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, **H**COH), 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, **H**COH); 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.

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]

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[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.

[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.

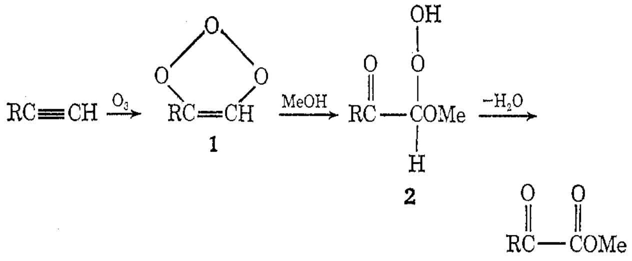
[3] P. S. Bailey, Y.-G. Chang, and W. W. L. Kwie, *J. Org. Chem.*, **27**, 1198 (1962).

TABLE I

Registry no.	Starting material	Registry no.	α-Keto ester obtained[a]	Bp, °C (mm)	Yield, %
1119-64-8	$C_4H_9C{\equiv}CBr$	6395-83-1	$C_4H_9COCOOMe$	48–52 (12)	40
38761-67-0	$C_6H_{13}C{\equiv}CBr$	41172-04-7	$C_6H_{13}COCOOMe$	82–85 (5)	50
932-87-6	$PhC{\equiv}CBr$	15206-55-0	$PhCOCOOMe$	87–90 (2)	50

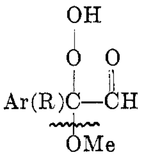
[a] The ir, pmr, and mass spectra are identical with those of authentic specimens.

SCHEME I



1-Hexyne, 1-octyne, and phenylacetylene were used as starting materials. The ozonation reaction was carried out in dry methanol, and $SOCl_2$ was used for the dehydration.

The corresponding α-keto methyl esters were prepared in 10–20% yield. The reason for the low yield is probably because the cleavage of the unstable intermediate **1** is controlled by resonance and inductive effects which promote the formation of α-hydroperoxy-α-methoxy aldehydes such as **3**;[3] dehydration of these compounds does not give α-keto esters.



3

The above reaction was then modified using 1-bromoacetylenes, which are readily available from terminal acetylenes by treatment with alkaline aqueous solutions of sodium or potassium hypobromite,[4] as starting materials. The bromine atom was introduced assuming that it would facilitate zwitterion formation on the terminal carbon atom, while zwitterion formation on the "internal" carbon atom should give an acylic bromine easily esterified by methanolic acylation.

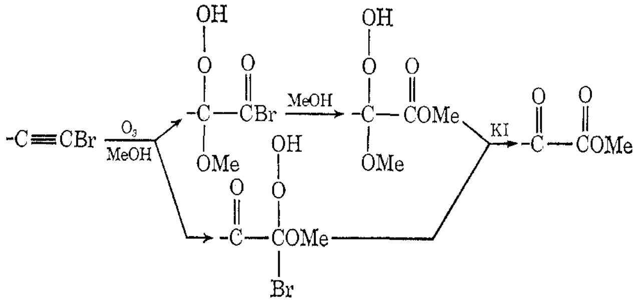
Finally, the ozonolysis of 1-bromoacetylenes in methanol solution should give two peroxides, both of which can be converted to α-keto esters by reduction with potassium iodide (Scheme II).

By this route, 1-bromohexyne,[5] 1-bromooctyne,[6] and bromophenylacetylene[7] were converted to the corresponding α-keto esters in 40–50% yields (Table I).

In both reactions considerable amounts of the carboxylic acid methyl esters were obtained as side products from the decomposition of the intermediate hydroperoxides in methanolic solution.[3,8]

The present work opens a new route to this important class of α-keto esters. Work is in progress on generalization of the method and on improving the yields.

SCHEME II



Experimental Section

α-Keto Methyl Esters from 1-Acetylenes. General Procedure.—An ozone–oxygen stream was passed through a solution of 0.04 mol of the terminal acetylene in 100 ml of dry methanol at −30°, until 90–95% of the starting material had reacted (determined by glc). The solvent was removed at low temperature under reduced pressure. Then 50 ml of cold, dry chloroform was added and a cold mixture of 7.3 ml (0.1 mol) of $SOCl_2$ and 16.1 ml (0.2 mol) of dry pyridine in 9 ml of dry chloroform was added dropwise with stirring at about −10°. The resulting mixture was allowed to warm to room temperature, added to water, and extracted with chloroform. The chloroform extract was neutralized with a saturated sodium bicarbonate solution and dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. Fractional distillation of the yellow-brown oil under reduced pressure gave the α-keto esters.

α-Keto Methyl Esters from 1-Bromoacetylenes. General Procedure.—An ozone–oxygen stream was passed through a solution of 0.04 mol of the 1-bromoacetylene in 100 ml of dry methanol at −30° until 90–95% of the starting material had reacted (determined by glc). Dry nitrogen was passed through the solution to remove excess ozone. Then 33.2 g (0.2 mol) of potassium iodide was added portionwise at about −30° with stirring. The reaction mixture was allowed to stand at room temperature for about 30 min and then 0.1 *N* aqueous sodium thiosulfate was added to neutralize the liberated iodine. The solution was extracted with ether, and the extract was dried over anhydrous sodium sulfate and evaporated under reduced pressure. Fractional distillation of the yellow-brown oil under reduced pressure gave the α-keto esters.

[4] R. G. Viehe, "Chemistry of Acetylenes," Marcel Dekker, New York, N. Y., 1969, p 680.

[5] W. Chodkiewicz, *Ann. Chim. (Paris)*, **2**, 819 (1957).

[6] G. Eglington and W. McCrae, *J. Chem. Soc.*, 2295 (1963).

[7] S. I. Miller, G. R. Ziegler, and R. Wieleseck, *Org. Syn.*, **45**, 86 (1965).

[8] P. S. Bailey and Y.-G. Chang, *J. Org. Chem.*, **27**, 1192 (1962).

The Preparation of Diacyl Dithiosulfites

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Although esters of sulfurous acid, $(RO)_2SO$, are readily prepared from alcohols and thionyl chloride,[1] thio esters of sulfurous acid, $(RS)_2SO$, have not been reported.

Mercaptans react with thionyl chloride to give the corresponding disulfides and trisulfides instead of the thio esters.[2] On the other hand, Tommasi reported

[1] W. E. Bessinger and F. E. Kung, *J. Amer. Chem. Soc.*, **69**, 2158 (1947).

[2] B. Holmberg, *Justus Liebigs Ann. Chem.*, **359**, 81 (1908); B. Holmberg, *Ber.*, **43**, 226 (1910); S. F. Birch, T. V. Cullum, and R. A. Dean, *J. Inst. Petrol. Technol.*, **39**, 206 (1953).