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.

(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).

(10) I. M. Downie, J. B. Holmes, and J. B. Lee, *Chem. Ind. (London)*, 900 (1966); J. B. Lee, *J. Amer. Chem. Soc.*, **88**, 3440 (1966).

Synthesis of Spiro Ketals from Japanese Hops

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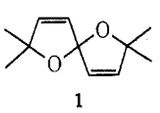
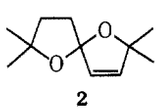
Among the volatile components of the pistillate cones of "Shinshu-wase," a variety of hop plant (*Humulus lupulus*, L.) cultivated in Japan, are two C_{11} unsaturated spiro ketals having a pleasant, apple-like odor.[1] On the basis of spectral properties and hydrogenation to the known[2] saturated spiro 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**.



1



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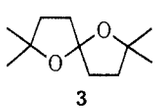


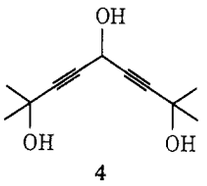
3

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.

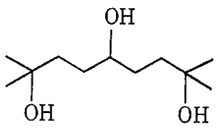
(1) Y. Naya and M. Kotake, *Nippon Kagaku Zasshi*, **88**, 1302 (1967); *Chem. Abstr.*, **69**, 44038 (1968).

(2) T. Ström, *J. Prakt. Chem.*, **48**, 209 (1893).

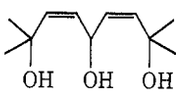
(3) Y. Naya and M. Kotake, *Tetrahedron Lett.*, 1715 (1967).



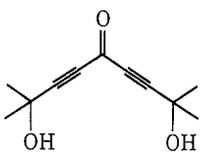
4



5



6



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.

(4) H. Lindlar and R. Dubuis, *Org. Syn.*, **46**, 89 (1966).

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

(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.

4-Hydroxy-4-methyl-2-pentynal.—This compound was prepared for use in place of ethyl formate in the foregoing reaction. A solution of 2.0 g (17.5 mmol) of 4-methyl-2-pentyne-1,4-diol[8] in 100 ml of methylene chloride was stirred for 0.5 hr with 20 g of active manganese dioxide.[5] After filtration and concentration, distillation afforded 0.5 g (25%) of 4-hydroxy-4-methyl-2-pentynal: bp 58–60° (0.6 mm); ir ($CHCl_3$) 2.75, 2.95 (b), 3.35, 3.50, 3.65 (w), 4.5 (s), 6.0 (s), 8.6, 9.55, 10.5 μ; nmr ($CDCl_3$) δ 1.43 (6 H, s, $-CH_3$), 3.93 (1 H, s, –OH), 9.10 (1 H, s, –CHO); mass spectrum m/e 112 (M^+), 97, 43, 32, 28 (base); 2,4-DNP (from ethanol–water) mp 103–105°.

Anal. (2,4-DNP). Calcd for $C_{12}H_{12}N_4O_5$: C, 49.32; H, 4.14; N, 19.17. Found: C, 49.11; H, 3.99; N, 18.96.

Although spectral analysis indicated the formation of **4** from the addition of this aldehyde to the dimagnesium salt of 2-methyl-3-butyn-2-ol, no crystalline product was obtained.

2,8-Dimethyl-2,5,8-nonatriol (5).—A solution of 235 mg (1.2 mmol) of **4** in 40 ml of ethyl acetate was stirred with 6 mg of 5% palladium on charcoal under 1 atm of hydrogen at 25°. After 1 hr, uptake of hydrogen (4.8 mmol) was complete. After removal of the catalyst and solvent, **5** was recovered as an analytically pure, clear, viscous oil (228 mg, 93%): ir ($CHCl_3$) 2.7, 2.9 (b), 7.2, 7.3, 8.65, 11.0 μ; nmr (DMSO-d_6) δ 1.05 (12 H, s, $-CH_3$), 0.73–2.20 (8 H, m, $-CH_2CH_2-$), 3.35 (1 H, m, HCOH), 4.07 (2 H, b, –OH), 5.43 (1 H, m, –OH).

Anal. Calcd for $C_{11}H_{24}O_3$: C, 64.67; H, 11.84. Found: C, 64.80; H, 12.00.

2,8-Dimethyl-3-*cis*,6-*cis*-nonadiene-2,5,8-triol (6).—To a mixture of 186 mg of synthetic quinoline and 157 mg of hydrogen-equilibrated 5% palladium on barium sulfate in 100 ml of ethyl acetate was added 2.94 g (15 mmol) of diynetriol **4** in 50 ml of the same solvent. After the mixture was stirred for 45 min at 25°, 30 mmol of hydrogen was absorbed. Filtration and evaporation afforded 3.18 g of a pale yellow oil which slowly solidified. The nmr spectrum indicated 95% conversion of **4** to **6**. Chromatography of 107 mg of the crude product on 10 g of silica gel (Grace, neutral) gave 18 mg of analytically pure **6**: mp 75.5–77.5°; ir (KBr) 2.65, 3.0 (b), 3.3, 7.25, 7.3, 8.55, 10.05, 10.4, 11.15, 12.70 μ; nmr ($CDCl_3$) δ 1.37 (12 H, s, $-CH_3$), 4.80 (3 H, b, –OH), 5.50 (4 H, s, =CH–), 5.85 (1 H, m, HCOH); mass spectrum m/e 185 ($M^+ - CH_3$), 149, 43, 28 (base).

Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 66.28; H, 9.99.

Attempts to hydrogenate **4** in the presence of an active Lindlar catalyst[4] capable of reducing diphenylacetylene to *cis*-stilbene were unsuccessful.

2,2,7,7-Tetramethyl-1,6-dioxaspiro[4.4]nona-3,8-diene (1).—Crude **6** (3.06 g, 15.3 mmol) in 100 ml of methylene chloride was added to a suspension of 60 g of active manganese dioxide[5] in 240 ml of the same solvent. The mixture was stirred for 2 hr at 25° and filtered and the solvent was removed, leaving 2.19 g of a clear, fragrant oil containing 1.43 g of **1** by nmr spectral analysis. Distillation afforded 1.26 g (46%) of **1**: bp 74–76° (11 mm) [lit.[3] bp 82° (12 mm)]; ir ($CHCl_3$) 3.3, 6.1, 7.35, 7.4, 9.2, 10.0, 11.3, 11.9 μ; nmr ($CDCl_3$) δ 1.30 (6 H, s, $-CH_3$), 1.38 (6 H, s, $-CH_3$), 5.55 (2 H, d, J = 5.5 Hz, =CH–), 6.05 (2 H, d, J = 5.5 Hz, =CH–), [lit.[3] nmr (solvent not given) δ 1.33 (6 H, s), 1.36 (6 H, s), 5.40 (2 H, d, J = 5 Hz), 5.89 (2 H, d, J = 5 Hz)]; mass spectrum m/e 180 (M^+), 165, 43, 32, 28 (base).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.50; H, 8.99.

2,2,7,7-Tetramethyl-1,6-oxaspiro[4.4]non-3-ene (2).—To a suspension of prereduced platinum oxide (25 mg) in 30 ml of ether, 541 mg (3.0 mmol) of **1** was added under hydrogen. After the solution was stirred for 0.5 hr, 1.5 mmol of hydrogen was absorbed. Filtration and evaporation afforded an oil which was resolved into three components by glc on a 6-ft column of 15% Carbowax 20M on Chromosorb W at 100° with a flow rate of 40 ml/min. The first fraction (6.75 min) was 2,2,7,7-tetramethyl-1,6-oxaspiro[4.4]nonane (**3**) (see below); the third fraction (12.25 min) was starting material (**1**). The middle fraction (9.5 min) was identified as **2**[9] by the nmr spectrum ($CDCl_3$): δ 1.09 (3 H, s, $-CH_3$), 1.17 (3 H, s, $-CH_3$), 1.25 (3 H, s, $-CH_3$), 1.27 (3 H, s, $-CH_3$), 1.87–2.03 (4 H, m, $-CH_2CH_2-$), 5.38 (1 H, d, J = 5.5 Hz, C=CH), 5.83 (1 H, d, J = 5.5 Hz, =CH–) [lit.[3] nmr (solvent not given) δ 1.11 (3 H, s), 1.20 (3 H, s), 1.27 (3 H, s), 1.30 (3 H, s), 1.86–2.0 (4 H, m), 5.39 (1 H, d, J = 5 Hz), 5.84 (1 H, d, J = 5 Hz)].

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.54; H, 10.27.

The ratio of **2** to **3** was *ca.* 55:45.

2,2,7,7-Tetramethyl-1,6-oxaspiro[4.4]nonane (3). A. From 2,8-Dimethyl-2,8-dihydroxy-3,6-nonadiyn-5-one (7).—Treatment of 197 mg (1.0 mmol) of **4** with a slight excess of Jones reagent in 2 ml of acetone for 1 hr gave 181 mg (93%) of product which slowly solidified. Distillation onto a cold finger condenser at 60° (0.02 mm) afforded an analytical sample of **7**: mp 37–42°; ir ($CHCl_3$) 2.8, 2.95 (b), 3.35, 4.55, 6.15, 8.05 μ; nmr ($CDCl_3$) δ 1.60 (12 H, s, $-CH_3$), 2.98 (2 H, b, –OH); mass spectrum m/e 194 (M^+), 161, 59, 58, 43 (base), 28; 2,4-DNP (from ethanol–water) mp 156.5–158°.

Anal. (2,4-DNP). Calcd for $C_{17}H_{18}N_4O_6$: C, 54.54; H, 4.85; N, 14.97. Found: C, 54.50; H, 4.71; N, 15.01.

For conversion to **3**, **7** (1.97 g, 10.0 mmol) was added to a suspension of 212 mg of hydrogen-equilibrated 5% palladium on charcoal in 40 ml of methanol. After 45 min 40 mmol of hydrogen was adsorbed. Filtration, evaporation of the solvent, and elution of the yellow residue through acidic alumina with ether gave, after short-path distillation, 0.89 g (48%) of **3** as a colorless oil: bp 70–72° (12 mm) [lit.[2] bp 178.5° (760 mm)]; ir (CCl_4) 3.35, 3.45, 6.85, 7.25, 7.3, 8.8, 9.6, 10.1, 10.35, 11.55 μ; nmr (CCl_4) δ 1.09 (6 H, s, $-CH_3$), 1.27 (6 H, s, $-CH_3$), 1.45–1.95 (8 H, m, $-CH_2CH_2-$) [lit.[3] nmr (solvent not given) δ 1.13 (6 H, s), 1.30 (6 H, s), 1.60–1.93 (8 H, m)]; mass spectrum m/e 184 (M^+), 115, 43, 32, 28 (base).

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.57; H, 11.11.

B. From 2,8-Dimethyl-2,5,8-nonatriol (5).—Treatment of 133 mg (0.65 mmol) of **5** in 4 ml of acetone with a slight excess of Jones reagent[6] for 15 min gave, after extraction and passage through acidic alumina with ether, 65 mg (54%) of **3**, the spectral properties of which were identical with those of material prepared above in part A.

Registry No.—**1**, 15129-55-2; **2**, 15031-05-7; **3**, 15031-07-9; **4**, 41189-22-4; **5**, 41189-23-5; **6**, 41189-24-6; **7**, 41189-25-7; **7** 2,4-dinitrophenylhydrazone, 41189-26-8; 2-methyl-3-butyn-2-ol, 115-19-5; 4-hydroxy-4-methyl-2-pentynal, 41189-27-9; 4-hydroxy-4-methyl-2-pentynal 2,4-dinitrophenylhydrazone, 18938-43-7; 4-methyl-2-pentyne-1,4-diol, 10605-66-0; quinoline, 91-22-5.

(8) W. Reppe, *et al.*, *Justus Liebigs Ann. Chem.*, **596**, 36 (1955).

(9) Isolated by preparative glc on a 10-ft column of 15% SF-96 on ABS at 110° with a flow rate of 60 ml/min.

A New Approach to α-Keto Esters

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During the past few years several asymmetric syntheses of α-amino acids from their biological precursors (α-keto acids) have been reported.[1]

This paper describes the possibility of preparing α-keto esters from readily available terminal acetylenes by ozonation followed by dehydration, as shown in Scheme I.[2]

This hypothesis is based on the behavior of ozone toward internal acetylenes,[2] and on the formation of α-hydroperoxy-α-methoxyacetophenone by ozonation of phenylacetylene in methanol.[3]

(1) (a) E. J. Corey, R. J. McCaully, and H. S. Sachdev, *J. Amer. Chem. Soc.*, **92**, 2476 (1970), and references cited therein; (b) E. J. Corey, H. S. Sachdev, J. Z. Gougoutas, and W. Saenger, *ibid.*, **92**, 2488 (1970); (c) K. Harada and T. Yoshida, *Bull. Chem. Soc. Jap.*, **43**, 921 (1970).

(2) (a) T. L. Jacobs, *J. Amer. Chem. Soc.*, **58**, 2272 (1936); (b) P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958), and references cited therein.

(3) P. S. Bailey, Y.-G. Chang, and W. W. L. Kwie, *J. Org. Chem.*, **27**, 1198 (1962).