane-3-*anti*-carboxamide (8).**—To a solution of 25 g (0.164 mol) of the acid of **7**[6] in 100 ml of ether was added 98.5 g (0.828 mol) of thionyl chloride over 25 min. The resulting mixture was heated at reflux for 15 hr after which the excess thionyl chloride was removed by distillation under aspirator vacuum. Addition of 150 ml of anhydrous ether to the residue was followed by passage of ammonia gas through the solution for 2 hr. The white precipitate was removed by filtration and extracted with benzene in a Soxhlet apparatus for 24 hr. The extracts and the original ether filtrate were combined and cooled, whereupon 22.2 g (90%) of colorless crystals formed, mp 172–175°. Crystallization from benzene raised the melting point to 173.5–175°.

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.40; H, 8.50; N, 8.98.

***exo*-Tricyclo[3.2.1.0^{2,4}]octane-3-*anti*-carbinylamine (9).**—A solution of 6.0 g (0.040 mol) of amide **8** in 300 ml of benzene was treated with 3.04 g (0.080 mol) of lithium aluminum hydride over a period of 0.5 hr. The resulting slurry was heated at reflux for 20 hr. Hydrolysis was effected by cautious addition of 7.7 ml of water. The salts formed were collected and washed twice with ether. The combined extracts were evaporated to yield 5.42 g (92%) of an oil which was characterized by the preparation of the phenylurea derivative, mp 158–159.5°.

Anal. Calcd for $C_{16}H_{20}N_2O$: C, 74.96; H, 7.86; N, 10.93. Found: C, 74.94; H, 8.01; N, 10.88.

Nitrous Acid Deamination of 9.—A solution of 1.5 g (0.01 mol) of amine **9** in 62 ml of glacial acetic acid was cooled and treated with 8.01 g (0.010 mol) of sodium nitrite. The resulting solution was stirred at room temperature for 24 hr after which it was poured into a cold aqueous solution which contained an excess of sodium carbonate. The crude acetates were removed by ether extraction. The dried ($MgSO_4$) extracts were added dropwise to a stirred suspension of 0.50 g (0.013 mol) of lithium aluminum hydride in 50 ml of ether. After stirring for 2 hr the reaction mixture was treated with water. The precipitate was collected and washed with ether. The combined extracts were washed with dilute hydrochloric acid, sodium carbonate solution, and water. Removal of the ether yielded 1.04 g (69%) of product. Analysis of the mixture by gas chromatography (C, 175°) indicated the presence of three major components in the

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[21] The recent results of R. Baker and J. Hudec, *Chem. Commun.*, 929 (1967) with the benzotricyclo[4.2.1.0^{2,5}] nonyl system also are consistent with this generalization.

[22] P. von R. Schleyer and M. M. Donaldson, *J. Amer. Chem. Soc.*, **82**, 4645 (1960).

[23] For references and a recent discussion of this problem, see P. von R. Schleyer, *ibid.*, **89**, 701 (1967).

ratio 1:1:1.6. The last peak proved to be identical in retention time with **10**. The nmr spectrum of a collected sample was superimposable on the spectrum of **10**.

The first two components were collected and submitted for elemental analysis.

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.20. Found for peak 1: C, 78.11; H, 10.24. Found for peak 2: C, 78.40; H, 10.21.

The nmr spectrum of peak 1 showed complex vinyl absorption extending from 6.2 to 5.0 ppm and strong vinyl absorptions in the infrared spectrum at 9.9, 10.0, 10.3, and 11.0 μ. The second peak likewise showed nmr absorptions from 5.7 to 5.0 ppm (3 H) and strong infrared maxima at 9.9, 10.1, and 11.0 μ.

Isoamyl Nitrite Deamination of 9.[9]—A solution of 2 g (0.013 mol) of amine **9** in 50 ml of chloroform was treated successively with 1.3 g (0.01 mol) of isoamyl nitrite and 0.66 g (0.01 mol) of acetic acid. The resulting solution was heated at reflux for 12 hr. Sodium carbonate solution was added to neutralize the acid. Evaporation of the chloroform yielded 0.54 g of an oil, bp 135–145°. Gas chromatographic analysis (D, 95°) revealed two major peaks in the ratio 1:7. The nmr spectrum of the minor product displayed a complex vinyl group pattern extending from 4.8 to 6.15 ppm. Superimposed were absorptions due to norbornene olefinic protons at 5.90 ppm. The total relative area of the low field protons was 5. Bridgehead proton absorption (2 H) appeared at 2.85 ppm and other complex absorptions (5 H) extended from 2.20 to 0.8 ppm. The infrared spectrum displayed strong absorptions at 7.5 and 11.0 μ characteristic of vinyl groups.

The major product **12** likewise displayed a complex vinyl group pattern (3 H) centered at 5.38 ppm in the nmr spectrum. The infrared spectrum displayed vinyl group absorptions at 7.2, 10.2, and 11.05 μ.

Anal. Calcd for C_9H_{12}: C, 89.93; H, 10.07. Found: C, 89.95; H, 9.97.

The high boiling (75–85° at 0.25 mm) fraction of the product was converted into alcohols with lithium aluminum hydride and shown to consist of the rearranged alcohols and **10** in the ratios 1:1:10, respectively. The yield of the alcohols was 0.77 g (38%).

Ozonolysis of 12.—Ozone was passed through a solution of 0.10 g of the mixed olefinic products of the preceding experiment in 10 ml of methanol at 0°. After warming to room temperature a solution of 1.6 g of sodium hydroxide in 25 ml of water was added followed by 4.0 ml of 30% hydrogen peroxide solution. The resulting solution was heated at reflux for 12 hr and then evaporated in a stream of air. Acidification followed by ether extraction yielded 0.075 g of crude acid. Crystallization from pentane gave 0.015 g of **13**, mp 48–50° (lit.[24] mp 48–50°). Infrared and nmr spectra were identical with those of an authentic sample upon comparison.

***exo*-Tricyclo[3.2.1.$0^{2,4}$]octane-3-*anti*-carboxaldehyde (16). Hydride Reduction of Amide 17.**—The dimethylamide **17** was prepared using the same procedure as was used for the unsubstituted amide. From 11.5 g of the acid of **7**[6] there was obtained 11.07 g (83%) of amide **17**, mp 84.5–86°.

Anal. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.63; H, 9.64; N, 7.78.

The methyl protons appeared as a broad singlet (6 H) at 2.95 ppm in the nmr spectrum. Amide carbonyl absorption appeared at 6.12 μ in the infrared spectrum.

The reduction was carried out according to the procedure of Brown and Tsukamoto[13] using a solution of mixed hydride prepared from 1.5 g (0.039 mol) of lithium aluminum hydride and 3.5 g (0.040 mol) of ethyl acetate in 87 ml of ether. The resulting solution was added to a stirred solution of 11.0 g (0.062 mol) of amide **17** in 43 ml of ether at 0°. The resulting mixture was heated at reflux for 1.5 hr and hydrolyzed with sulfuric acid. The salts were removed by filtration and the filtrate was evaporated to give 3.69 g (43%) of a liquid, bp 60–80° (1 mm). Gas chromatography (C, 145°) revealed two major products in the ratio 1:5.6. The major product proved to be aldehyde **16** as determined by nmr absorptions at 9.1 (1 H, doublet J = 5 cps), 2.45 (2 H), 1.28 (1 H, quintuplet, 2.5 cps splitting), and complex absorptions between 1.45–0.5 ppm. The infrared spectrum showed carbonyl absorption at 5.85 μ.

The 2,4-dinitrophenylhydrazone had mp 208.5–209.5° after crystallization from ethanol–ethyl acetate.

Anal. Calcd for $C_{15}H_{16}N_4O_4$: C, 56.96; H, 5.10; N, 17.71. Found: C, 56.69; H, 5.15; N, 17.36.

Manganese Dioxide Oxidation of 10.[12]—A solution of 5 g (0.036 mol) of **10** in 350 ml of methylene chloride was stirred with 75 g of manganese dioxide[25] for 2 hr at reflux. The mixture was filtered and the solids were washed with more methylene chloride. The combined extracts were washed with sodium carbonate solution prior to evaporation. There was obtained 3.35 g (68%) of aldehyde **16**, bp 70° (1 mm), on distillation of the residue.

***exo*-Tricyclo[4.2.1.$0^{2,5}$]non-3-ene (18).**—The tosylhydrazone of **16** was prepared by the procedure of Kirmse and Pook[11] and had mp 118–120°.

Anal. Calcd for $C_{16}H_{20}N_2O_2S$: C, 63.12; H, 6.57; N, 9.20. Found: C, 62.73; H, 6.59; N, 9.44.

To a solution of 5.50 g (0.018 mol) of the tosylhydrazone in 100 ml of dry tetrahydrofuran was added 11.35 ml of 1.6 M butyllithium in n-hexane (0018 mol). After stirring for 30 min the solvents were removed on a rotary evaporator at aspirator pressure. The last traces of solvents were removed with a vacuum pump at 0.25 mm and 40°. The salt was then pyrolyzed at 95–110° (0.25 mm) over 45 min. The volatile products (0.65 g) were collected in a Dry Ice trap as an orange oil which showed absorptions at 4.90 and 4.50 μ in the infrared spectrum. On standing, the color disappeared. Gas chromatography of this material (A, 145°) revealed two components in the ratio 1:3.4. The minor component proved to be norbornene by comparison of its infrared spectrum with that of an authentic sample. The major product **18** showed a singlet (2 H) at 5.85, a singlet (2 H) at 2.45, a broad singlet (2 H) at 1.90, and a complex multiplet (6 H) centered at 1.2 ppm. The infrared spectrum showed absorptions at 3.22, 3.30, 3.42 (s), 3.49, 6.44 (w), 6.80, 7.74, 11.95, and 14.30 (vs) μ.

Anal. Calcd for C_9H_{12}: C, 89.94; H, 10.06. Found: C, 90.13; H, 10.06.

Catalytic Reduction of 18.—A solution of 0.10 g of **18** in 3 ml of ether was reduced with hydrogen in the presence of platinum oxide. Within 20 min hydrogen uptake (96%) had ceased. Gas chromatography (A, 160°) revealed one component. Infrared and nmr spectra were identical with those of the sample of **1** prepared below.

***exo*-Tricyclo[4.2.1.$0^{2,5}$]nonan-3-ol.**—Addition of 5.5 ml of 0.5 M diborane solution to a solution of 1.97 g of the mixture of **18** and norbornene in 40 ml of tetrahyrofuran was followed by stirring at 25° for 2 hr. The boranes were oxidized by addition of 1.82 ml of 3 N sodium hydroxide solution followed by 1.82 ml of 30% hydrogen peroxide. The reaction mixture was poured into 200 ml of water and extracted with ether. The combined extracts were washed with sodium bisulfite solution prior to evaporation. A viscous oil (1.43 g) was obtained which displayed two main peaks on gas chromatography (C, 150°) in the ratio 1:3.4. The minor peak had the same retention time as *exo*-norbornanol. The major product displayed a complex nmr peak at 3.75 ppm assigned to the proton adjacent to the hydroxyl group. The infrared spectrum showed absorptions at 3.00 (s), 3.45 (s), 6.85, 7.02, 8.65, and 9.50 μ.

Anal. Calcd for $C_9H_{14}O$: C, 78.20; H, 10.15. Found: C, 78.51; H, 10.32.

***exo*-Tricyclo[4.2.1.$0^{2,5}$]nonan-3-one (19).**—The above mixture of alcohols was oxidized using a two-phase system[26] of ether and sodium dichlormate solution. The oxidation of 0.4 g of alcohols was incomplete after 12 hr as shown by gas chromatography. Preparative gas chromatography (C, 165°) yielded 0.11 g of ketone **19** as an oil. The infrared spectrum showed a strong carbonyl absorption at 5.62 μ. Other absorptions appeared at 6.75, 6,80, 7.20, 7.55, 7.70, 9.22 (s), and 11.70 (s) μ.

Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.68; H, 9.07.

3-*anti*-Acetyl-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane (20).—To a stirred solution of 16.5 g (0.11 mol) of the acid of **7**[6] in 100 ml of ether was added 175 ml of 1.67 M methyllithium (0.29 mol) in ether. The addition required 2 hr and was followed by stirring 4.5 hr at reflux temperature. Hydrolysis was effected by addition of 200 ml of water. The organic layer was washed with saturated ammonium chloride solution and water. The aqueous layer was neutralized with ammonium chloride and extracted with ether.

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[24] J. D. Roberts, E. R. Trumbull, Jr., W. Bennett, and R. Armstrong, *J. Amer. Chem. Soc.*, **72**, 3116 (1950).

[25] J. Attenburrow, A. F. Cameron, J. H. Chapman, R. M. Evans, B. A. Heins, A. B. Jansen, and T. Walker, *J. Chem. Soc.*, 1094 (1952).

[26] H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, **83**, 2952 (1961).

The combined extracts were dried ($MgSO_4$) and evaporated to give 13.8 g (85%) of a crude solid. Two components in the ratio of 1:9 were present as shown by gas chromatography (C, 170°). The major constituent was isolated and had mp 38–40°.

Anal. Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 80.00; H, 9.41.

Infrared absorptions ($CHCl_3$) appeared at 3.30, 5.90 (s), 7.20, 7.60, 8.40, 8.60, 10.90, and 11.80 μ. The nmr spectrum showed a sharp singlet (3 H) at 2.10, bridgehead protons (2 H) at 2.25, and other complex peaks (9 H) in the high field region from 1.8 to 1.0 ppm.

The tosylhydrazone of **20** was prepared in boiling 60% aqueous methanol and had mp 158.0–159.0° after crystallization from methanol.

Anal. Calcd for $C_{17}H_{22}N_2SO_2$: C, 64.12; H, 6.96; N, 8.80. Found: C, 64.18; H, 6.92; N, 8.74.

***exo*-3-Methyltricyclo[4.2.1.0^{2,5}]non-3-ene** (**21**).—The lithium salt of the above tosylhydrazone was prepared and pyrolyzed by the above procedure. From 4.06 g there was obtained 2.4 g of a light yellow oil. Gas chromatography (C, 95°) indicated two components in the area ratio 13:87. The nmr spectrum of the major component was consistent with structure **21** in showing a broad singlet (1 H) at 5.60, broad singlets at 2.30 (2 H), and 1.90 (2 H) and complex high field absorptions (9 H) superimposed on a sharp singlet between 0.8 and 1.8 ppm. The infrared spectrum displayed absorptions at 3.35, 3.41, 6.17, 6.96 (s), 7.30, 7.60, 7.75 and 12.50 (s) μ.

Anal. Calcd for $C_{10}H_{14}$: C, 89.49; H, 10.51. Found: C, 89.54; H, 10.43.

The minor component presumably had structure **22** as evidenced by the appearance of vinyl absorptions at 4.9 (3 H) in the nmr spectrum and strong infrared absorptions at 10.15, 11.3, and 12.05 μ.

Anal. Calcd for $C_{10}H_{14}$: C, 89.49; H, 10.51. Found: C, 89.45; H, 10.65.

***endo*-Tricyclo[4.2.1.0^{2,5}]non-7-ene** (**24**).—The diiodide **26** was prepared as described by Alder and Roth[16] and was obtained as a yellow oil in agreement with the literature. The crude product (59.0 g, 0.16 mol) in 100 ml of ether was added rapidly to an ice-cold solution of phenyllithium which had been prepared from 7.0 g (1 g-atom) of lithium and 33.0 g (0.21 mol) of bromobenzene in 100 ml of ether. After stirring at 25° for 2 hr the reaction mixture was filtered through a Büchner funnel (no paper) onto crushed Dry Ice. After the mixture warmed to room temperature, 500 ml of water was added. The ether layer was washed with water, dried, and distilled through a short Vigreux column. The residual oil was distilled in a Holzman column to yield 13.99 g of a colorless oil, bp 81–84° (67–68 mm). Gas chromatographic analysis (A, 135°) revealed 18% of an impurity. A pure sample was collected and had mp 54.5–55.5°.

Anal. Calcd for C_9H_{12}: C, 89.93; H, 10.07. Found: C, 89.66; H, 10.28.

The infrared spectrum of **24** displayed absorptions at 3.22, 6.02 (s), 6.13 (w), 6.36 (w), 10.93, 11.17, 11.43, and 14.42 (s) μ. The nmr spectrum consisted of a poorly resolved triplet (2 H) at 6.34, a broad multiplet (4 H) at 2.68, and complex absorption (6 H) between 2.28 and 0.69 ppm.

***exo*-Tricyclo[4.2.1.0.^{2,5}]non-7-ene** (**23**).—The *exo*-diiodide was prepared according to the literature[16] and was obtained as a crystalline solid, mp 48.5–50° (lit.[16] oil). Cyclization was effected as in the previous experiment on 31.8 g (0.085 mol) of **25**. The distilled product (8.04 g) was collected between 41 and 43° (14–15 mm) and was 90% homogeneous. A pure sample of **23** was collected by gas chromatography (A, 135°).

Anal. Calcd for C_9H_{12}: C, 89.93; H, 10.07. Found: C, 89.68; H, 9.93.

The infrared spectrum of **23** showed absorptions at 3.17, 6.41 (w), 6.23 (w), 6.06 (s), 11.04, 11.20, and 14.57 (s) μ. The nmr spectrum consisted of a poorly resolved triplet at 5.89 (2 H), a multiplet at 2.57 (2 H), and complex absorption (8 H) between 2.38 and 0.83 ppm.

***exo*-Tricyclo[4.2.1.0^{2,5}]nonane** (**1**).—Catalytic reduction of 0.512 g of **23** in 5 ml of anhydrous ether was rapid in the presence of platinum oxide. The product was isolated as an oil by gas chromatography (A, 135°).

Anal. Calcd for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.27; H, 11.50.

Double-bond absorptions were absent in the nmr spectrum. Two broad areas of absorption were seen of equal integrated centered area at 2.03 and 1.2 ppm. Distinctive infrared absorptions appeared at 10.42, 10.68, and 11.01 μ.

***endo*-Tricyclo[4.2.1.0^{2,5}]nonane** (**2**).—The *endo* olefin **24** was similarly hydrogenated. Purification by gas chromatography gave a solid, mp 62–63° (sealed capillary).

Anal. Calcd for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.10; H, 11.63.

The nmr spectrum displayed extremely complex absorptions between 3.00 and 0.94 ppm. The infrared spectrum showed strong bands at 11.51, 10.44, and 9.92 μ.

Addition of Formic Acid to 23 and 24.—In separate experiments, mixtures of 0.20 g of **23** and 1.0 ml of 97% formic acid and 0.135 g of **24** and 1.0 ml of formic acid were shaken vigorously for 4 days. Both reactions were homogeneous at this time. The solutions were quenched with 10 ml of water and the products were extracted into ether. After washing with sodium bicarbonate solution and water, the extracts were evaporated. The crude formates were reduced with lithium aluminum hydride in ether. From the *exo* olefin, there was obtained 80 mg (50%) of crude alcohols. From the *endo* olefin there was obtained 140 mg (61%) of crude alcohols. Gas chromatography (C, 170°) revealed two products in 97:3 and 99:1 ratios from the two experiments. The major product was collected in both cases and shown to be identical with *exo*-7-hydroxy-*exo*-tricyclo[4.2.1.0^{2,5}]nonane (**35**) by comparative infrared and nmr spectra. The minor peak had a retention time identical with that of **36** (U, 115°).

***exo*-7-Hydroxy-*exo*-tricyclo[4.2.1.0^{2,5}]nonane** (**35**).—Hydroboration–oxidation of **23** was carried out as described by Brown and coworkers[19] using the sodium borohydride–boron trifluoride etherate system in tetrahydrofuran. From 2.40 g of olefin there was obtained 1.65 g (60%) of a viscous oil, bp 77–84° (0.2 mm). Purity was assessed at greater than 95% by gas chromatography (C, 170°).

Anal. Calcd for $C_9H_{14}O$: C, 78.22; H, 10.21. Found: C, 78.17; H, 10.00.

The nmr spectrum consisted of a multiplet (1 H) centered at 3.55, a singlet (OH) at 2.73, and complex peaks (12 H) between 2.40 and 0.95 ppm. The infrared spectrum showed absorptions at 11.26, 11.00, 10.82, and 10.37 μ.

The *p*-bromobenzenesulfonate **38** was prepared in pyridine and had mp 62.5–63.5° on crystallization from petroleum ether (30–60°).

Anal. Calcd for $C_{15}H_{17}BrO_3S$: C, 50.43; H, 4.80; Br, 22.37. Found: C, 50.70; H, 4.90; Br, 22.13.

***exo*-7-Hydroxy-*endo*-tricyclo[4.2.1.0^{2,5}]nonane** (**36**).—The *endo* olefin (**24**) was similarly converted into the alcohol in 72% yield. The product was purified by gas chromatography (C, 170°) and had mp 56–60° (sealed capillary).

Anal. Calcd for $C_9H_{14}O$: C, 78.22; H, 10.21. Found: C, 78.37; H, 10.26.

The nmr spectrum showed a doublet at 4.37 (1 H), a singlet at 2.28 (OH) and complex absorption (12 H) extending from 3.00 to 0.83 ppm. The infrared spectrum had peaks at 11.14, 10.85, 10.08, and 9.86 μ.

The *p*-bromobenzenesulfonate derivative **37** had mp 83.7–84.7° after crystallization from petroleum ether (30–60°).

Anal. Calcd for $C_{15}H_{17}BrO_3S$: C, 50.43; H, 4.80; Br, 22.37. Found: C, 50.47; H, 4.90; Br, 22.38.

Acetolyses Products.—The brosylate **37** was shown to rearrange rapidly to the *exo-exo* isomer **38** at room temperature in glacial acetic acid–sodium acetate solution. The reaction could be followed by nmr spectroscopy. From 53 mg of **37** in 0.50 ml of acetic acid there was recovered 44 mg of crude **38** after 18 hr at 25°. After crystallization the melting point was 59.0–60.5°. A preparative acetolysis on 2.73 g of **37** in 25 ml glacial acetic acid which contained 0.7 g of sodium acetate was carried out for 20 hr at 90°. Quenching with water and ether extraction gave 1.57 g of crude acetates. Reduction with lithium aluminum hydride in ether gave essentially pure *exo*-7-hydroxy-*exo*-tricyclo[4.2.1.0^{2,5}]nonane (0.63 g, 60%) as shown by gas chromatography and comparative nmr spectroscopy.

***endo*-Tricyclo[4.2.1.0^{2,5}]nonan-7-one** (**39**).—The alcohol **36** was oxidized in a two-phase ether–water system[26] From 1.106 g (8.0 mmol) of **36**, there was obtained 289 mg of crude product which contained 17% of unreacted alcohol by gas chromatography (C, 170°). A preparatively purified sample of the ketone had mp 91.2–93.2° (sealed capillary).

Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.68; H, 8.99.

The infrared spectrum revealed a strong carbonyl absorption at 5.71 μ.

The 2,4-dinitrophenylhydrazone was prepared and recrystallized from ethanol–ethyl acetate mixtures, mp 159.0–160.0°.

Anal. Calcd for $C_{15}H_{16}N_4O_4$: C, 56.96; H, 5.09; N, 17.71. Found: C, 57.08; H, 5.33; N, 17.52.

The same ketone was obtained *via* manganese dioxide oxidation in methylene chloride and by Sarett oxidation.[27] The yields in the latter case (43%) were superior to those in the other procedures.

endo-7-Hydroxy-*endo*-tricyclo$[4.2.1.0^{2,5}]$nonane (40).—The ketone **39** was reduced with lithium aluminum hydride in ether. From 3.29 g (24 mmol) of **39** there was obtained 2.48 g of alcohol. Gas chromatography (C, 170°) revealed the presence of *ca.* 6% of alcohol **36**. A pure sample of **40** was collected for analysis.

Anal. Calcd for $C_9H_{14}O$: C, 78.22; H, 10.21. Found: C, 77.95; H, 10.29.

The infrared spectrum displayed distinctive absorptions at 10.53, 11.12, and 11.39 μ. The nmr spectrum showed a broad multiplet (1 H) at 4.45 attributed to the H–C–O proton and complex absorptions extending from 3.20 to 0.83 ppm.

The bromobenzene sulfonate **41** was recrystallized from petroleum ether (30–60°) and had mp 82.8–83.8°.

Anal. Calcd for $C_{15}H_{17}BrO_3S$: C, 50.43; H, 4.80; Br, 22.37. Found: C, 50.44; H, 4.56; Br, 22.56.

Acetolysis of brosylate **41** by the above procedure led to a 58% yield of alcohols which contained 95.5% **35**, 3% **26**, and 1.5% **40**, as shown by gas chromatography (U, 115°). The major component was isolated by preparative gas chromatography (C, 170°) and shown by nmr spectroscopy to be identical with **35**. The small amount of **40** found may have resulted from reduction of unreacted **41** (sulfide odor).

Registry No.—**1,** 16526-27-5; **2,** 16526-28-6; *exo-syn* **7,** 16545-17-8; *exo-anti* **7,** 16529-68-3; **8,** 16529-69-4; **9,** 16529-70-7; **10,** 16529-71-8; **10** 3,5-dinitrobenzoate, 10414-10-5; **12,** 16545-19-0; **16,** 16529-72-9; **16** 2,4-dinitrophenylhydrazone, 16529-73-0; **16** tosylhydrazone, 16529-74-1; **17,** 16529-75-2; **18,** 16529-76-3; **19,** 16529-77-4; *exo*-tricyclo$[4.2.1.0^{2,5}]$nonan-3-ol, 16545-20-3; **20,** 16529-78-5; **20** tosylhydrazone, 16529-79-6; **21,** 16529-80-9; **22,** 16529-81-0; **23,** 16529-82-1; **24,** 16529-83-2; **35,** 16529-84-3; **36,** 16529-91-2; **37,** 16529-85-4; **38,** 16529-86-5; **39,** 16529-87-6; **39** 2,4-dinitrophenylhydrazone, 16529-90-1; **40,** 16529-88-7; **41,** 16529-89-8.

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[27] G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Amer. Chem. Soc.*, **75**, 422 (1953); see also S. J. Cristol, W. K. Seifert, and S. B. Soloway, *ibid.*, **82**, 2351 (1960).

Synthesis of (−)-(3*S*)- and (+)-(3*R*)-4-Methyl-3D1-pentan-1-ols and (−)-(3*S*)- and (+)-(3*R*)-3D1-Isocaproic Acids[1a,b]

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The (+)-(3*R*)- and (−)-(3*S*)-hydroxytetrahydropyranyl ethers (IVb) were prepared by asymmetric reduction of the keto ether (V) using (+)- and (−)-diisopinocampheylborane,[3] respectively. The absolute configurations at C-3 of the two hydroxy ethers were determined by the method of Horeau and the results were rationalized on the basis of Brown's model for the (+)- and (−)-diisopinocampheylboranes. The enantiomeric hydroxy ethers were converted into the mesylates and hydrogenolyzed with lithium aluminum deuteride. It is assumed that introduction of deuterium proceeded with inversion at the asymmetric center. However, in addition to hydrogenolysis, other significant side reactions were noted. Removal of the tetrahydropyranyl moiety from the resulting (−)-(3*S*)-3D1 and (+)-(3*R*)-3D1 ethers (VIb) gave the alcohols (VIa) which were oxidized to the corresponding (−)-(3*S*)-3D1 and (+)-(3*R*)-3D1 acids (VII).

For studies of the biosynthesis of polyisoprenoids the enantiomeric (3*R*)- and (3*S*)-3D1-4-methylpentan-1-ols and (3*R*)- and (3*S*)-3D1-4-methylpentanoic acids were required. The synthesis of the four specimens and their configurational assignments are described.

Two synthetic approaches were projected both of which were based on the use of optically active dialkylboranes.[2] In one instance it was planned to hydroborate asymmetrically the olefin $(CH_3)_2C{=}CHCH_2R$ (II or III) (Figure 1) and displace stereospecifically the derived hydroxyl with deuterium. The alternative route, which proved successful, consisted of the asymmetric reduction of the carbonyl in $(CH_3)_2CHCOCH_2CH_2R$ (V) and subsequent displacement of the hydroxyl with deuterium.

Diisopinocampheylborane has been used as a highly selective reagent for the preparation of optically active alcohols from olefins and ketones.[2,3] Recently Streitwieser, *et al.*,[4] employed optically active diisopinocampheylborane to synthesize optically active 1-butanol-1-D from *cis*-1-butene-1-D. Preparation of optically active benzyl alcohol-1-D by reduction of benzaldehyde with diisopinocampheyldeuterioborane has also been reported.[5] The reduction of carbonyl groups with fermenting yeast is not practical for α-branched ketones.[6]

The starting material for the syntheses, methyl 4-methyl-3-pentenoate (IIb), was prepared from I,

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