ppm (NH_2, broad, 2 H). The molecular weight was determined to be 357 (calcd for $C_{20}H_{11}N_3O_4$, 357.31) by means of high resolution mass spectrometry.

Anal. Calcd for $C_{20}H_{11}N_3O_4$: C, 67.22; H, 3.10; N, 11.76. Found: C, 66.50; H, 3.16; N, 11.86.

Reaction of Compound 5a and Acetic Anhydride.—Acetic anhydride (9 ml) was added to a solution of **5a** (0.2 g) dissolved in pyridine (5 ml) and refluxed for 4 hr. After cooling, water (3 ml) was added to the reaction mixture; a crystalline precipitate was formed. Recrystallization from glacial acetic acid gave 0.15 g of 4-acetamido-2-(3′-coumarinyl)-5-oxo-6-oxa-5,6-dihydrobenzo[*h*]quinazoline, mp 312–313°.

Anal. Calcd for $C_{22}H_{13}N_3O_5$: C, 66.16; H, 3.28; N, 10.52. Found: C, 65.93; H, 2.99; N, 10.65.

4-Amino-2-(8′-methoxy-3′-coumarinyl)-7-methoxy-5-oxo-6-oxa-5,6-dihydrobenzo[*h*]quinazoline (5b).—To a solution of ethyl cyanoacetate (3.39 g, 0.03 mol) and 2-hydroxy-3-methoxybenzaldehyde (4.56 g, 0.03 mol) dissolved in ethanol (8 ml), ammonium acetate (3.08 g, 0.04 mol) was added and refluxed for 20 min. A pale yellow crystalline matter precipitated out during the reaction; this was collected and washed with ethanol and then with water. Recrystallization from pyridine–water afforded 2.2 g (35%) of pale yellow crystals: mp 303–306°; ν_{max}^{KBr} 3410, 3300, 3210 (NH_2), 1735, 1700 (C=O), and 1640 cm^{-1} (δ NH_2); nmr spectrum (CF_3CO_2H) gave signals at 4.15 (OCH_3, singlet, 6 H), 7.5–8.0 and 8.2–8.6 (coumarin ring, 7 H), 9.5–10.1 ppm (NH_2, broad, 2 H).

Anal. Calcd for $C_{22}H_{15}N_3O_6$: C, 63.31; H, 3.62; N, 10.07. Found: C, 63.21; H, 3.85; N, 9.85.

Reaction of Ethyl Cyanoacetate and Salicylaldehyde in Glacial Acetic Acid at Room Temperature.—To a solution of ethyl cyanoacetate (2.26 g, 0.02 mol) and salicylaldehyde (2.44 g, 0.02 mol) in glacial acetic acid (5 ml), ammonium acetate (2.31 g, 0.03 mol) was added and allowed to stand at room temperature. After 7 hr, a crystalline compound (B) separated; B was filtered off and water was added to the filtrate; the deposited crystals were then collected and recrystallized from ethanol–water to give 4.6 g of 3-ethoxycarbonylcoumarin, mp 92–94° (lit.[7] mp 94°). The compound B was recrystallized from glacial acetic acid to afford 0.3 g of **5a**, mp 275–277°.

Reaction of Ethyl Acetoacetate and Salicylaldehyde.—To a solution of ethyl acetoacetate (5.2 g, 0.04 mol) and salicylaldehyde (4.9 g, 0.04 mol) in ethanol (7 ml), ammonium acetate (3.08 g, 0.05 mol) was added. After the reaction mixture was refluxed for 1 hr, a crystalline precipitate was formed. The crystals were collected and washed with methanol and dried. Recrystallization from pyridine gave 2.2 g (31%) of 2-(3′-coumarinyl)-4-methyl-5-oxo-6-oxa-5,6-dihydrobenzo[*h*]quinoline (**6**): mp 291–292°; nmr spectrum (CF_3CO_2H) revealed signals at 3.50 (CH_3, singlet, 3 H), 7.5–8.5 (hetero ring, multiplet, 8 H), 9.13 and 9.4 ppm (hetero ring, singlet, 2 H). The molecular weight determined by mass spectrometry was 356 (calcd for $C_{22}H_{13}NO_4$, 355.33).

Anal. Calcd for $C_{22}H_{13}NO_4$: C, 74.36; H, 3.69; N, 3.94. Found: C, 74.59; H, 3.72; N, 4.00.

Registry No.—**1a,** 21537-68-8; **1b,** 21537-69-9; **1c,** 21537-70-2; **1d,** 21537-71-3; **2,** 21545-00-6; **3a,** 21545-01-7; **3b,** 21545-02-8; **5a,** 21545-03-9; **5b,** 21537-66-6; **6,** 21537-67-7; ammonium acetate, 1066-32-6; 2-(*o*-acetyloxyphenyl)-4-phenyl-10-oxa-5H-benzo[*g*]quinazoline, 21545-04-0; 2-(2′-acetyloxy-3′-methoxyphenyl)-9-methoxy-4-phenyl-10-oxa-5H-benzo-[*g*]quinazoline, 21545-05-1; 4-acetamido-2-(3′-coumarinyl)-5-oxo-6-oxa-5,6-dihydrobenzo[*h*]quinazoline, 21545-06-2.

Acknowledgment.—The authors wish to express their thanks to Dr. Taro Hayashi and Dr. Tatsuo Takeshima for their kind advice. Thanks are also due to Dr. Haruo Homma and his staff for their microanalyses, to Mr. Jun Uzawa for his measurements of the nmr spectra, and to Mr. Hironori Ogawa for his measurements of the infrared spectra.

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[7] E. Knoevenagel, *Chem. Ber.*, **31**, 2593 (1898).

Conjugate Addition Reactions with Lithium Diallylcuprate[1a]

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Although the conjugate addition of an allyl group from lithium diallylcuprate to 2-cyclohexenone (1) was successful, the more hindered ketone, 3,5,5-trimethylcyclohexenone (2), underwent 1,2 addition with the same reagent. Attempts to effect or to catalyze the conjugate addition of acetylide anions or enolate anions to unsaturated ketones by the presence of copper(I) derivatives were not successful.

The pronounced tendency of metal organocuprate derivatives, *e.g.*, $LiCuR_2$ where R = alkyl, vinyl, or aryl, to add in a conjugate fashion to α,β-unsaturated carbonyl compounds[2] raises the question whether the conjugate addition of more stable carbanionic intermediates could be catalyzed by copper(I) derivatives. The answer to the question is of particular interest for the allylic, acetylide, and enolate anions since the conjugate addition of these systems has substantial synthetic utility (*e.g.*, the Michael reaction[3]). A previous study of the reaction of 2-cyclohexenone (**1**) with β-methylallylmagnesium chloride indicated that addition of catalytic amounts of the ether-insoluble copper(I) chloride did not yield a conjugate addition product; only the alcohol from 1,2 addition was isolated.[4] In this study we have synthesized allylic and acetylenic copper(I) derivatives and have examined their behavior as potential reagents for conjugate addition. Also, we have examined one possible route to copper(I) enolates.

Reaction of cyclohexenone (**1**) with lithium diallylcuprate (**3**) in ether solution at −70° did indeed produce the conjugate addition product **4** in 90–94% yield. The phosphine complex **8** of allylcopper(I) also produced the adduct **4**, but in very poor yield (10–15%) accompanied by high molecular weight by-products. This problem of high molecular weight by-products was encountered earlier[2a] when phosphine and phosphite complexes of methylcopper(I) were allowed to react with cyclohexenone derivatives. Thus, the lithium cuprate reagents are generally more satisfactory

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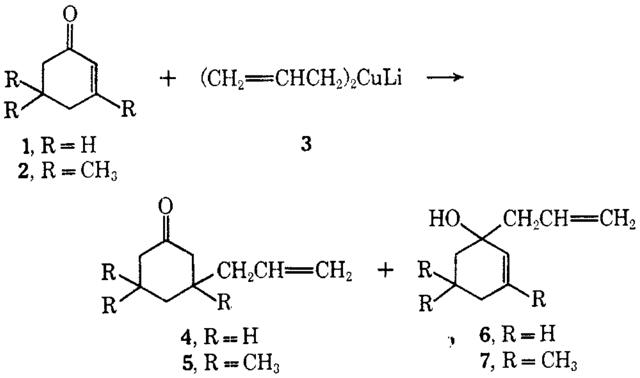
[1] (a) This research has been supported by Grant No. AFOSR-68-1518 from the Directorate of Chemical Sciences, Air Force Office of Scientific Research; (b) National Institutes of Health Predoctoral Fellow, 1966–1969.

[2] See (a) H. O. House and W. F. Fischer, Jr., *J. Org. Chem.*, **33**, 949 (1968); (b) H. O. House, W. L. Respess, and G. M. Whitesides, *ibid.*, **31**, 3128 (1966); (c) H. O. House, R. A. Latham, and C. D. Slater, *ibid.*, **31**, 2667 (1966); and references cited in these papers.

[3] E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. Reactions*, **10**, 179 (1959).

[4] L. Mandell and J. M. Brodmann, *J. Org. Chem.*, **31**, 591 (1966).

as synthetic intermediates. However, even the cuprate 3 failed to react with the substituted cyclohexenone 2 to give any appreciable amount of the conjugate addition product 5; instead, we isolated the allylic alcohol 7, the 1,2-addition product. Similarly, $\Delta^{1,9}$-octal-2-one (9) reacted with the cuprate 3 to produce a crude product which exhibited no appreciable carbonyl absorption in the infrared. Since both of these unsaturated ketones, 2 and 9, react with either lithium dimethylcuprate or methylmagnesium halide plus a copper(I) salt to give good yields of the conjugate addition products (*e.g.*, 5 with allyl replaced by methyl),[2] it is clear that the copper(I) derivatives of allylic carbanions have a lesser tendency to undergo conjugate addition than do the corresponding alkyl, vinyl, and aryl derivatives.



1, R = H
2, R = CH_3

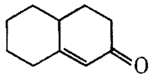
3

4, R = H
5, R = CH_3

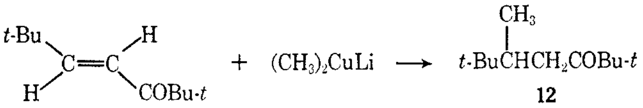
6, R = H
7, R = CH_3

$CH_2{=}CHCH_2CuP(C_4H_9\text{-}n)_3$

8



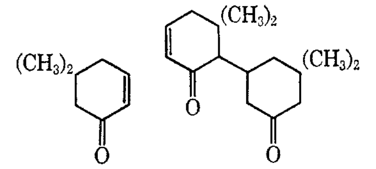
9



10 11 12

We observed no tendency for conjugate addition with the lithium cuprate derivatives 13 and 14 derived from lithium acetylides. Although both ketones 10 and 15[2] undergo ready conjugate addition of a methyl group from the cuprate 11, reaction of either acetylide 13 or 14 with the ketone 15 yields predominately a dimeric diketone. This diketone, believed to possess structure 16, is presumably derived from formation of an enolate ion from ketone 15 and subsequent Michael addition to a second molecule of the unsaturated ketone. Attempts to add the acetylide 13 to the ketone 10 (where enolate formate is unlikely) produced a crude product which lacked carbonyl absorption in the infrared. The reaction mixture prepared from 2 equiv of triphenylmethyllithium and 1 equiv of bis(di-*n*-butyl sulfide)copper(I) iodide in 1,2-dimethoxyethane solution was also treated with the unsaturated ketone 10; in this case the starting material 10 was recovered quantitatively after a reaction period of 4 hr at −78 to 0°.

$(RC{\equiv}C)_3CuLi_2$
13, R = C_6H_5
14, R = $n\text{-}C_4H_9$



15 16

Finally, we examined briefly several Michael reactions including the addition of diethyl sodio- and lithiomalonates to cyclohexenone and the addition of the lithium enolate of acetophenone to mesityl oxide. In no case did the presence of a stoichiometric amount of a copper(I) derivative [*e.g.*, CuI, $(n\text{-}Bu_2S)_2CuI$, or $(n\text{-}Bu_3P)CuI$] in the reaction solution have any substantial effect on the rate or product distribution of the Michael reaction.

From the foregoing observations, it would appear that the tendency of cuprate species to undergo conjugate addition is retarded by the presence of carbon ligands which could form reasonably stable anions. It is not clear whether the loss of reactivity of these species is actually attributable to the following dissociation. However, it is appropriate to note that the

$$\underset{17}{R_2Cu^-} \rightleftharpoons \underset{18}{RCu} + R^-$$

previously suggested[2] mechanism involving initial electron transfer from the copper species to the conjugated system would be more difficult if the dissociation indicated above were taking place. The reactivity of various metal cuprates in coupling reactions with alkyl halides also decreases as the attached carbon ligands are changed to species (*e.g.*, $RC{\equiv}C^-$ and $N{\equiv}C^-$) which form relatively stable anions.[5,6]

Experimental Section[7]

Starting Materials.—Previously described[6] procedures were followed to prepare Et_2O solutions of $LiCuMe_2$, lithium diallylcuprate, and the dilithium derivative of tris(phenylethynyl)cuprate. Commercial samples of cyclohexenone and isophorone were used and 2,2,6,6-tetramethyl-*trans*-4-hepten-3-one (10), mp 43.9–44.5°, was prepared by the aldol condensation of pivaldehyde with pinacolone.[8] The reaction of MeLi with Ph_3CH in 1,2-dimethoxyethane (DME) solution yielded Ph_3CLi.

Reaction of Lithium Diallylcuprate with Cyclohexenone Derivatives. A. 2-Cyclohexenone (1).—To a cold (−78°) solution of lithium diallylcuprate, prepared from 1.45 g (3.00 mmol) of $(n\text{-}Bu_2S)_2CuI$ and 6.00 mmol of allyllithium in 11.2 ml of Et_2O, was added 2.5 ml of an Et_2O solution containing 2.50 mmol of 2-cyclohexenone and a known amount of naphthalene (internal standard). During the addition a red precipitate [presumably allylcopper(I)][6] separated, The mixture was allowed to warm to 0° [during which time any unchanged copper(I) reagent decomposed with the separation of metallic copper] and then was partitioned between Et_2O and an aqueous solution (pH 8) of NH_3 and NH_4Cl. After the Et_2O solution had been washed (aqueous NaCl) and dried, it was concentrated and analyzed by

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[5] H. O. House and W. F. Fischer, Jr., *J. Org. Chem.*, **34**, 3626 (1969).

[6] G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, *J. Amer. Chem. Soc.*, **91**, 4871 (1969).

[7] All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer Model 237 grating spectrophotometer. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The nmr spectra were determined at 60 MHz, with a Varian Model A-60 nmr spectrometer. The chemical-shift values are expressed in hertz or δ values (parts per million) relative to a tetramethylsilane internal standard. The mass spectra were obtained with a CEC Model 21-130 or a Hitachi (Perkin-Elmer) mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates. All reactions involving organometallic or strongly basic intermediates were performed under a nitrogen atmosphere.

[8] (a) The characterization of this substance in our laboratories by Roger W. Giese will be described elsewhere. Very brief descriptions of this ketone have been given by (b) K. Dimroth and W. Mach, *Angew. Chem.*, **80**, 489, 490 (1968); and (c) W. Rundel and K. Besserer, *Tetrahedron Lett.*, 4333 (1968).

glpc.[9] The crude product contained di-*n*-butyl sulfide (retention time 11.2 min), 3-allylcyclohexanone (**4**) 14.8 min), and naphthalene (17.1 min); the calculated yields of the cyclohexanone **4** from two reactions were 90 and 94%. A collected[9] sample was identified with a subsequently described sample by comparison of ir spectra and glpc retention times.

After a cold (−70°) solution of 32.4 mmol of allyllithium[10] in 90 ml of Et_2O had been treated with 100 ml of a cold (−70°) Et_2O solution of 12.7 g (32.4 mmol) of $[(n\text{-}Bu_3P)CuI]_4$, the resulting bright yellow suspension of the phosphine complex of allylcopper(I) was treated with a solution of 3.20 g (32.4 mmol) of 2-cyclohexenone in 5 ml of Et_2O. The resulting mixture was stirred at −70° for 10 min and then subjected to the previously described isolation procedure. The crude liquid product was distilled in a short-path still to separate a fraction, bp 44–48° (1 mm), which contained[11] 3-allylcyclohexanone (**4**) and a number of more rapidly eluted materials thought to be various dienes from 1,2 addition and dehydration. The crude product also contained a substantial amount of unidentified higher molecular weight material. In subsequent comparable reactions containing an internal standard (naphthalene), the calculated[11] yields of 3-allylcyclohexanone (**4**) ranged from 10 to 15%. A collected sample of the allylcyclohexanone **4** was obtained as a colorless liquid: ir (CCl_4), 1715 ($C=O$), 1640 ($C=C$), and 915 cm^{-1} ($CH=CH_2$); nmr (CCl_4), δ 4.7–5.3 (3 H, m, vinyl CH) and 1.1–2.6 (11 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 138 (M^+, 10), 97 (36), 69 (46), 55 (52), 41 (100), and 39 (30).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 77.94; H, 10.25.

A solution of 18.8 mg (0.13 mmol) of the allyl ketone **4** in 2.0 ml of EtOH was hydrogenated at 25–30° (1 atm) over 7.2 mg of a 5% Pd–C catalyst. After 45 min the uptake of H_2 ceased; the crude liquid product, isolated in the usual way, contained[12] one major component. A collected[12] sample of this component was identified with the subsequently described sample of 3-propylcyclohexanone by comparison of ir spectra and glpc retention times.

The reaction of 81.5 mmol of *n*-PrMgBr and 5.3 mmol of CuI and with 41.6 mmol of 2-cyclohexenone for 10 min yielded, after the usual isolated procedure, 86% 3-propylcyclohexanone as a colorless liquid: bp 51–53° (1.0 mm); $n^{25}\mathrm{D}$ 1.4525 [lit.[13] bp 41–42° (0.7 mm); $n^{20}\mathrm{D}$ 1.4530]; ir (CCl_4), 1720 cm^{-1} ($C=O$); nmr (CCl_4), δ 0.6–2.6 (m, aliphatic CH); mass spectrum *m/e* (rel intensity) 140 (M^+, 11), 97 (100), 69 (23), 56 (22), 55 (59), 42 (22), 39 (28), and 27 (27).

B. 3,5,5-Trimethyl-2-cyclohexenone (2).—The red, insoluble allylcopper(I), obtained from 1.45 g (3.00 mmol) of $(n\text{-}Bu_2S)_2CuI$ and 3.00 mmol of allyllithium in 7.0 ml of Et_2O at −78°, was washed with four portions of cold (−78°) Et_2O and then dissolved in 5.0 ml of Et_2O solution containing 2.50 mmol of allyllithium. When 250 mg (1.82 mmol) of the ketone **2** was added to the cold (−78°) pale yellow solution of lithium diallylcuprate, an immediate red precipitate [allylcopper(I)] was observed. The resulting mixture was allowed to warm to room temperature and then subjected to the previously described isolation procedure. Distillation of the crude product (320 mg of yellow liquid) in a short-path still (6 mm and 60° bath) afforded 231 mg (71.4%) of the alcohol **7** as a colorless liquid, $n^{22}\mathrm{D}$ 1.4857, identified with the subsequently described sample by comparison of ir and nmr spectra.

An authentic sample of the alcohol **7** was obtained by reaction of 104 mmol of allyllithium with 11.50 g (90 mmol) of the unsaturated ketone **2** in 120 ml of Et_2O at 0–25° for 30 min. The crude organic product (19.8 g of yellow liquid) isolated in the usual way after drying over Na_2CO_3 was distilled in a short-path still. A 6.0-g aliquot of the distillate (13.4 g or 89.6%) was fractionally distilled to separate 4.48 g of the pure alcohol **7** as fractions, bp 52–53° (0.6 mm), $n^{22}\mathrm{D}$ 1.4845–1.4851. A lower boiling fraction, bp 40–52° (0.6 mm), $n^{22}\mathrm{D}$ 1.4866, appeared (ir analysis) to be a mixture of the desired alcohol **7** and its dehydration products. The pure alcohol **7** is a colorless liquid: ir (CCl_4), 3590, 3540, 3540 (br, free and associated OH), 1665, 1630 ($C=C$), and 910 cm^{-1} ($CH=CH_2$); nmr (CCl_4), δ 4.7–6.1 (4 H, m, vinyl CH), 2.16 (2 H, d of t, *J* = 7.1 and 2.2 Hz, allyl CH_2), 2.13 (1 H, s, exchanges with D_2O, OH), 1.66 and 1.64 (5 H, partially resolved singlets, vinyl CH_3 and CH_2), 1.42 (2 H, s, CH_2), 1.01 (3 H, s, CH_3), and 0.93 (3 H, s, CH_3); mass spectrum *m/e* (rel intensity) 162 (58), 147 (82), 119 (71), 106 (39), 105 (100), 91 (48), 44 (65), and 41 (72).

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.89; H, 10.93.

A comparable attempt to add lithium diallylcuprate to $\Delta^{1,9}$-octal-2-one yielded a crude reaction product with only very weak ir absorption attributable to a $C=O$ function which contained (glpc[12]) at least four products; the ir and mass spectra of collected[12] samples suggested that only one minor component was a ketone (ir 1710 cm^{-1}). The remaining products appeared to be dehydration products of alcohol from 1,2 addition.

Reactions of Lithium Dimethylcuprate and the Dilithum Derivative of Tris(hexynyl)cuprate. A. 2,2,6,6-Tetramethyl-*trans*-4-hepten-3-one (10).—To a cold (0°) solution of $LiCuMe_2$ [from 740 mg (3.9 mmol) of CuI and 7.8 mmol of MeLi in 12.5 ml of Et_2O] was added 442 mg (2.63 mmol) of the ketone **10**. The formation of a red-brown color immediately after addition was followed by the precipitation of MeCu within 5–8 sec. After the resulting mixture had been stirred for 2 hr at 0°, the usual isolation procedure separated the crude product as 380 mg (79%) of pale yellow oil which exhibited a single glpc peak;[12] none of the dihydro dimer[8a] derived from the radical anion of ketone **10** was detected by glpc.[14] The major product, the saturated ketone **12**, was collected[12] as a colorless liquid: ir (CCl_4), 1710 cm^{-1} ($C=O$); nmr (CCl_4), δ 1.7–2.4 (3 H, m, aliphatic CH), 1.10 (9 H, s, *t*-Bu), 0.86 (9 H, s, *t*-Bu), and 0.77 (3 H, d, *J* = 6.3 Hz, CH_3); mass spectrum *m/e* (rel intensity) 184 (M^+, 1), 125 (100), 85 (42), 57 (97), 43 (30), and 41 (26).

Anal. Calcd for $C_{12}H_{24}O$: C, 78.19; H, 13.13. Found: C, 78.16; H, 13.06.

Reaction of MeLi with 1-hexyne in Et_2O afforded hexynyllithium as a white solid which was insoluble in Et_2O. A solution of this lithium reagent in dioxane reacted with 1 equiv of CuI to form the yellow insoluble copper(I) derivative. An additional 2 equiv of $n\text{-}BuC{\equiv}CLi$ was required to discharge the yellow color of the copper derivative forming a partial solution with additional white solid suspended in dioxane, suggesting that the reagent has the composition $(n\text{-}BuC{\equiv}C)_3CuLi_2$. Reaction of this reagent with the ketone **10** at 50° for 24 hr afforded a crude product (a yellow oil) with no ir absorption in the 6-μ region attributable to a carbonyl function. Similarly, when the red-orange suspension obtained by adding 1.08 g (2.33 mmol) of $(n\text{-}Bu_2S)_2CuI$ to a solution of 4.65 mmol of Ph_3CLi in 8.5 ml of DME at −78° was stirred with 328 mg (1.96 mmol) of the ketone **10** for 4 hr at −78°, the starting ketone **10** was recovered quantitatively (glpc[15]).

When 4.65 mmol of the ketone **10** was stirred with 4.65 mmol of Ph_3CLi in DME at 25° for 4 hr (red color of Ph_3C anion diminished but not discharged) and then hydrolyzed, the reaction mixture contained[14,15] the starting ketone **10** (24% recovery) but no other lower molecular products such as the *cis* isomer[8a] of ketone **10**, the saturated analog[8a] of ketone **10**, or the dihydro dimer[8a] of ketone **10**.

B. 5,5-Dimethyl-2-cyclohexenone (15).—To a partial solution–partial suspension of $(n\text{-}BuC{\equiv}C)_3CuLi_2$ [white solid from 486 mg (2.56 mmol) of CuI and 7.68 mmol of $n\text{-}BuC{\equiv}CLi$) in 6.0 ml of dioxane] was added 91 mg (0.73 mmol) of the unsaturated ketone **15**. The mixture, from which a yellow-brown precipitate settled immediately, was stirred at 25–30° for 10 min and then subjected to the usual isolation procedure. The crude product (106 mg) was recrystallized (pentane) to separate 56.1 mg (61.5%) of material believed to be the diketone **16** as pale yellow needles: mp 87.8–88.8°; ir (CCl_4), 1718 ($C=O$) and 1675 cm^{-1} (conjugated $C=O$); nmr (CCl_4), δ 6.77 (1 H, d of t, *J* = 4.0 and 10.5 Hz, β-vinyl CH), 5.94 (1 H, d of t, *J* = 2.0 and 10.5 Hz, α-

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[9] A glpc column packed with silicone gum, no. SE-30, suspended on Chromosorb P was employed.

[10] Allyllithium for this reaction was obtained by reaction of tetrallyltin [K. V. Vijayaraghavan, *J. Indian Chem. Soc.*, **22**, 135 (1945)] with *n*-butyllithium in pentane. The pentane-insoluble allyllithium was collected and dissolved in Et_2O.

[11] A glpc column packed with LAC-728 (diethylene glycol succinate) suspended on Chromosorb P was employed.

[12] A glpc column packed with silicone gum, no. XE-60, suspended on Chromosorb P was employed.

[13] G. F. Woods, P. H. Griswald, B. H. Armbrecht, D. I. Blumenthal, and R. Plapinger, *J. Amer. Chem. Soc.*, **71**, 2028 (1949).

[14] A glpc column packed with silicone gum, no. SE-52, suspended on Chromosorb P was employed.

[15] A glpc column packed with TCEP [1,2,3-tris(β-cyanoethoxy)propane] suspended on Chromosorb P was employed.

vinyl CH), 1.2–2.5 (10 H, m, aliphatic CH), and four singlets (3 H each, CH_3) at 1.13, 1.06, 1.04, and 0.87; mass spectrum *m/e* (rel intensity) 248 (M^+, 11) 125 (22), 124 (25), 109 (100), 55 (23), 41 (36), and 39 (16).

Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 77.08; H, 9.64.

A comparable reaction of 0.75 mmol of the unsaturated ketone **15** with an Et_2O solution of 1.5 mmol of $(PhC{\equiv}C)_3CuLi_2$ yielded a crude reaction product which contained[9] $PhC{\equiv}CH$ and the starting ketone **15** accompanied by two minor, higher molecular weight materials and the major product, the previously described diketone **16**, identified by comparison of ir spectra and glpc retention times.

Registry No.—**3,** 21500-57-2; **4,** 20498-05-9; **7,** 21436-26-0; **12,** 14705-56-7; **16,** 21436-17-9.

β-Keto Sulfoxides. VI. Conversion of ω-(Methylsulfinyl)acetophenone into Di- and Tri-ω-(methylmercapto)acetophenone. Synthesis of α-Hydroxy Aldehydes, α-Keto Thio Esters, α-Keto Esters, α-Hydroxy Thio Esters, and α-Hydroxy Esters. The Chemistry of α-Keto Mercaptals[1]

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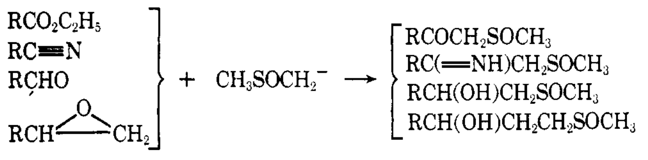
A convenient synthetic conversion of β-keto sulfoxides to α-hydroxy aldehydes involves the sequence, $RCOCH_2SOCH_3 \rightarrow RCOCH(Cl)SCH_3 \rightarrow RCOCH(SCH_3)_2 \rightarrow RCH(OH)CH(SCH_3)_2 \rightarrow RCH(OH)CHO$. Convenient syntheses of mandelaldehyde, atrolactaldehyde, benzilaldehyde, and 2-phenyl-2-ethylglycolaldehyde were developed. The α-chloro β-keto sulfides are readily converted to α-keto acetals. α-Keto mercaptals undergo O-alkylations and O-acylations in the presence of base. Bromination of the α-keto mercaptal followed by hydrolysis yielded S-methyl phenylthioglyoxylate ($C_6H_5COCOSCH_3$). Reaction of phenylglyoxal methyl mercaptal with methanesulfenyl chloride in the presence of base yielded ω,ω,ω-tri(methylmercapto)acetophenone which can also be converted to S-methyl phenylthioglyoxalate. A convenient synthesis of S-methyl thiomandelate is described: $C_6H_5COC(SCH_3)_3 \rightarrow C_6H_5CH(OH)C(SCH_3)_3 \rightarrow C_6H_5CH(OH)COSCH_3$. Bromination of the methyl mercaptal of phenylglyoxal in basic solution in the absence of water leads to *cis-* and *trans-*1,2-dibenzoyl-1,2-di(methylmercapto)ethylene, a product also formed in the pyrolysis of ω-chloro-ω-(methylmercapto)acetophenone.

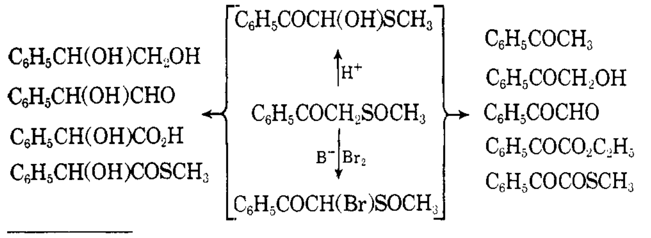
The methylsulfinylcarbanion $(CH_3SOCH_2^-)$[2] reacts readily with a variety of electrophilic centers including esters,[3,4] aldehydes,[4,5] epoxides, and nitriles (Scheme I, also see Experimental Section).

Scheme I



The substituted sulfoxides are potentially important in organic synthesis. β-Keto sulfoxides can be readily converted by the Pummerer rearrangement to α-hydroxy β-keto sulfides.[3] From these materials we have demonstrated practical routes to seven of the nine derivatives shown in Scheme II.[6]

Scheme II



The present investigation was directed toward a convenient synthesis of α-hydroxy aldehydes starting from the β-keto sulfoxides. In addition, new syntheses were developed for α-keto and α-hydroxy esters and thio esters.

Results and Discussion

We initially attempted to prepare mandelaldehyde from the β-hydroxy sulfoxide available from the sodium borohydride reduction of the β-keto sulfoxide (see Scheme III).[7] However, 1-phenyl-2-(methylsulfinyl)ethanol proved to be quite resistant to the Pummerer rearrangement and forcing conditions produced either ω-hydroxyacetophenone or the dehydration product, β-styryl methyl sulfoxide.[7] Treatment of the β-hydroxy sulfoxide with iodine gave only a low yield of the hydroxy aldehyde although the β-keto sulfoxide may be converted to an α-keto aldehyde or α-keto acetal by this procedure.[8]

Scheme III

$$C_6H_5COCH_2SOCH_3 \xrightarrow{NaBH_4} C_6H_5CH(OH)CH_2SOCH_3 \xrightarrow{H_3O^+} [C_6H_5CH(OH)CH(OH)SCH_3 \longrightarrow C_6H_5CH(OH)CHO + CH_3SH]$$

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