spectra were consistent with those of an authentic sample of geranial, obtained from GLC separation of citral.

Jones Oxidation of Nerol. A solution of 500 mg (3.24 mmol) of 95% nerol and 10 ml of reagent-grade acetone was placed in a 50-ml round-bottom flask and cooled to 0° (ice–water bath). Oxidation as described for cinnamyl alcohol gave material which upon evaporative distillation (0.1 mm, 100°) yielded 420 mg (2.72 mmol, 84%) of a pale yellow oil having a citrus odor. GLC (Carbowax) showed a 7:1 ratio (87.5%) of neral to geranial as the only significant (97%) components. The NMR and ir spectra were consistent with those of an authentic sample of neral, obtained from GLC separation of citral.

Jones Oxidation of Benzyl Alcohol. A solution of 500 mg (4.63 mmol) of benzyl alcohol and 10 ml of reagent-grade acetone was placed in a 50-ml round-bottom flask and cooled to 0° (ice–water bath). Oxidation in the same manner gave material which upon evaporative distillation (water aspirator pressure, 100°) yielded 380 mg (3.52 mmol, 76%) of a clear oil (>99% pure by GLC) identified by ir and NMR as benzaldehyde.

Acknowledgments. We thank the Robert A. Welch Foundation and the National Cancer Institute (PHS Research Grant CA 15736) for support of this research.

Registry No.—Cinnamyl alcohol, 104-54-1; cinnamaldehyde, 104-55-2; geraniol, 106-24-1; geranial, 141-27-5; neral, 106-26-3; nerol, 106-25-2; benzyl alcohol, 100-51-6; benzaldehyde, 100-52-7; chromic acid, 7738-94-5.

References and Notes

(1) (a) H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, p 270; (b) W. Carruthers, "Modern Methods of Organic Synthesis", Cambridge University Press, New York, N.Y., 1971, p 245; (c) K. L. Rinehart, Jr., "Oxidation and Reduction of Organic Compounds", Prentice-Hall, Englewood Cliffs, N.J., 1973, pp 70–71; (d) R. O. C. Norman, "Principles of Organic Synthesis", Methuen, London, 1968, p 518; (e) C. A. Buehler and D. E. Pearson, "Survey of Organic Syntheses", Wiley-Interscience, New York, N.Y., 1970, pp 545–549; (f) L. J. Chinn, "Selection of Oxidants in Synthesis", Marcel Dekker, New York, N.Y., 1971, pp 41–43.

(2) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946); C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

(3) K. E. Harding and R. C. Ligon, *Synth. Commun.*, **4**, 297 (1974); K. E. Harding and R. C. Ligon, unpublished observations.

(4) J. R. Holum, *J. Org. Chem.*, **26**, 4814 (1961).

(5) A recent communication has described oxidation of cinnamyl alcohol in 85% yield using sodium dichromate and sulfuric acid in dimethyl sulfoxide: Y. S. Rao and R. Filler, *J. Org. Chem.*, **39**, 3304 (1974).

220-MHz Nuclear Magnetic Resonance Spectra of Bicyclo[3.2.1]octan-6-ones

William C. Agosta* and Steven Wolff*

Laboratories of The Rockefeller University, New York, New York 10021

Received December 2, 1974

Over the past few years we have accumulated a number of substituted bicyclo[3.2.1]octan-6-ones, both as substrates and as products in diverse photochemical investigations. Examination of the 220-MHz NMR spectra of these compounds has permitted consistent assignments for the various low-field proton resonances in each case, and these results are presented here. Other investigators have previously underscored the advantages and value of NMR studies of this bicyclic ring system,[1] and indeed our results allow worthwhile comparisons with the large store of information now on hand for norbornanes.[2] Furthermore, they permit generalizations which should facilitate future determinations of structure and stereochemistry for related bicyclooctanes.

Synthesis of most of these ketones has been described in earlier work,[3] and details of the preparation of the epimeric methoxy ketones **15** and **16** are given at the end of the present article. The remaining new compounds, **5–7**, are formed on photolysis of appropriate cyclopentenones,[4] and their preparation and other data defining their structures will be reported in a forthcoming publication.

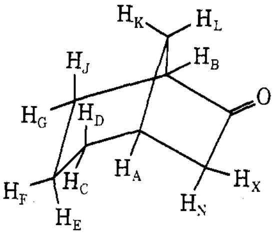
The methyl and low-field resonances of the 220-MHz NMR spectra of these 16 bicyclooctanones are collected in Table I. For comparison the completely interpreted spectrum[3] of the closely related oxabicyclic ketone **17** is also presented.

Typically the lowest field signals in the simple alkylated ketones of this series are those of the bridgehead positions at C(1) and C(5), H_A and H_B, respectively, with H_A the farther downfield (compare, for example, **1**, **2**, and **4**). The positions of these protons closely parallel those of the bridgehead hydrogens of norbornanone (**18**): C(4) H, δ 2.57, 2.61, and C(1) H, 2.39, 2.41 ppm.[2b,5] Interestingly, these effects do not appear in bicyclo[2.2.2]octanone (**19**); here the two bridgehead protons at C(1) and C(4), along with the C(3) methylene protons, all appear at 2.15 ppm ($W_{1/2}$ = 5 Hz).[5] The bridgehead proton more distant from the carbonyl both in norbornanones and in bicyclo[3.2.1]octan-6-ones then appears downfield from the bridgehead proton adjacent to the carbonyl. The reason for this is not known with certainty; for norbornanones it has been suggested[5] that excess s character and abnormal polarizability in the bridgehead bonding orbital may be responsible. In this regard it is noteworthy that in the bicyclo[3.2.1]octanones a qualitatively similar low-field shift is also seen for methyl groups at the distant bridgehead position. For example, the C(1) methyl of **2** appears well downfield from the C(5) methyl of **4** (1.13 vs. 0.936 ppm).

The next two signals upfield are those of the endo and exo protons at C(7), H_N and H_X. These are characterized by two, and occasionally three, coupling constants. First, the geminal coupling is typically 18 Hz (J_{NX}). Second, H_X shows a vicinal coupling constant (J_{XA}) of 6–7 Hz, while the corresponding interaction for H_N is not seen or else is small (J_{NA} = 0–1 Hz). Finally, there are long-range splittings over four bonds; H_N couples with H_K in all cases (J_{NK} = 3–4 Hz),[6] and H_X occasionally does so with H_D (J_{XD} = 0–0.5 Hz). All these interactions are analogous to those well documented in norbornanes, although the range of values observed is slightly different in some cases. Thus, in norbornanes the vicinal coupling constant corresponding to J_{XA} is a little smaller (3–4 Hz[2]), and the long-range coupling constant corresponding to J_{XD} is a little larger (1–1.5 Hz[2]). The noted difference in vicinal coupling constants between the two systems would appear primarily attributable to the increase in the dihedral angle involving H_A and H_X on passing from the bicyclo[3.2.1]octane to the bicyclo[2.2.1]heptane skeleton. The high value of the geminal coupling in the bicyclooctanes (J_{NX} = 18 Hz) is due largely to the effect of the carbonyl group. There is good evidence[7] that adjacent π bonds can enhance geminal coupling if the geometry is appropriate, and models indicate that the rigid geometry of the five-membered ring here should lead to a maximum contribution from the carbon–oxygen double bond to the value of J_{NX}.

H_N and H_X appear at about 2.0 ppm, with the exact position of each influenced by substitution not only at the adjacent bridgehead position but also at C(2) and C(3). The difference in chemical shift between these protons is usually 0.2 ppm or less. For these reasons assignment of the two signals to one or the other of the C(7) protons is based on the magnitude of the observed vicinal and long-range coupling constants, as discussed above, and not on the chemical shifts of these protons. In the ketones bearing hydrogen at C(1), H_X appears at lower field in six of the nine exam-

Table I
NMR Spectra of Bicyclo[3.2.1]octan-6-ones



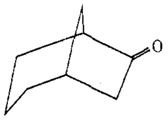
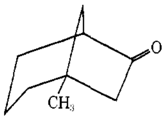
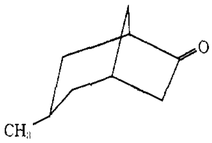
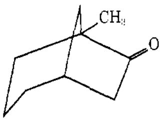
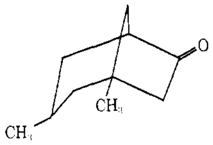
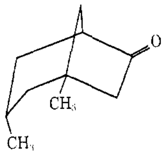
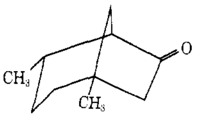
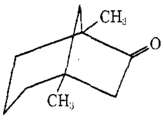
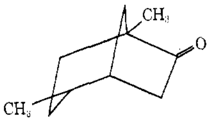
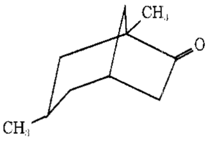
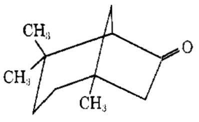
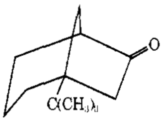
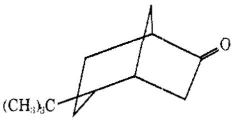
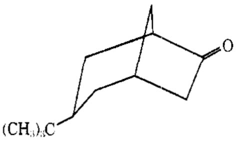
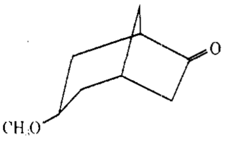
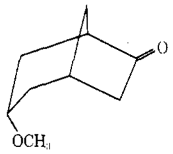
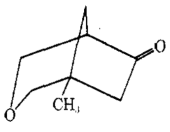
	Chemical shifts, δ, and coupling constants, Hz					
Compd	H_A	H_B	H_N	H_X	C(1) CH_3	Other
 1	2.57, br	2.23, br	1.96, dd J_{NK} = 3 J_{NX} = 18	2.16, dd J_{XA} = 7 J_{XN} = 18		
 2		2.33, br	1.98, dd J_{NK} = 3 J_{NX} = 18	1.83, dd J_{XD} = 0.5 J_{XN} = 18	1.13, s	
 3	2.54, br	2.23, br	1.95, dd J_{NK} = 3 J_{NX} = 18	2.12, ddd J_{XD} = 0.5 J_{XA} = 7 J_{XN} = 18		C(3) CH_3: 0.900, d $J = 6$
 4	2.50, br		2.00, dd J_{NK} = 3.5 J_{NX} = 18	2.19, dd J_{XA} = 7 J_{XN} = 18		C(5) CH_3: 0.936, s
 5		2.33, br	1.98, dd J_{NK} = 4 J_{NX} = 18	1.80, dd J_{XD} = 0.5 J_{XA} = 18	1.12, s	C(3) CH_3: 0.905, d $J = 7$
 6		2.29, br	2.18, dd J_{NK} = 3 J_{NX} = 18	1.73, d J_{XN} = 18	1.14, s	C(3) CH_3: 1.01, d $J = 7$
 7		2.09, br	1.93, dd J_{NK} = 4 J_{NX} = 18	1.81, d J_{XN} = 18	1.14, s	C(4) CH_3: 0.927, d $J = 7$
 8			2.01, dd J_{NK} = 4 J_{NX} = 18	1.85, d J_{XN} = 18	1.12, s	C(5) CH_3: 0.945, s
 9	2.19, br		2.09, dd J_{NK} = 4 J_{NX} = 18	1.98, dd J_{XA} = 7 J_{XN} = 18		C(2) CH_3: 0.891, d $J = 6$ C(5) CH_3: 0.927, s

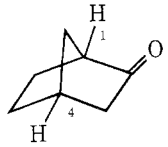
Table I (*Continued*)

	Chemical shifts, δ, and coupling constants, Hz					
Compd	H_A	H_B	H_N	H_X	C(1)CH_3	Other
 10	2.47, br		2.00, ddd J_{NA} = 0.5 J_{NK} = 4 J_{NX} = 18	2.15, dd J_{XA} = 7 J_{XN} = 18		C(3) CH_3: 0.886, d $J = 6$ C(5) CH_3: 0.935, s
 11		~1.82	1.92, dd J_{NK} = 4 J_{NX} = 18	1.74, dd J_{XD} = 0.5 J_{XN} = 18	1.13, s	C(4) CH_3: 0.932, s C(4) CH_3: 0.986, s
 12		2.34, br	1.80, dd J_{NK} = 3 J_{NX} = 18	2.09, dd J_{XD} = 0.5 J_{XN} = 18		$C(CH_3)_3$: 0.91, s
 13	2.63, br	2.19, br	2.16, dd J_{NK} = 3 J_{NK} = 18	2.02, dd J_{XA} = 6 J_{XN} = 18		$C(CH_3)_3$: 0.89, s
 14	2.58, br	2.26, br	1.94, ddd J_{NA} = 0.5 J_{NK} = 3.5 J_{NX} = 18	2.11, dd J_{XA} = 6.5 J_{XN} = 18		$C(CH_3)_3$: 0.84, s
 15	2.63, br	2.34, br	1.98, ddd J_{NA} = 1 J_{NK} = 3 J_{NX} = 18	2.12, dd J_{XA} = 6 J_{XN} = 18		H_E: 3.31, m OCH_3: 3.21, s
 16	2.52, br	2.14, br	2.47, dd J_{NK} = 3 J_{NX} = 17	~1.93		H_F: 3.45, m OCH_3: 3.14, s
 17		2.26, br	2.18, dd J_{NK} = 3 J_{NX} = 17	1.96, d J_{XN} = 17	1.07, s	H_C: 3.53, dd J_{CD} = 11 J_{CL} = 3 H_D: 3.44, d J_{DC} = 11 H_G: 3.98, ddd J_{GJ} = 10 J_{GB} = 2 J_{GL} = 3 H_J: 3.47, d J_{JG} = 10 H_K: 1.74, dd J_{KN} = 3 J_{KL} = 13 H_L: 1.89, br

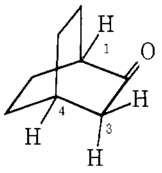
ples.[8] In the exceptional cases (**9**, **13**, and **16**) there is endo substitution at either C(2) or C(3), placing a substituent rather close in space to C(7). Interestingly, substitution of a methyl group at C(1) causes a sizable upfield shift of H_X but not H_N, with the result that in all six C(1)-methyl compounds H_N appears at lower field than H_X. In contrast to these observations, it has been known for some years that in norbornanes an exo proton appears reliably at lower field than the corresponding endo proton, and that this is true whether the adjacent bridgehead bears hydrogen or methyl.[9]

In six of the ketones the three-carbon bridge [C(2)–C(4)] of the cyclohexane ring bears a single methyl group. It is noteworthy that the one axial methyl in this series (in **6**) exhibits the expected[10] downfield shift relative to the five equatorial ones ($\delta_{ax} = 1.01$, $\delta_{eq} = 0.90 \pm 0.03$ ppm).

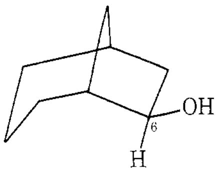
Preparative Experiments. The methoxy ketones **15** and **16** were prepared from hydroxy ketal **22**.[11] Reaction of this alcohol with methyl iodide and base gave the methoxy ketal, which was hydrolyzed to **15** in dilute acid. For **16** the configuration of the hydroxyl group of **22** was inverted through oxidation to **23** as previously described,[11] followed by reduction to **24**. We found lithium tri-*sec*-butyl hydride[12] to be highly stereoselective in this reduction, with no detectable amount (<2%) of **22** accompanying formation of **24**. Etherification and subsequent hydrolysis of **24** following the procedures noted above then gave **16**.



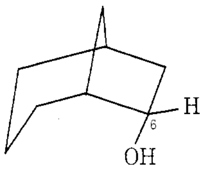
18



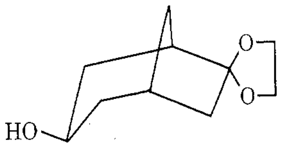
19



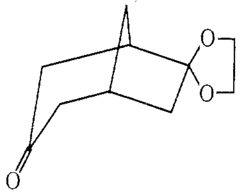
20



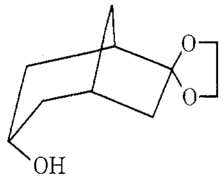
21



22



23



24

Experimental Section

Materials and Equipment. All VPC was carried out with a 10 ft × 0.375 in. aluminum column containing DEGS (30%) absorbed on 45/60 Chromosorb W in a Varian Aerograph Model A-90-P3. The column oven was operated at 145–175° and the helium carrier gas flow rate was 120–150 ml/min. NMR spectra were recorded for dilute CCl_4 solutions using a Varian HR-220 (220-MHz) spectrometer. Ir spectra were obtained for CCl_4 solutions with a Perkin-Elmer Model 237B spectrometer. Mass spectra were obtained on a Du Pont 21-492 double-focusing mass spectrometer with a resolution of 10^4, and the results were processed with a AEI DS-30 data system. Boiling points are uncorrected; all products were obtained as colorless oils.

***exo*-3-Methoxybicyclo[3.2.1]octan-6-one (15).** Hydroxy ketal **22** (184 mg, 1 mmol) was methylated using NaH and methyl iodide in dimethyl sulfoxide as previously described for the synthesis of 4-methyl-4-methoxymethylcyclopentanone ethylene ketal.[3] Deketalization was effected by vigorous stirring of the crude ether with 5 ml of 10% HCl for 1 hr at room temperature. The reaction mixture was poured into brine and extracted three times with pentane. The combined pentane extracts were washed with brine, saturated $NaHCO_3$, and brine and dried over $MgSO_4$. Removal of the pentane by distillation through a Vigreux column yielded a residue which was distilled bulb-to-bulb (120°, 12 mm) to afford 144 mg of oil. The major component of this crude product was purified by preparative VPC and identified as **15**: ir 2980 (m), 2895 (w), 2850 (w), 1742 (s), 1400 (w), 1098 (s), 1058 (m), 975 cm^{-1} (w); NMR δ 3.31 (seven-line m, 1 H), 3.21 (s, 3 H), 2.63 (br m, 1 H), 2.34 (br m, 1 H), 2.30–1.82 (br m, 3 H), 2.12 (dd, J = 6, 18 Hz, 1 H), 1.98 (ddd, J = 1, 3, 18 Hz, 1 H), 1.67 (dd, J = 3, 12 Hz, 1 H), 1.46 (m, 1 H), 1.33 (ddd, J = 2, 11, 11 Hz, 1 H); mass spectrum m/e 154.1005 (M^+, calcd for $C_9H_{14}O_2$, 154.0993).

***endo*-3-Methoxybicyclo[3.2.1]octan-6-one (16).** An anhydrous tetrahydrofuran solution (5 ml) of keto ketal **23** (338 mg), obtained from **22** by the method of Monti,[11] was added to lithium tri-*sec*-butylborohydride (4.65 ml of a 1 *M* solution) at −78° under a nitrogen atmosphere. After stirring at this temperature for 3 hr, the reaction mixture was warmed to room temperature and oxidized with 3 *M* aqueous NaOH (3 ml) and 30% H_2O_2 (5 ml). The mixture was poured into water and extracted three times with ether. The organic phases were combined, washed with brine, and dried. Removal of solvents in vacuo gave 542 mg of a viscous oil. Without further attempt to remove 2-butanol, the crude hydroxy ketal was methylated and worked up as described for **15** above. Hydrolysis of the ketal by vigorous stirring with 5 ml of 3% H_2SO_4 for 1 hr at room temperature and extractive work-up with pentane yielded impure **16**. This was distilled bulb-to-bulb (135°, 12 mm) to give 184 mg of an oil which was purified by preparative VPC. There was no evidence of **15** in the distilled material. The major component was collected and identified as **16**: ir 2980 (s), 2900 (m), 2850 (w), 1745 (s), 1360 (m), 1260 (m), 1148 (m), 1082 (s), 962 (m), 880 cm^{-1} (m); NMR δ 3.45 (br, 1 H), 3.14 (s, 3 H), 2.52 (br, 1 H), 2.47 (dd, J = 3, 17 Hz, 1 H), 2.38–1.54 (br m, 7 H), 1.93 (d, J = 17 Hz, 1 H); mass spectrum m/e 154.0998 (M^+, calcd for $C_9H_{14}O_2$, 154.0993).

Acknowledgments. The NMR spectra were obtained on an instrument at The Rockefeller University and operated by a consortium supported in part by NSF Grant GB-43257. We thank Miss Luz Catan for technical assistance and The Rockefeller University Mass Spectrometry Laboratory for mass spectra.

Registry No.—**1**, 6553-12-4; **2**, 54277-28-0; **3**, 54277-29-1; **4**, 20608-68-8; **5**, 54831-14-0; **6**, 54831-15-1; **7**, 54831-16-2; **8**, 38857-63-5; **9**, 54788-70-4; **10**, 54788-71-5; **11**, 33315-89-8; **12**, 54277-32-6; **13**, 54788-72-6; **14**, 54277-33-7; **15**, 54788-73-7; **16**, 54788-74-8; **17**, 39921-29-4; **22**, 31444-22-1; **23**, 31444-23-2.

References and Notes

(1) C. W. Jefford and K. C. Ramey, *Tetrahedron*, **24**, 2927 (1968).
(2) For leading references, see (a) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed, Pergamon Press, Oxford, 1969; (b) J. L. Marshall and S. R. Walter, *J. Am. Chem. Soc.*, **96**, 6358 (1974).
(3) **1**, K. B. Wiberg and B. A. Hess, Jr., *J. Org. Chem.*, **31**, 2250 (1966); **2–4**, **9**, **12–14**, W. C. Agosta and S. Wolff, *ibid.*, **40**, 1027 (1975); **8**, **10**, S. Wolff and W. C. Agosta, *ibid.*, **38**, 1694 (1973); **11** and **17**, S. Wolff, W. L. Schreiber, A. B. Smith, III, and W. C. Agosta, *J. Am. Chem. Soc.*, **94**, 7797 (1972).
(4) S. Wolff, unpublished work in this laboratory; similar photochemical reactions lead to **11** and **17** (see ref 3).
(5) D. G. Farnum and G. Mehta, *J. Am. Chem. Soc.*, **91**, 3256 (1969).
(6) Direct evidence for J_{NK} is seen in labeled **17**, in which H_K is replaced by deuterium. In this compound H_N appears as a simple doublet, J_{NX} = 17 Hz: S. Wolff and W. C. Agosta, *J. Chem. Soc., Chem. Commun.*, 502 (1973).
(7) M. Barfield and D. M. Grant, *J. Am. Chem. Soc.*, **85**, 1899 (1963). For examples involving cyclic ketones, see N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Francisco, Calif., 1964, pp 57–61.
(8) In the spectra of *exo*- and *endo*-bicyclo[3.2.1]bicyclooctan-6-ol (**20** and **21**), as well as the derived acetates and tosylates, the C(6) proton also appears at lower field when exo: R. A. Appleton, J. C. Fairlee, R. McCrindle, and W. Parker, *J. Chem. Soc. C*, 1716 (1968).
(9) J. I. Musher, *Mol. Phys.*, **6**, 93 (1963); W. D. Kumler, J. N. Shoolery, and F. V. Brutcher, Jr., *J. Am. Chem. Soc.*, **80**, 2533 (1958); T. J. Flautt and W. F. Erman, *ibid.*, **85**, 3212 (1963); K. Tori, Y. Hamashima, and A. Takamizawa, *Chem. Pharm. Bull.*, **12**, 924 (1964); P. V. Demarco, D. Doddrell and E. Wenkert, *Chem. Commun.*, 1418 (1969).
(10) A. Segre and J. I. Musher, *J. Am. Chem. Soc.*, **89**, 706 (1967); D. K. Dalling and D. M. Grant, *ibid.*, **89**, 6612 (1967).
(11) S. A. Monti and S.-S. Yuan, *J. Org. Chem.*, **36**, 3350 (1971). We thank Professor Monti for a generous gift of **22**.
(12) H. C. Brown and S. Krishnamurthy, *J. Am. Chem. Soc.*, **94**, 7159 (1972).