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.

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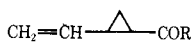
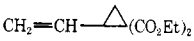
(11) For various examples of this reaction, see (a) E. J. Corey and P. L. Fuchs, *J. Am. Chem. Soc.*, **94**, 4014 (1972); (b) G. Daviaud and P. Miginiac, *Tetrahedron Lett.*, 997 (1972); (c) R. D. Clark and C. H. Heathcock, *ibid.*, 529 (1975); (d) P. A. Grieco and R. Finkelhor, *J. Org. Chem.*, **38**, 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.

(13) J. G. Aston, J. T. Clarke, K. A. Burgess, and R. B. Greenburg, *J. Am. Chem. Soc.*, **64**, 300 (1942).

(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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(20) P. Ramart-Lucas and J. Hoch, *Bull. Soc. Chim. Fr.*, 422 (1952).

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(23) Our product was identified with an authentic sample by comparison of ir spectra. We are grateful to Professor James A. Marshall for providing this authentic sample.

(24) (a) C. R. Johnson, R. A. Kirchoff, R. J. Reischer, and G. F. Katekar, *J. Am. Chem. Soc.*, **95**, 4287 (1973); (b) F. Rocquet and A. Sevin, *Bull. Soc. Chim. Fr.*, 888 (1974); (c) U. Mende, B. Radüchel, W. Skuballa, and H. Vorbrüggen, *Tetrahedron Lett.*, 629 (1975); (d) In order to separate the ketone **24** from small amounts of residual starting benzalacetophenone, the product was initially purified by chromatography on alumina with pentane as an eluent.

(25) We are grateful to Professor Erling Grovenstein and Dr. Leslie Gelbaum for an authentic sample of this ketone. It was prepared by the addition of PhMgBr to 1-cyano-2,2-dimethylcyclopropane [E. R. Nelson, M. Maienthal, L. A. Lane, and A. A. Benderly, *J. Am. Chem. Soc.*, **79**, 3467 (1957)]. The preparation of this ketone has been described by J. M. Watson, J. L. Irvine, and R. M. Roberts, *ibid.*, **95**, 3348 (1973).

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(28) For examples and leading references concerning the reaction of α-bromo ketones with Ag^+ ion to form either esters or α-alkoxy ketones, see (a) D. N. Kevill and N. H. Cromwell, *J. Org. Chem.*, **29**, 499 (1964); (b) D. J. Pasto and K. Garves, *ibid.*, **32**, 778 (1967); (c) D. Baudry and M. Charpentier-Morize, *Tetrahedron Lett.*, 3013 (1973); D. Baudry J. P. Begue, and M. Charpentier-Morize, *ibid.*, 4707 (1970); J. P. Begue, M. Charpentier, and C. Pardo, *Tetrahedron*, **31**, 1919 (1975).

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(34) L. I. Smith and V. A. Engelhardt, *J. Am. Chem. Soc.*, **71**, 2671 (1949).

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(37) (a) A. C. Lespagnol, J. Claude, and M. Cazin, *Bull. Soc. Chim. Fr.*, 1507 (1964); (b) E. Middleton, *J. Am. Chem. Soc.*, **45**, 2763 (1923).

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(40) Since neither of the ketones used reacts with Me_2CuLi at −60 °C, this procedure was followed to ensure complete mixing of the cuprate and the ketones before any reaction occurred.

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

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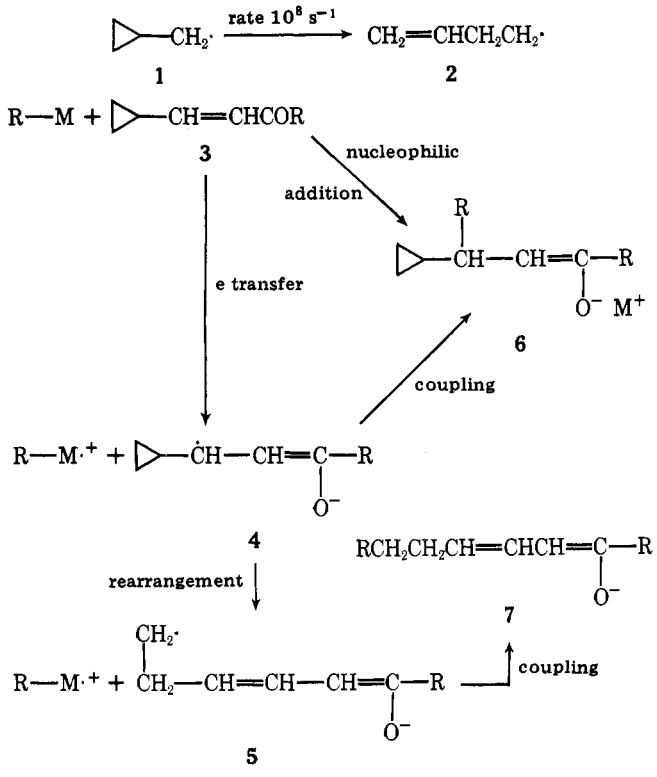
The cyclopropyl enone **16** has been prepared as an example of an enone whose anion radical **39** will have a geometry very favorable for the rearrangement **39** → **40**. Reaction of this enone **16** with Me_2CuLi yielded a mixture of rearranged product **33** (72% of the product) and unrearranged 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

Scheme I

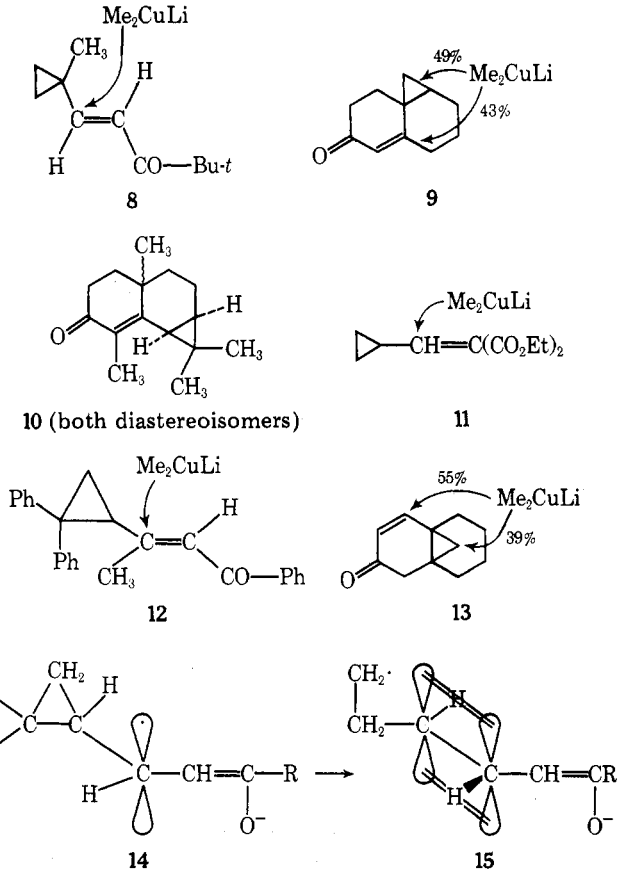


involved transfer of only an electron, the resulting anion radical intermediate **4** could follow two different pathways leading to addition products. In cases where recombination of the ion radical intermediates was *faster* than the intramolecular rearrangement **4** → **5** of the anion radical **4**, the same unrearranged product **6** would result. Alternatively, if the rate of rearrangement **4** → **5** was *faster than* or *comparable to* the rate of coupling of the ion radical intermediates, then at least part of the product would be the rearranged adduct **7** rather than **6**. This later result would be particularly useful in supplying evidence that the electron-transfer step lies on the reaction path leading to an addition product and is not merely a parasitic equilibrium that is unrelated to the formation of addition products.

For this experimental test to be useful, it was clear that the lifetime of the anion radical **4** formed in a two-stage addition process must be sufficient to permit the rearrangement **4** → **5** to be at least competitive with the recombination of ion radical intermediates. Earlier study[4] of this idea employed conjugate addition of lithium dimethylcuprate and conjugate reduction with solutions of lithium in ammonia as model reactions that almost certainly involve an initial electron transfer.[2] Among the β-cyclopropyl enones **8–10** (Scheme II) examined, cyclic voltammetry measurements indicated the half-lives of the anion radicals from these enones to be **8**, 10^{-2} s; **9**, 10^{-3} s; **10**, $<10^{-3}$ s. Thus, the delocalization of the unpaired electron possible in the enone anion radicals **4**, but not in radical **1**, resulted in rearrangement **4** → **5** being slower than **1** → **2** by a factor of 10^4–10^6.

Since both enone systems **8**[4] and **10**[5] were reduced without rearrangement by Li–NH_3 solutions, we concluded that the lifetime of the enone anion radical present in these reactions was $<10^{-4}$ s. In reactions with Me_2CuLi (see Scheme II), only unrearranged product was isolated from enone **8** whereas about equal amounts of rearranged and unrearranged product were obtained from enone **9**.[6] These observations suggested a lifetime of about 10^{-3} s for the enone anion radical formed during these Me_2CuLi–enone reactions. In other studies involving Me_2CuLi addition, both of the unsaturated carbonyl compounds **11**[7] and **12**[8] gave unrearranged addition products

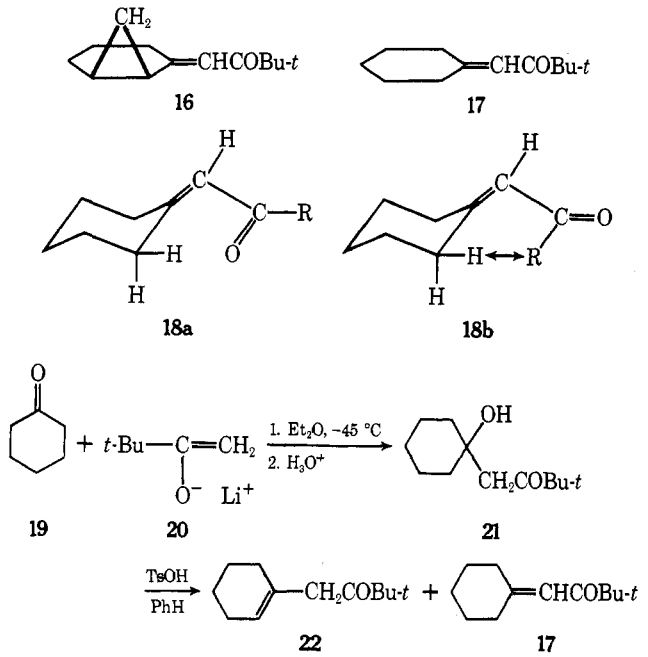
Scheme II



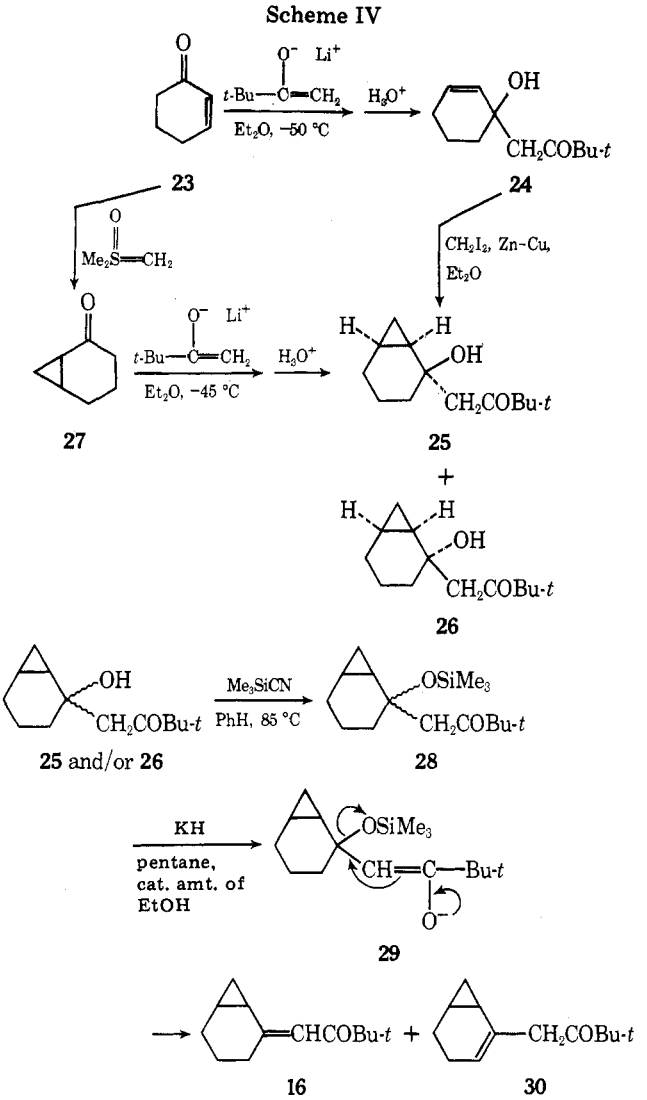
whereas the enone **13**[6] gave comparable amounts of rearranged and unrearranged products. These various results suggest that the anion radical rearrangement **4** → **5** is definitely more rapid with anion radicals derived from the polycyclic enones **9, 10,** and **13** than with the anion radicals from unsaturated carbonyl compounds **8, 11,** and **12.** Since even the enone **12,** containing two phenyl substituents that could stabilize a rearranged radical ion (cf. **5**), gave an unrearranged product with Me_2CuLi,[8] the presence of substituents on the cyclopropane ring is apparently not particularly effective in increasing the rate of the rearrangement **4** → **5.** Instead, it appeared that the appropriate structural feature to enhance this rate of rearrangement **4** → **5** would be to prepare cyclopropyl enones whose structures would maintain the geometry of the anion radical indicated in structure **14.** This arrangement **14,** with one cyclopropyl C–C bond and the p orbital at the β carbon in the same plane and approximately parallel, would offer the best opportunity for continuous orbital overlap during the rearrangement **14** → **15.** Such a geometrical arrangement is maintained in each of the enones **9, 10,** and **13** but is not required in systems **8, 11,** and **12.**

Since rapid rearrangement **4** → **5** is one of the requirements of a β-cyclopropyl enone system **3** if it is to be useful in testing for an anion radical intermediate, we sought to prepare an enone system **3,** different from the octalone derivatives **9, 10,** and **13,** that would meet the geometrical requirements of structure **14.** This paper describes the preparation of such a derivative, the β-cyclopropyl enone **16,** as well as the related model substance **17** (Scheme III). Both of these compounds, like previously studied α-cyclohexylidene ketones and esters,[9] are believed to exist in the cisoid conformation **18a** in order to avoid a serious nonbonding interaction (arrow in structure **18b**) that would be present in the transoid conformation **18b.** Thus, although the enone **16** and the decalones **9, 10,** and **13** share the geometric feature (structure **14**) believed appropriate for rapid rearrangement **14** → **15** of the anion radical,

Scheme III



Scheme IV



in other respects the cisoid enone **16** and the transoid enones **9**, **10**, and **13** have quite different geometries.

The model enone **17** was readily synthesized (Scheme III) by use of a directed aldol condensation[10] followed by acid-catalyzed dehydration of the hydroxy ketone **21**. Although prolonged contact with this acid catalyst gave a mixture of enones **17** and **22** containing mainly the more stable β,γ isomer **22**, under carefully controlled dehydration conditions the initially formed conjugated isomer **17** was the major reaction product.

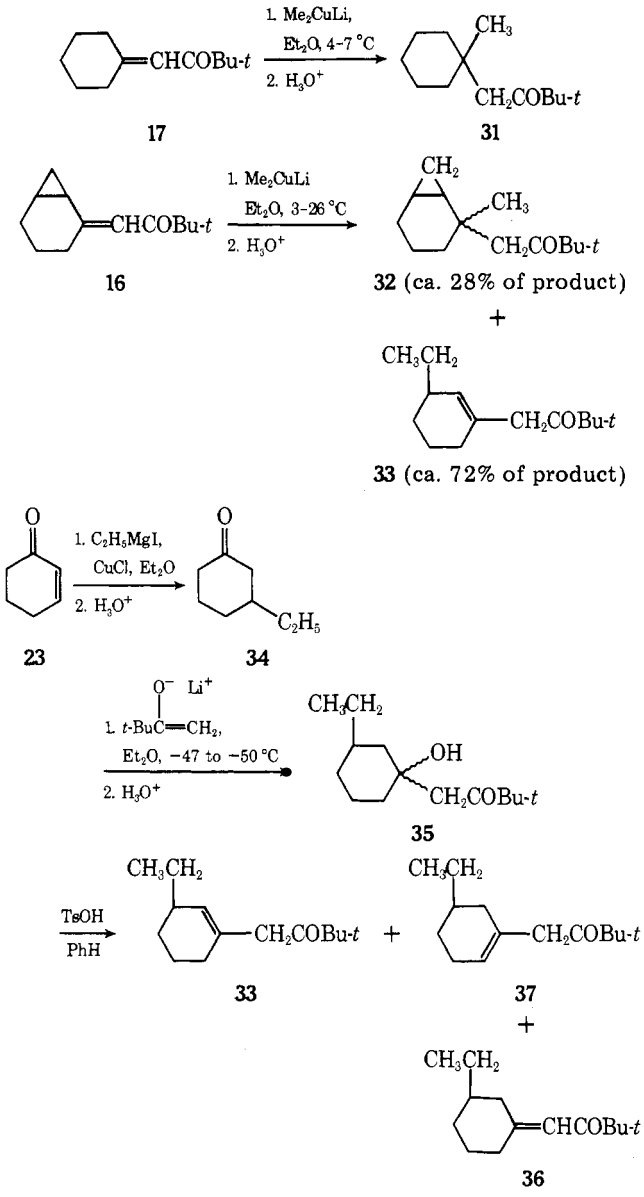
We had hoped to obtain the cyclopropyl enone **16** by an analogous process involving initial aldol condensation of the enolate **20** with the cyclopropyl ketone **27** (Scheme IV). Unfortunately, in spite of considerable experimentation, we were able to effect this aldol condensation only in ca. 25% yield with the remaining bicyclic ketone **27** being recovered unchanged. The products from this aldol reaction were the diastereoisomeric ketols **25** (minor product) and **26** (major product). A more satisfactory route to these ketols **25** and **26** involved initial condensation of the enolate **20** with cyclohexenone (**23**) to yield the hydroxy ketone **24**.[11] Reaction of this allylic alcohol **24** with the CH_2I_2–Zn–Cu reagent[12] afforded a mixture of the diastereoisomeric ketols **25** (major) and **26** (minor). The major diastereoisomer formed in this reaction was assigned the stereochemistry **25** based on the expectation[12] that the cyclopropyl CH_2 group should be introduced cis to the allylic hydroxyl group.

Our efforts to obtain the desired enone **16** by acid-catalyzed dehydration of the ketols **25** and/or **26** also posed an unexpected difficulty since the ketols **25** and **26** dehydrated only under conditions more vigorous than those required to dehydrate the model ketol **21**. As a result all of our successful acid-catalyzed dehydration experiments yielded mixtures of enones **16** and **30** in which the more stable β,γ isomer **30** was the major product. To circumvent this problem we elected to convert the acid- and base-labile ketols **25** and **26** to their trimethylsilyl ethers **28**. Although the conventional silylating procedures were unsatisfactory, heating the ketols **25** and **26** with Me_3SiCN with escape of the HCN as it formed did allow us to achieve the desired silylation under essentially neutral conditions. Subsequent reaction of the β-trimethylsilyloxy ketone **28** with KH and a catalytic amount of EtOH effected the desired elimination (see structure **29**) to give a mixture of enones **16** and **30** containing primarily the desired conjugated isomer **16**. It is appropriate to note that the ketone **28**, formed in the presence of Me_3SiCN (which is an efficient scavenger for alcohol impurities), failed to react with the KH suspension to form the enolate **29** until a catalytic amount of alcohol was added. These observations suggest that KH, like NaH,[13] does not react directly with ketones to form enolates but rather reacts with some alcohol present to form a potassium alkoxide that abstracts a proton from the ketone.

Reaction of the model enone **17** with Me_2CuLi formed the expected conjugate addition product **31** (Scheme V). The same reaction with the cyclopropyl enone **16** afforded a mixture of structurally isomeric products in which the unrearranged adduct **32** (a mixture of diastereoisomers) was the minor product accompanied by the rearranged adduct **33**. To establish the structure of the rearranged product **33**, the crude ketol **35**, obtained from ketone **34** and enolate **20**, was dehydrated with acid to yield a mixture of the rearranged adduct **33** and at least two other products believed to be the isomeric enones **36** and **37**.

Although the polarographic reduction potentials of the two enones **16** and **17** (Scheme VI) were approximately the same, reduction by cyclic voltammetry demonstrated that the stabilities of the initial anion radical products **38** and **39** were very different. In particular, the half-life ($<10^{-3}$ s) of the anion radical **39** derived from the cyclopropyl enone **16** was significantly less than the half-life for **38** (0.3 s) and was comparable to the values previously observed for the octalone derivatives **9** and **10**. Both this observation and the fact that the enone **16** reacted with Me_2CuLi to form mainly rearranged product **33**

Scheme V

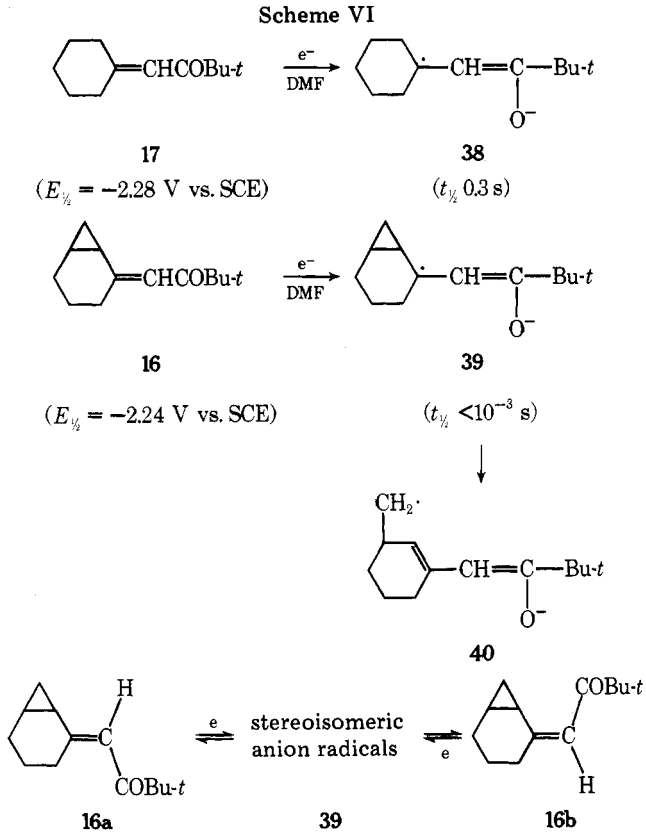


are consistent with the hypothesis that the anion radical rearrangement **4** → **5** can be expected to be most rapid when the anion radical is held in the geometric arrangement shown in structure **14.**

Thus, in the reaction of Me_2CuLi with the various cyclopropyl enones **8, 9,** and **16,** there is a clear relationship between the stability of the enone anion radicals and the formation of a rearranged product. Consequently, the reaction of the cyclopropyl enone **16** with Me_2CuLi to form mainly the rearranged adduct **33** provides compelling evidence that *the major reaction pathway in this case involves initial formation of an anion radical intermediate* **39** *and not initial nucleophilic addition to enone* (as in structure **6,** Scheme I).

A stereochemical result of incidental interest was also observed in the reaction of enone **16** with Me_2CuLi. After preparation of the enone **16** (Scheme IV), purification by a combination of preparative liquid chromatography and low temperature crystallization separated the two geometrical isomers **16a** and **16b** of enone **16.** We have tentatively assigned stereochemistry to these isomers **16a** [λ_{max} 263 nm (ϵ 14 800), eluted first from silica gel] and **16b** [λ_{max} 264 nm (ϵ 9260), eluted second from silica gel] based on the assumption that isomer **16a** will have less steric hinderance to coplanarity so that its ultraviolet absorption maximum would be expected to have a larger extinction coefficient. In agreement with this

Scheme VI



sterochemical assignment, the NMR spectrum of isomer **16a** exhibits a signal for the allylic CH_2 group at unusually low field as expected[9] for this isomer **16a** in a cisoid conformation **18a.** Similarly, the NMR spectrum of isomer **16b** (also in the cisoid conformation **18a**) exhibits a signal for the allylic cyclopropyl CH group at unusually low field. After reaction of this enone (12% **16a** and 88% **16b**) with Me_2CuLi, the small amount of enone **16** recovered contained appreciable amounts of both stereoisomers (29% **16a** and 71% **16b**). Although the mechanistic significance of this observation is dubious, the result is compatible with our previous observations[2,14] that a catalytic amount of an anion radical (e.g., **39**) can catalyze the interconversion of stereoisomeric enones such as **16a** and **16b.**

This observation does raise the question: is the stereochemical isomerization of β-cyclopropyl enones **16a** ⇌ **16b,** catalyzed by electron exchange with a small amount of the anion radical **39,** faster than the structural isomerization **39** → **40?** Earlier indirect evidence[2,14] had suggested that this was the case. To explore this question in a more direct manner, a DMF solution of the enone **16b** (which was stable if not electrolyzed) was subjected to partial controlled-potential electrolysis to convert approximately 1% of the enone **16b** to its anion radical **39.** The enone **16** recovered from this partial electrolysis was a mixture of 37% of isomer **16a** and 63% isomer **16b.** Partial isomerization of the conjugated enones **16** to the more stable β,α isomer **30** also occurred as a result of catalysis by the base produced during the partial electrolysis. However, several control experiments (see Experimental Section) established that further equilibration accompanying this base-catalyzed isomerization **16** → **30** could not account for the amount of stereochemical isomerization **16b** → **16a** observed in the partial electrolysis experiment. Consequently, these observations provide direct evidence that the interconversion of stereoisomeric enones such as **16a** and **16b** by electron exchange with their anion radical **39** is more rapid than anion radical structural isomerizations such as **39** → **40.**

Experimental Section[15]

Aldol Condensation with Cyclohexanone (19). To a cold (−45 °C) pink-orange solution of *i*-Pr_2NLi, prepared by the dropwise addition of 15.7 ml of a hexane solution containing 24 mmol of *n*-BuLi to a cold (−72 °C), stirred solution of 2.593 g (25.6 mmol) of *i*-Pr_2NH and several milligrams of 2,2′-bipyridyl (an indicator) in 54 ml of Et_2O, was added, dropwise and with stirring, 2.319 g (23.2 mmol) of pinacolone. After the resulting yellow-orange solution of the enolate **20** had been stirred at −45 °C for 50 min, a solution of 2.310 g (23.5 mmol) of cyclohexanone (**19**) in 5 ml of Et_2O was added to the cold solution, dropwise and with stirring during 8 min. After the resulting pale yellow solution had been stirred at −45 °C for 15 min, it was poured into 150 ml of cold (0 °C) aqueous 1 M HCl. The combined Et_2O layer and Et_2O extract of the aqueous phase were washed successively with aqueous $NaHCO_3$ and aqueous NaCl and then dried and concentrated. The residual crude aldol product **21**, 4.535 g of white solid, was recrystallized from pentane to separate 3.604 g (78.5%) of the pure aldol **21** as white needles: mp 61–62 °C; ir (CCl_4) 3490 (OH) and 1692 cm^{-1} (C=O); NMR ($CDCl_3$) δ 4.17 (1 H, s, OH, exchanged with D_2O), 2.61 (2 H, s, CH_2CO), 1.2–2.0 (10 H, m, aliphatic CH), and 1.11 (9 H, s, *t*-Bu); uv max (95% EtOH) 290.5 nm (ϵ 37); mass spectrum *m/e* (rel intensity) 198 (M^+, 1), 180 (11), 141 (30), 123 (86), 100 (55), 99 (85), 98 (70), 95 (30), 85 (51), 83 (21), 81 (88), 70 (37), 69 (45), 67 (24), 57 (100), 56 (40), 55 (77), 53 (23), 43 (62), 42 (61), 41 (65), and 39 (46).

Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.78; H, 11.20.

A series of small-scale experiments were performed in which solutions of 0.5 mmol of the aldol **21** in 4.2 ml of PhH were mixed with various amounts of *p*-TsOH and refluxed for various periods of time. The resulting mixtures were partitioned between Et_2O and aqueous $NaHCO_3$ and the Et_2O solutions were dried, concentrated, and analyzed by NMR (CCl_4) employing the vinyl CH signals at δ 6.13 (attributable to **17**) and 5.38 (attributable to **22**). With 0.5 mmol of the aldol **21**, 0.026 mmol (5 mol %) of *p*-TsOH, and a reflux period of 30 min, dehydration was complete and the mixture contained ca. 77% of the conjugated olefin **17** and ca. 23% of the unconjugated olefin **22**. With less acid catalyst or shorter reaction times, the dehydration was incomplete while longer reaction times resulted in mixtures containing increased amounts of the unconjugated isomer **22**. The mixture of isomers could also be analyzed by use of GLC (TCEP on Chromosorb P) using peaks for olefins **17** (retention time 21.8 min) and **22** (25.0 min), although some interconversion of **17** and **22** during GLC analysis was observed.

After a solution of 1.986 g (10.0 mmol) of the aldol **21** and 104 mg (0.55 mmol) of *p*-TsOH in 84 ml of PhH had refluxed for 36 min with continuous separation of H_2O and then subjected to the previously described isolation procedure, 1.913 g of the crude mixture (GLC) of olefins **17** (ca. 83%) and **22** (ca. 17%) was obtained. Fractional crystallization of this mixture from pentane at dry ice temperatures enriched the conjugated isomer **17** in the crystalline fractions and the nonconjugated isomer **22** in the mother liquors. After two crystallizations, the pure (ir analysis) conjugated isomer **17** was obtained as 1.226 g (70%) of colorless liquid, $n^{25}D$ 1.4797. A collected (GLC) sample of the conjugated olefin **17** was obtained as a colorless liquid: $n^{25}D$ 1.4801;[16] ir (CCl_4) 1680 (conjugated C=O) and 1618 cm^{-1} (conjugated C=C); uv max (95% EtOH) 238 nm (ϵ 14 500) and 324.5 (102); NMR (CCl_4) δ 6.13 (1 H, m, vinyl CH), 1.4–3.1 (10 H, m, aliphatic CH), and 1.10 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 180 (M^+, 10), 123 (100), 95 (16), 55 (28), 54 (23), and 41 (17).

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.82; H, 11.20.

A collected (GLC) sample of the unconjugated olefin **22** was obtained as a colorless liquid: $n^{25}D$ 1.4673; ir (CCl_4) 1710 cm^{-1} (C=O); uv max (95% EtOH) 293.5 nm (ϵ 71); NMR (CCl_4) δ 5.38 (1 H, m, vinyl CH), 3.02 (2 H, broad s, CH_2CO), 1.3–2.3 (8 H, m, aliphatic CH), and 1.09 (9 H, s, *t*-Bu): mass spectrum *m/e* (rel intensity) 180 (M^+, 8), 123 (14), 85 (25), 57 (100), 41 (18), and 40 (17).

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.95; H, 11.18.

Aldol Condensation with Cyclohexenone (23). To a cold (−50 °C) solution of *i*-Pr_2NLi, from 10.70 g (106 mmol) of *i*-PrNH, 67 ml of a hexane solution containing 105 mmol of *n*-BuLi, and 150 ml of Et_2O, was added, dropwise and with stirring, 10.22 g (102 mmol) of pinacolone. After the enolate solution had been stirred at −50 °C for 45 min, a solution of 9.886 g (103 mmol) of cyclohexenone (**23**) in 20 ml of Et_2O was added, dropwise and with stirring during 5 min. After the reaction solution had been stirred at −50 °C for 10 min, it was poured into cold (0 °C), aqueous 1 M HCl and then subjected to the previously described isolation procedure. The crude neutral liquid product was concentrated at 85 °C and 0.06 mm pressure to leave 18.58 g (93%) of the crude aldol product **24** as a yellow liquid. Two crystallizations from pentane at −50 °C separated 6.63 g (33%) of the aldol product **24** as colorless plates, mp 26–29 °C. An additional crystallization gave the aldol product **24** as colorless plates, mp 31–33 °C, that appeared to react rapidly if exposed to air: ir (CCl_4) 3490 (OH) and 1690 cm^{-1} (C=O); uv max (95% EtOH) 292.5 nm (ϵ 19); NMR (CCl_4) δ 5.3–5.8 (2 H, m, vinyl CH), 3.83 (1 H, broad s, OH), 2.60 (2 H, s, CH_2CO), 1.3–2.3 (6 H, m, aliphatic CH), and 1.10 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 178 (2), 121 (7), 100 (11), 97 (16), 96 (17), 68 (92), 57 (100), 43 (50), 42 (25), 41 (100), 40 (34), and 39 (75).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.36; H, 10.28.

Preparation of the Hydroxy Ketone 25. To a suspension of 7.204 g of Zn–Cu couple[17] in 35 ml of Et_2O containing several milligrams of I_2 was added, dropwise and with stirring during 10 min, 23.11 g (86 mmol) of CH_2I_2. After the resulting mixture had been heated to 40 °C for 70 min, a solution of 7.791 g (39.7 mmol) of the hydroxy olefin **24** in 8 ml of Et_2O was added, dropwise and with stirring during 22 min. After the reaction mixture had been refluxed for 23 h, it was partitioned between Et_2O and aqueous NH_4Cl. The Et_2O solution was washed successively with aqueous K_2CO_3 and with aqueous NaCl and then dried over Na_2SO_4 and concentrated (finally at 48 °C and 0.4 mm to remove CH_2I_2). The residual yellow oil, 7.290 g, which slowly solidified on standing, was fractionally recrystallized from pentane at −25 °C to separate 2.477 g (29.7%) of the pure hydroxy ketone **25** as white needles: mp 47.7–48.4 °C; ir (CCl_4), 3510 (OH), 3060 (cyclopropyl CH), and 1695 cm^{-1} (C=O); uv max (95% EtOH) 294 nm (ϵ 34); NMR (CCl_4) δ 3.61 (1 H, broad s, OH), 2.76 (2 H, s, CH_2CO), 1.1–2.0 (8 H, m, aliphatic CH), 1.14 (9 H, s, *t*-Bu), and 0.3–0.8 (2 H, m, cyclopropyl CH_2); mass spectrum *m/e* (rel intensity) 210 (M^+, 1), 110 (18), 67 (23), 57 (100), 55 (36), 54 (30), 43 (31), 41 (59), and 39 (27).

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.25; H, 10.56.

The NMR spectrum of the crude product, before separation of ketone **25** by recrystallization, suggests that in addition to the major product, ketone **25**, a small amount of the stereoisomeric ketone **26** is also present.

Preparation of the Hydroxy Ketone 26. A previously described procedure[18] was used to convert cyclohexenone (**23**) to the cyclopropyl ketone **27** (57% yield), bp 36–37 °C (0.25–0.3 mm), $n^{25}D$ 1.4871 [lit. bp 91 °C (15 mm),[19a] $n^{25}D$ 1.4878[19b]]. To a cold (−45 °C) solution of *i*-Pr_2NLi, from 526 mg (5.20 mmol) of *i*-Pr_2NH, 3.18 ml of a hexane solution containing 4.99 mmol of *n*-BuLi, and 50 ml of Et_2O, was added, dropwise and with stirring, 519 mg (5.18 mmol) of pinacolone. After the cold solution of the enolate **20** had been stirred for 38 min, a solution of 598 mg (5.43 mmol) of the cyclopropyl ketone **27** in 2 ml of Et_2O was added, dropwise and with stirring during 1.8 min. The resulting solution was stirred at −45 to −50 °C for 15 min and then poured into 50 ml of cold (0 °C) aqueous 1 M HCl and subjected to the usual isolation procedure. The concentration of the crude neutral product was completed with warming at 0.1 mm pressure to facilitate removal of the unchanged pinacolone and cyclopropyl ketone **27**. Analysis (NMR) of the residual crude product suggested that the total yield of aldol product was about 25% and that the crude product contained mainly the hydroxy ketone **26** accompanied by minor amounts of the stereoisomer **25**. Crystallization of this crude product from cold pentane separated 142 mg (13.5%) of the pure hydroxy ketone **26** as white plates: mp 60–61 °C; ir (CCl_4) 3490 (OH), 3060 (cyclopropyl CH), and 1695 cm^{-1} (C=O); uv max (95% EtOH) 292 nm (ϵ 30); NMR (CCl_4) δ 3.99 (1 H, broad s, OH), an AB pattern (J = 17 Hz) with signals at 2.79 and 2.44 (2 H, CH_2CO), 1.0–2.0 (17 H, m, aliphatic CH including a *t*-Bu singlet at 1.12) and multiplets at 0.5–0.9 and −0.4 to −0.1 (2 H, cyclopropyl CH_2); mass spectrum *m/e* (rel intensity) 192 (3), 135 (12), 110 (19), 100 (17), 67 (20), 57 (100), 55 (24), 54 (25), 43 (26), 41 (52), 40 (27), and 39 (24).

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.23; H, 10.56.

Preparation of the Unsaturated Ketones 16 and 30. Preliminary experiments in which PhH solutions of the ketols **25** and **26** and TsOH were heated for varying periods of time indicated that the conditions required to dehydrate the ketols also caused isomerization of the conjugated enone **16** to its β,γ isomer **30** so that the product mixture contained mainly ketone **30**. To explore an alternative procedure, Me_3SiCN was prepared by a published procedure[20] in which a mixture of 116.2 mg (0.44 mmol) of 18-crown-6 polyether, 6.596 g (101 mmol) of anhydrous KCN, 12 g (0.11 mmol) of Me_3SiCl, and 20 ml of anhydrous CH_2Cl_2 was refluxed with stirring for 36 h. Fractional distillation of the mixture through a 10-cm Vigreux column separated 3.712

g (37%) of Me_3SiCN as a colorless liquid: bp 114–116.5 °C (lit. bp 114–117,[21a] 117.9–118.2[21b]); ir (CCl_4) 2195 cm^{-1} (C≡N); NMR (CCl_4) δ 0.33 (s, CH_3Si). A solution of 2.095 g (9.96 mmol) of the hydroxy ketones **25** and **26** in 3.0 ml of Me_3SiCN and 1.0 ml of PhH was heated to 85 °C under an N_2 atmosphere for 20 h and then concentrated under reduced pressure and shaken with a mixture of 30 ml of pentane and 30 ml of cold (0 °C) aqueous buffer (pH 7) to remove any residual Me_3SiCN.[22] The pentane solution was dried (Na_2SO_4) and concentrated to leave 2.23 g (97%) of the crude siloxy ketone **28** as a yellow liquid: NMR (CCl_4) δ 2.87 (s), 2.6–2.7 (m, CH_2CO of two diastereoisomers in a ratio of ca. 6:1), 0.9–2.2 (m, aliphatic CH including a *t*-Bu singlet at 1.10), and 0.05–0.8 [m, cyclopropyl CH including a $(CH_3)_3SiO$ singlet at 0.09].

To a cold (−5 °C) solution of 2.21 g (7.82 mmol) of the siloxy ketone **28** and 2.5 μl (0.07 mmol) of EtOH[22] in 20 ml of pentane was added, portionwise and with stirring during 2.5 min, 316 mg (7.9 mmol) of KH (washed with pentane). The cold, orange-colored reaction mixture was stirred for an additional 5.5 min and then poured into 30 ml of cold (0 °C) aqueous buffer (pH 7) and extracted with pentane. The pentane extract was washed with aqueous NaCl, dried (Na_2SO_4), and concentrated to leave 1.61 g of yellow liquid containing (NMR analysis) the conjugated enone **16** (ca. 75%, a mixture of stereoisomers) and the isomeric ketone **30** (ca. 25%). This mixture was subjected to fractional crystallization from pentane at −70 °C to separate 624 mg of the enone **16** (a mixture of stereoisomers) that melted as it warmed to room temperature to form a colorless liquid, $n^{25}D$ 1.5092. The mother liquors from this fractional crystallization were subjected to preparative liquid chromatography (silica gel with 1.5% Et_2O in hexane as an eluent) to separate early fractions containing the unconjugated ketone **30** and later fractions containing the conjugated isomers **16**. Fractional crystallization of these latter fractions from pentane at −70 °C separated an additional 228 mg of the enones **16** (total yield 852 mg or 56%): ir (CCl_4) 1675 (conjugated C=O) and 1595 cm^{-1} (conjugated C=C);[23] uv max (95% EtOH) 264 nm (ε 11 900) and 330 (shoulder, 168); NMR (CCl_4) δ 6.37 (t, *J* = 2.0 Hz, vinyl CH of minor stereoisomer) and 6.1–6.3 (m, vinyl CH of major stereoisomer, total 1 H), 2.0–3.2 (2 H, m, allylic CH_2 including an apparent triplet of doublets, *J* = 2.0 and 6.5 Hz, at 2.70 shown by decoupling to be the allylic CH_2 group of the minor stereoisomer), and 0.4–2.0 (19 H, m, aliphatic CH including a *t*-Bu singlet at 1.09); mass spectrum *m/e* (rel intensity) 192 (M^+, 9), 177 (8), 138 (33), 135 (50), 107 (60), 93 (38), 91 (50), 79 (100), 77 (39), 57 (65), 41 (98), and 39 (66). Analysis by GLC (Apiezon M on Chromosorb P) exhibited partially resolved peaks with retention times of 9.7 (major) and 11.0 min (minor) corresponding to the two stereoisomers tentatively assigned structures **16b** and **16a**, respectively.

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.34; H, 10.75.

The liquid chromatography fractions containing (GLC, Apiezon M on Chromosorb P) mainly the unconjugated enone **30** (retention time 8.6 min) with lesser amounts of the stereoisomeric conjugated enones **16b** (11.2 min) and **16a** (12.4 min) were used to collect (GLC) a pure sample of the unconjugated enone **30** as a colorless liquid: $n^{25}D$ 1.4841; ir (CCl_4) 1710 cm^{-1} (C=O); NMR (CCl_4) δ 5.1–5.3 (1 H, m, vinyl CH), 3.1–3.3 (2 H, m, CH_2CO), 0.9–2.2 (15 H, m, aliphatic CH including a *t*-Bu singlet at 1.12), and 0.4–0.9 (2 H, m, cyclopropyl CH_2); mass spectrum *m/e* (rel intensity) 192 (M^+, 1), 91 (9), 79 (10), 77 (7), 57 (100), 41 (24), and 39 (13).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 80.96; H, 10.45.

The analysis of mixtures of the unconjugated enone **30** and the stereoisomeric conjugated enones **16a** and **16b** (not resolved) could be obtained both by the previously described GLC analysis and by integration of that portion of the NMR spectrum containing the vinyl CH signals. Since neither of these methods was well suited for determining the composition of mixtures of the stereoisomeric enones **16a** and **16b**, the composition of mixtures of these stereoisomeric enones **16** was determined by high-pressure liquid chromatography (HPLC) employing a Waters liquid chromatograph, Model ALC-202, fitted with a uv detector (254 nm), a 30-cm μ-Porasil column, and 2.5% (by volume) of $CHCl_3$ in pentane as an eluent. Known amounts of $PhCOCH_3$ were added as an internal standard and the apparatus was calibrated with known mixtures prepared from pure samples of $PhCOCH_3$, **16a**, and **16b**. The retention times were **30**, 4.3 min; **16a**, 6.2 min; **16b**, 6.8 min; and $PhCOCH_3$, 9.0 min. Mixtures of the stereoisomeric enones **16** were separated by preparative low-pressure (15 psi) liquid chromatography employing columns packed with silica gel (E. Merck) and eluted with 1.5% (by volume) of Et_2O in hexane. The early fractions containing (HPLC) the isomer **16a** were subjected to low-temperature crystallization from pentane to separate the enone, tentatively assigned stereochemistry **16a**, as colorless crystals: mp 26.5–27.5 °C; uv max (95% EtOH) 263 nm (ε 14 800); ir (CCl_4) 1671 (less intense, C=O) and 1588 cm^{-1} (more intense, C=C); NMR (CCl_4) δ 6.33 (1 H, t, *J* = 1.9 Hz, vinyl CH), 2.67 (2 H, apparently a triplet of doublets, *J* = 1.9 and 6.3 Hz, allylic CH_2), and 0.6–2.1 (17 H, m, aliphatic CH including a *t*-Bu singlet at 1.10); mass spectrum *m/e* (rel intensity) 192 (M^+, 23), 177 (5), 135 (93), 107 (19), 93 (22), 91 (22), 79 (32), 57 (100), 55 (22), 41 (55), and 39 (32).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.19; H, 10.51.

The later chromatography fractions containing (HPLC) isomer **16b** were subjected to low-temperature crystallization to separate the enone, tentatively assigned stereochemistry **16b**, as colorless crystals: mp 12.5–13.5 °C; uv max (95% EtOH) 264 nm (ε 9260); ir (CCl_4) 1671 (less intense, C=O) and 1595 cm^{-1} (more intense, C=C); NMR (CCl_4) δ 6.20 (1 H, broad, vinyl CH), 2.7–3.2 (1 H, m, allylic cyclopropyl CH), 0.9–2.3 (17 H, m, aliphatic CH including a *t*-Bu singlet at 1.10), and 0.4–0.7 (1 H, m, one H of cyclopropyl CH_2, shown by a spin-decoupling experiment to be coupled to the low-field allylic cyclopropyl CH signal); mass spectrum *m/e* (rel intensity) 192 (M^+, 28), 177 (11), 138 (48), 135 (100), 107 (22), 93 (27), 91 (26), 79 (42), 57 (40), 55 (24), 41 (71), and 39 (34).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.18; H, 10.50.

Reaction of Enone 17 with Me_2CuLi. To a cold (4 °C) solution of Me_2CuLi, from 875 mg (4.25 mmol) of Me_2SCuBr, and 7.8 mmol of MeLi in 17 ml of Et_2O and 5 ml of Me_2S, was added, dropwise with stirring and cooling, a solution of 546 mg (3.03 mol) of the enone **17** in 1.5 ml of Et_2O. The reaction solution, from which yellow $(MeCu)_n$ began to precipitate after 10 s, was stirred at 4–7 °C for 40 min and then partitioned between Et_2O and an aqueous solution (pH 8) of NH_4Cl and NH_3. The ethereal layer was washed successively with aqueous $NaHCO_3$ and with aqueous NaCl and then dried and concentrated. The residual liquid (630 mg) was chromatographed on silica gel with an Et_2O–hexane eluent (1:130 v/v) to separate 518 mg (87%) of the pure ketone **31** as a colorless liquid: $n^{25}D$ 1.4564; ir (CCl_4) 1705 cm^{-1} (C=O); uv max (95% EtOH) 295 nm (ε 30); NMR (CCl_4) δ 2.33 (2 H, s, CH_2CO), 1.2–1.8 (10 H, m, CH_2), 1.07 (9 H, s, *t*-Bu), and 1.00 (3 H, s, CH_3); mass spectrum *m/e* (rel intensity) 196 (M^+, 2), 139 (31), 97 (100), 69 (10), 57 (13), 55 (24), and 41 (13).

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.56; H, 12.34.

Reaction of the Enone 16 with Me_2CuLi. To a cold (3 °C) solution of Me_2CuLi, from 719 mg (3.50 mmol) of Me_2SCuBr, 7.0 mmol of MeLi, 5 ml of Me_2S, and 14.4 ml of Et_2O, was added a solution of 490 mg (2.55 mmol) of the enone **16** in 1.1 ml of Et_2O. The resulting solution was stirred at 3 °C for 4 h, during which time a precipitate of $(MeCu)_n$ slowly separated, and at 26 °C for 45 min. After the resulting mixture had been partitioned between Et_2O and an aqueous solution (pH8) of NH_3 and NH_4Cl, the ethereal phase was washed successively with aqueous $NaHCO_3$ and with aqueous NaCl and then dried and concentrated. The crude product (520 mg of pale yellow liquid) contained (GLC, Carbowax 20M on Chromosorb P) mainly a mixture of the adducts **32** and **33** (unresolved, retention time 5.9 min) accompanied by minor amounts of the enones **16** (9.6 min) and the unconjugated enone **30** (7.4 min) and three minor unidentified materials (3.0, 3.4, and 4.6 min). On a second GLC column (TCEP on Chromosorb P), the components eluted were the three minor unidentified materials (retention times 6.1, 8.0, and 11.6 min), the stereoisomeric ketones **32** (19.7 and 20.4 min, ca. 28% of the product), the enone **33** (24.0 min, ca. 72% of the product), the unconjugated isomer **30** of the starting material (34.6 min), and the starting enones **16** (45.1 min, isomers not resolved).

A 372-mg aliquot of this product was subjected to preparative low-pressure liquid chromatography (LC) employing a column packed with silica gel and an Et_2O–hexane eluent (1:66 v/v). After separation of initial fractions (14 mg) containing (GLC) the minor, unidentified materials, the next fraction, amounting to 56.5 mg (15% yield), contained the stereoisomeric ketones **32** as a colorless liquid: ir (CCl_4) 3060 (cyclopropyl CH) and 1705 cm^{-1} (C=O); NMR (CCl_4) δ 2.2–2.6 (2 H, m, CH_2CO) and 0.3–2.2 [22 H, m, aliphatic CH including singlets for the minor stereoisomer at 1.13 (*t*-Bu) and 1.06 (CH_3) and singlets for the major stereoisomer at 1.26 (CH_3) and 1.12 (*t*-Bu)]; mass spectrum *m/e* (rel intensity) 208 (M^+, 30), 193 (100), 151 (36), 109 (83), 81 (20), 67 (40), 57 (59), and 41 (28); calcd for $C_{14}H_{24}O$; 208.1827; found; 208.1847.

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 81.02; H, 11.79.

The next LC fractions eluted (148.8 mg or 39% yield) contained (GLC) the β,λ-unsaturated ketone **33** as a colorless liquid: $n^{25}D$ 1.4665;

ir (CCl_4) 1710 cm^{-1} (C=O); uv max (95% EtOH) 295 nm (ϵ 82); NMR (CCl_4) δ 5.29 (1 H, broad, vinyl CH), 3.05 (2 H, broad, CH_2CO), and 0.5–2.2 (21 H, m, aliphatic CH including at *t*-Bu singlet at 1.10); mass spectrum *m/e* (rel intensity) 208 (M^+, 4), 79 (18), 57 (100), and 41 (20); calcd for $C_{14}H_{24}O$, 208.1827; found, 208.1847.

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 81.01; H, 11.80.

The next LC fraction (20 mg or 4% yield) contained (GLC) the unconjugated isomer **30** of the starting enone **16**. The material was identified with the previously described sample by comparison of GLC retention times and ir and NMR spectra. The final LC fraction (58 mg or 12% recovery) contained (GLC, ir and NMR analysis) a mixture of starting enones **16**. Although the starting enone **16** for this reaction contained (HPLC) mainly one stereoisomer (12% **16a** and 88% **16b**), the enone sample recovered from this reaction contained (HPLC) substantial amounts of both stereoisomers (29% **16a** and 71% **16b**).

Synthesis of the Enone 33. A cold (−4 °C), stirred solution of EtMgI, from 3.65 g (150 mg-atoms) of Mg, 25.0 g (160 mmol) of EtI, and 45 ml of Et_2O, was treated with 219 mg (2.2 mmol) of CuCl and then a solution of 9.62 g (100 mmol) of 2-cyclohexenone in 20 ml of Et_2O was added, dropwise with stirring and cooling during 85 min. After the addition was complete, the mixture was stirred for 30 min while it was allowed to warm to room temperature and then the mixture was added slowly to a vigorously stirred mixture of 150 g of ice and 80 ml of aqueous 10% H_2SO_4. The resulting mixture was extracted with Et_2O and the ethereal extract was washed with aqueous $Na_2S_2O_3$, dried, concentrated, and fractionally distilled to separate 7.145 g (57%) of the ketone **34** as a pale yellow liquid: bp 44–45 °C (0.8 mm) [lit.[24] bp 190 °C (732 mm)], $n^{25}D$ 1.4493; ir (CCl_4) 1712 cm^{-1} (C=O); uv max (95% EtOH) 285 nm (ϵ 21); NMR (CCl_4) δ 0.8–2.5 (m, aliphatic CH); mass spectrum *m/e* (rel intensity) 126 (M^+, 39), 98 (22), 97 (79), 83 (100), 82 (27), 70 (35), 69 (26), 56 (20), 55 (87), 42 (28), 41 (82), and 39 (39).

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.06; H, 11.18.

To a cold (−47 to −50 °C) solution of the enolate **20**, from 4.68 g (46.2 mmol) of *i*-Pr_2NH, 75 ml of Et_2O, 25.3 ml of a hexane solution containing 45.8 mmol of *n*-BuLi, and 4.48 g (44.7 mmol) of *t*-$BuCOCH_3$, was added, dropwise with stirring and cooling during 4 min, a solution of 5.34 g (42.3 mmol) of the ketone **34** in 8 ml of Et_2O. The resulting cold (−47 to −50 °C) solution was stirred for an additional 7 min and then poured into cold (0 °C) aqueous 1 M HCl and extracted with Et_2O. The ethereal extract was washed successively with aqueous $NaHCO_3$ and with aqueous NaCl and then dried and concentrated. The residual pale yellow liquid (10.6 g) was fractionally crystallized from pentane at −70 °C to separate the crude aldol **35** as white crystals that melted below 25 °C to give the aldol **35** (presumably a mixture of diastereoisomers) as a colorless liquid: ir (CCl_4) 3495 (associated OH) and 1690 cm^{-1} (hydrogen bonded C=O); NMR (CCl_4) δ 3.64 (1 H, broad, OH), 2.48 (2 H, s, CH_2CO), and 0.7–2.1 (23 H, m, aliphatic CH including a *t*-Bu singlet at 1.11).

A solution of 52.2 mg (0.27 mmol) of $TsOH \cdot H_2O$ and 1.174 g (5.12 mmol) of the hydroxy ketone **35** in 41 ml of PhH was refluxed for 46 min and then partitioned between Et_2O and aqueous $NaHCO_3$. The crude product (1.075 g of yellow liquid) recovered from the Et_2O solution contained (ir and GLC, TCEP on Chromosorb P) mainly a component (retention time 22.3 min) believed to be the conjugated isomer **36** with lesser amounts of the enone **33** (23.6 min) and a component believed to be enone **37** (25.6 min). A 1.039-g aliquot of this crude product mixture in 41 ml of PhH containing 194 mg (1.02 mmol) of $TsOH \cdot H_2O$ was refluxed for 1.5 h and subjected to the same isolation procedure to yield 993 mg of yellow liquid containing the same three components noted above but with the major products being the β,γ isomers **33** and **37**. A collected (GLC) sample of the component believed to be enone **37** was obtained as a colorless liquid: ir (CCl_4) 1710 cm^{-1} (C=O); NMR (CCl_4) δ 5.2–5.5 (1 H, m, vinyl CH), 3.04 (2 H, broad, CH_2CO), and 0.8–2.3 (21 H, m, aliphatic CH including a *t*-Bu singlet at 1.11); mass spectrum *m/e* (rel intensity) 208 (M^+, 4), 151 (11), 57 (100), and 41 (16); calcd for $C_{14}H_{24}O$, 208.1827; found, 208.1847.

A collected (GLC) sample of the enone **33** was identified with the previously described sample by comparison of GLC retention times and NMR and mass spectra.

Electrochemical Measurements. The polarography, cyclic voltammetry, and electrolysis 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.[25] In all cases the solvent was anhydrous DMF containing 0.5 M *n*-$Bu_4N^+BF_4^-$ as the supporting electrolyte. Previously described procedures[25b,c,26] were used to estimate $E_{1/2}$ values and half-lives from cyclic voltammetry measurements.

Solutions of the enone **17** (2.5–5.4 × 10^{-3} M), upon polarographic reduction, exhibited $E_{1/2}$ −2.28 V vs. SCE (n = 1.2, i_d = 5–15 μA). Cyclic voltammetry indicated the reduction ($E_{1/2}$ −2.29 V vs. SCE) to be reversible at moderate scan rates (1 V/s) with the anion radical having an estimated half-life of 0.3 s. Polarographic reduction of solutions of the enone **16** (3.0–5.1 × 10^{-3} M) gave $E_{1/2}$ = −2.24 V vs. SCE (n = 1.4, i_d = 9–18 μA). Cyclic voltammetry measurements on these solutions exhibited only a cathodic current peak with no evidence for reversibility up to scan rates of 500 V/s. We therefore estimate the half-life of the radical anion from enone **16** to be less than 10^{-3} s.

The preparative electrolysis experiments employed a previously described[25c] three-compartment H-cell with a Pt anode, a Hg-pool cathode, and an SCE reference electrode fitted with a salt bridge. The potential between the reference electrode and the cathode was measured with a high-input impedance buffer amplifier connected to a digital voltmeter and the current passing through the cell was measured by continuously monitoring the potential drop across a precision resistor in series with the cell circuit. After a solution containing 0.42 M *n*-Bu_4NBF_4 in anhydrous DMF had been placed in each cell compartment, a potential (−2.4 V vs. SCE) was applied to reduce any impurities present and then 246 mg (1.28 mmol) of the enone **16b** was added to the catholyte (total volume 10 ml). A potential (−2.1 V vs. SCE) was applied to the cell and reduction was to proceed for 8 min at which time 1.50 × 10^{-5} Faradays of current (sufficient to reduce 1.2% of the enone **16** to its anion radical **39** and/or **40**) had passed through the cell. The catholyte solution was then removed and partitioned between H_2O and pentane. After the organic phase had been dried (Na_2SO_4) and concentrated, the crude liquid product (244 mg) contained (GLC and NMR analysis) ca. 53% of the unconjugated enone **30** and ca. 47% of the conjugated enones **16**. After an aliquot of the crude product had been mixed with a known amount of internal standard ($PhCOCH_3$) for HPLC analysis, the calculated yields of the stereoisomeric enones were 19% of **16a** (37% of the recovered enone **16**) and 32% of enone **16b** (63% of the recovered enone **16**).

In this electrochemical experiment both interconversion of the gemetrically isomeric enones **16a** and **16b** and structural isomerization of the conjugated enones **16** to the *more stable* unconjugated enone **30** were occurring. The latter structural isomerization is presumably catalyzed by the base(s) generated on further electrochemical reduction of the rearranged anion radical **40**. Several control experiments were performed to establish the cause of the geometrical isomerism **16a** ⇌ **16b**. When a 17.7-mg (0.92 mmol) sample of the enone **16b** (containing 2.3% of **16a**) was stirred at 25 °C in 1.0 ml of a DMF solution containing 0.41 M *n*-Bu_4NBF_4 for 1 h and subjected to the same isolation and analysis procedures used in the electrochemical experiment, the crude recovered enone **16b** (22 mg) contained 2.4% of the stereoisomer **16a**. In another experiment, 1.0 ml of a 0.42 M solution of *n*-Bu_4NBF_4 in DMF was treated with 0.002 mmol of *n*-BuLi and then 28 mg (0.14 mmol) of the enone **16b** (containing 7.0% of stereoisomer **16a**) was added. After this solution had been stirred for 20 min at 25 °C, the recovered crude enone **16b** (22 mg) contained 7.3% of the stereoisomer **16a**. To explore the effect of a higher concentration of base, 22 mg (0.11 mmol) of the enone **16b** (containing 7.2% of stereoisomer **16a**) was added to 1.0 ml of a solution prepared from 0.42 M *n*-Bu_4NBF_4 in DMF and 0.05 mmol of *n*-BuLi and the solution was stirred at 25 °C for 20 min. The yields (HPLC analysis) of enones **16** in the crude liquid product (40 mg) were 10% of enone **16a** (15% of the recovered enones **16**) and 56% of enone **16b** (85% of the recovered enones **16**). The crude liquid product contained (NMR analyses) ca. 61% of the stereoisomeric enones **16** and ca. 39% of the unconjugated enone **30**. These observations strongly suggest that the rapid stereochemical isomerization **16b** → **16a** observed in the electrochemical experiment was caused by the presence of the anion radical **39** and not by the small amount of base generated during the partial electrolysis.

Registry No.—**16a**, 59671-43-1; **16b**, 59671-44-2; **17**, 775-10-0; **19**, 108-94-1; **20**, 34865-75-3; **21**, 59671-45-3; **22**, 775-09-7; **23**, 930-68-7; **24**, 59671-46-4; **25**, 59671-47-5; **26**, 59671-48-6; **27**, 5771-58-4; **28** isomer A, 59671-49-7; **28** isomer B, 59686-32-7; **30**, 59671-50-0; **31**, 59671-51-1; **32** isomer A, 59671-52-2; **32** isomer B, 59671-53-3; **33**, 59671-54-4; **34**, 22461-89-8; *cis*-**35**, 59671-55-5; *trans*-**35**, 59671-56-6; **37**, 59671-57-7; *i*-Pr_2NLi, 4111-54-0; pinacolone, 75-97-8; Me_3SiCN, 7677-24-9; Me_2CuLi, 15681-48-8.

References and Notes

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Reactions Involving Electron Transfer. 11. Reaction of Lithium Dimethylcuprate with Diaryl Ketones[1]

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When cold, colorless solutions of PhCOPh and Me_2CuLi were mixed, an intermediate red-colored solution was formed. When this red solution, thought to arise from a charge-transfer absorption, was allowed to warm above 0 °C, a deep blue solution was formed and yellow $(MeCu)_n$ precipitated. This solution contained a mixture of the blue ketyl, $Ph_2\dot{C}-O^-Li^+$, and the salt of the 1,2 adduct **9**. When the more hindered diaryl ketone **3**, selected to retard 1,2 addition, was mixed with Me_2CuLi a yellow solution was formed that underwent no further change even at 25 °C. However, treatment of ketone **3** with a cold solution containing both Me_2CuLi and MeLi produced an initial yellow solution that turned red with precipitation of $(MeCu)_n$ as the solution was warmed above 0 °C. This red solution contained a mixture of the red ketyl **16** and the salt of the 1,2 adduct **14**. The observations with ketone **3** and mixtures of Me_2CuLi and MeLi suggest the formation of at least a small concentration of some more powerful reducing agent such as Me_4CuLi_3.

As noted in a recent paper,[2] it was of interest to examine the reactions of lithium dimethylcuprate (Me_2CuLi or $Me_4Cu_2Li_2$)[3] with alkyl aryl ketones (typical E_{redn} values −1.8 to −2.2 V) and with diaryl ketones (typical E_{redn} values −1.8 to −2.0 V) because the reduction potentials (E_{redn}) of these ketone substrates are sufficiently positive to permit[4] reactions with Me_2CuLi by a process involving an initial electron transfer step. Our study of reactions with alkyl aryl ketones is described elsewhere[2] and this paper describes our observations when the diaryl ketones **1–3** (Scheme I) were treated with Me_2CuLi.

Some time ago we reported[5] that treatment of either Me_2CuLi or $MeCuP(Bu\text{-}n)_3$ with the very easily reduced[6] diaryl ketone **1** (Scheme I) formed immediately a deep green colored ethereal solution containing (EPR) a paramagnetic species. Hydrolysis of this solution yielded a mixture containing approximately equal amounts of the alcohol **6** and the diol **7** as well as minor amounts of the alcohol **8** and the starting ketone **1**. These observations indicate that the reaction of the ketone **1** with Me_2CuLi formed approximately equal amounts of the 1,2 adduct **5** and the ketyl **4**. This mixture, containing excess Me_2CuLi, underwent further change only very slowly.

Since reduction of the ketone **1** to the ketyl **4** occurs with unusual ease (E_{redn} = −1.29 V), we were concerned that the formation of the anion radical **4** in this case might not be indicative of the behavior with typical enones having E_{redn} values in the range −1.6 to −2.4 V. Consequently, we have examined the analogous reaction with benzophenone (**2**, E_{redn} = −1.80 and −2.34 V).[7] As summarized in Scheme II, mixing