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Reactions Involving Electron Transfer. 9. Reaction of Lithium Dimethylcuprate with Alkyl Aryl Ketones[1]

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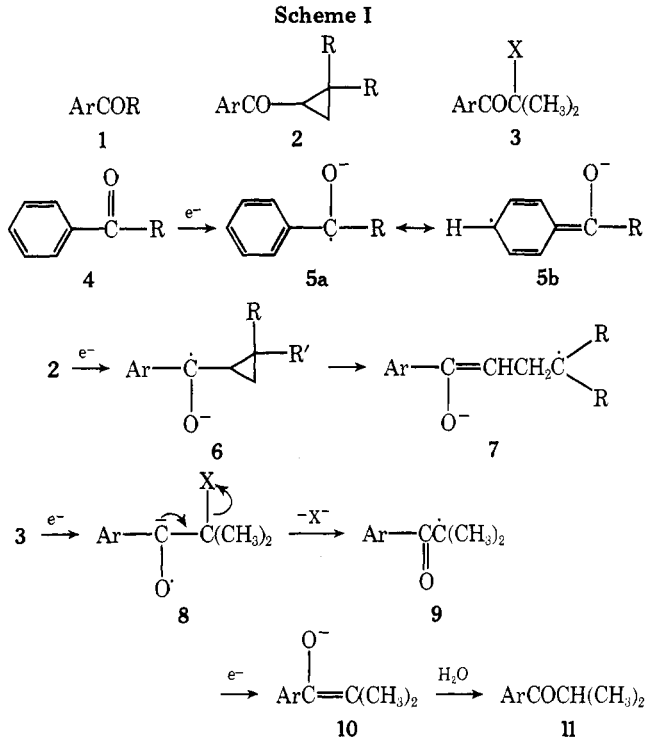
The reactions of several aryl alkyl ketones **12–15, 22–24,** and **40–42** with Me_2CuLi have been studied. Each of these ketones has a sufficiently positive reduction potential so that reduction by Me_2CuLi to form an anion radical is energetically feasible. The major products formed from those ketones whose anion radicals are relatively stable were the 1,2-addition products. This 1,2-addition reaction was significantly slower than the conjugate addition of Me_2CuLi to α,β-unsaturated ketones. The aryl alkyl ketones **41** and **42,** whose anion radicals are relatively unstable, reacted rapidly with Me_2CuLi to form the product of reductive elimination rather than 1,2 addition.

Previous study[2] of the reaction of Me_2CuLi with carbonyl compounds revealed that α,β-unsaturated carbonyl compounds having reduction potentials within the range −1.4 to −2.35 V (vs. SCE in an aprotic solvent) could be expected to react by way of an initial electron-transfer step to form products derived from the net conjugate addition of a methyl anion to the unsaturated carbonyl compound. Substrates with less negative reduction potentials (more easily reduced) yielded reduction rather than addition products while substrates with more negative reduction potentials (more difficulty reduced) either failed to react with Me_2CuLi or reacted, with liberation of CH_4, to form the metal enolate of the starting unsaturated ketone. Saturated ketones (which have reduction potentials more negative than −2.9 V) reacted with Me_2CuLi either with evolution of CH_4 to form the metal enolates of the ketones or by a very slow process leading to 1,2 addition.[2c]

Since aryl alkyl ketones typically have reduction potentials in the range −1.8 to −2.2 V (vs. SCE in an aprotic solvent),[3] these compounds appeared to be substrates that might react with Me_2CuLi by a process that involved an initial electron transfer step. To learn what types of products might result, we have studied the reaction of Me_2CuLi with three types of aryl alkyl ketone systems **1–3** (Scheme I). Reaction of ketones of type **1** (e.g., **4**) by an electron-transfer process would yield anion radicals **5** in which spin density would be distributed between the carbonyl carbon atom (**5a**) and various positions of the aromatic ring (e.g., **5b**).[4] Thus, further reaction of such an intermediate could introduce a methyl substituent either at the carbonyl carbon atom or at one of the positions in the aromatic ring.[5]

Reaction of Me_2CuLi with an aryl cyclopropyl ketone **2** offered the possibility that an intermediate anion radical **6** might rearrange to the structurally isomeric ion radical **7** prior to further reaction. Provided that this rearrangement occurred within a time period of 10^{-3} s or less,[2b,6] rearranged addition products derived from ion radical **7** might be expected.

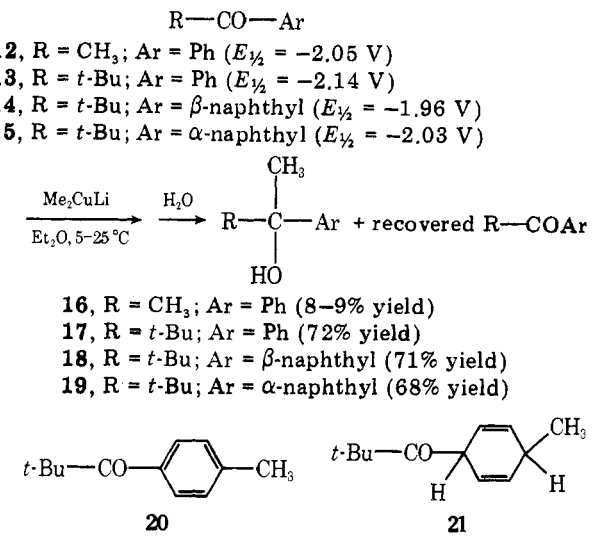
Scheme I



Compounds of the type **3,** where X is a group that can be lost as a relatively stable anion, offered the possibility that an intermediate anion radical might eliminate an anion X^- provided that this elimination would occur within time periods of the order of 10^{-3} s or less. The elimination of X^- would yield an easily reduced radical **9** that would be expected to react with additional Me_2CuLi to form the enolate **10** and finally the reduction product **11**.[2,7]

Ketones **12–15** (Scheme II) were studied as examples of aryl alkyl ketones of type **1**. Acetophenone (**12**) reacted relatively

Scheme II

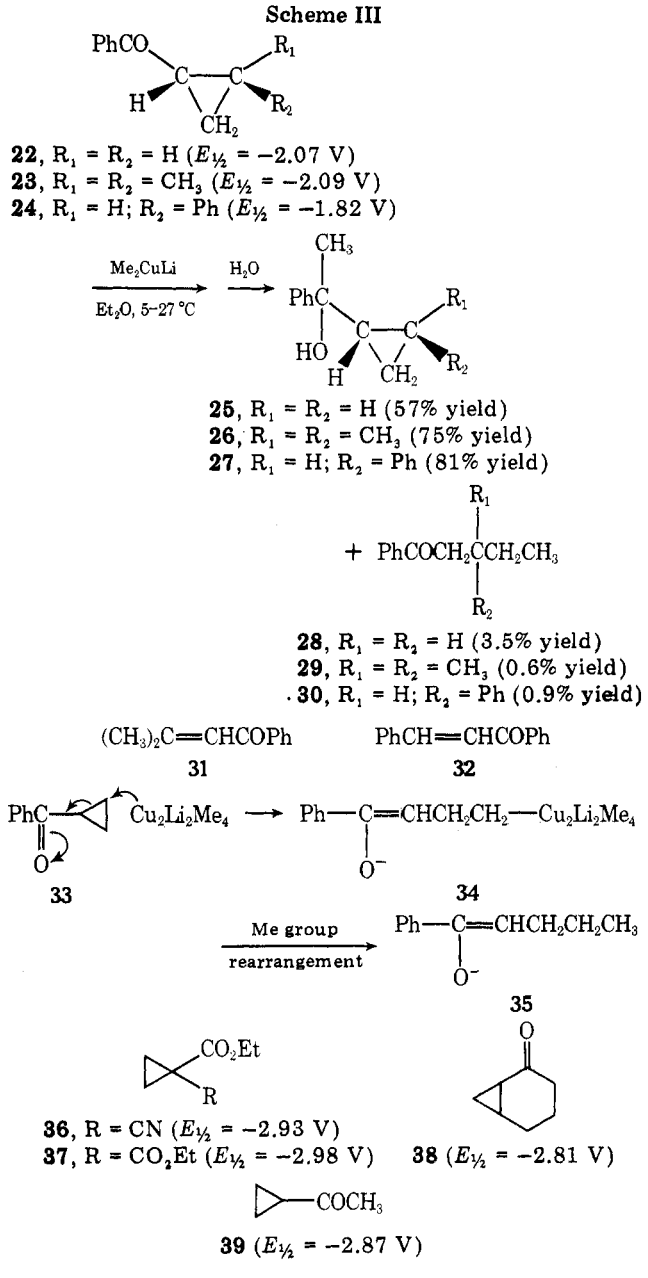


rapidly with Me_2CuLi with evolution of gas and precipitation of $(MeCu)_n$. The predominant reaction was formation of the enolate of ketone **12**; the 1,2 adduct **16** was obtained in only 8–9% yield after reaction periods of either 11 min or 3.5 h with excess Me_2CuLi.[8] This major side reaction leading to enolate formation is also observed[2c] in reaction of Me_2CuLi with aliphatic methyl ketones and *n*-alkyl ketones. To avoid this side reaction, the nonenolizable ketones **13–15** were used for further study. Each compound underwent a relatively slow reaction with Me_2CuLi to form the 1,2 adducts **17–19.** Minor components detected in these reaction mixtures were the unchanged ketones **13–15** and/or olefinic products derived from dehydration of the alcohols **17–19.** Examination of these minor compounds by mass spectrometry gave no indication that ring-methylated products, such as **20** or **21** from ketone **13,** were present. Consequently, we conclude that if anion radicals of the type **5** are intermediates in these reactions, recombination with the cluster $[Me_4Cu_2Li_2]\cdot^+$ occurs only at the carbonyl carbon atom (structure **5a**) that appears to be the site of highest spin density in these intermediates. It should be noted that each of the ketones **12–15** has a reduction potential (see Scheme II and Table I) within the range (less negative than −2.2 V) where electron transfer from Me_2CuLi is feasible. Furthermore, the anion radicals formed from these ketones **12–15** are relatively stable with half-lives greater than 0.1 s (see Table I).

We next examined the reactions of Me_2CuLi with ketones **22–24** (Scheme III) as representative aryl cyclopropyl ketones **2.** In each case these ketones **22–24** underwent a relatively slow reaction with Me_2CuLi to form mainly the 1,2 adducts **25–27.** However, small amounts of ring-opened by-products **28–30** were also formed. The structures of each of these by-products **28–30** were established by comparison with authentic samples, samples of ketones **29** and **30** being obtained by CuCl-catalyzed conjugate addition of EtMgBr to the enones **31** and **32.** The reduction potentials (Scheme III and Table I) of each of the ketones **22–24** lie in the range −1.8 to −2.1 V. The anion radicals **6** formed from ketones **22** and **23** are relatively stable with half-lives of 4–5 s (Table I) but the half-life of the anion radical from ketone **24** is much less ($<10^{-2}$ s).[9]

Several facts indicate that the minor ring opened products **28–30** *are not derived from an anion radical intermediate* **6** by rearrangement **6** → **7** followed by recombination of **7** with $[Me_4Cu_2Li_2]\cdot^+$. Thus, the greatest amount of ring-opened product **28** is obtained from ketone **22** whose anion radical rearranges (**6** → **7**) very slowly and in which the rearranged radical ion **7** (R = R′ = H) has no stabilizing substituents. Not only do stabilizing substituents (as in ketones **23** and **24**) diminish the yields of ring-opened products, but the products **29** and **30** obtained are derived from addition of a methyl group to the cyclopropane carbon atom with no stabilizing substituents. All of these observations are better explained by a relatively slow direct nucleophilic attack of the cuprate at the least substituted cyclopropane carbon atom as illustrated in structures **33** → **34** → **35.** This process is, of course, analogous to the nucleophilic displacement believed operative in the reaction of cuprates with alkyl halides or epoxides.[2d,10] This type of nucleophilic displacement readily accounts for the slow ring opening observed when various cyclopropyl esters (e.g., **36** and **37**) react with Me_2CuLi.[11] Although the reduction potentials of these esters **36** and **37** are clearly too negative for an electron-transfer process to be probable, the fact that aliphatic nitriles and esters fail to react with Me_2CuLi[2c,11e] would clearly allow time for a slow nucleophilic ring opening process analogous to **33** → **34** → **35.** Although aliphatic cyclopropyl ketones such as **38** and **39** have less negative reduction potentials than the esters **36** and **37,** each of the ketones **38**[11b] and **39**[5b] failed to undergo any opening with Me_2CuLi and the ketones were recovered. Since both of these ketones have relatively acidic α-CH_2 groups, we suspect that the failure to observe a slow ring opening in these cases

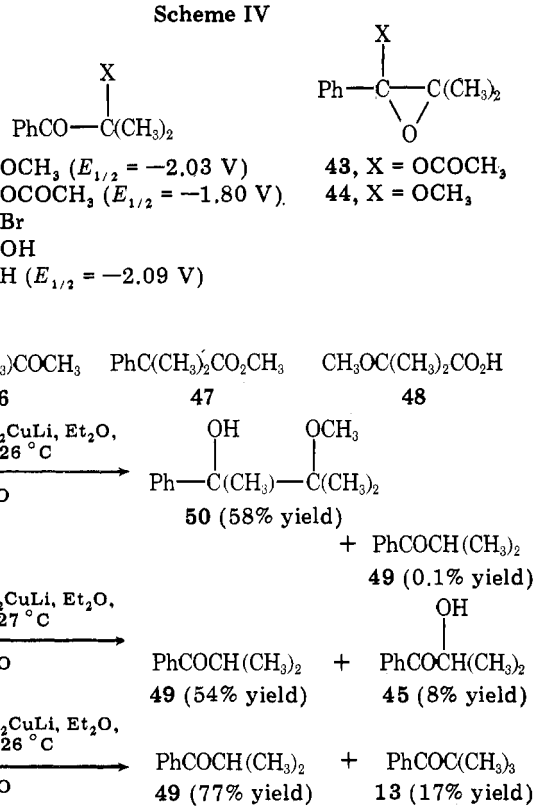
Scheme III



is attributable to the rapid conversion of each ketone to its enolate by the cuprate reagent.[12]

The last type of aryl alkyl ketones to be examined were the α-substituted ketones **40–42** (Scheme IV). Although the ac-

Scheme IV



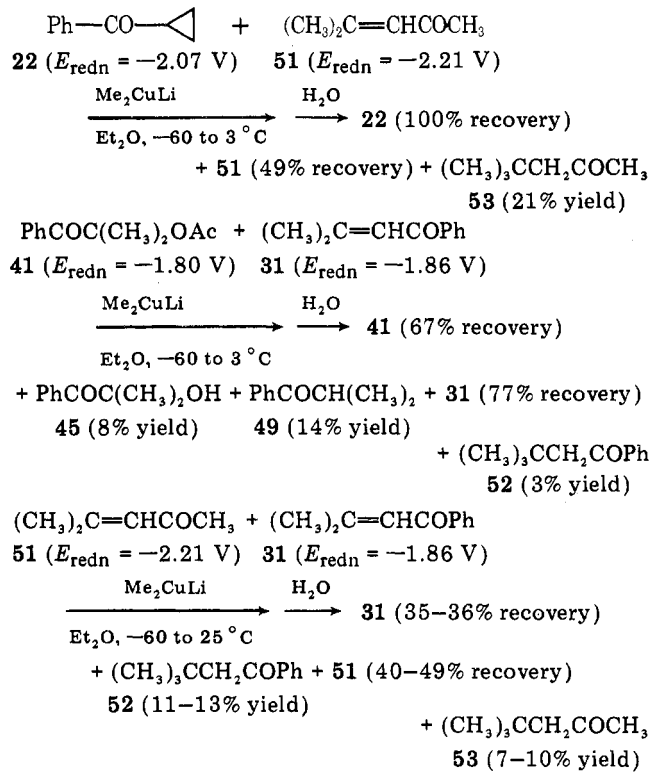
etoxy ketone **41** was readily prepared by reaction of the bromo ketone **42** with KOAc (presumably via the unstable epoxide **43**), the analogous reaction of the bromo ketone **42** with NaOMe yielded not the reported[13] methoxy ketone **40** but rather the epoxy ether **44**. Acid-catalyzed hydrolysis of the epoxy ether **44** yielded the ketol **45** and acid-catalyzed rearrangement of **44** yielded the methoxy ketone **46**. Silver nitrate catalyzed solvolysis of the bromo ketone **42** in MeOH produced a mixture of the desired methoxy ketone **40** (ca. 10% of the mixture) and the rearranged ester **47** (ca. 90% of the mixture). In view of these problems, we finally synthesized the methoxy ketone **40** by reaction of the methoxy acid **48** with excess PhLi. Although the reduction potentials (Scheme IV and Table I) of ketones **40** and **41** were similar, the half-life (see Table I) of the ketyl **8** derived from the methoxy ketone **40** ($t_{1/2}$ 0.7 s) was distinctly longer than the half-life ($<10^{-2}$ s) for the ketyl **8** from the acetoxy ketone **41**. The instability of the bromo ketone **42** in our solvent–electrolyte system prevented us from obtaining satisfactory electrochemical data for this compound.

Although the methoxy ketone **40** reacted with Me_2CuLi to form the 1,2 adduct **50** accompanied by only traces of the reduction product **49**, the analogous reaction with the acetoxy ketone **41** yielded primarily the reduced ketone **49**. This differing behavior of ketones **40** and **41** with Me_2CuLi is analogous to the differing behavior[7c] of a 4-alkoxy-2-cyclohexen-1-one (conjugate addition) and a 4-acetoxy-2-cyclohexen-1-one (reductive elimination) with Me_2CuLi. In both cases, reductive elimination, presumably by the sequence **8** → **9** → **10** → **11**, is observed only if a reasonably good leaving group X is present so that the initial elimination **8** → **9** can occur within the lifetime (ca. 10^{-3} s)[2b,d,6] of the anion radical in a cuprate reaction. Thus, the different reactions of ketones **40** and **41** seem to be determined not by a mechanistic difference in the first step of the reaction but rather by the relative stabilities of the initially formed radical ions **8**.

As might be expected, the bromo ketone **42** with an even better leaving group as a substituent reacted with Me_2CuLi to form mainly the reduction product **49** accompanied by a minor amount of the ketone **13** in which substitution of a methyl group for bromine has occurred. The formation of both reduction and substitution products upon reaction of α-bromo ketones with cuprates has been observed in a number of cases.[14] The substitution products (such as **13** from **42**) are presumably formed[14c] by reaction of the enolate **10** with CH_3X (X = I or Br), this methyl halide being formed in the reaction mixture[7a] from reaction of the halide ion present (I^- or Br^-) with an oxidized derivative of the cuprate such as $[Me_4Cu_2Li_2]\cdot^+$ or $[Me_4Cu_2Li_2]^{2+}$.

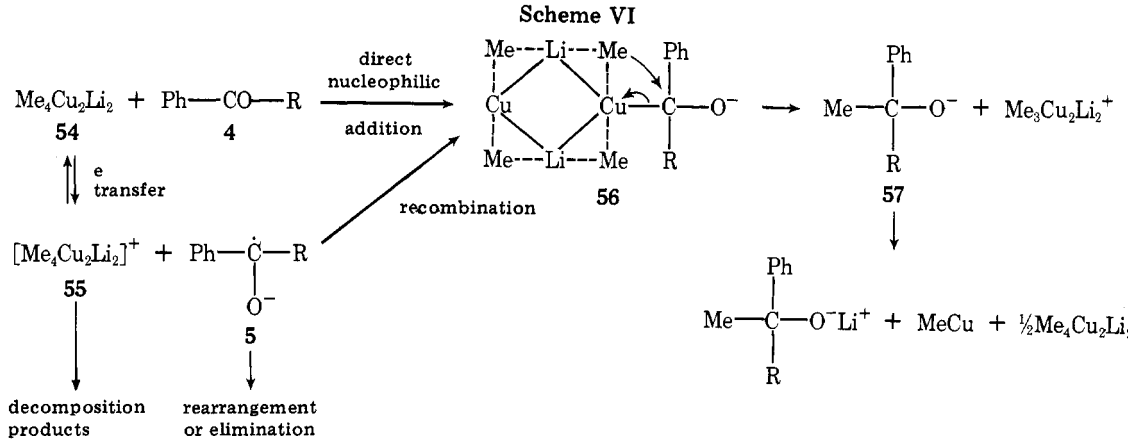
Finally, to obtain estimates of the relative rates at which Me_2CuLi reacts with typical enones and with aryl alkyl ketones, we performed the competition experiments summarized in Scheme V. In a competition between an enone **51** and an

Scheme V. Competition Experiments in Which the Ketone Reactants Are Present in Excess



aryl alkyl ketone **22** that reacts to give a 1,2 adduct, addition of Me_2CuLi to the enone was clearly more rapid. The same conclusion has been derived from a related study[15] of a competitive reaction of Me_2CuLi with a mixture of the enone **31** and PhCOPh (E_{redn} = −1.80 V, reacts with Me_2CuLi to give mainly a 1,2 adduct). In a competition reaction involving an enone **31** and an aryl alkyl ketone **41** whose anion radical undergoes a rapid secondary reaction, the overall rates of the two processes were similar with the reaction involving reductive elimination (**41** → **49**) being slightly more rapid. In each of the foregoing rate comparisons, ketones having comparable E_{redn} values were compared. In conjugate additions of Me_2CuLi to enones the relative reaction rates appear not to be directly related to E_{redn} values. Thus, the relative rates of conjugate addition of Me_2CuLi to the two enones **31** and **51** were similar although the E_{redn} values differ by 0.35 V. Although experimental difficulties in this competition experiment (see Experimental Section) created some ambiguity

Scheme VI



in our results, the reaction of Me_2CuLi with the more easily reduced enone **31** does appear to be slightly faster than the reaction with enone **51.**

From these studies we conclude that if the radical anion **5** (Scheme VI) derived from an aryl alkyl ketone **4** can undergo a further intramolecular reaction within a time period of 10^{-3} s or less, reaction of this ketone **4** with Me_2CuLi is likely to form a reduced or a rearranged product in a reaction that is comparable in rate to the conjugate addition of Me_2CuLi to an enone. However, if the anion radical **5** does not undergo a rapid intramolecular reaction, reaction of the ketone **4** with Me_2CuLi will yield a 1,2 adduct via a reaction path that is significantly slower than conjugate addition of Me_2CuLi to an enone. There appear to be at least two reaction pathways (Scheme VI) that can lead to the 1,2 adduct **57.** One pathway is a direct nucleophilic addition of the cuprate cluster **54** to the ketone to form an intermediate **56** that can rearrange to form the 1,2 adduct **57.** This process, which is analogous to the mechanism believed operative[10] in the relatively slow reaction of cuprates with alkyl halides, seems most probable for the slow 1,2 addition of cuprates to difficulty reduced (E_{redn} more negative than −2.8 V) saturated ketones. With the more easily reduced aryl alkyl ketones, a second process involving initial electron transfer to form intermediates **5** and **55** followed by recombination to form the intermediate **56** is a reasonable alternative. Although we are inclined to favor this second pathway (**4** → **5** → **56** → **57**), it should be noted that the recombination step (**5** + **55** → **56**) must be slow to be consistent with the relative reaction rates observed. This slow recombination rate could be attributed to the fact that a relatively small amount of the *total spin density* in the ketyl **5** is centered at the carbonyl carbon atom.[4] By contrast, a significantly larger fraction of the *total spin density* in ketyls derived from α,β-unsaturated ketones is centered at the β-carbon atom.[2] Also, in species such as **7** and **9** derived from rearrangement of or elimination of an anion from a radical anion, the bulk of the spin density will be located at a single carbon atom. To decide if this conjecture has merit, we clearly need more information about the relationship between spin densities in ion radical intermediates and their rates of recombination.

Experimental Section[16]

Preparation or Purification of the Starting Materials. All anhydrous ethereal solvents were freshly distilled from $LiAlH_4$, commercial Et_2O solutions of MeLi (halide free, Foote Mineral Co.) were standardized by a double titration procedure,[17] and the colorless, crystalline complex, Me_2SCuBr, was prepared from commercial CuBr (Fisher Scientific) as previously described.[2c] Commercial samples of ketones **12, 22,** and **39** were purified by distillation and the ketone **13** was obtained from PhCOCl by a literature procedure.[18] This same procedure[18] was used with β-$C_{10}H_7COCl$ and with α-$C_{10}H_7COCl$ to obtain ketones **14** and **15.** The ketone **15** was obtained in 72% yield as colorless needles from hexane: mp 74–75 °C [recrystallization raised the mp to 76–77 °C (lit.[19] mp 73–74 °C)]; ir (CCl_4) 1688 cm^{-1} (C=O); uv max (95% EtOH) 220 nm (ϵ 65 000) and 282 (5600) with shoulders at 271 (5100) and 293 (5100); NMR (CCl_4) δ 7.1–7.9 (7 H, m, aryl CH) and 1.23 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 212 (M^+, 14), 155 (100), 127 (36), 77 (4), and 57 (4).

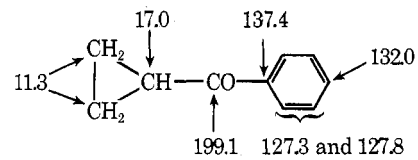
The ketone **14** was obtained in 88% yield as a pale yellow liquid, bp 134–136 °C (0.8 mm) [lit.[19] bp 184–186 °C (16 mm)], that solidified on cooling, mp 55–59 °C. Recrystallization from hexane afforded the pure ketone **14** as colorless prisms: mp 59–60 °C (lit.[20] mp 66 °C); ir (CCl_4) 1675 cm^{-1} (C=O); uv max (95% EtOH) 213 nm (ϵ 29 700), 222 (26 700), 242 (33 600), 248 (32 500), and 283 (6910); NMR (CCl_4) δ 7.3–8.3 (7 H, m, aryl CH) and 1.40 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 212 (M^+, 17), 156 (13), 155 (100), 128 (5), 127 (32), 126 (4), 97 (3), 57 (3), and 41 (5).

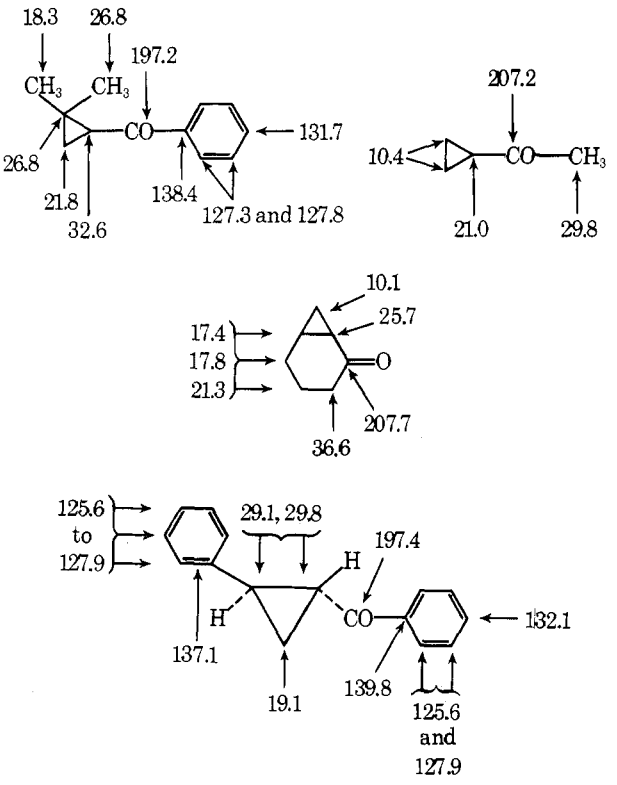
Anal. Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 84.84; H, 7.62.

Ketones **38** and **24** were prepared by previously described procedures.[21] The bicyclic ketone **38** was obtained in 51% yield as a colorless liquid: bp 96 °C (18 mm); $n^{25}D$ 1.4898 [lit.[22] bp 90 °C (15 mm)]; ir (CCl_4) 1691 cm^{-1} (C=O);[23] NMR (CCl_4) δ 0.8–1.4 (2 H, m, cyclopropyl CH_2) and 1.5–2.5 (8 H, m, aliphatic CH); mass spectrum *m/e* (rel intensity) 110 (M^+, 73), 82 (48), 81 (55), 68 (53), 67 (58), 55 (66), 54 (100), 53 (33), 41 (34), and 39 (68). The ketone **24** was obtained in 54% yield as colorless needles from hexane: mp 43–44 °C[24d] (lit. mp 45.5–50,[21] 45–48,[24a] 45,[24b] 43–45 °C[24c]); ir ($CHCl_3$) 1667 cm^{-1} (conjugated C=O); uv max (95% EtOH) 244 nm (ϵ 20 200); NMR ($CDCl_3$) δ 7.1–8.2 (10 H, m, aryl CH), 2.5–3.1 (2 H, m, benzylic CH and COCH), and 1.3–2.1 (2 H, m, CH_2); mass spectrum *m/e* (rel intensity) 222 (M^+, 100), 221 (58), 117 (67), 116 (57), 115 (75), 106 (26), 105 (94), 91 (40), 78 (32), 77 (86), and 51 (32).

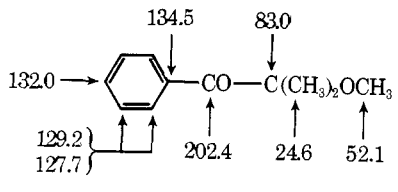
An authentic sample of the ketone **23** was obtained as a colorless liquid:[25] ir (CCl_4) 1675 cm^{-1} (C=O); uv max (95% EtOH) 245 nm (ϵ 13 000); NMR (CCl_4) δ 7.2–8.0 (5 H, m, aryl CH), 2.2–2.6 (1 H, m, CHCO), and 0.6–1.8 (8 H, m, cyclopropyl CH_2 and two CH_3 singlets at 1.05 and 1.33); mass spectrum *m/e* (rel intensity) 174 (M^+, 75), 159 (30), 154 (39), 115 (23), 106 (23), 105 (100), 77 (65), 51 (25), and 41 (20). The cyclopropyl ketone **22** had the following spectral properties: ir (CCl_4) 1670 cm^{-1} (C=O); uv max (95% EtOH) 242 nm (ϵ 23 200) and 273 (1830); NMR (CCl_4) δ 7.0–8.0 (5 H, m, aryl CH), 2.3–2.9 (1 H, m, COCH), and 0.7–1.4 (4 H, m, cyclopropyl CH_2); mass spectrum *m/e* (rel intensity) 146 (M^+, 72), 145 (25), 106 (26), 105 (100), 77 (73), 69 (23), 51 (36), 43 (38), 41 (22), and 39 (30). The spectral properties of the cyclopropyl ketone **39** were ir (CCl_4) 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 2.48 (3 H, s, $COCH_3$), 2.0–2.5 (1 H, m, CHCO), and 0.8–1.3 (4 H, m, cyclopropyl CH_2); mass spectrum *m/e* (rel intensity) 84 (M^+, 74), 83 (21), 69 (100), 43 (92), 42 (30), 41 (72), and 39 (61).

The natural abundance ^{13}C NMR spectra of the various cyclopropyl ketones **22–24, 38,** and **39,** determined in $CDCl_3$ solution, are summarized in the following structures. In each case off-resonance decoupling was used to support the assignments given.





Preparation of the Methoxy Ketone 40. A solution of $NaOCH_3$ [from 2.45 g (107 mg-atoms) of Na] and 8.41 g (50.3 mmol) of α-bromoisobutyric acid in 75 ml of MeOH was stirred at 26 °C for 3 h and then refluxed for 1.5 h. After the reaction mixture had been concentrated it was partitioned between Et_2O and saturated aqueous HCl. The ethereal solution was dried (Na_2SO_4) and concentrated to leave 5.16 g of pale yellow liquid. Fractional distillation separated 3.85 g (65%) of the methoxy acid **48** as a colorless liquid: bp 95–96 °C (19 mm); $n^{25}D$ 1.4188 [lit.[26] bp 99.5 °C (18 mm)]; ir (CCl_4) 2980 (broad, associated OH) and 1710 cm^{-1} (carboxyl C=O); NMR (CCl_4) δ 10.16 (1 H, s, OH), 3.27 (3 H, s, OCH_3), and 1.40 (6 H, s, CH_3); mass spectrum *m/e* (rel intensity) 118 (M^+, <1), 103 (2), 73 (100), 59 (8), 57 (8), 45 (10), 43 (29), and 41 (26). To a cold (−45 °C) solution of 1.21 g (10.2 mmol) of the acid **48** in 15 ml of Et_2O was added, dropwise with stirring and cooling during 10 min, 10 ml of an Et_2O solution containing 10.7 mmol of PhLi. The resulting mixture was warmed to −10 °C and an additional 9.5 ml of Et_2O solution containing 10 mmol of PhLi was added, dropwise and with stirring while the reaction mixture was kept at −10 to 1 °C. After the reaction mixture had been stirred at 1 °C for 15 min, it was warmed to 27 °C and poured, with vigorous stirring, into dilute aqueous HCl. After the aqueous phase had been saturated with NaCl, the mixture was extracted with Et_2O and the Et_2O extract was washed with aqueous $NaHCO_3$ and with aqueous NaCl and dried (Na_2SO_4). Concentration left 1.67 g of pale yellow liquid that was chromatographed on silica gel to separate 329 mg of early fractions containing PhPh and other impurities followed by 1.36 g (75%) of fractions (eluted with Et_2O–hexane mixtures, 2:98 v/v) containing (GLC, Carbowax 20M on Porasil) the ketone **40**. A collected (GLC) sample of the ketone **40** was obtained as a colorless liquid: $n^{25}D$ 1.5094; ir (CCl_4) 1680 cm^{-1} (conjugated C=O); NMR (CCl_4) δ 8.1–8.4 (2 H, m, aryl CH), 7.3–7.6 (3 H, m, aryl CH), 3.13 (3 H, s, OCH_3), and 1.43 (6 H, s, CH_3); uv max (95% EtOH) 247 nm (ε 10 200), 280 (shoulder, 1020), and 330 (72); mass spectrum *m/e* (rel intensity) 178 (M^+, <1), 105 (9), 77 (12), and 73 (100). The natural abundance ^{13}C NMR spectrum of the ketone **40** in $CDCl_3$ solution is summarized in the following structure.



Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.87; H, 7.78.

To examine a reaction reported[13] to form the methoxy ketone **40**, a mixture of NaOMe [from 409 mg (17.8 mg-atoms) of Na] and 3.45 g (15.2 mmol) of the bromo ketone **42** in 20 ml of Et_2O was stirred for 16 h at 25 °C and then partitioned between Et_2O and aqueous NaCl. The Et_2O solution was dried and concentrated to leave 2.54 g of a pale yellow liquid that contained no halogen and exhibited no ir absorption in the 6-μ region attributable to a carbonyl group. A 203-mg aliquot of the product was distilled under reduced pressure (0.6 mm) in a short-path still to separate 159 mg (78%) of the epoxy ether **44** as a colorless liquid: $n^{25}D$ 1.4898; ir (CCl_4) no OH or C=O absorption in the 3- and 6-μ regions; NMR (CCl_4) δ 7.1–7.6 (5 H, m, aryl CH), 3.14 (3 H, s, OCH_3), 1.48 (3 H, s, CH_3), and 0.97 (3 H, s, CH_3); mass spectrum *m/e* (rel intensity) 178 (M^+, <1), 105 (100), 77 (45), 73 (14), and 43 (15); uv (95% EtOH), series of weak maxima (ε 64–727) in the region 244–281 nm.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.03; H, 7.94.

An attempt to obtain the pure epoxy ether **44** by GLC collection (silicone SE-30 on Chromosorb P) resulted in isomerization to the methoxy ketone **46** that was collected as a colorless liquid: $n^{25}D$ 1.5049; ir (CCl_4) 1720 cm^{-1} (C=O); NMR (CCl_4) δ 7.1–7.6 (5 H, m, aryl CH), 3.28 (3 H, s, OCH_3), 1.97 (3 H, s, CH_3CO), and 1.55 (3 H, s, CH_3); uv max (95% EtOH) 255 nm (ε 810) and 291 (256); mass spectrum *m/e* (rel intensity) 135 (52), 105 (10), 77 (21), and 43 (100).

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.20; H, 7.94.

A solution of 792 mg (4.45 mmol) of epoxy ether **44** and 0.15 ml of aqueous 36% HCl in 10 ml of MeOH was stirred at 27 °C for 80 min and then partitioned between Et_2O and aqueous NaCl. After the Et_2O solution had been washed with H_2O and with aqueous NaCl and dried (Na_2SO_4), concentration left 667 mg of the crude hydroxy ketone **45** as a pale yellow liquid. A 150-mg aliquot of the crude product was distilled at 0.05 mm in a short-path still to separate 124 mg (75% yield) of the hydroxy ketone **45** as a colorless liquid: $n^{25}D$ 1.5260 [lit. $n^{25}D$ 1.5276,[27a] bp 91–93 °C (0.7 mm),[27a] 120 °C (3 mm)[27b]]; ir (CCl_4) 3590, 3460 (OH), and 1670 cm^{-1} (C=O); uv max (95% EtOH) 244 nm (ε 7190) and 325 (63); NMR (CCl_4) δ 7.2–8.2 (5 H, m, aryl CH), 3.85 (1 H, broad, OH, exchanged with D_2O), and 1.50 (6 H, s, CH_3); mass spectrum *m/e* (rel intensity) 164 (M^+, <1), 121 (50), 106 (23), 105 (30), 77 (30), 59 (97), and 43 (100).

To explore the possible synthesis of the methoxy ketone **40** by reaction of the bromo ketone **42** with Ag^+ ion in MeOH solution,[28] a solution of 510 mg (3.0 mmol) of $AgNO_3$, 0.6 ml of H_2O, and 647 mg (2.85 mmol) of the bromo ketone **42** in 11 ml of MeOH was stirred in the dark for 30 min during which time a white precipitate separated. The mixture was filtered and the filtrate was partitioned between Et_2O and aqueous NaCl. After the Et_2O solution had been dried ($NaSO_4$), concentration left 419 mg of yellow liquid that contained (GLC, Carbowax 20M on Porasil) the ester **47** (ca. 90%, retention time 22.4 min) and the methoxy ketone **40** (ca. 10%, 25.6 min). A collected (GLC) sample of the ketone **40** was identified with the previously described material by comparison of ir and mass spectra and GLC retention times. A collected (GLC) sample of the ester **47** was obtained as a colorless liquid: $n^{25}D$ 1.5040; ir (CCl_4) 1735 cm^{-1} (ester C=O); uv (95% EtOH), a series of weak maxima (ε 408–831) in the region 248–262 nm with intense end absorption; NMR (CCl_4) δ 7.1–7.4 (5 H, m, aryl CH), 3.60 (3 H, s, OCH_3), and 1.53 (6 H, s, CH_3); mass spectrum *m/e* (rel intensity) 178 (M^+, 17), 119 (100), 91 (45), 77 (15), and 41 (20).

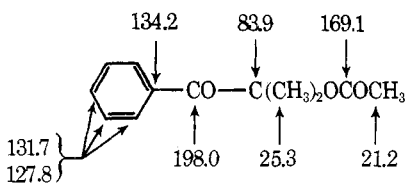
Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.12; H, 7.93.

Preparation of the Acetoxy Ketone 41. A solution of 10.00 g (44 mmol) of the bromo ketone **42** and 7.2 g (73 mmol) of KOAc in 75 ml of 95% EtOH was refluxed for 19 h and then cooled, filtered, and partitioned between Et_2O and aqueous NaCl. After the Et_2O solution had been dried (Na_2SO_4) and concentrated, distillation of the residual yellow liquid (7.75 g) separated 2.90 g of an early fraction, bp 82–90 °C (0.9–1.3 mm), containing (NMR analysis) a mixture of the acetoxy ketone **41** and an olefinic impurity. The subsequent distillation fraction (3.05 g), bp 90–96 °C (0.9–1.3 mm), containing the desired product was crystallized from hexane to separate 2.52 g (28%) of the acetoxy ketone **41** as white needles: mp 59–60 °C (lit.[29] mp 61 °C); ir (CCl_4) 1742 (ester C=O) and 1690 cm^{-1} (conjugated C=O); uv max (95% EtOH) 249 nm (ε 13 300), 269 (1000), and 314 (96); NMR (CCl_4) δ 7.8–8.1 (2 H, m, aryl CH), 7.2–7.5 (3 H, m, aryl CH), 1.88 (3 H, s, $COCH_3$), and 1.66 (6 H, s, CH_3); mass spectrum *m/e* (rel intensity) 206 (M^+, <1), 163 (59), 106 (16), 105 (100), 101 (17), 77 (45), 59 (32), and 43 (51). The natural abundance ^{13}C NMR spectrum of the ketone **41** in $CDCl_3$ solution is summarized in the following structure.

Table I. Electrochemical Reduction of the Ketones at 25 °C in DMF Solution Containing 0.5 M n-Bu_4NBF_4

Registry no.	Ketone (concn, M × 10^3)	Polarography $E_{1/2}$, V vs. SCE	Polarography n	Polarography i_d, μA	Cyclic voltammetry $E_{1/2}$, V vs. SCE	Cyclic voltammetry Half-life, s
98-86-2	**12** (6.3)	−2.05	1.1	17–18	−2.12	0.2
938-16-9	**13** (5.6–5.8)	−2.14	1.0	17–25	−2.15	3
		−2.82	ca. 2	23		
7270-99-7	**14** (2.9–3.1)	−1.96	1.0	8–11	−1.95	>10
		−2.44	1.1	6–7	*a*	*a*
25540-73-2	**15** (3.8–4.8)	−2.03	1.1	14–18	−2.04	3
		−2.41	1.0	4	*a*	*a*
765-43-5	**39** (7.6–11.7)	ca. −2.87[b]			*a*	*a*
5771-58-4	**38** (7.6–8.3)	ca. −2.81[b]			*a*	*a*
3481-02-5	**22** (3.6–6.6)	−2.07	1.1	15–18	−2.08	ca. 5
		−2.73	1.4	12		
5685-43-8	**23** (2.6–4.3)	−2.09	1.1	9–16	−2.09	4
1145-92-2	**24** (1.8–4.2)	−1.82	0.8	8–23	−1.85	$<10^{-2}$
5650-07-7	**31** (6.4–7.0)	−1.86	0.9	11–25	−1.89	0.7
141-79-7	**51** (8.0–10.2)	−2.21	0.9	15–26	−2.26	0.07
611-70-1	**49** (3.8–6.2)	−2.09	1.1	12–22	−2.09	0.3
		−2.73	1.3	5–13		
7476-41-7	**41** (6.1–6.2)	−1.80[c]	1.0	22–24	−1.83[d]	$<10^{-2}$
59671-36-2	**40** (6.2)	−2.03	1.2	32–35	−2.01	0.7
		−2.76	1.2	16–21		

[a] Value not determined. [b] Since the reduction wave for this ketone was almost as negative as the reduction wave for the supporting electrolyte, only approximate $E_{1/2}$ values could be obtained. [c] An additional wave with $E_{1/2}$ = −2.10 V corresponding to the formation and reduction of ketone **49** was also observed. [d] At slow scan rates (<10 V/s), the cyclic voltammetry scans also exhibited a reversible reduction wave, with $E_{1/2}$ = −2.10 V, corresponding to the formation and reversible reduction of the ketone **49**.



Electrochemical Measurements. The polarographic and cyclic voltammetry measurements employed a custom-made polarographic module, utilizing solid-state amplifiers, that followed the typical three electrode design. Descriptions of the cells, working electrodes, reference electrodes, and reagent purification procedures have been published previously.[30] In all cases the solvent was anhydrous DMF containing 0.5 M n-$Bu_4N^+BF_4^-$ as the supporting electrolyte. Previously described procedures[30b,31] were used to estimate the $E_{1/2}$ values and half-lives from cyclic voltammetry measurements. The results of these measurements are summarized in Table I. Since the reduction waves for the saturated cyclopropyl ketones **38** and **39** were almost as negative as the discharge potential for the supporting electrolyte, only approximate $E_{1/2}$ values were obtained from the polarographic measurements and it was not possible to obtain data for these two ketones by cyclic voltammetry.

Reactions with Me_2CuLi. A. Ketone 13. To a solution of Me_2CuLi, prepared by adding 10.1 ml of an Et_2O solution containing 18 mmol of MeLi to a solution of 1.77 g (8.6 mmol) of Me_2SCuBr in 12 ml of Et_2O and 9 ml of Me_2S, was added 1.00 g (6.2 mmol) of the ketone **13** in 2 ml of Et_2O. The resulting solution, from which yellow $(MeCu)_n$ began to precipitate within 5 min, was stirred at 27 °C for 1 h and then partitioned between Et_2O and an aqueous solution of NH_4Cl and NH_3. The ethereal layer was dried and concentrated to leave 966 mg of crude liquid product. After an aliquot of the product had been mixed with a known weight of internal standard (n-$C_8H_{17}Ph$), GLC analysis (silicone SE-30 on Chromosorb P) indicated the presence of the unchanged ketone **13** (retention time 4.5 min, 10% recovery), the alcohol **17** (6.5 min, 72% yield), and n-$C_8H_{17}Ph$ (10.4 min). The mixture of the ketone **13** (R_f 0.48) and the alcohol **17** (R_f 0.34) was separated by preparative TLC [silica gel with an Et_2O–pentane (1:19 v/v) eluent] and the alcohol fraction was distilled under reduced pressure in a short-path still to separate the alcohol **17** as a colorless liquid: bp 140–141 °C (18 mm); $n^{25}D$ 1.5123 [lit.[32] bp 116–117 °C (15 mm), $n^{25}D$ 1.5135]; ir (CCl_4) 3590 cm^{-1} (OH); uv (95% EtOH) series of weak maxima (ε 125–204) in the region 247–254 nm; NMR (CCl_4) δ 6.9–7.5 (5 H, m, aryl CH), 1.4–1.6 (4 H, OH and CH_3 singlet at 1.52), and 0.88 (9 H, s, t-Bu); mass spectrum m/e (rel intensity) 160 ($M^+ - H_2O$, 16), 145 (49), 121 (100), 105 (42), 91 (20), 77 (35), 57 (21), 51 (21), 43 (65), and 41 (20).

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.83; H, 10.18.

Reaction of 969 mg (5.98 mmol) of the ketone **13** with 6.58 mmol of MeLi in 24 ml of Et_2O afforded 1.02 g (96%) of the alcohol **17**, $n^{25}D$ 1.5145, that was identified with the previously described sample by comparison of ir and NMR spectra.

The ketone fraction from the preparative TLC separation was identified as ketone **13** by comparison of ir and mass spectra. The absence of peaks in the mass spectrum at m/e values larger than 162 (e.g., 176 and 178) indicated the absence of ketone products in which a CH_3 group had been added to the aromatic ring.

B. Ketone 14. To a cold (4 °C) solution of Me_2CuLi, from 10.0 mmol of MeLi, 1.03 g (5.0 mmol) of Me_2SCuBr, 4 ml of Me_2S, and 5.9 ml of Et_2O, was added 336 mg (1.6 mmol) of ketone **14** in 4 ml of Et_2O. The reaction solution was stirred at 0–8 °C for 1 h, during which time a small amount of yellow $(MeCu)_n$ precipitated, and then at 25 °C for 16 h. After the usual isolation procedure, the crude liquid product was subjected to preparative TLC (silica gel with an Et_2O–pentane eluent, 1:19 v/v) to separate 28 mg of a ketone fraction and 269 mg of an alcohol fraction (eluted second). The alcohol fraction was distilled in a short-path still at 0.4 mm to separate 260 mg (71%) of the alcohol **18** as a light yellow liquid, $n^{25}D$ 1.5843. This material crystallized on standing and was recrystallized from pentane at low temperatures to separate the pure alcohol **18** as colorless needles: mp 57.5–59 °C; ir (CCl_4) 3595 cm^{-1} (OH); uv max (Et_2O) 224 nm (ε 94 300) with a series of weak maxima (ε 3250–5190) in the region 248–288 nm; NMR (CCl_4) δ 7.3–8.0 (7 H, m, aryl CH), 1.67 (3 H, s, CH_3), 1.57 (1 H, s, OH, exchanged with D_2O), and 0.97 (9 H, s, t-Bu); mass spectrum m/e (rel intensity) 228 (M^+, 33), 172 (53), 171 (100), 155 (41), 153 (22), 129 (25), 128 (58), 127 (40), 77 (20), and 57 (40).

Anal. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.09; H, 8.84.

An authentic sample of the alcohol **18**, mp 58–59 °C, was obtained in 64% yield by reaction of the ketone **14** with excess ethereal MeLi for 30 min at 25 °C. The two samples were identified by a mixture melting point determination and by comparison of ir, NMR, and uv spectra.

The crude ketone fraction (28 mg) from the TLC separation contained (GLC, silicone SE-30 on Chromosorb P) the ketone **14** (retention time 14.0 min, ca. 73% of the mixture) accompanied by two more rapidly eluted components (10.2 min, ca. 14%, and 11.7 min, ca. 13%), believed to be olefins derived from the alcohol **18**. The mass spectrum of this mixture exhibited abundant peaks corresponding to the ketone **14** with a less abundant peak at m/e 210 attributable

to an olefin formed from alcohol **18**. There were no higher mass peaks that would be expected from ketones in which a Me group had been added to the aromatic ring of ketone **14**.

C. Ketone 15. A cold (5 °C) solution of Me_2CuLi, from 11.9 mmol of MeLi, 1.23 g (6.0 mmol) of Me_2SCuBr, 6 ml of Me_2S, and 7.3 ml of Et_2O, was treated with 424 mg (2.0 mmol) of the ketone **15** in 5 ml of Et_2O. The resulting mixture was stirred at 5–10 °C for 1 h and at 25 °C for 18 h and then subjected to the usual isolation procedure. The crude liquid product (500 mg) was subjected to preparative TLC (silica gel with an Et_2O–pentane eluent, 1:19 v/v) to separate 70 mg of an unidentified hydrocarbon fraction (ir analysis) and 410 mg of an alcohol fraction (eluted second). A 375-mg aliquot of the alcohol fraction was distilled in a short-path still at 1.6 mm to separate 282 mg (68%) of the alcohol **19** as a viscous yellow liquid: n^{25}D 1.5892; ir (CCl_4) 3590 cm^{-1} (OH); uv max (Et_2O) 224 nm (ϵ 79 000) with a series of weak maxima (ϵ 4780–8410) in the region 260–295 nm; NMR (CCl_4) δ 7.1–7.9 (7 H, m, aryl CH), 1.77 (3 H, s, CH_3), 1.70 (1 H, s, OH, exchanged with D_2O), and 0.99 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 210 ($M^+ - H_2O$, 49), 195 (50), 171 (51), 170 (25), 165 (37), 155 (70), 154 (100), 153 (94), 152 (83), 151 (24), 127 (53), 57 (32), 56 (28), 43 (28), and 41 (28).

Anal. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.38; H, 8.90.

Reaction of the ketone **15** with excess ethereal MeLi at 25 °C for 1 h yielded 81% of the alcohol **19** as a viscous liquid, n^{25}D 1.5880, that was identified with the previously described sample by comparison of ir, NMR, and uv spectra.

D. Ketone 22. To a cold (4 °C) solution of Me_2CuLi, from 9.3 mmol of MeLi, 1.01 g (4.9 mmol) of Me_2SCuBr, 5.3 ml of Me_2S, and 5.7 ml of Et_2O, was added a solution of 512 mg (3.5 mmol) of ketone **22** in 1 ml of Et_2O. As the ketone was added an exothermic reaction occurred with precipitation of $(MeCu)_n$. The mixture was stirred at 27 °C for 3.5 h and then subjected to the usual isolation procedure to separate 476 mg of crude product as a yellow liquid. A 454-mg aliquot of this product was chromatographed on silica gel to separate 18 mg (3.5%) of ketone **28** (eluted with hexane, identified with an authentic sample by comparison of ir, NMR, and mass spectra and GLC retention times), followed by 29 mg of fractions (eluted with hexane) containing (GLC, silicone DC-10 on Chromosorb P) a mixture of ketone **22** (retention time 9.1 min) and ketone **28** (9.6 min) and 54 mg (11%) of ketone **22** (eluted with 2% Et_2O in hexane, identified by comparison of GLC retention times and ir and mass spectra). Subsequent chromatography fractions, eluted with 2% Et_2O in hexane, contained 289 mg (57%) of the crude alcohol **25**. A 120-mg aliquot was distilled at 0.5 mm in a short-path still to separate 86 mg of the pure alcohol **25** as a colorless liquid: n^{25}D 1.5332; ir (CCl_4) 3590 cm^{-1} (OH); uv (95% EtOH), series of weak maxima (ϵ 75–187) in the region 247–267 nm; NMR (CCl_4) δ 7.0–7.5 (5 H, m, aryl CH), 1.60 (1 H, s, OH, exchanged with D_2O), 1.41 (3 H, s, CH_3), 0.9–1.3 (1 H, m, cyclopropyl CH), and 0.2–0.5 (4 H, m, cyclopropyl CH_2); mass spectrum *m/e* (rel intensity) 147 (22), 144 (43), 143 (26), 134 (100), 129 (81), 128 (45), 121 (32), 115 (30), 105 (44), 103 (30), 91 (43), 77 (40), 51 (23), 43 (43), and 39 (20).

Reaction of the ketone **22** with excess ethereal MeLi at 26 °C for 2 h yielded 79% of the alcohol **25** as a colorless liquid, n^{25}D 1.5330 [lit.[33] bp 78–81 °C (0.3 mm), n^{27}D 1.5324], that was identified with the previously described sample by comparison of ir, NMR, and mass spectra.

E. Ketone 23. To a cold (3 °C) solution of Me_2CuLi, from 9.3 mmol of MeLi, 1.02 g (4.9 mmol) of Me_2SCuBr, 5.0 ml of Me_2S, and 6.0 ml of Et_2O, was added a solution of 613 mg (3.5 mmol) of the ketone **23** in 2.0 ml of Et_2O. During the addition, a mildly exothermic reaction occurred with precipitation of $(MeCu)_n$. After the mixture had been stirred at 27 °C for 4.5 h, it was subjected to the usual isolation procedure to give 640 mg of crude product as a pale yellow liquid. A 610-mg aliquot of this product was chromatographed on silica gel with an Et_2O–petroleum ether eluent (1:99 v/v) to separate 76 mg of early fractions containing (ir analysis) a mixture of alcohol and ketone products. Subsequent fractions contained 467 mg (75%) of the alcohol **26**. A 130-mg portion of the alcohol was distilled in a short-path still to separate 95 mg of the pure alcohol **26** as a colorless liquid: n^{25}D 1.5145; ir (CCl_4) 3610 cm^{-1} (OH); uv (95% EtOH), series of weak maxima (ϵ 92–257) in the region 240–266 nm; NMR (CCl_4) δ 7.1–7.6 (5 H, m, aryl CH), 0.8–1.7 (11 H, m, cyclopropyl CH, OH, and three CH_3 singlets at 1.54, 1.04, and 0.88), and 0.2–0.7 (2 H, m, cyclopropyl CH); mass spectrum *m/e* (rel intensity) 172 (46), 157 (100), 143 (38), 142 (50), 134 (27), 129 (58), 128 (39), 115 (46), 91 (41), and 77 (29).

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 82.11; H, 9.58.

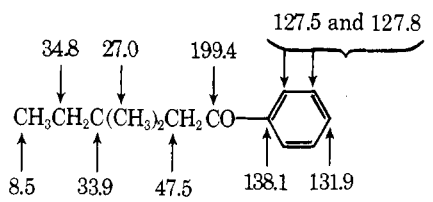
Reaction of the ketone **23** with excess ethereal MeLi at 27 °C for 3 h yielded 90% of the alcohol **26** as a colorless liquid, n^{25}D 1.5155, that was identified with the previously described sample by comparison of ir, NMR, and mass spectra and TLC R_f values on silica gel.

The early chromatographic fractions (70 mg) were rechromatographed on silica gel to separate 9 mg of an early fraction containing (GLC, silicone SE-30 on Porasil) the starting ketone **23** (retention time 16.0 min, ca. 60% of the mixture) and the ketone **29** (22.2 min, ca. 40% of the mixture corresponding to a 0.6% yield). Subsequent chromatographic fractions contained 22 mg of the starting ketone **23** (GLC analysis) and 30 mg of the alcohol **26**. A collected (GLC) sample of the ketone **29** was identified with a subsequently described authentic sample by comparison of mass spectra and GLC retention times.

An authentic sample of the ketone **29** was prepared from β,β-dimethylacryloyl chloride: bp 78–82 °C (42 mm); n^{25}D 1.4750 [lit.[34] bp 59–61 °C (30 mm)]; ir (CCl_4) 1785, 1755 (C=O), and 1620 cm^{-1} (C=C); NMR (CCl_4) δ 6.03 (1 H, m, vinyl CH), 2.15 (3 H, broad, CH_3), and 1.98 (3 H, broad, CH_3). To a cold (−8 °C) solution of 13.5 g (114 mmol) of this acid chloride in 25 ml of Et_2O was added, dropwise and with stirring, 75 ml of an ethereal solution of PhMgBr (prepared from 100 mmol of PhBr). After the resulting solution had been stirred for 30 min, it was quenched with H_2O and then partitioned between Et_2O and aqueous NaCl. The organic solution was washed successively with aqueous $NaHCO_3$ and with aqueous NaCl and then dried (Na_2SO_4) concentrated, and distilled to separate 7.15 g (45%) of β,β-dimethylacrylophenone (**31**) as a pale yellow liquid: bp 89–93 °C (1.2 mm); n^{25}D 1.5598 [lit. bp 104–106 °C (5 mm),[34] 120–121 °C (4 mm),[35] n^{23}D 1.5579,[34] n^{19}D 1.5598[35]]; ir (CCl_4) 1665 (C=O) and 1615 cm^{-1} (C=C); uv max (95% EtOH) 259 nm (ϵ 19 700) and 346 (155); NMR (CCl_4) δ 7.2–8.0 (5 H, m, aryl CH), 6.69 (1 H, broad, vinyl CH), 2.20 (3 H, broad, CH_3), and 1.96 (3 H, broad, CH_3); mass spectrum *m/e* (rel intensity) 160 (M^+, 72), 159 (100), 145 (83), 115 (40), 105 (72), 83 (64), 77 (81), 55 (38), 51 (59), and 39 (42). A cold (2 °C) solution of EtMgBr, prepared from 1.80 g (75 mg-atoms) of Mg, 10.9 g (100 mmol) of EtBr, and 75 ml of Et_2O, was treated successively with 91 mg (1.0 mmol) of CuCl and a solution of 4.80 g (30 mmol) of the enone **31** in 25 ml of Et_2O. The resulting mixture was stirred for 2.5 h while it was allowed to warm to 27 °C and then the mixture was partitioned between Et_2O and cold dilute aqueous H_2SO_4. The ethereal solution was washed with aqueous NaCl, dried, and concentrated to leave 5.30 g (93%) of crude product as a pale yellow oil containing (GLC, silicone SE-30 on Porasil) one major component, the ketone **29** (retention time 23.8 min). A collected (GLC) sample of the pure ketone **29** was obtained as a colorless liquid: n^{25}D 1.5100; ir (CCl_4) 1692 and 1680 cm^{-1} (conjugated C=O);[36] uv max (95% EtOH) 241 nm (ϵ 10 300) and 277 (1190); NMR (CCl_4) δ 7.3–8.1 (5 H, m, aryl CH), 2.80 (2 H, s, CH_2CO), and 0.7–1.7 [11 H, m, CH_3CH_2 and a $C(CH_3)_2$ singlet at 1.00]; mass spectrum *m/e* (rel intensity) 190 (M^+, 6), 120 [$PhC(OH)=CH_2^+$, 100], 105 (90), and 77 (36).

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 82.00; H, 9.55.

The natural abundance ^{13}C NMR spectrum of ketone **29**, determined in $CDCl_3$, is summarized in the following formula.



F. Ketone 24. To a cold (4 °C) solution of Me_2CuLi, from 6.8 mmol of MeLi, 0.73 g (3.5 mmol) of Me_2SCuBr, 4.0 ml of Me_2S, and 6.0 ml of Et_2O, was added a solution of 560 mg (2.5 mmol) of ketone **24** in 3.0 ml of Et_2O. The addition was accompanied by a mild exothermic reaction and precipitation of $(MeCu)_n$ began within 20 min. After the reaction mixture had been stirred for 5 h at 27 °C, it was subjected to the usual isolation procedure to give 572 mg of crude product as a yellow liquid. A 565-mg aliquot of this product was chromatographed on silica gel with Et_2O–hexane mixtures as eluents. After separation of 28 mg of early fractions containing (GLC) a mixture of ketones **24** (ca. 4% recovery) and **30** (ca. 0.9% yield), the next fraction contained 36 mg (6% recovery) of the starting ketone **24**, mp 42.5–43 °C, identified by a mixture melting point determination and by comparison of ir, NMR, and mass spectra and GLC retention times. Subsequent fractions contained 484 mg (81%) of the alcohol **27** as a colorless liquid: n^{25}D 1.5805; ir ($CHCl_3$) 3580 and 3460 cm^{-1} (OH); uv (95% EtOH), series of weak maxima (ϵ 440–900) in the region 249–272 nm; NMR ($CDCl_3$) δ 6.9–7.6 (10 H, m, aryl CH), 1.8–2.2 (1 H, m, benzylic CH), 1.70 (1 H, s, OH, exchanged with D_2O), and 0.6–1.6 (6 H, m, cyclo-

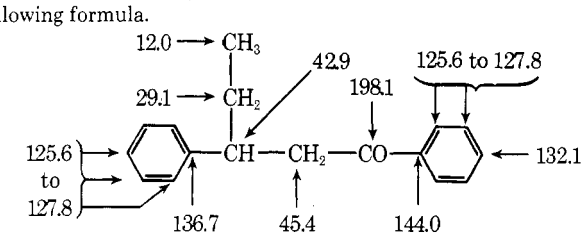
propyl CH and a CH_3 singlet at 1.55); mass spectrum *m/e* (rel intensity) 221 (16), 220 (78), 205 (96), 142 (26), 134 (32), 130 (81), 129 (100), 128 (72), 115 (73), 106 (59), 105 (66), 103 (31), 91 (40), 77 (66), and 51 (37).

Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.71; H, 7.65.

Reaction of the ketone **24** with excess ethereal MeLi at 26 °C for 2 h yielded, after column chromatography, 94% of the alcohol **27** as a colorless liquid, $n^{25}D$ 1.5790, that was identified with the previously described sample by comparison of ir, NMR, and mass spectra.

The early chromatographic fractions (23 mg) were rechromatographed on silica gel to separate in early fractions 3 mg of the ketone **30** followed by 11.5 mg of fractions containing (GLC, silicone SE-30 on Porasil) both ketone **30** (retention time 29.4 min) and ketone **24** (34.4 mm), and 5 mg of ketone **24.** Recrystallization of the crude ketone **30** from EtOH afforded 1 mg of the pure ketone **30,** mp 57–58 °C, that was identified with the subsequently described authentic sample by a mixture melting point determination and by comparison of ir and mass spectra.

To obtain an authentic sample of ketone **30,** a cold (6 °C) solution of EtMgBr, prepared from 21.8 g (200 mmol) of EtBr, 3.60 g (150 mg-atoms) of Mg, and 75 ml of Et_2O, was treated successively with 0.20 g (2 mmol) of CuCl and a solution of 12.48 g (60 mmol) of ketone **32** in 20 ml of Et_2O. The mixture was stirred for 3 h while it was allowed to warm to 25 °C and then it was partitioned between Et_2O and cold, dilute aqueous H_2SO_4. the organic layer was washed with aqueous NaCl, dried, and concentrated to leave 12.4 g (87%) of the crude ketone **30** as a yellow liquid that solidified on standing. A 1.80-g aliquot of the crude product was chromatographed on Al_2O_3 with a pentane eluent to separate 1.15 g of the ketone **30** as a colorless solid. Recrystallization from EtOH afforded the ketone **30** as colorless needles: mp 59–60 °C (lit.[37] mp 63 °C); ir ($CHCl_3$) 1682 cm^{-1} (conjugated C=O); uv max (95% EtOH) 243 nm (ε 13 400); NMR ($CDCl_3$) δ 7.1–8.2 (10 H, m, aryl CH), 3.1–3.4 (3 H, m, benzylic CH and CH_2CO), 1.4–2.0 (2 H, m, CH_2), and 0.80 (3 H, t, J = 7.5 Hz, CH_3); mass spectrum *m/e* (rel intensity) 238 (M^+, 32), 209 (65), 120 (20), 118 (100), 105 (95), 91 (32), and 77 (45). The natural abundance ^{13}C NMR spectrum of ketone **30,** determined in $CDCl_3$, is summarized in the following formula.



G. Ketone 12. A cold (5 °C) solution of Me_2CuLi, from 10.7 mmol of MeLi, 1.25 g (6.06 mmol) of Me_2SCuBr, 6.5 ml of Me_2S, and 8.5 ml of Et_2O, was treated with a solution of 563 mg (4.69 mmol) of ketone **12** in 3 ml of Et_2O. The addition was accompanied by a mildly exothermic reaction with evolution of gas (presumably CH_4) and precipitation of $(MeCu)_n$. After the mixture had been stirred at 27 °C for 3.5 h, it was subjected to the usual isolation procedure to separate 532 mg of crude product as a pale yellow oil. A 434-mg aliquot was chromatographed on silica gel with an Et_2O–hexane eluent (1:19 to 1:3 v/v) to separate 354 mg (77% recovery) of starting ketone **12** followed by 46 mg (9%) of the alcohol **16.** Both products were identified with authentic samples by comparison of ir, NMR, and either mass spectra (for alcohol **16**) or GLC retention times (for ketone **12**). A comparable experiment was performed with a solution of 540 mg (4.5 mmol) of ketone **12** and a cold (4 °C) solution of Me_2CuLi, from 1.66 g (8 mmol) of Me_2SCuBr, 14 mmol of MeLi, 8 ml of Me_2S, and 7 ml of Et_2O. After reaction for 11 min at 4–8 °C [with gas evolution and precipitation of $(MeCu)_n$], a 446-mg aliquot of the crude liquid product (484 mg) was chromatographed to separate 357 mg (72% recovery) of ketone **12** and 48 mg (8%) of the alcohol **16,** $n^{25}D$ 1.5159.

An authentic sample of the alcohol **16,** prepared by reaction of ketone **12** with excess ethereal MeLi, was obtained as a colorless liquid: $n^{25}D$ 1.5169 [lit. bp 60–65 °C (4 mm),[38a] $n^{27}D$ 1.510,[38a] $n^{35}D$ 1.51502[38b]]; ir (CCl_4) 3590 and 3420 cm^{-1} (OH); NMR (CCl_4) δ 7.0–7.6 (5 H, m, aryl CH), 2.18 (1 H, s, OH, exchanged with D_2O), and 1.47 (6 H, s, CH_3); mass spectrum *m/e* (rel intensity), 136 (M^+, 1), 121 (25), 105 (3), 78 (6), 77 (9), 59 (4), 51 (10), and 43 (100); uv (95% EtOH), series of weak maxima (ε 78–177) in the region 239–265 nm.

H. Ketone 31. To a cold (4 °C) solution of Me_2CuLi, from 1.03 g (5.0 mmol) of Me_2SCuBr, 8.6 mmol of MeLi, 6 ml of Me_2S, and 9 ml of Et_2O, was added, dropwise with stirring and cooling, a solution of 480 mg (3.0 mmol) of the ketone **31** in 4 ml of Et_2O. As the ketone **31** was added a mildly exothermic reaction occurred with precipitation of $(MeCu)_n$. The resulting cold (8 °C) mixture was stirred for 15 min at 4–8 °C and then subjected to the usual isolation procedure. The crude product, 490 mg of yellow liquid, contained (ir and NMR analyses) the ketone **52.** A 157-mg aliquot was distilled at 0.9 mm in a short-path still to separate 135 mg (80%) of the ketone **52:** $n^{25}D$ 1.5078 [lit.[36] bp 112–114 °C (10 mm), $n^{25}D$ 1.5056]; ir (CCl_4) 1690 and 1675 cm^{-1} (C=O); NMR (CCl_4) δ 7.2–8.0 (5 H, m, aryl CH), 2.79 (2 H, s, CH_2CO), and 1.05 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 176 (M^+, 12), 120 (56), 105 (100), 77 (54), 57 (15), 51 (25), and 41 (19). This product, which exhibited a single GLC peak (silicone SE-30 on Chromosorb P), was identified with an authentic sample[36] by comparison of ir and NMR spectra and GLC retention times.

I. Ketone 51. To a cold (5 °C) solution of Me_2CuLi, from 1.144 g (5.57 mmol) of Me_2SCuBr, 10 mmol of MeLi, 6 ml of Me_2S, and 7 ml of Et_2O, was added, dropwise with stirring and cooling, a solution of 394 mg (4.00 mmol) of the enone **51** in 5 ml of Et_2O. The reaction mixture, which warmed to 11 °C with precipitation of $(MeCu)_n$ during this addition, was stirred at 5–11 °C for 15 min and then subjected to the usual isolation procedure. The crude product, 407 mg (89%) of yellow liquid containing (ir and NMR analyses) the ketone **53,** was distilled at 20 mm in a short-path still to separate 280 mg (61%) of the ketone **53:** $n^{25}D$ 1.4034 (lit. bp 125–126 °C;[39a] $n^{31}D$ 1.3989;[39a] $n^{25}D$ 1.4018[39b]); ir (CCl_4) 1715 cm^{-1} (C=O); NMR (CCl_4) δ 2.27 (2 H, s, CH_2CO), 2.03 (3 H, s, CH_3CO), and 1.00 (9 H, s, *t*-Bu). This product was identified with an authentic sample[39a] by comparison of ir and NMR spectra and GLC retention times.

J. Bromo Ketone 42. A cold (5 °C) solution of Me_2CuLi, from 1.025 g (5.0 mmol) of Me_2SCuBr, 9.6 mmol of MeLi, 7 ml of Me_2S, and 9 ml of Et_2O, was treated with a solution of 690 mg (3.04 mmol) of the bromo ketone **42** in 3 ml of Et_2O. After the addition [accompanied by an exothermic reaction and precipitation of $(MeCu)_n$] was complete, the mixture was stirred for 30 min at 5 °C and for 90 min at 26 °C and then subjected to the usual isolation procedure. After the crude product (405 mg of yellow liquid) had been mixed with a weighed amount of internal standard (n-$C_{11}H_{24}$), analysis (GLC, silicone SE-30 on Porasil) indicated the presence of n-$C_{11}H_{24}$ (retention time 11.7 min), ketone **49** (18.8 min, 77% yield), and ketone **13** (22.2 min, 17% yield). Collected (GLC) samples of ketones **13** and **49** were identified with authentic samples by comparison of GLC retention times and ir and mass spectra.

K. Methoxy Ketone 40. To a cold (5 °C) solution of Me_2CuLi, from 1.028 g (5.0 mmol) of Me_2SCuBr, 9.45 mmol of MeLi, 6 ml of Me_2S, and 9 ml of Et_2O, was added, dropwise and with stirring, a solution of 540 mg (3.03 mmol) of the methoxy ketone **40** in 4 ml of Et_2O. The mixture, from which $(MeCu)_n$ began to precipitate immediately, was stirred at 4–7 °C for 30 min and at 26 °C for 1 h and then subjected to the usual isolation procedure. A 506-mg aliquot of the crude product (510 mg of yellow liquid) was chromatographed on silica gel with Et_2O–hexane mixtures as the eluent. After separation of 202 mg of early fractions containing mixtures of ketone and alcohol products, the subsequent fractions contained 312 mg (53%) of the alcohol **50** as a colorless liquid. Short-path distillation of a 95-mg aliquot of this product under reduced pressure afforded 75 mg of the pure liquid alcohol **50:** $n^{25}D$ 1.5131; ir (CCl_4) 3600 and 3550 cm^{-1} (OH); NMR (CCl_4) δ 7.0–7.6 (5 H, m, aryl CH), 3.22 (3 H, s, OCH_3), 2.82 (1 H, s, OH, exchanged with D_2O), 1.53 (3 H, s, CH_3), 1.32 (3 H, s, CH_3), and 0.98 (3 H, s, CH_3); mass spectrum *m/e* (rel intensity) 194 (M^+, <1), 121 (5), 105 (2), 77 (4), 74 (5), 73 (100), and 43 (22), uv (95% EtOH), series of weak maxima (δ 236–440) in the region 247–264 nm.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.18; H, 9.35.

Reaction of the ketone **40** with excess ethereal MeLi at 27 °C for 1.5 h followed by isolation of the crude neutral product and chromatography on silica gel afforded 92% of the alcohol **50** as a colorless liquid, $n^{25}D$ 1.5118–1.5120, that was identified with the previously described sample by comparison of ir, NMR, and mass spectra.

A 185-mg portion of the first fraction from the initial chromatography was rechromatographed on silica gel to separate an additional 29 mg of the pure alcohol **50** (total yield 58%), 95 mg of fractions containing (ir and NMR analysis) mainly the alcohol **50,** and 22 mg of early fractions that contained (GLC, Carbowax 20M on Chromosorb P) the starting ketone **40** (ca. 83%, retention time 22.4 min) accompanied by ca. 2% (corresponding to a 0.1% yield) of the ketone **49** (14.8 min) and ca. 15% of the alcohol **50** (42.6 min). A collected (GLC) sample of the ketone **49** was identified with an authentic sample by comparison of GLC retention times and mass spectra.

L. Acetoxy Ketone 41. To a cold (3–5 °C) solution of Me_2CuLi, from 1.03 g (5.0 mmol) of Me_2SCuBr, 9.6 mmol of MeLi, 9 ml of Et_2O, and 6 ml of Me_2S, was added, dropwise and with stirring, a solution

of 618 mg (3.0 mmol) of the ketone **41** in 2 ml of Et_2O. The resulting solution, from which $(MeCu)_n$ began to precipitate immediately, was stirred at 3–5 °C for 40 min and at 27 °C for 80 min and then subjected to the usual isolation procedure. A 420-mg aliquot of the crude liquid product (426 mg) was subjected to preparative TLC on silica gel (E. Merck, no. PF 254) with an Et_2O–hexane eluent (3:25 v/v, three successive elutions). The fastest moving band (R_f 0.63) contained 169 mg (39%) of the ketone **49** as a colorless liquid identified with an authentic sample by comparison of the R_f values and ir, NMR, and mass spectra. The second TLC band (R_f 0.32) contained 128 mg of liquid that was crystallized from hexane to separate 94 mg (15% recovery) of the starting acetoxy ketone **41**, mp 59–60 °C, that was identified with an authentic sample by a mixture melting point determination and by comparison of ir, NMR, and mass spectra. The slowest moving band (R_f 0.18) contained 39 mg (8%) of the hydroxy ketone **45** as a pale yellow liquid that was identified with a previously described sample by comparison of ir, NMR, and mass spectra.

In a comparable experiment reaction of 4.8 mmol of Me_2CuLi with 532 mg (2.58 mmol) of the acetoxy ketone **41** for 2 h at 3–5 °C and for 2.5 h at 25 °C yielded 361 mg of crude liquid product that was mixed with a known weight of internal standard (n-$C_{11}H_{24}$). The crude product contained (GLC, silicone SE-30 on Chromosorb P) n-$C_{11}H_{24}$ (retention time 11.2 min), the ketone **49** (54% yield, 18.0 min), and two minor unidentified components (26.6 and 58.4 min). A collected (GLC) sample of the ketone **49** was identified with an authentic sample by comparison of GLC retention times and ir, NMR, and mass spectra.

Competition Experiments with Me_2CuLi. A. Ketones 22 and 51. A solution of Me_2CuLi, prepared at 4 °C from 216 mg (1.05 mmol) of Me_2SCuBr in 1.6 ml of Me_2S and 2 ml of Et_2O and 2.04 mmol of MeLi in 3 ml of Et_2O, was cooled to −70 °C. While the solution was maintained at −60 to −70 °C,[40] a solution of 301 mg (2.06 mmol) of the ketone **22** and 207 mg (2.11 mmol) of the ketone **51** in 2 ml of Et_2O was added dropwise and with stirring. After the solution had been stirred for 15 min at −60 to −70 °C (during which time no reaction was apparent), it was allowed to warm to 3 °C during approximately 5 min; separation of significant quantities of $(MeCu)_n$ from the reaction solution occurred as the temperature rose above −35 °C. After the mixture had been stirred at 3 °C for 45 min, it was subjected to the usual isolation procedure; aliquots of the crude product were mixed with known amounts of an internal standard (either tetralin or n-$C_{12}H_{26}$) and subjected to GLC analysis (Carbowax 20M on Porasil). Employing a GLC analysis at 85 °C, the mixture contained ketone **53** (retention time 3.8 min, 21% yield), ketone **51** (6.6 min, 49% recovery), and n-$C_{12}H_{26}$ (11.0 min). At higher temperatures (158 °C), GLC analysis indicated the presence of tetralin (7.0 min) and ketone **22** (28.6 min, 100% recovery). Collected (GLC) samples of each of the ketones **22**, **51**, and **53** were identified with authentic samples by comparison of GLC retention times and mass spectra.

B. Ketones 31 and 41. A solution of Me_2CuLi, from 209 mg (1.02 mmol) of Me_2SCuBr in 1.5 ml of Me_2S and 2 ml of Et_2O and 2.8 ml of an Et_2O solution containing 1.96 mmol of MeLi, was cooled to −72 °C and then a solution of 321 mg (2.0 mmol) of enone **31** and 411 mg (2.0 mmol) of acetoxy ketone **41** in 3 ml of Et_2O was added, dropwise with stirring and cooling. After the resulting orange solution had been stirred at −60 °C for 10 min,[40] it was allowed to warm to 3 °C during 5 min. Precipitation of $(MeCu)_n$ from the solution was observed as the temperature rose above −35 °C. The resulting mixture was stirred at 3 °C for 35 min and then subjected to the usual isolation procedure. The crude liquid product was mixed with a known weight of internal standard (tetralin) and subjected to GLC analysis (Carbowax 20M on Porasil). The product contained (GLC) tetralin (retention time 5.6 min), ketone **49** (9.3 min, 14% yield), ketone **52** (13.6 min, 3% yield), enone **31** (25.7 min, 77% recovery), hydroxy ketone **45** (32.1 min, ca. 8% yield), and the acetoxy ketone **41** (38.8 min, 67% recovery). Collected (GLC) samples of ketones **31**, **49**, **41**, **45**, and **52** were identified with authentic samples by comparison of GLC retention time and mass spectra.

C. Ketones 31 and 51. After a solution of Me_2CuLi, prepared at 4 °C from 216 mg (1.05 mmol) of Me_2SCuBr in 1.5 ml of Me_2S and 2 ml of Et_2O and 2.04 mmol of MeLi in 3 ml of Et_2O, had been cooled to −70 °C, the solution was maintained at −60 to −70 °C[40] while a solution of 324 mg (2.03 mmol) of ketone **31** and 201 mg (2.05 mmol) of ketone **51** in 2 ml of Et_2O was added, dropwise, with stirring. After the resulting orange-colored mixture had been stirred at −70 °C for 10 min, it was warmed to 4 °C during approximately 5 min. During this warming, the orange color faded and a yellow precipitate of $(MeCu)_n$ separated as the solution was warmed above −30 °C. The reaction mixture was stirred at 4 °C for 25 min and at 27 °C for 20 min and then subjected to the usual isolation procedure. Aliquots of the crude product were mixed with known amounts of an internal standard (tetralin or n-$C_{12}H_{26}$) for GLC analysis (Carbowax 20M on Porasil). Analysis (GLC) at 85 °C indicated the presence of ketone **53** (retention time 3.9 min, 10% yield), ketone **51** (6.9 min, 49% recovery), and n-$C_{12}H_{26}$ (12.6 min). Analysis (GLC) at 170 °C indicated the presence of tetralin (retention time 5.7 min), ketone **52** (14.2 min, 11% yield), and ketone **31** (26.2 min, 36% recovery). Collected (GLC) samples of ketones **31**, **51**, **52**, and **53** were identified with authentic samples by comparison of GLC retention times and mass spectra.

Repetition of this experiment resulted in the following yields of products or reactants: **31**, 35%; **51**, 40%; **52**, 13%; and **53**, 7.4%. These consistently low yields (or recoveries) of products and reactants indicated that portions of these materials were being converted to higher molecular weight materials that were not eluted in our GLC analysis. This is presumably the result of Michael and/or aldol condensation of the product enolate anions with the excess enones present in the reaction mixture. In an effort to minimize this problem, a series of comparable reactions were performed in which the mixtures were quenched after shorter reaction times at lower reaction temperatures. In an experiment in which a cold reaction solution was warmed to −30 °C, stirred at −30 °C for 30 min, and then quenched, the yields were 93% of **31**, 86% of **51**, 6% of **52**, and 0.9% of **53**. When the reaction solution was warmed from −70 to −20 °C during 10 min and then quenched immediately, the yields were 96% of **31**, 86% of **51**, 3.8% of **52**, and 1.4% of **53**. When the cold (−70 °C) reaction solution was warmed to −10 °C during 10 min, stirred at −10 °C for 10 min, and then quenched, the yields were 97% of **31**, 79% of **51**, 3% of **52**, and 0.7% of **53**. Thus, it appears that the reaction of the more easily reduced enone **31** with Me_2CuLi is slightly more rapid than the corresponding reaction with the enone **51**.

Registry No.—**16**, 617-94-7; **17**, 21811-48-3; **18**, 59671-37-3; **19**, 59671-38-4; **25**, 5558-04-3; **26**, 59671-39-5; **27**, 59671-40-8; **28**, 1009-14-9; **29**, 59671-41-9; **30**, 1454-61-1; **32**, 94-41-7; **42**, 10409-54-8; **44**, 13694-96-7; **45**, 7473-98-5; **46**, 18913-16-1; **47**, 57625-74-8; **48**, 13836-62-9; **50**, 59671-42-0; **52**, 31366-07-1; **53**, 590-50-1; α-bromoisobutyric acid, 2052-01-9; Me_2CuLi, 15681-48-8.

References and Notes

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(2) (a) H. O. House and M. J. Umen, *J. Org. Chem.*, **38**, 3893 (1973); *J. Am. Chem. Soc.*, **94**, 5495 (1972); (b) H. O. House and P. D. Weeks, *ibid.*, **97**, 2770, 2778, 2785 (1975); (c) H. O. House, C.-Y. Chu, J. M. Wilkins, and M. J. Umen, *J. Org. Chem.*, **40**, 1460 (1975); (d) For a brief review, see H. O. House, *Acc. Chem. Res.*, **9**, 59 (1976).

(3) For an extensive survey of electrode potentials, see H. Siegerman in "Technique of Electroorganic Synthesis", Part II, N. L. Weinberg, Ed., Wiley-Interscience, New York, N.Y., 1975, pp 667–1056.

(4) The hyperfine coupling constants observed in the EPR spectra of benzaldehyde and acetophenone anion radicals suggest that about one-third of the spin density is centered at the carbonyl carbon atom with the remainder being distributed among the ortho, meta, and para positions of the benzene ring: P. B. Ayscough, "Electron Spin Resonance in Chemistry", Methuen, London, 1967, pp 274–279.

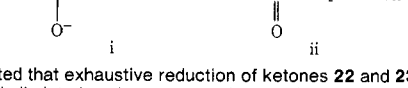
(5) One apparent example of this possibility is the reaction of various benzophenone derivatives with *t*-BuMgCl to form both products with the *t*-Bu group bound to the carbonyl carbon atom and dihydroaromatic products with the *t*-Bu group at the ortho or para position of the dihydroaromatic ring. T. Holm and I. Crossland, *Acta Chem. Scand.*, **25**, 59 (1971).

(6) (a) H. O. House and K. A. J. Snoble, *J. Org. Chem.*, following paper in this issue; (b) J. A. Marshall and R. A. Ruden, *ibid.*, **37**, 659 (1972).

(7) For examples of this type of reaction sequence with enones, see (a) D. J. Hannah and R. A. J. Smith, *Tetrahedron Lett.*, 187 (1975); (b) A. Nilsson and A. Ronlán, *ibid.*, 1107 (1975); (c) R. A. Ruden and W. E. Litterer, *ibid.*, 2043 (1975).

(8) E. Barreiro, J. L. Luche, J. Zweig, and P. Crabbé [*Tetrahedron Lett.*, 2353 (1975)] also reported obtaining only a low yield (13%) of the adduct **16** from ketone **12**. These authors obtained good yields (>90%) of 1,2 adducts from reaction of Me_2CuLi with both aromatic and aliphatic aldehydes.

(9) The substantial decrease in the stability of the ketyl **6** with a phenyl substituent (from ketone **24**) when compared with the analogous ketyl with two methyl substituents (from ketone **23**) presumably reflects the fact that the phenyl substituent can stabilize both radical and carbanionic structures i and ii. H. Shiota, K. Ohkata, and T. Hanafusa [*Chem. Lett.*, 1153 (1974)]



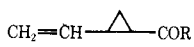
have reported that exhaustive reduction of ketones **22** and **23** with Na in NH_3 yielded alkylated cyclopropanes whereas the comparable reduction of ketone **24** yielded 1,4-diphenylbutane. Although the latter result could be regarded as an example of the ion radical rearrangement **6** → **7**, the facts that ketone **24** reacts with Me_2CuLi without appreciable ring opening

and that anion radical intermediates appear to have longer lifetimes in cuprate reactions than in metal–NH_3 reductions (ref 2b,d) lead us to believe that this ring opening occurred after initial reduction of the carbonyl group.

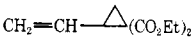
(10) (a) H. O. House, *Proc. Robert A. Welch Found. Conf. Chem. Res.*, **16**, 101–149 (1973); (b) C. R. Johnson, R. W. Herr, and D. M. Wieland, *J. Org. Chem.*, **38**, 4263 (1973).

(11) For various examples of this reaction, see (a) E. J. Corey and P. L. Fuchs, *J. Am. Chem. Soc.*, **94**, 4014 (1972); (b) G. Daviaud and P. Miginiac, *Tetrahedron Lett.*, 997 (1972); (c) R. D. Clark and C. H. Heathcock, *ibid.*, 529 (1975); (d) P. A. Grieco and R. Finkelhor, *J. Org. Chem.*, **38**, 2100 (1973); (e) For a study of the reactions of Me_2CuLi with other esters, see S. A. Humphrey, J. L. Herrmann, and R. H. Schlessinger, *Chem. Commun.*, 1244 (1971).

(12) N. Miyaura, M. Itoh, N. Sasaki, and A. Suzuki [*Synthesis*, 317 (1975)] have reported successful ring opening reactions with cuprates and ketones of the type iii. We presume that these reactions, like the analogous reaction



iii, R = Me, Ph



iv

with iv (see ref 11d), are instances in which nucleophilic ring opening with cuprate reagents is sufficiently rapid to compete with other possible side reactions.

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(14) For examples and leading references, see (a) C. Lion and J. E. Dubois, *Tetrahedron*, **31**, 1223, 1227 (1975); (b) G. H. Posner, J. J. Sterling, C. E. Whitte*, C. M. Lentz, and D. J. Brunelle, *J. Am. Chem. Soc.*, **97**, 107 (1975); (c) J. E. Dubois, P. Fournier, and C. Lion, *Tetrahedron Lett.*, 4263 (1975).

(15) H. O. House and C. Y. Chu, *J. Org. Chem.*, accompanying paper in this issue.

(16) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated $MgSO_4$ was employed as a drying agent. The ir spectra were determined with a Perkin-Elmer Model 257 infrared recording spectrophotometer fitted with a grating. The uv spectra were determined with a Cary Model 14 or a Perkin-Elmer Model 202 recording spectrophotometer. The ^1H NMR spectra were determined at 60 MHz with a Varian Model A-60 or Model T-60-A NMR spectrometer and the ^{13}C NMR spectra were determined at 100 MHz with a JEOL Fourier transform spectrometer, Model PFT-100. The chemical shift values are expressed in δ values (ppm) relative to a Me_4Si internal standard. The mass spectra were obtained with an Hitachi (Perkin-Elmer) Model RMU-7 or a Varian Model M-66 mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere.

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Reactions Involving Electron Transfer. 10. The Use of β-Cyclopropyl α,β-Unsaturated Ketones to Detect Anion Radical Intermediates[1]

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The cyclopropyl enone **16** has been prepared as an example of an enone whose anion radical **39** will have a geometry very favorable for the rearrangement **39** → **40**. Reaction of this enone **16** with Me_2CuLi yielded a mixture of rearranged product **33** (72% of the product) and unrearranged product **32** (28% of the product). This observation is considered compelling evidence that this reaction is proceeding by an initial electron transfer step rather than a direct nucleophilic addition. As part of the synthesis of the enone **16**, a new procedure was developed for the dehydration of the aldol intermediate **25** or **26** to form mainly the α,β isomer **16** rather than the β,γ isomer **30**.

Among various experimental tests that might be applied to distinguish between addition reactions proceeding by a polar nucleophilic addition and by a two-stage reaction involving initial electron transfer,[2] we were encouraged to study β-cyclopropyl α,β-unsaturated ketones **3** as reaction substrates because of the rapidity with which a cyclopropylcarbinyl radical **1** (see Scheme I) rearranges to a 3-butenyl radical **2**.[3] The nucleophilic addition of an organometallic reagent RM (or other nucleophile) to such an enone **3** could be expected to form an unrearranged product **6**. However, if the initial step