Tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one. Preparation, Characterization, and Physical and Chemical Properties[1]

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The preparation, characterization, and physical and chemical properties of tetracyclo[3.3.0.0^{2,8}.0^{4,6}]*octan-3-one* (**1**), *tetracyclo*[3.3.0.0^{2,8}.0^{4,6}]*octane, 3-methylenetetracyclo*[3.3.0.0^{2,8}.0^{4,6}]*octane, and bicyclo*[3.2.1]*oct-6-en-3-one are described.*

α-Cyclopropyl substitution has been shown to cause bathochromic shifts in the electronic absorption spectra of ketones,[3] olefins,[4] and aromatic compounds[5]; and the cyclopropane ring is known to participate in solvolytic reactions of carbinyl esters and halides.[6,7] Optimum orientation of this substituent in its interaction with adjacent, electron-deficient centers is still in doubt. In the present manuscript, we report the synthesis and some chemical and physical properties of tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one (**1**). The unique geometry of this compound requires a cross-conjugated dicyclopropyl ketone in which the two planes of the three-membered rings are at angles of ~117° with the plane of the carbonyl group.[8]

Bromination of 3-bromobicyclo[3.2.1]octa-2,5-diene (**2**)[9] in ether at $-10°$ led to a high yield of a sharp-melting, crystalline tribromide. The n.m.r. spectrum of this product (δ = 6.14 p.p.m., 1 H, doublet of doublets; δ = 4.45 p.p.m., 1 H, singlet; and δ = 4.35 p.p.m., 1 H, triplet) indicated a rearranged structure, that of either *exo-anti*-3,6,8-tribromobicyclo[3.2.1]oct-2-ene (**3a**) or the *exo-anti*-3,7,8-tribromo isomer **3b**. Although our data are as yet insufficient to distinguish these, the latter (**3b**) is favored because *exo* addition at C-6 of **2** could lead to a carbonium ion stabilized by homoallylic resonance; subsequent attack by bromide at C-1 would afford **3b**.

Hydrolysis of **3** in aqueous ethanol containing sulfuric acid furnished the bromo ketone **4a**, *anti*-8-bromotricyclo[3.2.1.0^{2,7}]octan-3-one. The n.m.r. spectrum of **4a** showed the C-8 hydrogen atom as a singlet at δ = 4.34 p.p.m., and the infrared spectrum had $\nu_{\max}^{\mathrm{CHCl_3}}$ 1720 cm.$^{-1}$. The dipole moment was found to be 1.71 ± 0.03 D., which is in good agreement with the calculated value (1.77 D.), assuming μ (C=O) = 3.0 D. and μ (C—Br) = 2.15 D. The moment calculated for the epimeric ketone was 4.92 D. When the hydrolysis of **3b** was performed in a deuterated medium, the bromo ketone **4b** containing 2.65 atoms of deuterium (65% d_3, 35% d_2) was isolated. Acid-catalyzed exchange of the enolizable deuterium atoms of **4b** gave the bromo ketone containing 95% of one deuterium atom (**4c**), and acid-catalyzed deuterium exchange of **4a** led to the introduction of 97.5% of two deuterium atoms (**4d**, 95% d_2, 5% d_1). The mass spectra of the bromo ketones **4a–d** gave the deuterium content, and the major fragmentation patterns may be given as

$$\mathrm{M^+} \longrightarrow \mathrm{Br\cdot} + \mathrm{C_8H_9O^+} \longrightarrow \mathrm{CH_2{=}C{=}O} + \mathrm{C_6H_7^+}$$
$$\mathrm{C_8H_9O^+} \longrightarrow \mathrm{CO} + \mathrm{C_7H_9^+} \longrightarrow \mathrm{C_7H_7^+}$$

These data suggest the positional assignment of the nonexchangeable deuterium atom in **4b** and **4c** as C-2, and make it appear certain that incorporation of deuterium into this position must occur *before* closure of the three-membered ring. A reasonable mechanism for the formation of **4** is given in eq. 1; it may be noted that interconversion between the tricyclic bromo ketone **4** and the unsaturated bicyclic ketone **7** (as the enol) is not established under these conditions, since this process would likely require that deuterium be incorporated into position 6(7) of **4**.

When the bromo ketone **4** was treated with potassium *t*-butoxide in *t*-butyl alcohol an excellent yield of a halogen-free ketone **1** was obtained. The structure of **1**, tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one, followed from its mass spectrum[1] and the absence of vinyl hydrogens in the n.m.r. spectrum. The two most striking physical properties measured for **1** are the low carbonyl frequency, $\nu_{\max}^{\mathrm{CCl_4}}$ 1731 ± 2 cm.$^{-1}$, and the unusually high dipole moment, μ = 3.74 ± 0.03 D. These latter values suggest a high degree of charge separation in **1** (*cf.* **6**), a fact supported by the observations that **1** shows a longer retention time on gas chromatography than alcohols of similar structure and that **1** is water soluble but does *not hydrate*. Similar properties have been observed for quadricyclanone.[10]

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[1] A preliminary communication describing a portion of this work has appeared: N. A. LeBel, A. G. Phillips, and R. N. Liesemer, *J. Am. Chem. Soc.*, **86**, 1876 (1964).

[2] Alfred P. Sloan Foundation Fellow, 1961–1965.

[3] E. M. Kosower and M. Ito, *Proc. Chem. Soc.*, 25 (1962).

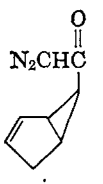
[4] R. Fuchs, C. A. Kaplan, J. J. Bloomfield, and L. F. Hatch, *J. Org. Chem.*, **27**, 733 (1962).

[5] A. L. Goodman and R. H. Eastman, *J. Am. Chem. Soc.*, **86**, 908 (1964).

[6] E. F. Cox, M. C. Caserio, M. S. Silver, and J. D. Roberts, *ibid.*, **83**, 2719 (1961).

[7] H. Hart and P. A. Law, *ibid.*, **86**, 1957 (1964).

[8] Subsequent to our initial report of the synthesis of **1**, two other approaches to this compound have been revealed, both of which utilize the bicyclic diazo ketone i. Copper-catalyzed decomposition of i afforded a 30% yield of crude **1** [J. Meinwald and G. P. Wahl, Jr., *Chem. Ind.* (London), 425 (1965)], whereas photolysis of i furnished a mixture of which **1** was a minor product [P. K. Freeman and D. G. Kuper, *ibid.*, 424 (1965)].[8a]

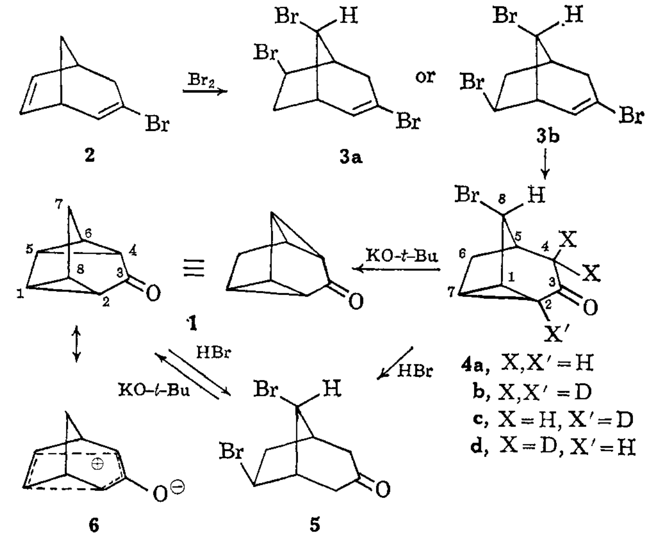


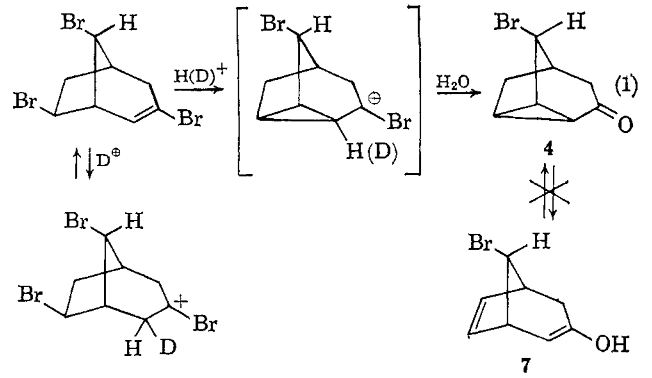
i

[8a] NOTE ADDED IN PROOF. Another approach to this tetracyclic system is photolysis of tricyclo[3.2.1.0^{2,4}]oct-6-ene derivatives: H. Prinzbach, W. Eberbach, and G. von Veh, *Angew. Chem.*, **77**, 455 (1965).

[9] W. R. Moore, W. R. Moser, and J. E. LaPrade, *J. Org. Chem.*, **28**, 2200 (1963).

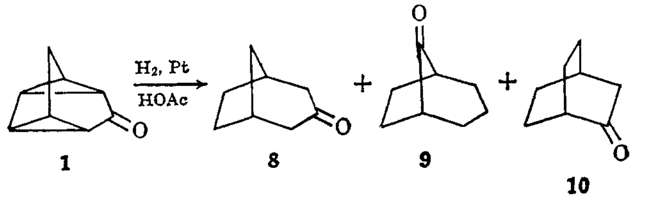
[10] P. R. Story and S. R. Fahrenholtz, *J. Am. Chem. Soc.*, **86**, 1720 (1964).



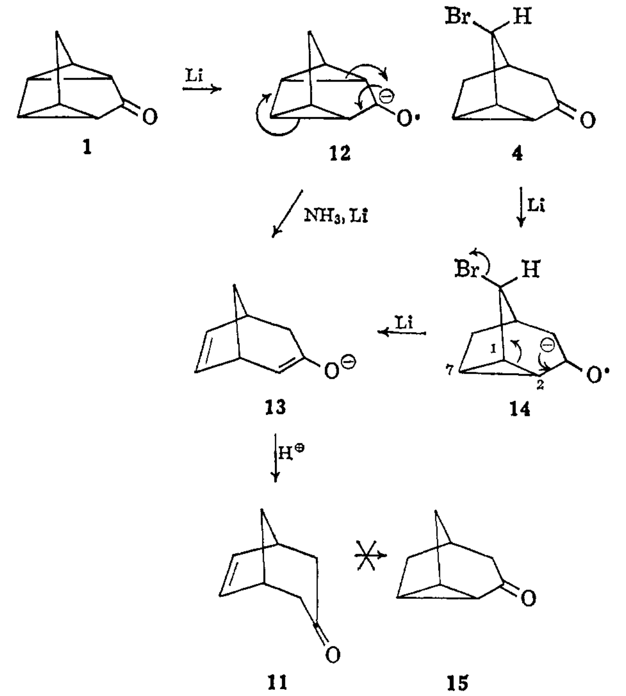


Tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one did not exchange deuterium under conditions of aqueous alcoholic acid or base. An unsuccessful attempt was made to prepare a stable O-alkylated salt of **1** by reaction with triethyloxonium fluoroborate. The ketone **1** was recovered in 72% yield after solution in concentrated sulfuric acid for 30 min.

Reactions of the Tetracyclic Ketone. I. Cleavage of the Cyclopropane Rings. Catalytic hydrogenolysis of **1** in acetic acid was stopped after the uptake of 2.0 molar equiv. of hydrogen, and a mixture of ketones and alcohols was obtained. Gas chromatographic analysis of this mixture and collection of several of the major products allowed the identification (comparison of infrared spectra and gas chromatographic retention times) of bicyclo[3.2.1]octan-3-one (**8**), bicyclo[3.2.1]octan-8-one (**9**), and bicyclo[2.2.2]octan-2-one (**10**). These results provide chemical confirmation for the structure of **1**.



Reduction of **1** with lithium in ammonia afforded a new ketone, bicyclo[3.2.1]oct-6-en-3-one (**11**); however, despite employment of a large excess of lithium, the yields of **11** were usually poor and large amounts of the tetracyclic ketone **1** were recovered. Minor amounts of alcohols from over-reduction were detected but were not identified. A more convenient route to **11** is represented by the lithium–ammonia reduction of the bromo ketone **4**. It can be seen that reduction of **1** by the metal will afford the radical anion **12** which, as a strong base, must abstract a proton from ammonia prior to a second electron transfer to form the enolate **13**. On the other hand, a thermodynamically favored expulsion of the weak base bromide is available to the radical anion **14**.



Complete directional control for opening of the C-1–C-2 bond of **4** rather than the C-2–C-7 bond is provided by the bromine atom at C-8. This observation may prove useful in other synthetic schemes.

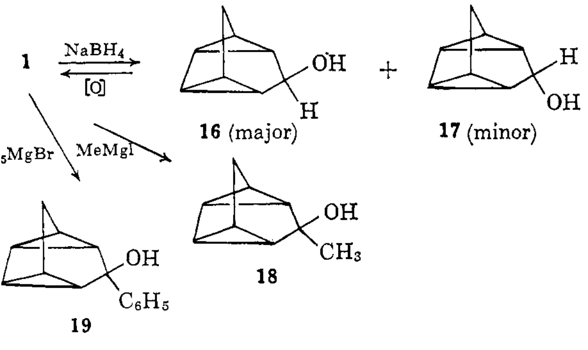
The n.m.r. spectrum of the ketone **11** showed the two vinyl protons as a narrow multiplet at δ = 6.20 p.p.m. Reduction afforded the known bicyclo[3.2.1]octan-3-one (**8**). Acid-catalyzed deuterium exchange led to the incorporation of four deuterium atoms per molecule (74% d_4, 26% d_3); the isomeric ketone **15**,[9] the product of possible transannular ketonization of the enol of **11**, was not detected in either this experiment or from base-catalyzed enolization of **11**.

The mass spectra of **11** and its deuterated analog support the structural assignment. The fragmentation pathway was that expected for this bicyclic ketone, namely, cleavage of the C–C bond α to the carbonyl group followed either by loss of ketene (or dideuterioketene) or by intramolecular hydrogen shift from the other α-position and subsequent loss of methyl (or perdeuteriomethyl).

Reaction of **1** with 2 equiv. of hydrogen bromide in dry chloroform gave the dibromo ketone **5**. Since the same product was obtained from **4** and hydrogen bromide, the stereochemistry of the C-8 bromine atom is thus established. The stereochemistry of the C-6 bromine atom is assumed to be *exo* because of the facile dehydrobromination of **5** to the tetracyclic ketone **1**.

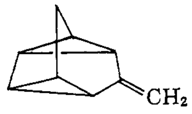
II. Additions to the Carbonyl Group. As a first approximation, one might expect the carbonyl stretching frequency and the carbonyl angle of **1** to be similar to those of cyclopentanone ($\nu_{\max}$ 1749.8 cm.$^{-1}$, C—CO—C angle $\approx 102°$).[11,12] That the observed value for **1** is lower is attributed to greater charge separation (**6**) resulting in more single-bond character to the carbonyl group. We felt it would be informative to determine the tendency of the ketone function of **1** to undergo the hybridization change sp^2 → sp^3 as measured by the dissociation constant for the cyanohydrin.[13] A value of ∞ (indistinguishable from a blank) was obtained, supporting our belief that, in this tetracyclic molecule, an equilibrium situation between a trigonal and a tetrahedral carbon atom at C-3 would prefer the former. This result must come about because of a severe interaction between the "bowsprit" and "flagpole" atoms at the C-3 and C-7 positions.

Reduction of tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one (**1**) with sodium borohydride in methanol or with diisobutyl aluminum hydride in hexane furnished an alcohol, which was shown to be a mixture of *exo* (**16**) and *endo* (**17**) epimers by gas chromatographic analysis. Repeated crystallization from pentane resulted in purification of one isomer, which by gas chromatographic analysis corresponded to the major isomer and to which we assign the structure *exo*-tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-ol (**16**) on the basis of steric approach control to the least hindered, bottom face of **1**. Pure *exo* isomer **16** and the mixture of **16** and **17** were readily oxidized to **1** by chromium trioxide–pyridine, manganese dioxide in pentane, and *t*-butyl hypochlorite. Interestingly, attempted sodium in alcohol reduction of **1** *did not give* isolable yields of alcohol. Moreover, the alcohols **16** and **17** were found to be quite unstable—the crystals, when allowed to stand at room temperature, appeared to lose water and yield a polymer. These latter observations again point to the fact that C-3 (or C-7) prefers the trigonal geometry.



Additions of methylmagnesium iodide and phenylmagnesium bromide followed by careful hydrolysis furnished the two carbinols **18** and **19**, respectively. *endo*-3-Methyltetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-ol (**18**) was obtained as a sharp-melting solid in 65% yield. Analysis of the mother liquors from crystallization by n.m.r. indicated the presence of small amounts of the epimer. Gas chromatographic analysis was impossible because of the great ease of dehydration of **18**. The structure **18** was inferred on the basis of steric approach control. *endo*-3-Phenyltetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-ol was obtained as a pure compound in 70% yield.

Reaction of **1** with triphenylphosphine methylide in dimethyl sulfoxide gave an excellent yield of 3-methylenetetracyclo[3.3.0.0^{2,8}.0^{4,6}]octane (**20**). The two *exo*-methylene protons showed resonance absorption at $\delta = 4.64$ p.p.m., bands at 1648 and 868 cm.$^{-1}$ were detected in the infrared spectrum, and the mass spectrum confirmed the molecular weight. The base peak on electron impact turned out to be (M − 1)$^+$, corresponding to $C_9H_9^+$. Measurements of the vapor phase ultraviolet spectrum of **20** showed broad absorption having much fine structure with a center of gravity at 204 mμ. This spectrum is consistent with a 1,1-disubstituted ethylene chromophore, with each cyclopropyl substituent providing a bathochromic perturbation of 10 mμ greater than a methyl group. No evidence for fulvene-type resonance can be seen. The olefin **20** could also be obtained by dehydration of the methylcarbinol **18**.



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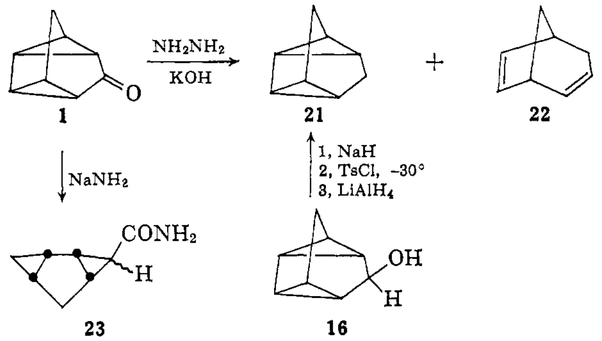
Miscellaneous Reactions. A Huang-Minlon modification of the Wolff–Kishner reduction of **1** gave the hydrocarbon **21**, tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octane, which was isolated in good yield. The product showed contamination by 15% by weight of bicyclo[3.2.1]octa-2,5-diene (**22**) as shown by gas chromatographic and n.m.r. analysis. Pure **21** was separated by gas chromatography, and its mass spectrum supported the structural assignment. An identical hydrocarbon was obtained by reduction of the *p*-toluenesulfonate (not isolated) of the alcohol **16**, albeit in poorer over-all yield. In the latter reaction, which presumably represents a trapping by hydride of the ion pair from ionization of the unstable tosylate of **16**, *none* of the diene **22** was detected.



The mass spectra of the two hydrocarbons **21** and **22** are quite similar, the only significant differences occurring in relative intensities. These spectra also show great similarity to those of other C_8H_{10} isomers.[14]

Haller–Bauer cleavage of **1** with sodium amide in dioxane afforded 3-carboxamidotricyclo[4.1.0.0^{2,4}]hep-

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(11) *Cf.* P. R. Schleyer and R. D. Nicholas, *J. Am. Chem. Soc.*, **83**, 182 (1961).

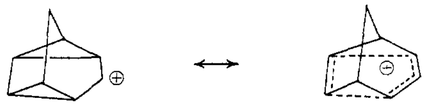
(12) The $\nu_{\max}$ of cyclopentanone is high presumably because puckering and accompanying angle strain reduces eclipsing strain, and that for **1** should be similar because of the constraint imparted by the bicyclic system.

(13) L. Ruzicka, P. A. Plattner, and H. Wild, *Helv. Chim. Acta*, **28**, 613 (1945).

(14) F. Meyer, P. Haynes, S. McLean, and A. Harrison, *Can. J. Chem.*, **43**, 211 (1965).

tane (**23**). Although the all-*cis* isomer of **23** must necessarily be the first product of cleavage, epimerization at C-3 may have resulted from the strongly basic conditions of the reaction.

We are currently exploring reactions that might be expected to occur by way of the carbonium ion **24**, and have initiated studies with carbanions and free radicals of this series.



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Experimental Section[15]

3,7,8-Tribromobicyclo[*3.2.1*]*oct-2-ene* (**3b**). A solution of 32.0 g. (0.173 mole) of 3-bromobicyclo[3.2.1]-octa-2,6-diene[9] in 150 ml. of ether was cooled to −10 to −15°, and a solution of 28.5 g. (0.178 mole) of bromine in 30 ml. of carbon tetrachloride was added with stirring. When the addition was complete, the flask was allowed to warm to room temperature. The contents were transferred to a separatory funnel and additional ether was added. The ether layer was shaken four times with a saturated sodium bisulfite solution, washed with water, dried, and concentrated. Crystallization of the residue from a mixture of ether and pentane afforded 49.78 g. (83.5%) of white crystals, m.p. 100–101°.

Anal. Calcd. for $C_8H_9Br_3$: C, 27.85; H, 2.60; Br, 69.51. Found: C, 27.62; H, 2.60; Br, 69.39.

The infrared spectrum showed $\nu_{\max}^{CCl_4}$ 2940 (w), 1652 (m), 1450 (m), 1350 (m), 1315 (m), 1258 (m), 1235 (m), 1208 (m), 1162 (w), 1063 (w), 1042 (w), 1000 (w), 980 (s), 945 (m), 908 (m), 865 (s), and 843 (s) cm.$^{-1}$. The n.m.r. spectrum showed 2 doublets (1 H) at δ = 6.14 p.p.m., J_1 = ~7.4 c.p.s., J_2 ~2.0 c.p.s. (C-2); δ = 4.45 p.p.m. (1 H), singlet (*syn*-C-8); δ = 4.35 p.p.m. (1 H), triplet, J = ≃5.0 c.p.s. (*endo*-C-6 or C-7); and a complex pattern between δ = 3.16 and 2.26 p.p.m. (6 H).

anti-8-Bromotricyclo[*3.2.1.0*^{2,7}]*octan-3-one* (**4a**). To a cooled solution of 10 ml. of water, 14 ml. of concentrated sulfuric acid, and 20 ml. of 95% ethanol was added 10.8 g. (0.0314 mole) of 3,7,8-tribromobicyclo-[3.2.1]oct-2-ene. The mixture was stirred and the temperature was raised and maintained at 50° until all of the solid material had dissolved (36 hr.). The solution was poured into ice water and was extracted with ether. The ether layer was washed with saturated sodium bicarbonate solution and water, and was dried and concentrated. Storage overnight at 0° afforded 3.58 g. (56%) of product, m.p. 54–56.5°

A portion of this material was chromatographed on Merck acid-washed alumina and was recrystallized from a mixture of pentane and ether to afford *anti*-8-bromotricyclo[3.2.1.0^{2,7}]octan-3-one (**4a**), m.p. 56.5–57.8°, $\nu_{\max}^{CCl_4}$ 3030 (w), 2940 (m), 2860 (w), 1720 (s), 1332 (s), 1220 (s), 1183 (m), 1100 (m), 1040 (m), 1010 (w), 1000 (w), 955 (m), 930 (m), 858 (m), and 850 (s) cm.$^{-1}$. The n.m.r. spectrum showed a singlet (1 H) at δ = 4.34 p.p.m. (*syn*-C-8), and complex patterns at δ = 1.74 p.p.m. (2 H), δ = 2.05 p.p.m. (2 H), and δ = 2.38 p.p.m. (4 H). The dipole moment was determined, μ = 1.71 ± 0.03 D.

Anal. Calcd. for C_8H_9BrO: C, 47.78; H, 4.51; Br, 39.75. Found: C, 47.81; H, 4.53; Br, 39.47.

Solvolysis of 3,7,8-Tribromobicyclo[*3.2.1*]*oct-2-ene in a Deuterated Solvent.* A medium was prepared by heating a mixture of 4.0 g. of diethyl sulfate and 2.0 g. of deuterium oxide at 100° for 6 hr. The solution was cooled to 50°, and 1.08 g. (0.00314 mole) of the tribromide **3b** was added with stirring. After 72 hr., the reaction mixture was poured onto cracked ice, and the aqueous mixture was extracted with ether. The combined ether layers were washed, dried, and concentrated. Crystallization from a mixture of ether and pentane afforded 280 mg. (48.2%) of bromo ketone **4b**, m.p. 57–59°. Examination of this material by n.m.r. showed a singlet at δ = 4.34 p.p.m. (1 H), and complex peaks at δ = 2.38 p.p.m. (4 H) and δ = 1.74 p.p.m. (1.33 H). The δ = 2.05 p.p.m. (2 H) peak was absent, and the δ = 1.74 p.p.m. (2 H) peak had decreased in area. The mass spectrum showed that the compound was a mixture of 31% d_2 and 69% d_3 species.

Acid-Catalyzed Hydrogen Exchange of anti-8-Bromotricyclo[*3.2.1.0*^{2,7}]*octan-3-one-*$d_{2,3}$. A solution of 1.4 ml. of concentrated sulfuric acid, 2.0 ml. of ethyl alcohol, and 1.0 ml. of water was heated to 50° and 0.070 g. (0.00035 mole) of the bromo ketone **4b** was added with stirring. After 2 hr., the mixture was worked up in the usual fashion. Crystallization from a mixture of ether and pentane afforded 280 mg. (48.2%) of bromo ketone **4b**, m.p. 57–59°. Examination of this material by n.m.r. showed a singlet at δ = 4.34 p.p.m. (1 H), and complex peaks at δ = 2.38 p.p.m. (4 H), δ = 2.07 p.p.m. (2 H), and δ = 1.77 p.p.m. (1.3 H). The mass spectrum showed that a mixture of 90% bromo ketone-d_1 (**4c**) and 10% bromo ketone-d_0 was present.

Acid-Catalyzed Deuterium Exchange of anti-8-Bromotricyclo[*3.2.1.0*^{2,7}]*octan-3-one.* A mixture containing 4.0 g. of diethyl sulfate and 2.0 g. of deuterium oxide was stirred for 4 hr. at 75° and was cooled to 55°, and 0.10 g. (0.0005 mole) of the bromo ketone **4a** was added with stirring. After 8 hr., the solution was cooled and worked up. Crystallization afforded 75 mg. (75%) of product, m.p. 56.5–58°. Examination of this material by n.m.r. showed a singlet at δ = 4.30 p.p.m. (1 H), and complex peaks at δ = 2.44 p.p.m. (4 H) and δ = 1.84 p.p.m. (2 H). The mass spectrum showed a mixture of 93% d_2 and 7% d_1 ketone (**4d**).

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[15] Melting points are corrected and boiling points are uncorrected. Infrared spectra were obtained with Beckman IR-4 or Perkin-Elmer Model 137B Infracord recording spectrophotometers. Analyses are by Midwest Microlab, Inc., Indianapolis, Ind. Gas chromatographic analyses were carried out on 8 mm. × 7 ft. glass U columns packed with (a) 20% by weight GE XE-60 on Chromosorb P and (b) 20% by weight γ-nitro-γ-methylpimelonitrile on Chromosorb P. Helium carrier gas inlet pressure was 9 p.s.i.g. for column A and analyses were performed at 47° for hydrocarbons and 147° for all other compounds. Column B was operated at 150° with a helium pressure of 23 p.s.i.g. A Varian Associates DP-60 high-resolution spectrometer was used for the n.m.r. spectra; carbon tetrachloride or deuteriochloroform were the solvents, and tetramethylsilane was the internal standard. Chemical shifts were obtained by the audio side band technique. The mass spectra were obtained from an Atlas CH/4 spectrometer with an ionization potential of 70 e.v. and an ionization current of 20 μa. This instrument was purchased with the assistance of Grant CP-1474 from the National Science Foundation. The ultraviolet spectra were measured with a Cary Model 14 recording spectrophotometer. The dipole moments were determined by measuring the dielectric constants and densities of solutions of various mole fractions at 25° in benzene, with the apparatus and method of calculation as described by N. L. Allinger, H. M. Blatter, M. A. DaRooge, and L. A. Freiberg, *J. Org. Chem.*, **26**, 2550 (1961).

Tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]*octan-3-one* (**1**). To a solution of 0.4 g. (0.0102 mole) of potassium metal in 15 ml. of dry *t*-butyl alcohol heated to 50° was added 1.0 g. (0.005 mole) of the bromo ketone. Within a few seconds a white precipitate had formed which was presumed to be potassium bromide. After 1 hr., the mixture was poured into ice water and was extracted with ether. The ether layers were combined and washed, dried, and concentrated. About one-half of the residual *t*-butyl alcohol was removed *in vacuo* and pentane was added. Low-temperature crystallization afforded 0.417 g. (70%) of tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]-octan-3-one, m.p. 69.5–71°. A second crop afforded 40 mg. (6%) of ketone, m.p. 65–69°.

Anal. Calcd. for C_8H_8O: C, 79.97; H, 6.71. Found: C, 79.76; H, 6.93.

The *2,4-dinitrophenylhydrazone* was prepared in the usual manner, m.p. 225–226° dec.

Anal. Calcd. for $C_{14}H_{12}N_4O_4$: C, 56.00; H, 4.03; N, 18.66. Found: C, 56.06; H, 4.28; N, 18.46.

The *oxime* was also prepared, m.p. 117–118°.

Anal. Calcd. for C_8H_9NO: C, 71.08; H, 6.72; N, 10.37. Found: C, 71.25; H, 6.89; N, 10.06.

The infrared spectrum showed $\nu_{\max}^{\mathrm{CHCl_3}}$ 3040 (m), 2930 (m), 2860 (m), 1730 (s), 1450 (w), 1410 (w), 1380 (w), 1332 (s), 1300 (w), 1268 (w), 1230 (m), 1189 (m), 1158 (w), 1100 (m), 1040 (m), 1015 (w), 1000 (w), 952 (m), 931 (m), 898 (m), 858 (s), and 850 (s) cm.$^{-1}$. The n.m.r. spectrum showed a complex pattern between δ = 1.30 and 2.6 p.p.m. The ultraviolet spectrum showed $\lambda_{\max}^{\mathrm{EtOH}}$ 281 mμ (ϵ 50) and 205 mμ (ϵ 5360); $\lambda_{\max}^{\mathrm{cyclohexane}}$ 286 mμ (ϵ 20). The dipole moment was obtained, μ = 3.74 ± 0.03 D. Analysis of the ketone by gas chromatography showed one broad peak with a retention time of 29 min.

Tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]*octan-3-one in Sulfuric Acid.* A solution of 0.100 g. (0.833 mmole) of the tetracyclic ketone in 0.5 ml. of concentrated sulfuric acid was prepared, and the n.m.r. spectrum was examined. A noticeable simplification of the spectrum took place. After 4 hr., the solution was poured onto crushed ice and extracted with ether. The ether layer was washed, dried, and concentrated. Sublimation of the residue afforded 0.035 g. (35%) of the ketone, m.p. 69–70.5°. When the time in solution was reduced to 30 min., the tetracyclic ketone was isolated in 72% yield, m.p. 69.5–70.5°. Analysis of the crude ether extract by gas chromatography showed only the starting ketone to be present.

Attempted Deuteration of Tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]-*octan-3-one. Procedure A.* A solution of 250 mg. (0.0021 mole) of the tetracyclic ketone in deuterioethanol containing sodium ethoxide (from 16 mg. of sodium in 10 ml. of deuterioethanol) was heated at 55° for 3 and for 36 hr. After work-up, sublimation at 60° afforded 100 mg. (40%) of ketone, m.p. 69–70°. The n.m.r. and mass spectra were identical with those of starting ketone.

Procedure B. A solution of 4.0 g. of ethyl sulfate and 2.0 g. of deuterium oxide was stirred at 75° overnight. The temperature was lowered to 50°, and 150 mg. (0.00125 mole) of the tetracyclic ketone was added. After 2 hr., the solution was cooled and worked up. Crystallization from pentane afforded 25 mg. (16.7%) of ketone. The mass spectrum showed that no deuterium had been incorporated into the molecule.

exo- and endo-Tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]*octan-3-ol.* A solution of 0.50 g. (0.00416 mole) of tetracyclo-[3.3.0.$0^{2,8}$.$0^{4,6}$]octan-3-one in 8 ml. of absolute methanol was cooled to 0°. Sodium borohydride (0.200 g., 0.0053 mole) was added in small portions. After 30 min., the ice bath was removed and the solution was allowed to stir for 3 hr. The mixture was cooled and was hydrolyzed with 8 ml. of water and 8 ml. of 15% potassium hydroxide solution. The mixture was poured into water and extracted with ether. The ether layer was washed, dried, and concentrated. Analysis by gas chromatography showed two major peaks in the ratio approximately 70:30 with retention times of 13.5 and 13 min., respectively. A third, smaller peak corresponded to the starting ketone. The yellow, oily residue was crystallized from pentane at 0° to afford 0.20 g. (40%) of product, m.p. 82–85°. The mother liquors were also examined by gas chromatography and showed only the alcohols to be present. However, attempts to obtain a second crop were unsuccessful; only an oily residue resulted. Infrared analysis of the crystalline product showed $\nu_{\max}^{\mathrm{CCl_4}}$ 3340 (s), 3040 (s), 2940 (s), 2860 (s), 1390 (m), 1350 (m), 1315 (w), 1290 (m), 1063 (s), 1040 (s), 1010 (s), 910 (w), and 875 (w) cm.$^{-1}$. The n.m.r. spectrum showed a broad singlet at δ = 4.64 p.p.m. (1 H) and a complex pattern between δ = 2.25 p.p.m. and δ = 1.31 p.p.m. (9 H). An analytical sample was prepared by repeated crystallization from pentane, m.p. 89.5–90.5° (assigned the *exo* structure); gas chromatographic analysis indicated that this isomer was the major isomer produced in the reduction of **1**.

Anal. Calcd. for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.88; H, 8.04.

Diisobutylaluminum Hydride Reduction of Tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]*octan-3-one.* A solution of 250 mg. (0.00181 mole) of diisobutylaluminum hydride in 15 ml. of dry hexane was cooled to 0°, and 100 mg. (0.833 mmole) of the tetracyclic ketone in 10 ml. of dry ether was added dropwise. After the reaction had stirred for 1 hr., 15 ml. of saturated ammonium chloride solution followed by 0.5 g. of potassium hydroxide in 5 ml. of water were added. The mixture was poured onto ice and was extracted with ether. The combined ether layers were washed, dried, and concentrated. Starting ketone (30%) was removed by crystallization, and gas chromatographic analysis of the residue showed both *exo*- and *endo*-tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]octan-3-ol to be present in a ratio 55:45 (based on the assignment made above); a small amount of the starting ketone was also present.

Sodium and Alcohol Reduction of Tetracyclo[3.3.-0.$0^{2,8}$.$0^{4,6}$]*octan-3-one.* A solution of 200 mg. (0.00166 mole) of the tetracyclic ketone in 50 ml. of absolute ethanol was cooled in an ice bath, and 775 mg. (0.0337 mole) of sodium metal was added over a period of 1.5 hr. The solution was concentrated *in vacuo* to a volume of 10 ml. and was poured onto cracked ice. The aqueous solution was extracted with pentane and the pentane layer was washed, dried, and concentrated. Analysis of the residue by gas chromatography showed only a small amount (1–2%) of the tetracyclic alcohols in about equal amounts. The only other peak detected corresponded to the starting ketone.

Oxidation of exo- and endo-Tetracyclo[*3.3.0.0*^{2,8}*.0*^{4,6}]*-octan-3-ol. A. Chromium Trioxide–Pyridine.* To a mixture of 300 mg. (0.0033 mole) of chromic anhydride in 5.0 ml. of pyridine at 0° was added with stirring 190 mg. (0.0016 mole) of the mixture of tetracyclic alcohols. After 6 hr., water was added, and the aqueous mixture was extracted with ether. The combined extract was washed, dried, and concentrated. Analysis of the residue (40.7 mg., 22%) by gas chromatography showed one peak with the same retention time as that of tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one; mixture melting point comparison of infrared spectra and preparation of the *2,4-dinitrophenylhydrazone* confirmed the assignment.

B. t-Butyl Hypochlorite. To a solution of 50 mg. (0.00041 mole) of a mixture of the *exo-* and *endo*-tetracyclic alcohols in 3 ml. of chloroform was added three drops of pyridine. The flask was wrapped with aluminum foil, cooled to 0°, and 0.50 ml. (0.0046 mole) of *t*-butyl hypochlorite was added with stirring. The solution was allowed to warm to room temperature. Periodically, a test was made for hypochlorite using wet potassium iodide–starch paper. After 3 days the aluminum foil was removed and the reaction mixture was stirred for an additional 2 days. Sodium bisulfite was added, and, after 5 min., the mixture gave a negative hypochlorite test. The reaction mixture was poured onto cracked ice and extracted with ether. The organic layer was washed, dried, and concentrated. Analysis of the residue by gas chromatography showed 14 peaks, with the tetracyclic ketone accounting for approximately 80% of the mixture. The other peaks were not identified, but showed retention times much shorter than the tetracyclic ketone.

C. Manganese Dioxide. To a solution of 50 mg. (0.41 mmole) of the mixture of tetracyclic alcohols in 5 ml. of dry pentane was added 750 mg. (0.00864 mole) of manganese dioxide.[16,17] The mixture was stirred at room temperature for 15 hr. and filtered, and the filter paper was washed with 75 ml. of ether. The filtrate was concentrated. Analysis of the residue by gas chromatography showed only tetracyclo[3.3.0.-0^{2,8}.0^{4,6}]octan-3-one to be present. Evaporation of the ether afforded 42 mg. (85%) of the tetracyclic ketone, m.p. 69–71°, m.m.p. 70–71°.

Hydrogenation of Tetracyclo[*3.3.0.0*^{2,8}*.0*^{4,6}]*octan-3-one.* A solution of 0.10 g. (0.0008 mole) of the tetracyclic ketone in 11 ml. of acetic acid was hydrogenated employing 35 mg. of prereduced platinum oxide as the catalyst. After 1.25 hr., 50 ml. (0.002 mole) of hydrogen had been absorbed, and the solution was filtered and poured onto cracked ice. The aqueous mixture was extracted with ether, and the combined ether layers were washed, dried, and concentrated. Analysis of the residue by gas chromatography showed four peaks in a ratio of 16:11:8:15. The retention time of the first peak (6.5 min.) was identical with that for bicyclo[3.2.1]octan-3-one[9] and bicyclo[3.2.1]-octan-8-one.[18] A sample was collected from the column and its infrared spectrum was obtained and compared with that of the pure compounds. Bands at 1350 and 1220 cm.$^{-1}$ characteristic of the 3-ketone and bands at 1472 and 1100 cm.$^{-1}$ characteristic of the 8-ketone were found. The remainder of the spectra were identical. The retention time of the second peak (8.0 min.) was shown to be identical with bicyclo-[2.2.2]octan-2-one[19] by comparison of infrared spectra. The third and fourth peaks were collected together (retention time 15.7, 19.5 min.). The infrared spectrum showed that an alcohol and a ketone were present. The mixture was not identified further except that *exo*-bicyclo[3.2.1]octan-8-ol[20] (retention time 16.4 min.) was shown not to be a component.

Bicyclo[*3.2.1*]*oct-6-en-3-one* (**15**). *A. From the Tetracyclic Ketone.* Into a 50-ml. three-necked flask equipped with a mechanical stirrer, Dry Ice condenser, and a gas inlet tube was distilled 35 ml. of liquid ammonia. While the solution was stirred slowly, 33 mg. (0.0048 mole) of lithium metal was added. Without further cooling 200 mg. (0.00167 mole) of tetracyclo-[3.3.0.0^{2,8}.0^{4,6}]octan-3-one was added, and the solution turned white within 10 sec. The solution was stirred for 1 hr. and 2 ml. of saturated ammonium chloride solution was added, followed by 20 ml. of ether. The ammonia was allowed to evaporate, and the mixture was poured into ice water and was extracted with ether. The ether layer was washed, dried, and concentrated. Analysis by gas chromatography showed two peaks in a ratio of 2.5:1 with retention times of 29 and 12 min., respectively. The larger peak corresponded to the starting ketone. Capillary gas chromatography confirmed this assignment. The more volatile component was identified as bicyclo[3.2.1]oct-6-en-3-one by gas chromatographic comparison with the compound prepared in procedure B.

In another preparation employing 500 mg. (0.00417 mole) of the tetracyclic ketone and 350 mg. (0.504 mole) of lithium metal, the reaction mixture never lost the blue-black color. After 1 hr., ammonium nitrate crystals were added and the reaction mixture was worked up as described above. Analysis of the residue (273 mg., 55%) by gas chromatography showed the tetracyclic ketone and the product to be in a ratio of 1.4:1. Crystallization afforded 203 mg. of material, m.p. 35–55°. The residue was examined by infrared analysis and showed a weak hydroxyl band at 3450 cm.$^{-1}$.

B. From the Bromo Ketone. A solution of 450 mg. (0.065 mole) of lithium metal in 225 ml. of liquid ammonia was stirred for 20 min., and 1.50 g. (0.00745 mole) of *anti*-8-bromotricyclo[3.2.1.0^{2,7}]octan-3-one was added with stirring. After 1 hr., the blue-black color still remained. Ammonium nitrate was added followed by moist ether and a saturated ammonium chloride solution. The ammonia was allowed to evaporate and the solution was poured into ice water. The aqueous mixture was extracted with ether, and the combined ether layers were washed, dried, and concentrated. Analysis of the residue (885 mg.) by gas chromatography showed only one peak with a retention time of 12 min. Crystallization of the residue from pen-

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(16) J. Attenburrow, A. Cameron, J. H. Chapman, R. M. Evans, B. Hems, A. Jansen, and T. Walker, *J. Chem. Soc.*, 1094 (1952).

(17) L. Crombie and J. Crossley, *ibid.*, 4983 (1963).

(18) N. A. LeBel and L. A. Spurlock, *Tetrahedron*, **20**, 215 (1964).

(19) W. C. Wildman and D. R. Saunders, *J. Org. Chem.*, **19**, 381 (1954).

(20) A. C. Cope, S. Moon, C. H. Park, and G. L. Woo, *J. Am. Chem. Soc.*, **84**, 4865 (1962).

tane afforded 279 mg. (31%) of product, m.p. 99–100.5°. The mother liquors were concentrated and sublimed to afford an additional 366 mg. (40%), m.p. 92–97°. The material was homogeneous on gas chromatography. The infrared spectrum of the residue showed hydroxyl bands at 3570 and 3450 cm.$^{-1}$. The infrared spectrum of the pure, crystalline ketone showed $\nu_{\max}^{\mathrm{CCl_4}}$ 3020 (w), 2930 (s), 2860 (w), 1700 (s), 1662 (w), 1580 (w), 1445 (w), 1403 (m), 1342 (s), 1273 (w), 1203 (m), 1183 (m), 1139 (w), 1063 (m), 1052 (w), 1005 (m), 975 (m), 860 (m), and 838 (w) cm.$^{-1}$. The n.m.r. spectrum showed a narrow multiplet at $\delta = 6.20$ p.p.m. (2 H), a broad singlet at $\delta = 3.01$ p.p.m. (2 H), a doublet at $\delta = 2.16$ p.p.m. (4 H), and a complex pattern at $\delta = 2.03$ p.p.m. next to two singlets at $\delta = 1.84$ and 1.65 p.p.m. (2 H).

Anal. Calcd. for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.62; H, 8.38.

The *2,4-dinitrophenylhydrazone* was prepared in the usual manner, m.p. 187–188°.

Anal. Calcd. for $C_{14}H_{14}N_4O_4$: C, 55.58; H, 4.67; N, 18.54. Found: C, 55.79; H, 4.93; N, 18.34.

C. From the Bromo Ketone with Inverse Addition of Lithium. To a solution of 0.50 g. (0.0025 mole) of *anti*-8-bromotricyclo[3.2.1.0^{2,7}]octan-3-one in 80 ml. of dry liquid ammonia,[21] was added 120 mg. (0.017 mole) of lithium in small pieces. After 30 min. the blue color had disappeared, and ammonium chloride was added. The ammonia was allowed to evaporate, and ether and water were added. The aqueous mixture was extracted with ether. The combined ether layers were washed, dried, and concentrated. The residue (444 mg.) was examined by gas chromatography and showed one peak having a retention time identical with that of the unsaturated ketone. Sublimation of the residue afforded 181 mg. (60%), which was crystallized from pentane to afford 80 mg. (27%) of the unsaturated ketone, m.p. 90–95°.

D. Reduction of the Bromo Ketone with Zinc. To a solution of 0.500 g. (0.0025 mole) of *anti*-8-bromotricyclo[3.2.1.0^{2,7}]octan-3-one in 35 ml. of ethyl alcohol was added 200 mg. (0.00326 mole) of zinc powder. The mixture was heated to reflux and was stirred for 20 hr. The mixture was cooled, poured into water, and extracted with pentane. The combined pentane layers were washed, dried, and concentrated. Analysis of the residue (270 mg.) by gas chromatography showed the unsaturated ketone to be present. Crystallization afforded 197 mg. of material, m.p. 49.5–54°. The infrared spectrum was identical with that of the starting bromo ketone. Recrystallization afforded 114 mg. of the starting bromo ketone, m.p. 56–58°, m.m.p. 56.5–58°. The mother liquors were concentrated and sublimed to afford 29 mg. (9.6%) of product, m.p. 91–100°.

Stability of Bicyclo[3.2.1]oct-6-en-3-one. A. Acidic Conditions. To a solution of 1.4 ml. of concentrated sulfuric acid, 2 ml. of 95% ethyl alcohol, and 1 ml. of water at 50° was added 40 mg. (0.00033 mole) of the unsaturated ketone. The mixture was stirred for 1 hr. at 50° and poured onto cracked ice.

After work-up, analysis of the residue by gas chromatography showed only pure starting ketone to be present. The ether was evaporated and the residue was treated with an excess of 2,4-dinitrophenylhydrazine solution. The precipitate was collected on a filter and chromatographed on Merck acid-washed alumina to afford 35 mg. (35.4%) of the 2,4-dinitrophenylhydrazone, m.p. 188–189°, m.m.p. 187.5–189°.

B. Basic Conditions. A solution of 50 mg. (0.4 mmole) of the unsaturated ketone in 50 ml. of 50% aqueous ethanol, and containing a catalytic amount of dissolved sodium metal, was stirred at 70° for 1 hr. The residue obtained after work-up (59 mg.) was examined by gas chromatography and showed one peak having the identical retention time of the starting ketone.

Acid-Catalyzed Deuterium Exchange of Bicyclo[3.2.1]oct-6-en-3-one. A mixture containing 4.0 g. of diethyl sulfate and 2.0 g. of deuterium oxide was stirred for 3 hr. at 100° and cooled to 50°, and 50 mg. (0.41 mmole) of the unsaturated ketone was added with stirring. After 2 hr., the solution was cooled, poured into ice water, and extracted with pentane. The combined pentane layers were washed, dried, and concentrated. Analysis of the residue (43 mg.) by gas chromatography showed one peak having the retention time of the starting ketone. Crystallization afforded 5 mg. (10%) of deuterated ketone, m.p. 103–104.5° (sealed capillary). The mass spectrum showed a mixture consisting of 26% d_3 and 74% d_4 ketone.

exo-anti-6,8-Dibromobicyclo[3.2.1]octan-3-one (**5**). *A. From the Tetracyclic Ketone.* Gaseous hydrogen bromide (about 20 ml., 0.685 mole) was condensed, and cold chloroform (25 ml.) was added followed by 500 mg. (0.00415 mole) of tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one. The reaction mixture was allowed to stir overnight, and to warm to room temperature. The mixture was poured onto cracked ice and was extracted with ether. The ether solution was washed, dried, and concentrated. Crystallization from a mixture of ether and pentane afforded 614 mg. (38.5%) of the dibromo ketone, m.p. 84–86°. The infrared spectrum showed bands at $\nu_{\max}^{\mathrm{CHCl_3}}$ 3040 (s), 2940 (s), 2860 (m), 1725 (s), 1450 (s), 1420 (s), 1342 (s), 1325 (s), 1260 (s), 1175 (s), 1150 (s), 1125 (m), 1063 (w), 1000 (s), 975 (s), 935 (s), 915 (s), 870 (m), 860 (s), and 840 (m) cm.$^{-1}$. The n.m.r. spectrum showed a singlet at $\delta = 4.62$ p.p.m. (1 H), a complex peak between $\delta = 4.2$ and 4.0 p.p.m. (1 H), and a complex pattern between $\delta = 3.49$ and 2.28 p.p.m. (8 H).

Anal. Calcd. for $C_8H_{10}Br_2O$: C, 34.07; H, 3.57; Br, 56.68. Found: C, 34.28; H, 3.81; Br, 56.22.

B. From the Bromo Ketone. The identical procedure was employed except that *anti*-8-bromotricyclo[3.2.1.0^{2,7}]octan-3-one (**4a**) was used. The dibromo ketone was isolated in 56% yield, m.p. 85–87°. A mixture melting point with the material from procedure A showed 84.5–87°. The infrared spectra were identical. Thin layer chromatography on silica gel employing chloroform as the solvent and 2,4-dinitrophenylhydrazine as the spotting agent showed one spot only.

Conversion of exo-anti-6,8-Dibromobicyclo[3.2.1]octan-3-one to Tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one. To a solution of 0.2 g. (0.005 mole) of potassium metal in 8 ml. of dry *t*-butyl alcohol at 50° was added with stirring 235 mg. (0.000835 mole) of the 6,8-dibromo ketone.

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(21) G. Stork, P. Rosen, N. Goldman, R. V. Coombs, and J. Tsuji, *J. Am. Chem. Soc.*, 87, 280 (1965).

A white precipitate formed immediately. After 1 hr., the mixture was poured onto ice and was extracted with ether. The combined ether layers were washed, dried, and concentrated. Sublimation (65°) afforded 48 mg. (48%) of the tetracyclic ketone, m.p. 69–70.5°, m.m.p. 69–71°.

Bicyclo[3.2.1]octan-3-one from Bicyclo[3.2.1]oct-6-en-3-one (**15**). A solution of 0.05 g. of bicyclo[3.2.1]-oct-6-en-3-one (**15**) in 10 ml. of 95% ethanol was hydrogenated employing 25 mg. of 10% palladium on charcoal as the catalyst. The uptake of hydrogen ceased in 10 min. The solution was filtered, poured into water, and extracted with pentane. The combined pentane layers were washed, dried, and concentrated. The residue (75 mg.) was sublimed to afford 25 mg. (50%) of the saturated ketone, m.p. 125–139° (sealed tube).

The *2,4-dinitrophenylhydrazone* was prepared in the usual manner, m.p. 164.5–165.5° (lit.[9] m.p. 165–166.2°).

3-Methylenetetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]*octane* (**20**). *Method A.* A procedure similar to that described by Corey[22] was employed. Sodium hydride (0.40 g., 0.0083 mole, 51% mineral oil dispersion) was added to 45 ml. of dry (distilled from calcium hydride) dimethyl sulfoxide, and dry nitrogen was passed through the solution throughout the reaction. The flask was heated to 65° for 1 hr. and was cooled to room temperature. One crystal of triphenylmethane was added and a red color resulted. Four and one-half grams (0.0127 mole) of triphenylmethylphosphonium bromide was added, the mixture was stirred for 20 min., and a solution of 1.0 g. (0.00833 mole) of tetracyclo-[3.3.0.$0^{2,8}$.$0^{4,6}$]octan-3-one in 20 ml. of dimethyl sulfoxide was added. After the mixture had stirred overnight, water was added and the mixture was poured onto ice. The aqueous mixture was extracted with pentane and the combined pentane layers were washed, dried, and concentrated. Distillation of the residue afforded 650 mg. (65%) of olefin, b.p. 85° (20 mm.), $n^{26}\text{D}$ 1.5242. The infrared spectrum showed $\nu_{\max}^{\text{neat}}$ 3142 (m), 3015 (s), 2875 (s), 2840 (s), 1648 (s), 1562 (m), 1450 (w), 1349 (m), 1282 (w), 1270 (m), 1107 (w), 1043 (w), 1000 (w), 970 (m), 927 (m), 895 (m), 868 (s), 860 (s), 802 (s), 747 (s), and 733 (s) cm.$^{-1}$. The n.m.r. spectrum showed a singlet at δ = 4.77 p.p.m. (2 H), and a complex pattern between δ = 2.37 p.p.m. and δ = 1.35 p.p.m. (8 H). Analysis by gas chromatography showed a broad peak with a retention time of 47 min. The ultraviolet spectrum was complex, $\nu_{\max}^{\text{vapor}}$ 204 mμ with shoulder peaks at 195, 198, 216, 220, 224, 226, 227, and 228 mμ.

Anal. Calcd. for C_9H_{10}: C, 91.47; H, 8.53. Found: C, 91.69; H, 8.59.

Method B. A solution of 50 mg. (0.00037 mole) of 3-methyltetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]octan-3-ol and 2 crystals of iodine in 15 ml. of dry benzene was heated to reflux for 24 hr. The water was collected in an attached water trap. The solution was poured into water and extracted with pentane. The combined pentane layers were washed with a sodium thiosulfate solution and water, dried, and concentrated. Analysis of the residue by gas chromatography showed one peak having the retention time of the tetracyclic olefin **20**. The infrared spectrum of the residue showed a hydroxyl band at 3340 and a double bond at 1640 cm.$^{-1}$.

endo-3-Methyltetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]*octan-3-ol* (**17**). A Grignard reaction employing 50 mg. (0.00205 g.-atom) of magnesium turnings, 0.2 ml. (0.0032 mole) of methyl iodide, and 200 mg. (0.0017 mole) of tetracyclo-[3.3.0.$0^{2,8}$.$0^{4,6}$]octan-3-one was carried out. A saturated ammonium chloride solution was added, and the mixture was poured into ice water. The aqueous mixture was extracted with ether, and the combined ether layers were washed, dried, and concentrated. Crystallization afforded 40 mg. of product, m.p. 50–52.5°. A second crop was obtained, 100 mg. (62% total), m.p. 45–52°. These crops were combined and recrystallized from pentane. The first crop, 70 mg., was dried *in vacuo* for 3 hr. at 0.1 mm. and room temperature to afford an analytical sample of 10 mg., m.p. 53.5–54.5°.

Anal. Calcd. for $C_9H_{12}O$: C, 79.37; H, 8.91. Found: C, 79.43; H, 9.02.

The infrared spectrum showed $\nu_{\max}^{\text{CCl}_4}$ 3640 (w), 3450 (m), 3030 (s), 2950 (s), 2920 (s), 2870 (m), 1450 (m), 1400 (m), 1370 (m), 1350 (m), 1290 (m), 1142 (s), 1112 (m), 1089 (m), 1042 (m), 1005 (m), 975 (s), 895 (w), and 845 (m) cm.$^{-1}$. The n.m.r. spectrum showed a complex pattern between δ = 1.08 and 2.30 p.p.m. with a sharp singlet at δ = 1.43 p.p.m. (CH_3). The n.m.r. spectrum of the residue showed a complex pattern between δ = 1.26 and 2.42 p.p.m.: four singlets were observed at δ = 1.26, 1.50, 2.24, and 2.62 p.p.m. Analysis by gas chromatography at any temperature high enough to produce a reasonable retention time caused the molecule to eliminate water forming **20**.

endo-3-Phenyltetracyclo[3.3.0.0.$^{2,8}0^{4,6}$]*octan-3-ol* (**19**). A Grignard reaction with phenylmagnesium bromide afforded a 71% yield of a phenyl carbinol, m.p. 112–114°. The infrared spectrum showed $\nu_{\max}^{\text{CCl}_4}$ 3570 (w), 3390 (w), 3020 (s), 2970 (m), 2930 (m), 2850 (m), 1600 (w), 1490 (m), 1445 (s), 1380 (m), 1348 (m), 1282 (m), 1217 (s), 1089 (s), 1048 (s), 1010 (w), 985 (w), 962 (m), 925 (m), and 910 (w) cm.$^{-1}$. The n.m.r. spectrum consisted of two complex regions: δ = 7.78–7.23 p.p.m. (5 H) and δ = 2.32–1.14 p.p.m. (9 H). The fine structure in the aromatic region was similar to that observed for 1-phenyl-1-cyclohexanol.

Anal. Calcd. for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.98; H, 7.32.

Tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]*octane* (**21**). *Method A.* The Huang-Minlon adaptation of the Wolff-Kishner reduction was employed. A solution of 2.0 g. of potassium hydroxide, 3 ml. of 85% hydrazine sulfate, and 885 mg. (0.0074 mole) of tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]octan-3-one in 25 ml. of diethylene glycol was refluxed for 2 hr. A distillation head was added and the temperature was allowed to climb to 205°. The solution was stirred at this point for 3 hr. and the distillate was collected, poured into water, and extracted with pentane. The pentane layer was washed, dried, and concentrated. Distillation afforded 466 mg. (59.7%) of hydrocarbon, b.p. 138–139°, $n^{26}\text{D}$ 1.4920. Analysis by gas chromatography showed two peaks in the ratio of 1:7. The major product showed a retention time identical with that of the compound prepared by

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(22) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).

method B. The infrared spectrum showed $\nu_{\max}^{\text{neat}}$ 3070 (s), 2900 (s), 2840 (s), 1670 (w), 1628 (w), 1562 (m), 1460 (w), 1370 (w), 1332 (w), 1282 (m), 1265 (w), 1240 (w), 1112 (w), 1052 (w), 1030 (w), 980 (w), 930 (w), 920 (w), 905 (w), 894 (w), 874 (m), 842 (w), 793 (s), 738 (s), 727 (s), and 674 (m) cm.$^{-1}$. The minor product was shown to be bicyclo[3.2.1]octa-2,5-diene[9] by its gas chromatographic retention time and by its presence in the n.m.r. spectrum of this mixture. The n.m.r. spectrum of **21** showed complex peaks at δ = 1.53 and 1.25 p.p.m. in addition to the very small peaks from bicyclo[3.2.1]octa-2,5-diene.

Anal. Calcd. for C_8H_{10}: C, 90.50; H, 9.50. Found: C, 90.71; H, 9.60.

Method B. Into a 50-ml. three-necked flask equipped with a mechanical stirrer and an addition funnel were placed 120 mg. (0.0028 mole) of sodium hydride (56% in mineral oil) and 7 ml. of dry ether. A solution of 200 mg. (0.00164 mole) of tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-ol in 5 ml. of dry ether was added, and the solution was stirred for 20 min. and was then cooled to −30°. A concentrated solution of *p*-toluenesulfonyl chloride (400 mg., 0.0021 mole) in ether was added. The reaction mixture was stirred for 1 hr. at −30°, and approximately 100 mg. (0.00263 mole) of lithium aluminum hydride was added all at once. The mixture was allowed to warm to room temperature and stir overnight. The work-up was carried out by adding successively 1 g. of water, 3 ml. of 15% potassium hydroxide, and 1 g. of water. The mixture was extracted with pentane and the combined pentane layers were washed, dried, and concentrated. Analysis by gas chromatography showed four peaks in the ratio of 11:1:4:9. The peak with the longest retention time (9) was collected and analyzed by its mass spectrum. The molecular ion peak was of the correct molecular weight; the remainder of the mass spectrum was very similar to that of the parent ketone. The hydrocarbon showed an identical retention time (13.5 min.) with that of the compound prepared by method A. The other peaks were not identified, and have retention times shorter than bicyclo[3.2.1]octa-2,5-diene.[9] The infrared spectrum was identical with that obtained from method A except that the 3340 band is less intense, the 727 band is absent, and a band at 705 cm.$^{-1}$ is present.

Dissociation Constant of the Cyanohydrin of Tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one. The methods described by Wheeler[23] and Ruzicka[13] were employed. Ethanol was purified by storing over zinc and distilling from potassium hydroxide. Into one 50.00-ml. volumetric flask was placed 0.100 g. (0.000833 mole) of the tetracyclic ketone, into another was placed 0.134 g. (0.00137 mole) of cyclohexanone, and into another was placed 120 mg. (0.00097 mole) of bicyclo[3.2.1]octan-8-one.[18] Two drops of pyridine and 10.0 ml. of ethanolic hydrogen cyanide (0.485 *M*) solution were added to each flask. The flasks were filled to their proper level with purified ethanol. A blank was also prepared. After 24 and 48 hr., duplicate 10.0-ml. aliquots were taken and added to an excess of 0.100 *N* silver nitrate (25.00 ml.). The excess silver nitrate was titrated with 0.100 *N* potassium thiocyanate, using ferric sulfate as the indicator. Representative data are as follows.

	time, hr.	HCN blank	tetracyclic ketone	cyclohexanone	bicyclic ketone
ml. of KCNS required	24	15.3	15.3	18.0	16.2
	48	15.2	15.4	17.7	16.5

The formula used for the calculation of the dissociation constant was $K_D = (a - x)(b - x)/x$ where a = HCN employed in moles/l., b = ketone employed in moles/l., and x = HCN consumed in moles/l. With tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one, $K_D = \infty$ (no cyanohydrin formed); with cyclohexanone, $K_D = 0.382 \times 10^{-2}$ (lit.[13,23] av. 0.265×10^{-2}, as high as 0.328×10^{-2}); and with bicyclo[3.2.1]octan-8-one, $K_D = 5.6 \pm 0.3 \times 10^{-2}$.

cis,cis,cis-3-Carboxamidotricyclo[4.1.0.0^{2,4}]heptane (**23**). Into a dry, three-necked, 50-ml. flask equipped with a Dry Ice condenser and a mechanical stirrer was condensed 35 ml. of liquid ammonia. A small amount of sodium metal, a small amount of anhydrous ferric chloride, and 0.50 g. (0.0217 g.-atom) of sodium metal were added in that order. After the sodium amide had formed, the ammonia was allowed to evaporate. Dry nitrogen was passed through the flask continually from this point until the end of the reaction. An addition funnel containing 20 ml. of dry, purified dioxane was fitted into the reaction flask, and the dioxane was added dropwise. The flask was heated to 80° and cooled, and a solution of 0.200 g. (0.00166 mole) of tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one in 7 ml. of dry, purified dioxane was added rapidly. The temperature was slowly raised until the liquid refluxed gently, and was held there for 1.5 hr. The mixture was allowed to cool and stand overnight. Water and 1 ml. of glacial acetic acid were added, and the mixture was extracted with ether. The ether layer was washed, dried, and concentrated. Crystallization of the residue from aqueous ethyl alcohol afforded 73 mg. (32%) of the tricyclic amide, m.p. 208.5–210°. The infrared spectrum showed $\nu_{\max}^{\text{CHCl}_3}$ 3450 (w), 3000 (w), 1680 (s), 1590 (m), 1430 (m), and 855 (w) cm.$^{-1}$.

Anal. Calcd. for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.01; H, 8.24; N, 10.45.

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(23) (a) O. H. Wheeler, E. O. DeRodriguez, *J. Org. Chem.*, **29**, 718 (1964); (b) O. H. Wheeler and V. S. Gaind, *Can. J. Chem.*, **36**, 1735 (1958).