methine proton of *N*-retinylidene-*n*-butylammonium ion (**8**) resonates at 8.3 ppm. If in the nmr spectrum of rhodopsin the region around 8.3 ppm is not masked by bands from the aromatic protons of the protein moiety (opsin) and the resonance due to the azomethine proton is easily detectable, then this technique (nmr spectroscopy) may reveal whether the Schiff base linkage of the visual pigment is protonated or not. We would have been more confident if the resonance of the azomethine proton had occurred in the region below 9 ppm.

Acknowledgments.—This work was supported in part by NSF Grant No. GB-29946 and Grants from the Research Corporation and Sloan Foundation to a consortium at the Rockefeller University for 220-MHz nmr facilities. We wish to thank Peter Ziegler for assistance in obtaining the nmr spectra.

Registry No.—**1,** 1077-18-5; **2,** 7020-93-1; **3,** 3910-55-2; **4,** 15286-55-2; **7,** 36076-04-7; **8,** 32798-55-3.

The Methyl Signals in the Proton Magnetic Resonance Spectra of Some 2-Methylnorbornanes. A Cautionary Tale

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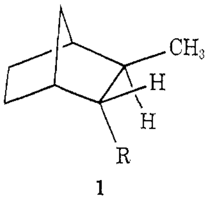
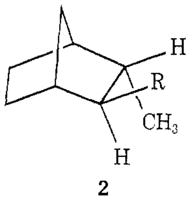
Proton magnetic resonance spectroscopy is frequently used for distinguishing between a methyl group bonded to a quaternary carbon atom and a methyl group bonded to an sp^3 carbon atom bearing a hydrogen atom. Although in the latter case the signal may deviate from a simple AX$_3$ doublet owing to strong or virtual coupling, it is usually readily distinguishable from the singlet signal in the former case, because the chemical shift differences between the methyl and methine protons is normally appreciable. If, however, there were accidental chemical equivalence between the methyl and methine protons because of special structural features in the molecule, the methyl signal could appear as a singlet, superimposed on the methine signal. We have observed examples of this circumstance in the spectra of the norbornanes **1a–c**.



1



2

a, R = CH$_2$OH
b, R = CH$_2$Cl
c, R = CH$_2$OAc
d, R = CO$_2$H

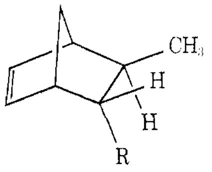
Compounds **1a–c** were prepared from the acid **1d**.[1] Although the methyl group of **1d** gives rise to a conventional CH$_3$CH doublet (Table I), the methyl groups of **1a–c** give rise to singlets. By contrast, the methyl groups of **2a–c** give rise to doublets; these compounds were prepared from the acid **2d**,[1] whose spectrum also showed a methyl doublet. It is known that the endo proton signal in norbornane occurs at unusually high field,[2,3] and we conclude that this effect, combined with a further upfield shift resulting from shielding by the endo C–CH$_2$X bond in **1a–c**,[4] results in accidental chemical equivalence of the methyl protons and the endo methine proton.[5] As expected for this interpretation, the methyl singlets are superimposed on multiplets, the total peak area corresponding to four protons. The absence of this effect in the spectrum of **1d** is attributable to deshielding of the endo methine proton by the carboxylic acid group and in the spectra of **2a–d** to the fact that exo protons are not shielded by the norbornane system.[2,3]

TABLE I
METHYL PROTON SIGNALS[a]

Compd	δ	Compd	δ
1a	0.93 (s)	**2a**	0.97 (d)
1b	0.98 (s)	**2b**	1.01 (d)
1c	0.95 (s)	**2c**	0.97 (d)
1d	0.97 (d)	**2d**	1.06 (d)
3a	1.10 (d)	**4a**	0.84 (d)
3b	0.79 (d), 1.03 (d)	**4c**	0.93 (d)
3c	1.18 (d)		

[a] For all doublets, J = 6–7 Hz.

Related observations have been made in the norbornene series. Compounds **3a** and **3b** give rise to methyl doublets in which the higher field component is considerably more intense than the lower field component,[6] whereas compounds **3c**, **4a**, and **4c** give rise to conventional CH$_3$CH doublets.[7] It is known that signals arising from endo protons in norbornene occur at yet higher field than those in norbornane.[2] Thus, the spectra of **3a** and **3b** can be interpreted in terms of a shift of the endo methine signals to higher field than those of the exo methyl protons; indeed, such signals are observed as multiplets as δ ∼ 0.90 and 0.80, respectively.



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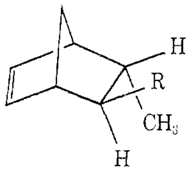

4

a, R = CH$_2$OH
b, R = CH$_3$
c, R = CO$_2$H

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(1) S. Beckmann, A. Dürkop, R. Bamberger, and R. Mezger, *Justus Liebigs Ann. Chem.*, **594**, 199 (1955).

(2) A. P. Marchand and N. W. Marchand, *Tetrahedron Lett.*, 1365 (1971).

(3) J. I. Musher, *Mol. Phys.*, **6**, 93 (1963); T. J. Flautt and W. F. Erman, *J. Amer. Chem. Soc.*, **85**, 3212 (1963); P. M. Subramanian, M. T. Emerson, and N. A. LeBel, *J. Org. Chem.*, **30**, 2624 (1965).

(4) R. G. Foster and M. C. McIvor, *Chem. Commun.*, 280 (1967).

(5) Broadening of the methyl singlets indicates that the chemical equivalence is not exact.

(6) In the case of **3b**, this refers to the lower field doublet, assigned to the exo methyl group; the endo methyl group gives rise to a conventional CH$_3$CH doublet.

(7) The pmr spectra of **3a** and **4a** have been discussed earlier,[8] but no reference was made to the methyl signal of **3a**.

(8) H. Christol, J. Coste, and F. Plénat, *Ann. Chim.* (*Paris*), **4**, 93, 105 (1969).

It is clear from these results that caution must be exercised in the interpretation of singlet methyl proton signals and that other evidence should be adduced, *e.g.*, from solvent or lanthanide shift studies, in order to exclude the possibility of accidental chemical equivalence of the methyl and vicinal methine protons.

Experimental Section

Materials.—Compounds **3c** and **4c** were prepared from cyclopentadiene and crotonic acid, and hydrogenated to give **1d** and **2d**.[9] These were reduced with lithium aluminum hydride to give **1a** and **2a**,[1] which were converted to **1b** and **2b** by treatment with triphenylphospine and carbon tetrachloride,[10] and to **1c** and **2c** by acetylation with acetic anhydride and sulfuric acid. Compounds **3a** and **4a** were prepared by reduction of **3c** and **4c** with lithium aluminum hydride.[8]

Spectra.—Pmr spectra were recorded in carbon tetrachloride solution at 100 MHz. Chemical shifts (δ) are reported in parts per million downfield from internal tetramethylsilane.

Acknowledgments.—We thank Dr. R. A. Blattel for the spectrum of **3b** and the National Research Council of Canada for support of this work.

Registry No.—**1a**, 18377-07-6; **1b**, 41476-85-1; **1c**, 41476-86-2; **1d**, 41476-87-3; **2a**, 18377-06-5; **2b**, 41476-89-5; **2c**, 41476-90-8; **2d**, 41476-91-9; **3a**, 24557-29-7; **3b**, 695-80-7; **3c**, 4397-23-3; **4a**, 24557-37-7; **4**, 4397-24-4.

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[9] G. Komppa and S. Beckmann, *Justus Liebigs Ann. Chem.*, **523**, 68 (1936); K. Alder, W. Günzl, and K. Wolff, *Chem. Ber.*, **93**, 809 (1960).

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Synthesis of Spiro Ketals from Japanese Hops

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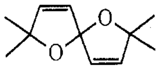
Among the volatile components of the pistillate cones of "Shinshu-wase," a variety of hop plant (*Humulus lupulus*, L.) cultivated in Japan, are two C_{11} unsaturated spiro ketals having a pleasant, apple-like odor.[1] On the basis of spectral properties and hydrogenation to the known[2] saturated spiro ketal **3**, structures **1** and **2** have been assigned[3] to these two compounds. Here we describe a simple confirmatory synthesis of **1** and **2** together with an alternative route to **3**.



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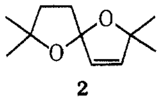

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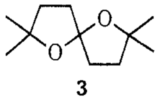
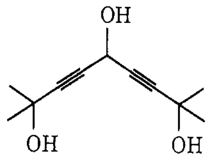


3

Addition of 2 mol of the dimagnesium salt of 2-methyl-3-butyn-2-ol to ethyl formate afforded the desired product, 2,8-dimethyl-3,6-nonadiyne-2,5,8-triol (**4**), in 33% yield as a solid which crystallized readily from chloroform. Reaction of the same salt with 4-hydroxy-4-methyl-2-pentynal gave material with spectral evidence for the presence of **4**; however, no crystalline product could be isolated.



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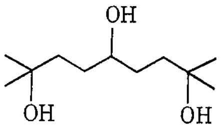

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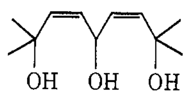

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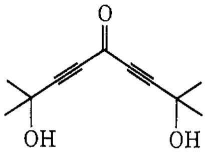

7

Hydrogenation of **4** to the saturated triol **5** proceeded smoothly over 5% palladium on charcoal. Partial hydrogenation of **4** was unsuccessful over a Lindlar catalyst[4] of demonstrated activity but was satisfactory over quinoline-poisoned, 5% palladium on barium sulfate, giving the crystalline dicisoid dienetriol **6** in 95% yield. Upon oxidation with active manganese dioxide,[5] crude **6** was converted in fair yield directly into the dienic spiro ketal **1**, the spectral properties of which correspond to those recorded[3] for the natural compound.

By partial hydrogenation, **1** gave a mixture containing the monounsaturated ketal **2** and the saturated ketal **3**, separable by gas chromatography. An alternative route to **3** was achieved by oxidation with accompanying cyclodehydration of the saturated triol **5** with Jones reagent[6] and also by similar oxidation of **4** to the dihydroxydiynone **7**, followed by hydrogenation and spontaneous ketal formation.

Experimental Section[7]

2,8-Dimethyl-3,6-nonadiyne-2,5,8-triol (**4**).—2-Methyl-3-butyn-2-ol (84 g, 1 mol) was added, with stirring, over a period of 1 hr at 20° to 2 mol of ethylmagnesium bromide in 1.2 l. of dry tetrahydrofuran (THF). To the resulting dimagnesium salt, 37 g (0.5 mol) of ethyl formate in 50 ml of dry THF was added slowly, with stirring, and the mixture was heated at reflux for 36 hr. With cooling, 500 ml of saturated ammonium chloride solution was added, and the mixture was extracted with four 500-ml portions of ether. The combined organic extracts were dried over powdered 4-A molecular sieves and then concentrated under reduced pressure to remove the ether, THF, and unreacted 2-methyl-3-butyn-2-ol. The residue was placed on a column of 80–100 mesh Alcoa alumina (3.5 × 50 cm) and washed with ether. A brown, foul-smelling oil was eluted and discarded. Further elution with ether and then methanol gave a nearly odorless brown syrup which when dissolved in chloroform crystallized in several crops, yielding a total of 32.8 g (33%) of triol **4**, mp 92–97°. Recrystallization from chloroform gave product with mp 95–98°; ir (KBr) 2.95 (b), 4.45 μ (w); nmr (DMSO-d_6) δ 1.33 (12 H, s, $-CH_3$), 5.10 (1 H, d, J = 6.5 Hz, HCOH), 5.28 (2 H, s, -OH), 5.94 (1 H, d, J = 6.5 Hz, -OH); mass spectrum m/e 181 ($M^+ - CH_3$), 163, 145, 91, 43 (base). The nmr absorptions at δ 5.28 and 5.94 disappeared upon addition of D_2O.

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.56; H, 8.50.

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[3] Y. Naya and M. Kotake, *Tetrahedron Lett.*, 1715 (1967).

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

[7] Melting points and boiling points are uncorrected. Microanalyses were performed by K. Widiger, University of Kansas Medicinal Chemistry microanalyst. Infrared spectra were recorded on a Perkin-Elmer Infracord 137B spectrophotometer; nmr spectra were taken on a Varian A-60 instrument; mass spectra were obtained on a Varian CH-5 spectrometer.