99-08-1; **17e**, 88-72-2; **18a**, 501-58-6; **18b**, 6257-64-3; **18c**, 501-60-0; **18d**, 588-04-5; **18e**, 584-90-7; **19a**; 37436-65-0; **19b**, 37436-66-1; **19c**, 37436-67-2; **19d**, 37436-68-3; **20a**, 37436-69-4; **20d**, 37436-70-7; **21**, 88-73-3; **22**, 37436-71-8; **23**, 2436-96-6; **24**, 230-17-1; **25**, 86-74-8; **26**, 2217-65-4; **28**, 88-75-5; 2-aminodiphenylamine, 534-85-0; 4-nitrosodiphenylamine, 156-10-5; 4-nitroaniline, 100-01-6; 3-nitroaniline, 99-09-2, 4-nitroacetanilide, 104-04-1; azoxybenzene, 495-48-7, 4,4′-azoxyanisole, 1562-94-3; 2,4-bromoazoxybenzene, 16109-68-5.

Acknowledgment.—The authors thank Professor C. N. R. Rao for helpful discussions. We are grateful to Dr. K. G. Das, National Chemical Laboratory, Poona, for his help in the recording of mass spectra, and Mr. A. H. Siddiqui (I. I. T., Kanpur) for microanalysis.

The Chemistry of Carbanions. XXII. C- *vs.* O-Acylation of Metal Enolates[1a]

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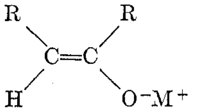
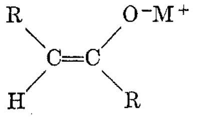
From a spectroscopic examination of metal enolates, the mercury(II) salts of ketones are found to exist as α-metalated ketones **2**, but salts with the metals lithium, sodium, zinc, and magnesium exist as enolate structures in which either contact ion pairs **4b** or solvent-separated ions **3** may be present. The existence of these metal enolates as solvent-separated ion pairs is favored (1) in a polar or a good solvating solvent, such as DME or DMF rather than ether; (2) by the presence of a metal cation such as lithium, sodium, or zinc rather than magnesium; and (3) by use of the trans (**1b**) rather than the cis (**1a**) stereoisomer of the enolate. In kinetically controlled reactions of metal enolates with acetylating agents, O-acylation is the favored reaction with α-metalated ketones **2** and with solvent-separated ion pairs **3**. The amount of of C-acylation is increased and may become the predominant reaction with metal enolates that exist as contact ion pairs **4b**. When the solvent and metal cation are kept constant, more C-acylation is obtained when acetyl chloride or acetyl bromide is used as the acylating agent rather than acetic anhydride or ketene.

Enolate anions **1** are members of a group of ambident nucleophiles that react wtih alkylating agents or acylating agents to form products with a new bond either at carbon or at oxygen.[2] When solutions of alkali metal enolates of monoketones in aprotic solvents are added slowly to an excess of reactive acylating agents such as $(CH_3CO)_2O$ or CH_3COCl, the major products of this kinetically controlled processes are usually the O-acetylated derivatives corresponding in structure and stereochemistry to the starting enolates.[2b,3] However, several groups have noted that, even with reaction procedures that result in kinetically controlled acylation, mixtures of C- and O-acylated products may result, especially when the metal cation is halomagnesium rather than lithium or sodium.[2b,3a,4] The proportion of C-acylation is also enhanced by the use of relatively nonpolar solvents,[2b,3a,4] by use of the metal enolate stereoisomer **1a** with the metal alkoxide and the β substituent trans[3a,b,4b] and by the use of acid chlorides rather than acid anhydrides as acylating agents.[4b]

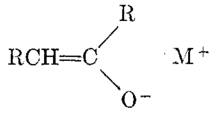

1a (cis enolate)

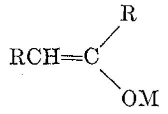

1b (trans enolate)

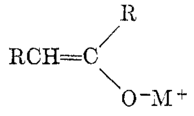
Consideration of this information has led us to the hypothesis that the reactions of ketone metal enolates can be explained by considering them to have one of three general structures: (1) structure **2** with a covalent carbon–metal bond; (2) solvent-separated ions **3**; or (3) either structure **4a** with a covalent metal–oxygen bond or the related contact ion pair **4b**. It is probable that many examples of the latter structures **4**

$$\mathrm{R\underset{M}{C}H\overset{O}{C}R}$$

2 (covalent)


3 (solvent-separated ions)


4a (covalent)


4b (contact ion pair)

will exist in solution as molecular aggregates (dimers, trimers, tetramers), especially with nonpolar solvents and in cases with small R groups which do not sterically impede aggregation.[5]

In light of earlier discussions of ambident anions,[2] it would be expected that treatment with reactive acylating agents would lead to predominant O-acylation of enolates **2** and **3** and predominant C-acylation of enolates **4**. For this study we have prepared solutions of several metal enolates, determined the products

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[1] (a) This research has been supported by Public Health Service Grant No. 7-R01-CA-12634 from the National Cancer Institute. (b) A portion of this work was taken from the Ph.D. dissertation of Martin Gall, Massachusetts Institute of Technology,1970.

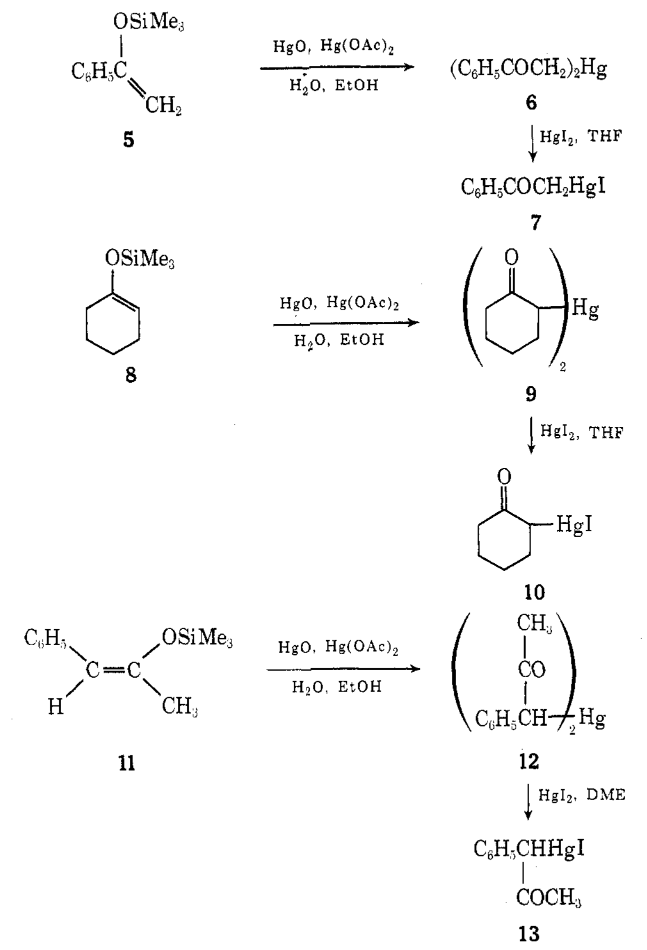
[2] For reviews, see (a) R. Gompper, *Angew. Chem., Int. Ed. Engl.*, **3**, 560 (1964); (b) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 520–530, 762–765.

[3] (a) H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966); (b) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *ibid.*, **34**, 2324 (1969); (c) H. O. House, W. F. Fischer, Jr., M. Gall, T. E. McLaughlin, and N. P. Peet, *ibid.*, **36**, 3429 (1971); (d) W. M. Muir, P. D. Ritchie, and D. J. Lyman, *ibid.*, **31**, 3790 (1966); (e) K. Yoshida and Y. Yamashita, *Tetrahedron Lett.*, 693 (1966).

[4] (a) J. P. Ferris, C. E. Sullivan, and B. G. Wright, *J. Org. Chem.*, **29**, 87 (1964); J. P. Ferris, B. G. Wright, and C. C. Crawford, *ibid.*, **30**, 2367 (1965). (b) P. Angibeaud, and M.-J. Lagrange, *C. R. Acad. Sci., Ser. C*, **272**, 1506 (1971); L. Alais, P. Angibeaud, M.-J. Lagrange, and R. Michelot, *Bull. Soc. Chim. Fr.*, 2731 (1971). (c) For examples of the C-acylation of enol silyl ethers with acid chlorides, see S. Murai, Y. Kuroki, K. Hasegawa, and S. Tsutsumi, *Chem. Commun.*, **No. 16**, 946 (1972).

[5] For examples and discussion, see (a) H. D. Zook, T. J. Russo, E. F. Ferrand, and D. S. Stotz, *J. Org. Chem.*, **33**, 2222 (1968); (b) H. D. Zook, W. L. Kelley, and I. Y. Posey, *ibid.*, **33**, 3477 (1968); (c) A. G. Pinkus, J. G. Lindberg, and A. B. Wu, *Chem. Commun.*, 1350 (1969); 859 (1970); (d) H. O. House, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **36**, 2361 (1971).

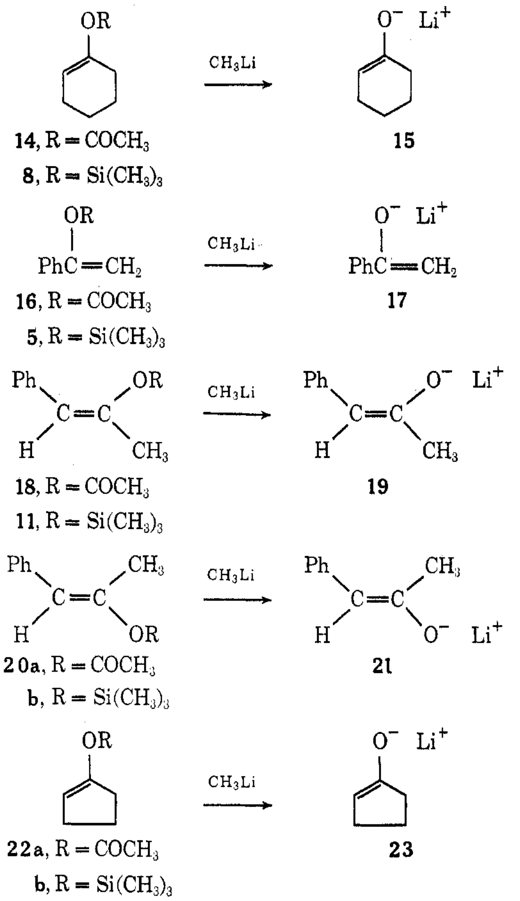
SCHEME I



formed upon acetylation, and examined the structures of certain metal enolates in solution by ir and nmr spectrometry.

Preparation and Properties of the Metal Enolate Solutions.—An earlier examination[6] of the ir (C=O at 1650 cm^{-1}) and nmr (δ_{CH_2} 2.80 with $J_{^{199}Hg-H}$ = 317 Hz and δ_{CH_3} 2.17 with $J_{^{199}Hg-H}$ = 14 Hz) spectra of α-chloromercuriacetone indicated that this metal enolate should be formulated as $ClHgCH_2COCH_3$, an enolate of the type **2** with a carbon–metal bond. To obtain additional α-mercuri ketones (Scheme I) we found the reaction of trimethylsilyl enol ethers with HgO and a catalytic amount of $Hg(OAc)_2$ in aqueous ethanol to be especially convenient.[7] Further reaction of the bisketomercurials **6**, **9**, and **12** with HgI afforded the relatively insoluble α-iodomercuri ketones **7**, **10**, and **13**. The ir, uv, and nmr spectra of these materials were compatible with the structures indicated and the nmr spectrum of each of the bisketomercurials exhibited satellite peaks corresponding to large ^{199}Hg–H coupling constants (172–200 Hz). Consequently, we conclude that each of these materials should be formulated as an enolate of type **2** with a covalent carbon–mercury bond.

SCHEME II



The various lithium enolates indicated in Scheme II were prepared by previously described methods employing the reaction methyllithium with the appropriate enol acetates[6] or trimethylsilyl enol ethers.[3b,5d,8] The sodium enolates **25** and **26** of phenylacetone (**24**) were conveniently generated by reaction with sodium hydride in various solvents (Scheme III). In all cases this procedure afforded solutions containing primarily the more stable[3b] trans enolate **25** as a result of enolate equilibration during the relatively slow reaction of phenylacetone with the insoluble sodium hydride. A solution containing at least in part the zinc enolate **27a** in DME solution was obtained by treatment of the lithium enolate **19** (from the silyl ether **11**) with 0.5 molar equiv of anhydrous zinc chloride. A solution of the corresponding magnesium enolate **27b** in an Et_2O–PhH mixture was obtained by an analogous reaction of the lithium enolate **19** (from the silyl ether **11**) with 0.5 molar equiv of anhydrous magnesium bromide and a solution of the same enolate **27b** in Et_2O was obtained from the enol acetate **18** and dimethylmagnesium. Similarly, a solution of the magnesium enolate **28** was produced by reaction of the corresponding enol acetate **14** with dimethylmagnesium.

In the 6-μ region of the infrared, DME solutions of both the cis (**21**) and trans (**19**) lithium enolates do not exhibit a normal C=O stretching band but rather a pair of strong bands at 1560 and 1585 cm^{-1}; a DME solution of the trans sodium enolate **25** has analogous bands at 1550 and 1575 cm^{-1}. Furthermore, the subsequently discussed nmr spectra clearly indicate that

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[6] H. O. House and B. M. Trost, *J. Org. Chem.*, **30**, 1341, 2502 (1965).

[7] This method is a modification of an earlier synthetic method employing enol acetates or alkyl enol ethers: (a) A. N. Nesmeyanov, I. F. Lutsenko, and Z. M. Lumanova, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 601 (1949); *Chem. Abstr.*, **44**, 7225 (1950); (b) I. F. Lutsenko and R. M. Khomutov, *Dokl. Akad. Nauk SSSR*, **102**, 97 (1955); *Chem. Abstr.*, **50**, 4773 (1956); (c) A. N. Nesmeyanov, I. F. Lutsenko, and R. M. Khomutov, *Dokl. Akad. Nauk SSSR*, **88**, 837 (1953); *Chem. Abstr.*, **48**, 4434 (1954); (d) also see ref 3a.

[8] G. Stork and P. F. Hudrlik, *J. Amer. Chem. Soc.*, **90**, 4462, 4464 (1968).

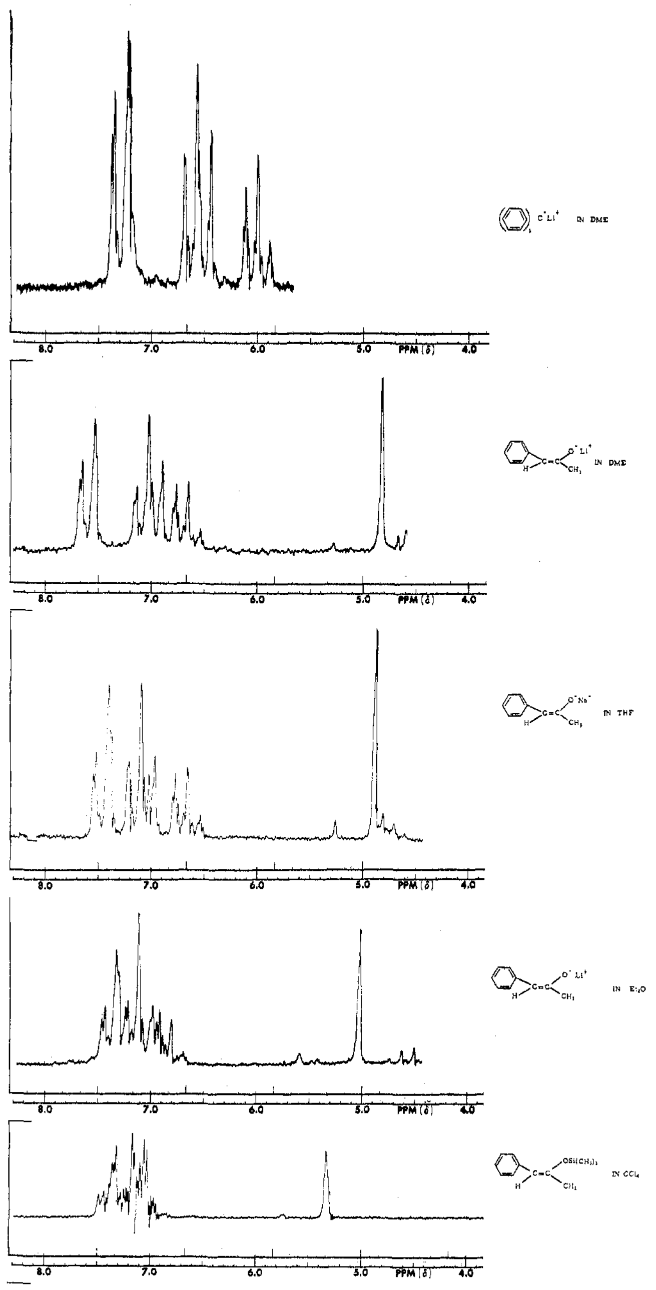
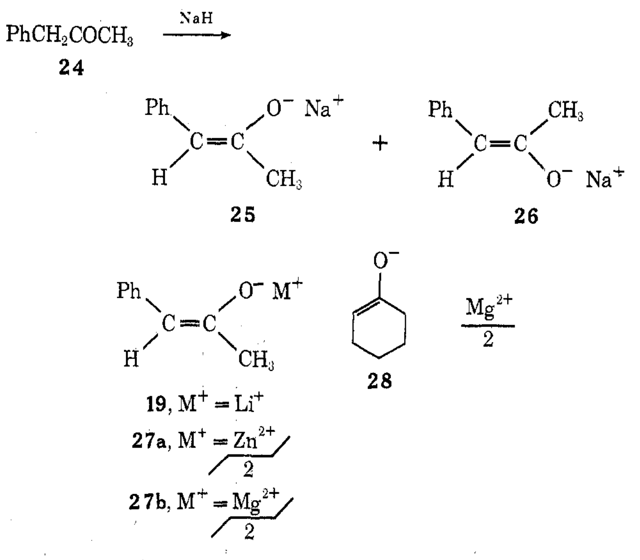


Figure 1.—Comparison of the nmr spectra of several trans enolates of phenylacetone with the spectra of the trans silyl ether **11** and triphenylmethyllithium.

these metal enolates have a vinyl CH bond. Thus, these enolates have structures of the type **3** or **4** and not **2**.

Scheme III



Although the nmr absorption of the various aliphatic metal enolates in ethereal solvents was obscured by solvent absorption, both the phenyl and vinyl CH absorption of the various phenylacetone enolates were at sufficiently low field to be examined. As noted earlier,[3b] the nmr spectra of the cis (**21** and **26**) and trans (**19** and **25**) phenylacetone enolates differ significantly and the composition of mixtures could be determined from the areas under the vinyl CH peaks. Representative spectra for the various phenylacetone enolates are presented in Figures 1 and 2. The sodium enolates prepared from phenylacetone (**24**) and excess sodium hydride in relatively polar solvents (THF, DME, DMF) contained primarily (92->98%) of the trans enolate **25** as a result of equilibration during the relatively slow formation of the enolates **25** and **26**. In ether solution, this equilibration was slower and the initial enolate solution (see Figure 2) contained 76–78% of the trans isomer **25** and 22–24% of the cis isomer **26**. When an additional equivalent of the unionized ketone **24** was added to this solution to permit enolate equilibration by proton transfers,[6] the proportion of trans isomer **25** in Et_2O solution increased to about 90% during 18 hr. In the more polar solvents (DME and DMF) proton exchange between the ketone and the enolate was much more rapid and resulted in substantial line broadening of the enolate nmr signals when these solutions contained equimolar amounts of the ketone **24** and the enolate **25**.

Figure 1 compares the nmr signals for triphenyllithium in DME solution (a solvent-separated ion pair[9]) and the trans trimethylsilyl enol ether **11** (a model for a covalent metal enolate **4a**) with the spectra of several representative metal trans enolates **19**, **25**, and **27** in various solvents. The nmr spectra of the sodium enolate **25** in either DMF or DME and the lithium enolate **19** in DME (shown in Figure 1) are practically identical and the phenyl absorption in these three spectra bears a striking resemblance to the phenyl absorption of triphenyllithium in DME. In THF solution the nmr spectra of the sodium (**25**) and lithium (**19**) enolates are practically the same with a phenyl absorption pattern intermediate between the patterns seen for the lithium enolate in DME and in Et_2O. The phenyl pattern in the nmr spectrum of an ether solution of the lithium enolate **19** resembles the pattern in the trans silyl ether **11**. The location of the vinyl CH signal exhibits a regular change, namely δ 4.83 for **19** in DME, 4.93 for **19** in THF, 5.02 for **19** in Et_2O, and 5.32 for the silyl ether **11**. This regular shift of the vinyl CH to lower field, like the progressive change in the phenyl pattern, is compatible with the presence of progressively less negative charge at the α carbon of the metal enolates as the solvent is changed from DME to THF to Et_2O. In spectra of the cis lithium enolate **21** and the related cis silyl ether **20b** (Figure 2) the vinyl CH is shifted downfield (δ 5.25 for **21** in DME, 5.57 for **21** in Et_2O, and 5.77 for **20b**) and little separation of the

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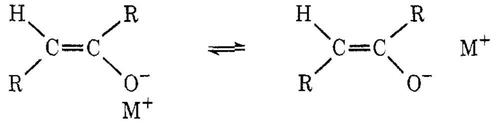
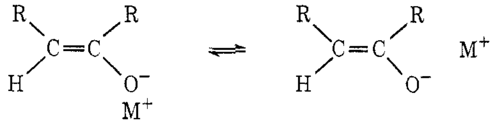
[9] J. B. Grutzner, J. M. Lawlor, and L. M. Jackman, *J. Amer. Chem. Soc.*, **94**, 2306 (1972).

ortho, meta, and para phenyl protons is observed. These changes in nmr chemical shift values clearly arise in part from steric interference with a conformation in which the phenyl ring and the enolate C=C are coplanar so that little negative charge is delocalized into the phenyl ring. However, the change in position of the vinyl CH signal again suggests that the negative charge at the α carbon of the cis enolates is substantially greater in DME than in Et_2O solution. The subsequently discussed acetylation studies suggest that, in a given solvent, dissociation of the contact ion pairs is greater with the trans metal enolate **1b** than with the cis isomer **1a**. This apparent tendency of the trans enolate **1b** to dissociate may be attributable to an unfavorable steric interaction between the solvated oxygen–metal ion pairs and the eclipsed α substituent in the trans enolate **1b** that is avoided in the cis enolate **1a** where the solvated oxygen–metal ion pair is relatively unhindered. An argument of this sort is based on the assumption that the solvated oxygen anion in a dissociated enolate has less steric bulk than a solvated (and possibly aggregated) oxygen–metal ion pair. The nmr spectrum of the zinc enolate **27a** (probably mixed with some lithium enolate **19**) in DME solution exhibits significant line broadening but the pattern of phenyl absorption and the position of the vinyl CH (δ 4.88) resemble the corresponding features in the spectrum of a DME solution of the lithium enolate **19**. The line broadening in the spectrum of an Et_2O solution of the magnesium enolate **27b** is sufficient to obscure the phenyl pattern. However, the low-field (δ 5.85) location of the vinyl CH absorption suggests that relatively little of the negative charge is located at the α-carbon atom of the enolate **27b**.



1b



1a

The above comparisons suggest that all of the trans enolate ions **19**, **25**, and **27a** in DME (or DMF) solution exist primarily as solvent-separated ions with an appreciable fraction of the negative charge in the phenyl ring and at the α-carbon atom. In Et_2O solution, the trans lithium (**19**) and sodium (**25**) enolates, and especially the cis lithium enolate (**21**) and the magnesium enolate **27b**, appear to be primarily contact ion pairs (or possibly covalent compounds).

Acetylation of the Metal Enolates.—The reactions of the various metal enolates with acetic anhydride and/or acetyl chloride (Scheme IV) were examined to determine the yield of O- and C-acetylated products. In an effort to obtain kinetically controlled mixtures of products the metal enolate solutions were added slowly with good mixing to a large excess of the acetylating agent. The reaction mixtures were quenched under conditions demonstrated not to remove either of the reaction products and the product mixtures were mixed with internal standards and analyzed with calibrated glpc equipment to determine the yields of acetylated products. Table I summarizes both the results of the present studies and also several earlier studies performed in our laboratory. The bulk of the material not accounted for as O- or C-acetylated product in these experiments was the recovered unacetylated ketone formed by a competing protonation of the metal enolate during the quenching process.

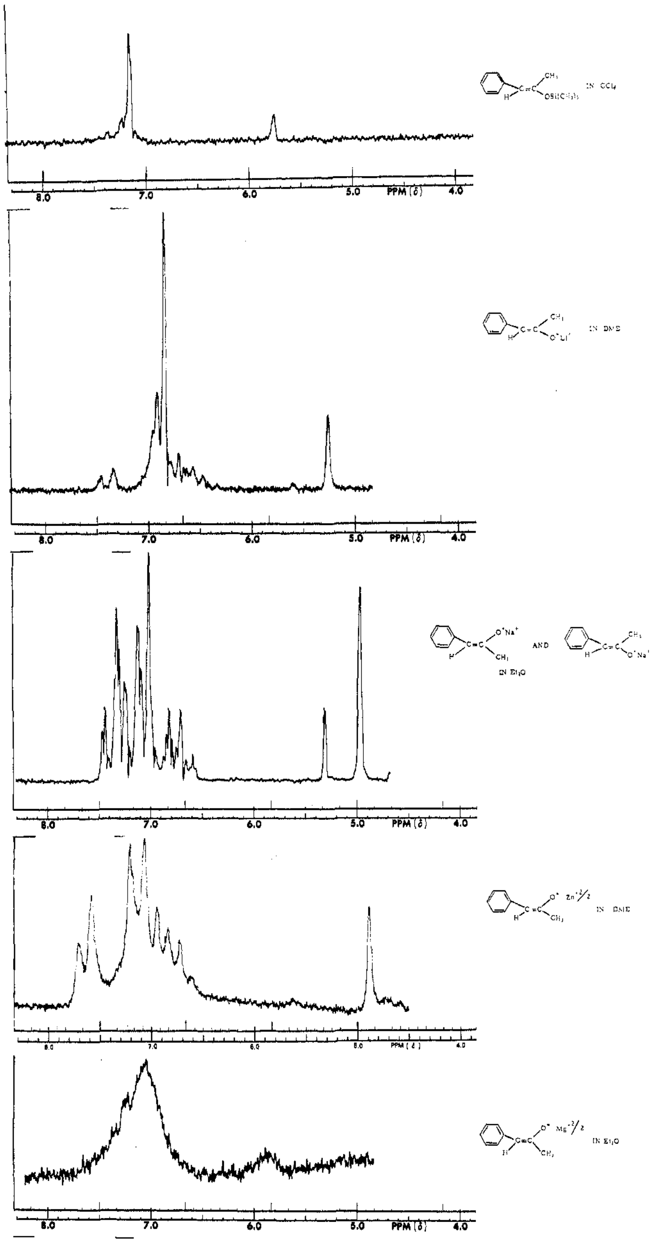
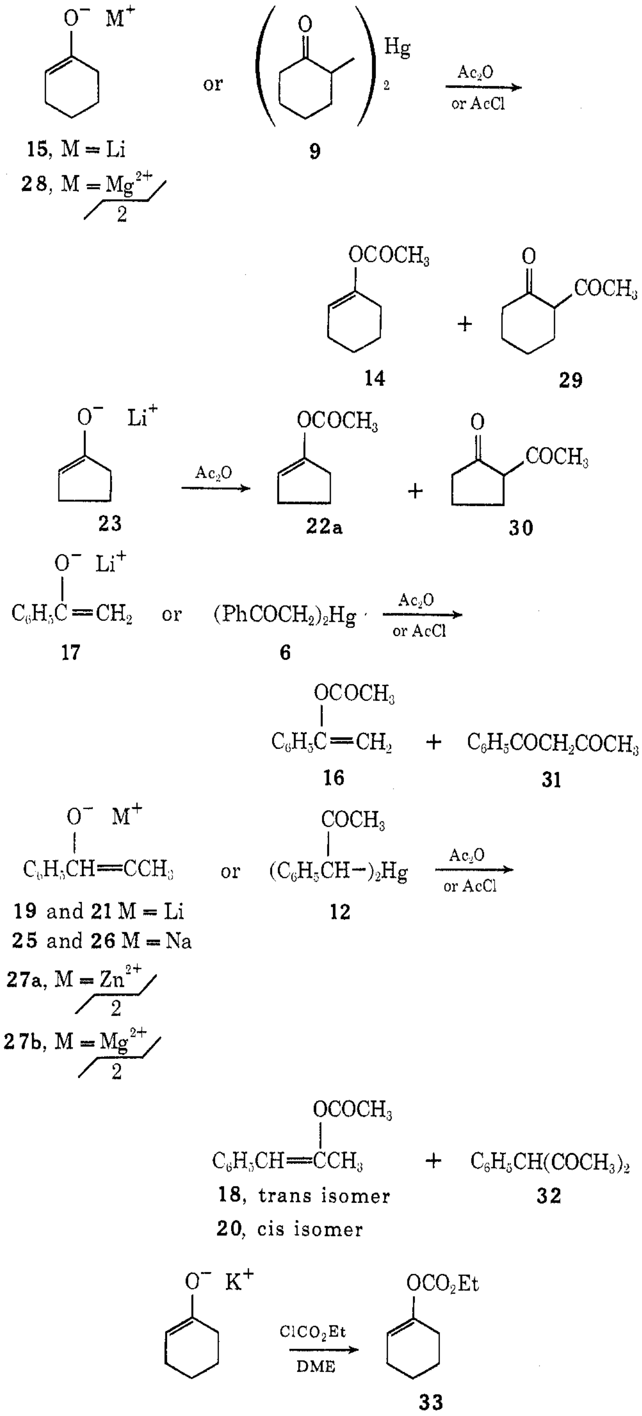


Figure 2.—Comparison of the nmr spectra of several cis and trans enolates of phenylacetone and the cis silyl ether **20b**.

Although the various α-mercuri ketones **6**, **9**, **12**, and **13** were relatively unreactive, they could be acetylated successfully with excess acetyl chloride. In every case the product was essentially only the O-acetylated material. The result can be interpreted[2] as either shielding of reaction at the α carbon by the α-mercuri substituent or as an intramolecular electrophilic catalysis by the α-mercuri substituent as implied in structure **34**. In any event the expectation that metal enolates of the type **2** should exhibit a preference for acylation at oxygen has clearly been realized.

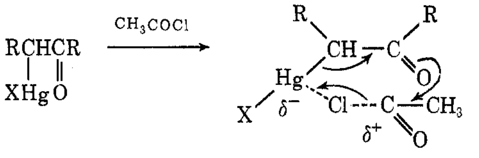
Scheme IV



The reaction of the various trans metal enolates **1b** (see Table I, entries 3, 4, and 11) and also certain of the cis enolates **1a** (see Table I, entries 1, 8, 9, and 10) in DME solution with acetic anhydride gave mixtures of acylated products in which more than 80% of the product arose from O-acylation. However, in every case where cis (**1a**) and trans (**1b**) metal enolates were compared (Table I, entries 2 *vs.* 3, 4 *vs.* 5, and 10 *vs.* 11), more C-acylation was observed with the cis isomer **1a**, and in some cases (Table I, entries 2, 5, 6, and 7) involving relatively unhindered cis enolates, a substantial fraction of the product was formed by C-acylation even in DME solution. As the metal enolate solvent was changed from DME to Et_2O favoring the existence of the metal enolates as contact ion pairs rather than solvent-separated ions, the reaction with acetic anhydride resulted in a moderate increase in the proportion of C-acylation (see Table I, entries 1, 10, and 11). Interestingly, in a given solvent and with a given acylating agent, the change in metal cation from Li^+ to Na^+ to $Zn^{2+}/2$ had little effect on the position of acylation, a result in keeping with the earlier observation that the nmr spectra of the enolates **19**, **25**, and **27a** were all very similar in a common solvent. However, when the cation was changed from Li^+ to either $Mg^{2+}/2$ or $BrMg^+$, a substantial increase in C-acylation was observed (see Table I, entries 1, 7, and 11). The reported[4c] C-acylation of enol silyl ethers with acid chlorides illustrates the tendency of fully covalent enol derivatives to react practically exclusively at carbon.

As had been noted previously,[4b] changing the acylating agent from acetic anhydride to acetyl chloride (or acetyl bromide) resulted in a significant increase in the proportion of C-acylation. That this result should not be attributed to the initial formation of ketene from the acetyl halides was shown by appropriate acylation reactions with ketene that gave predominantly O-acylated products as had been noted earlier[3e] in reactions of dimethylketene with metal enolates. Reaction of the metal enolate **15** with ethyl acetate lead to predominant C-acylation in a Claisen reaction where equilibration among the acylated products is almost certainly occurring. Reaction of the cyclohexanone enolate with ethyl chloroformate formed the O-acylated derivative **33**, suggesting that this process is a kinetically controlled acylation.

From the foregoing data we conclude that solvent-separated metal enolates **3** do react with acylating agents predominantly at oxygen and that any change that tends to favor the existence of metal enolates as contact ion pairs **4b** will enhance the amount of C-acylation. Either of the two previously advanced explanations,[2a] steric shielding of the enolate oxygen by the metal cation or an intramolecular electrophilic catalysis of the type indicated in structure **35**, could account for this trend. However, the differing amount of C-acylation with acetic anhydride and acetyl chloride (or acetyl bromide) appears to be better explained by the intramolecular electrophilic catalysis scheme **35**, since the formation of lithium (or sodium) chloride (from acetyl chloride) should be more energetically favorable than the formation of lithium (or sodium) acetate.



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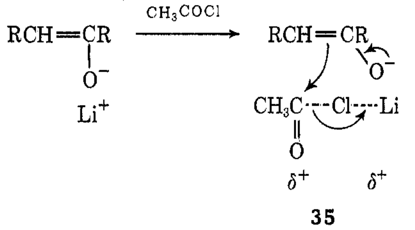

35

Experimental Section[10]

Reagents and Starting Materials.—Previous papers have described the preparation and characterization of the trimethylsilyl enol ethers **5**,[3b] **8**,[3b] **11**,[3b] **20b**,[3b] and **22b**,[3b] and the enol acetates **14**,[11] **16**,[11] **18**,[3b] and **20a**.[3b] Ethereal solutions of halide-free methyllithium were obtained from Foote Mineral Co. and the methylmagnesium reagents were prepared as described previously;[3a] these solutions were standardized by the titration procedure of Watson and Eastham.[12] The ether and 1,2-dimethoxyethane were distilled from $LiAlH_4$ immediately before use. In all reactions involving methyllithium, a few milligrams of either 2,2′-bipyridyl or triphenylmethane was added as an indicator to establish when excess methyllithium was present.[12,13]

Following a previously described procedure,[5d] cyclopentanone was allowed to react with a CCl_4 solution of Ac_2O in the presence of a catalytic amount of aqueous 70% $HClO_4$. Distillation of the crude product separated a colorless liquid fraction (11% yield), bp 82–83° (90 mm), which contained (glpc, silicone fluid, no. 710, on Chromosorb P) primarily the enol acetate **22a** accompanied by small amounts of lower boiling materials. A pure sample was collected (glpc): $n^{24.5}D$ 1.4492; ir (CCl_4) 1760 (enol ester C=O), 1665, and 1640 cm^{-1} (C=C); nmr (CCl_4) δ 5.3–5.5 (1 H m, vinyl CH), 2.05 (3 H s, $COCH_3$), and 1.7–2.6 (6 H m, aliphatic CH); mass spectrum *m/e* (rel intensity) 126 (35, M^+), 84 (100), 83 (94), 55 (34), and 43 (85).

Anal. Calcd for $C_7H_{10}O_2$: C, 66.64; H, 7.99. Found: C, 66.55; H, 7.87.

The preparation of an authentic sample of the diketone **32** was described in earlier work[3b] and a commercial sample of the diketone **31** was employed. 2-Acetylcyclohexanone (**29**), prepared by acetylation of a cyclohexanone enamine,[14] was obtained as a colorless liquid: bp 111° (22 mm), $n^{26}D$ 1.5055 [lit.[14] bp 97–104° (12–14 mm)]; ir (CCl_4) 1700 and 1600 cm^{-1} (broad) (enolic β diketone); uv max (95% EtOH), 290 mμ (ϵ 9400); nmr (CCl_4) δ 2.05 (3 H s, $COCH_3$) and 1.5–2.5 (9 H m, aliphatic CH); mass spectrum *m/e* (rel intensity), 140 (17, M^+), 125 (30), 55 (24), 43 (100), and 41 (27). The BF_3-catalyzed acetylation of cyclopentanone with Ac_2O[15] yielded 2-acetylcyclopentanone (**30**) as a colorless liquid: bp 91–92° (18 mm) [lit.[15] bp 72–75° (8 mm)]; ir (CCl_4) 1750, 1720, 1670, and 1625 cm^{-1} (partially enolic β-diketone); uv max (95% EtOH), 284 mμ (ϵ 2630); nmr (CCl_4) δ 13.1 (*ca.* 0.7 H, enolic OH), 3.3 (*ca.* 0.3 H m, COCHCO), and 1.5–2.7 (9 H m, aliphatic CH); mass spectrum *m/e* (rel intensity), 126 (24, M^+), 111 (57), 83 (33), 71 (27), 70 (37), 55 (77), 43 (100), 42 (21), 41 (25), and 37 (43).

Preparation of the α-Mercuri Ketone Derivatives. A. The Acetophenone Derivatives 6 and 7.—To a mixture of 5.4 g (25 mmol) of HgO, 0.2 g (0.6 mmol) of $Hg(OAc)_2$, 1 ml of H_2O, and 5 ml of EtOH was added, dropwise with mixing, 9.6 g (50 mmol) of the trimethylsilyl enol ether **5**. During this period, an additional 25 ml of EtOH was added to keep the mixture fluid. After the addition was complete, mixing was continued for 20 min and then the reaction mixture was diluted with 150 ml of warm $CHCl_3$, dried, and filtered. The filtrate was concentrated to *ca.* 40 ml, diluted with isooctane, and cooled. The crude mercurial **6** was collected as 9.8 g (89%) of white solid, mp 163–168°. Recrystallization from a $CHCl_3$–isooctane mixture afforded the pure bisketomercurial **6** as white needles: mp 171–172.5° (lit.[7a,b] mp 168–170°); ir (CCl_4) 1640 cm^{-1} (C=O); uv max (CH_3CN), 244 mμ (ϵ 26,400) and 320 (1380); nmr ($CDCl_3$) δ 7.3–8.1 (10 H m, aryl CH) and 2.95 (2 H s, $HgCH_2CO$, with satellites corresponding to $J_{H-^{199}Hg}$ = 172.8 Hz).

When a slurry of 4.39 g (10.0 mmol) of the bisketomercurial **6** in 50 ml of tetrahydrofuran was treated with 4.54 g (10.0 mmol) of HgI_2, the materials dissolved to give a clear, colorless solution. After the solution had been concentrated, the residue was crystallized from a $CHCl_3$–isooctane mixture to separate 8.4 g (94%) of the α-iodomercuri ketone **7** as white needles: mp 168–173° (lit.[7a] mp 163–170°); ir (Nujol mull) 1630 cm^{-1} (C=O); uv max (CH_3CN) 250 mμ (ϵ 18,200) and 322 (667).

B. The Cyclohexanone Derivatives 9 and 10.—The same procedure was followed with 8.5 g (50 mmol) of the silyl enol ether **8**, 5.4 g (25 mmol) of HgO, 0.2 g (0.6 mmol) of $Hg(OAc)_2$, 1 ml of H_2O, and 5 ml of EtOH. The crude product was obtained as 6.5 g (66%) of white solid, mp 125–130° dec. Recrystallization from a benzene–pentane mixture afforded the bisketomercurial **9** as a white solid: mp 137–139° (lit.[7c] mp 120°); ir ($CHCl_3$) 1645 cm^{-1} (C=O); nmr ($CDCl_2$) δ 2.98 (2 H broad singlet, COCHHg, with satellites corresponding to $J_{H-^{199}Hg}$ = *ca.* 174 Hz) and 1.1–2.7 (16 H m, aliphatic CH).

Anal. Calcd for $C_{12}H_{18}HgO_2$: C, 36.50; H, 4.59. Found: C, 36.83; H, 4.34.

A solution of 4.55 g (10.0 mmol) of HgI_2 in 50 ml of tetrahydrofuran was treated with 3.95 g (10.0 mmol) of the bisketomercurial **9**. The resulting solution was diluted with $CHCl_3$ and hexane and then cooled to precipitate 6.0 g (71%) of crude iodomercury compound **10**. This material was recrystallized from a $CHCl_3$–isooctane mixture to separate 4.3 g (50%) of the α-iodomercuri ketone **10** as white prisms: mp 115–117°; ir ($CHCl_3$) 1670 cm^{-1} (C=O); nmr ($CDCl_3$) δ 3.65 (1 H broad singlet, COCHHgI) and 1.3–2.9 (8 H m, aliphatic CH).

Anal. Calcd for C_6H_9HgIO: C, 16.97; H, 2.13; I, 29.89; Hg, 47.24. Found: C, 16.74; H, 2.14; I, 30.15; Hg, 47.30.

C. The Phenylacetone Derivative 12.—The same procedure was applied to 10.3 g (50.0 mmol) of the silyl enol ether **11**, 5.4 g (25 mmol) of HgO, 0.2 g (0.6 mmol) of $Hg(OAc)_2$, 1 ml of H_2O, and 5 ml of EtOH. The crude product (7.7 g or 63%, mp 106–133° dec) was crystallized from chloroform to separate the bisketomercurial **12** as a mixture of diastereoisomers: mp 126–133 dec; ir ($CHCl_3$) 1670 cm^{-1} (C=O); nmr ($CDCl_3$, spectrum at 100 MHz) δ 6.9–7.5 (10 H m, aryl CH), 4.22 (2 H s, HgCHCO, $J_{H-^{199}Hg}$ = 200 Hz), and two partially resolved singlets centered at δ 2.11 (6 H, $COCH_3$ groups of diastereoisomers). The separation of these two singlets is 1.90 Hz in the 100-MHz spectrum and 1.11 Hz in a 50-MHz spectrum.

Anal. Calcd for $C_{18}H_{18}HgO_2$: C, 46.26; H, 3.88; Hg, 42.96. Found: C, 46.27; H, 3.76; Hg, 42.97.

The Acetylation of Metal Enolates. The lithium or magnesium enolates acetylated in this study were formed in THF, Et_2O, or DME solution from the corresponding enol acetates or trimethylsilyl enol ethers by methods outlined previously.[3a–c,5d,6] Aliquots of the metal enolate solution were added, dropwise and with vigorous stirring, to a fivefold or greater excess of freshly distilled Ac_2O, AcCl, or AcBr. For reactions with ketene, a solution of the metal enolate was added to a cold (0°), freshly prepared solution of excess ketene in DME or the ketene was bubbled through a cold (−20 to −30°) solution of the enolate in DME. After the resulting mixtures had been stirred at 25° for 10–15 min they were partitioned between pentane and saturated aqueous $NaHCO_3$. The pentane solutions were separated, dried, and concentrated to leave the crude reaction product. For reactions involving the keto mercurials 0.50 mmol of the solid α-mercuri ketone was added, with stirring, to a mixture of 4.0 ml of AcCl and 4.0 ml of 1,2-dimethoxyethane. The resulting mixture was stirred at 25° for 15–60 min, during which time the solid dissolved to give a clear solution. These solutions were subjected to the same isolation procedure described above. In each case the crude product was mixed with a known amount of an internal standard and then subjected to analysis on glpc equipment which had been calibrated with known mixtures of authentic samples.

Products were identified by collecting (glpc) samples from representative reactions and comparing the glpc retention times and ir spectra for collected and authentic samples. The products from acetylation of the phenylacetone enolates **19**, **21**, **25**, and **26** and the α-mercuri ketones **12** and **13** were analyzed by glpc. On one glpc column (silicone fluid, no. 710, on Chromosorb P) the product retention times were: phenylacetone (**24**), 24.5 min; 1,3,5-triisopropylbenzene (the internal standard), 34.0

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[10] 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 237 or 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 nmr spectra were determined at 60 MHz with a Varian Model A-60 or Model T-60 nmr spectrometer. The chemical shift values are expressed in δ values (parts per million) relative to a Me_4Si internal standard. The mass spectra were obtained with a Hitachi Perkin-Elmer or a Varian Model M-66 mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere.

[11] H. O. House, D. S. Crumrine, A. Y. Teranishi, and H. D. Olmstead, to be published.

[12] S. C. Watson and J. F. Eastham, *J. Organometal. Chem.*, **9**, 165 (1967).

[13] Triphenylmethane may be used as an indicator for organolithium reagents in DME or THF solution where the red triphenylmethyl anion is formed.

[14] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

[15] R. M. Manyik, F. C. Frostick, Jr., J. J. Sanderson, and C. R. Hauser, *ibid.*, **75**, 5030 (1953).

TABLE I

THE ACETYLATION OF METAL ENOLATES

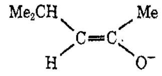
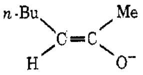
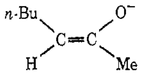
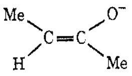
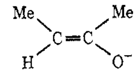
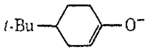
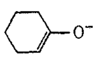
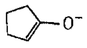
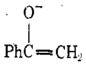
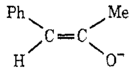
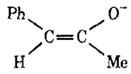
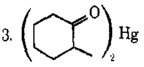
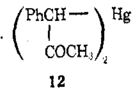
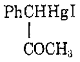
Enolate	Cation	Solvent	Acetylating agent	Product yields, %		Ref
				O-Acetyl derivative	C-Acetyl derivative	
1. 	Li$^{+a,b}$	DME	Ac_2O	75	<1	3a
	Li$^{+b,c}$	Et_2O	Ac_2O	68	4	3a
	BrMg$^{+a,b}$	Et_2O	Ac_2O	37	34	3a
2. 	Li^{+b}	DME	Ac_2O	24	43	3b
	Li^{+d}	DME	Ac_2O	38	28	3b
3. 	Li^{+b}	DME	Ac_2O	72	7	3b
	Li^{+d}	DME	Ac_2O	75	4	3b
4. 	Li$^{+d,e}$	DME	Ac_2O	53	9	3b
5. 	Li$^{+d,f}$	DME	Ac_2O	21	32	3b
6. 	Li^{+d}	DME	Ac_2O	63	12	3b
7.  15 or 28	Li^{+d}	DME	Ac_2O	49	16	
	Li^{+b}	DME	EtOAc	1	40	
	Mg^{+2}/2^{b,g}	Et_2O	Ac_2O	25	43	
8.  23	Li^{+d}	DME	Ac_2O	37	<1	
9.  $PhC(O^-)=CH_2$ 17	Li^{+d}	DME	Ac_2O	59	<1	
10.  21	Li^{+d}	DME	Ac_2O	75	2	
	Li^{+h}	DME	Ac_2O	87	3	
	Li^{+d}	Et_2O	Ac_2O	38	26	
11.  19, 25, or 27	Na^{+}	DME	Ac_2O	91–94	1	
	Na^{+}	DME	AcCl	50	14	
	Na^{+}	DME	Ketene	23–28	1–3	
	Na^{+}	THF	Ac_2O	92	<1	
	Na^{+i}	Et_2O	Ac_2O	73–79	7–9	
	Na^{+i}	Et_2O	AcCl	14–18	33	
	Na^{+i}	Et_2O	AcBr	12	46	
	Na^{+j}	Et_2O–hexane	Ac_2O	46–51	5–12	
	Li^{+d}	DME	Ac_2O	95–98	<1	
	Li^{+d}	DME	AcCl	24–47	16–22	
	Li^{+d}	THF	Ac_2O	61	<1	
	Li^{+d}	Et_2O	Ac_2O	68–76	5–9	
	Li^{+d}	Et_2O–PhH (1:3)	Ac_2O	54	12	
	Li^{+d} + 0.5 equiv $ZnCl_2$	Et_2O–DME (1:1)	Ac_2O	75	<1	
	Mg^{+2}/2^{b,g}	Et_2O	Ac_2O	41	43	
	Li^{+d} + 0.5 equiv $MgBr_2$	Et_2O–PhH (1:1)	Ac_2O	17	26	
12. $(PhCOCH_2-)_2Hg$ 6		DME	AcCl	82	<1	
13.  9		DME	AcCl	88	<1	
14.  $(PhCH(COCH_3)-)_2Hg$ 12		DME	AcCl	99	<1	

TABLE I

(*Continued*)

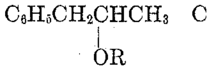
	Enolate	Cation	Solvent	Acetylating agent	Product yields, % *O*-Acetyl derivative	 C-Aetyl derivative	Ref
15.	 $\underset{\displaystyle COCH_3}{PhCHHgI}$ **13**		DME	AcCl	100	<1	

[a] The enolate anion contained 81% of the indicated cis isomer and 19% of the trans stereoisomer. [b] The enolate was prepared from the corresponding enol acetate. [c] The enolate anion contained 75% of the indicated cis isomer and 25% of the trans stereoisomer. [d] The enolate was prepared from the corresponding trimethylsilyl enol ether. [e] The enolate anion contained 92% of the indicated trans isomer and 8% of the cis isomer. [f] The enolate anion contained 97% of the indicated cis isomer and 3% of the trans isomer. [g] The enolate was prepared by the reaction of the enol acetate with 2 equiv of ethereal dimethylmagnesium. [h] This enolate, prepared from the ketone **24** and $(i\text{-}Pr)_2NLi$, contained 62–67% of the cis isomer **21** and 33–38% of the trans isomer **19**. [i] This enolate, prepared from the ketone **24** and NaH in Et_2O, contained 19–24% of the cis isomer **26** and 76–81% of the trans isomer **25**. [j] This enolate, prepared from 1 equiv of ketone **24**, 2 equiv of Et_2O, and excess NaH in hexane, contained 10–20% of the cis isomer **26** and 80–90% of the trans isomer **25**.

min; trans enol acetate **18**, 51.6 min; cis enol acetate **20a** and β-diketone **32** (not resolved), 56.4 min. On a second glpc column used (silicone gum, XE-60, on Chromosorb P), the retention times were: 1,3,5-triisopropylbenzene, 8.2 min; phenylacetone (**24**), 16.0 min; cis and trans enol acetates **18** and **20a** (not resolved), 24.4 min; β-diketone **32**, 27.6 min. On a third glpc column used (silicone QF_1 on Chromosorb P), the retention times were: 1,3,5-triisopropylbenzene, 4.0 min; phenylacetone (**24**), 6.1 min; cis and trans enol acetates **18** and **20a** (not resolved), 8.4 min; and β-diketone **32**, 9.5 min. The α-iodomercuri ketone **13** was generated *in situ* by adding 0.5 mmol of HgI_2 to a slurry of 0.5 mmol of the bisketomercurial **12** in 4.0 ml of DME. The resulting solution of the iodomercury compound **13** was then added to AcCl and subjected to the usual reaction and isolation procedures. For acetylations of the enolate **23**, the retention times (glpc, silicone fluid, no. 710, on Chromosorb P) of the possible products were: cyclopentanone, 4.8 min; enol acetate **22**, 10.0 min; *tert*-amylbenzene (internal standard), 19.1 min; β-diketone **30**, 27.6 min. For acetylations of the enolate **17** and the α-mercuri ketone **6**, the retention times (glpc, silicone fluid, No. 710, on Chromosorb P) of possible products were, acetophenone, 4.2 min; enol acetate **16**, 8.0 min; *n*-hexadecane (internal standard), 13.7 min; β-diketone **31**, 16.4 min. In the glpc (silicone fluid, no. 710, on Chromosorb P) used for the products from acetylation of the α-mercuri ketone **9**, the retention times were: cyclohexanone, 5.0 min; enol acetate **14**, 9.5 min; *n*-tridecane (internal standard), 14.6 min; β-diketone **29**, 27.8 min. For acetylation of the cyclohexanone enolates **15** and **28**, the product retention times [glpc, LAC-296 (diethylene glycol adipate) plus 3% (by weight) of H_3PO_4 suspended on Chromosorb W] were: cyclohexanone, 16.0 min; enol acetate **14**, 37.8 min; tetralin (internal standard), 46.2 min; β-diketone **29**, 85.0 min. For the reaction with EtOAc a solution of 1.4 mmol of the lithium enolate **15** in 3.5 ml of DME was added, dropwise and with stirring over 5 min, to 3.50 g (40 mmol) of EtOAc (freshly distilled from P_2O_5). After the resulting solution had been stirred for 30 min at 25° it was subjected to the usual isolation and analysis procedures.

Solutions of the sodium enolates **25** and **26** in various solvents were prepared by the dropwise addition of phenylacetone (**24**) to a suspension of excess NaH (dispersion washed with pentane before use) followed by a reaction period of 1–12 hr to ensure complete reaction. The resulting mixtures were allowed to settle and the supernatant solutions were removed; aliquots of these solutions were titrated with standard aqueous HCl for total base content and other aliquots were partitioned between pentane and aqueous NH_4Cl; the resulting pentane solutions were mixed with a known weight of internal standard and subjected to glpc analysis to determine the amount of phenylacetone (**24**) produced. Aliquots of these enolate solutions were also subjected to nmr analysis to determine the proportions of cis (**26**) and trans (**25**) isomers present. The procedures outlined above were employed for acetylation reactions and subsequent isolation and analysis.

In the reaction of phenylacetone with certain lots of NaH, either the alcohol **36a** (aqueous NH_4Cl quench) or the acetate **36b** (Ac_2O quench) was found as a by-product. Although the partial reduction of certain ketones with NaH has been reported,[16] we are inclined to attribute our reduction products, formed only with certain lots of NaH, to the presence of some metallic Na in some of the NaH samples. Another by-product found with enolate solutions prepared by the reaction of the ketone **24** with $(i\text{-}Pr)_2NLi$ was the amide **37**, formed during reaction of the enolate solution with Ac_2O. On one glpc column used (silicone fluid, DC-710, on Chromosorb P) the retention times of these components were: amide **37**, 14.9 min; alcohol **36a**,

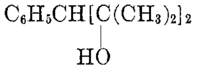


$$\underset{\displaystyle OR}{C_6H_5CH_2CHCH_3}$$

36a, R = H
b, R = COCH₃

$CH_3CON[CH(CH_3)_2]_2$

37



$$C_6H_5CH[\underset{\displaystyle HO}{C}(CH_3)_2]_2$$

38

20.6 min; ketone **24**, 21.6 min; 1,3,5-triisopropylbenzene, 29.9 min; and acetate **36b**, 33.1 min. On a second glpc column used (silicone QF_1 on Chromosorb P) the retention times were: 1,3,5-triisopropylbenzene, 3.4 min; alcohol **36a**, 3.9 min; ketone **24**, 5.3 min; amide **37**, 5.6 min; and acetate **36b**, 5.7 min. Collected (glpc) samples of the components **36a** and **36b** were identified with subsequently described authentic samples by comparison of glpc retention times and ir spectra.

A commercial sample of the alcohol **36a**, bp 103.5–104° (13 mm), $n^{25}D$ 1.5169, was acetylated with refluxing Ac_2O to form in 98% yield the acetate **36b**: bp 57.5° (0.4 mm); $n^{25}D$ 1.4880 [lit.[17] bp 107–108° (13 mm), $n^{20}D$ 1.4876]; ir (CCl_4) 1740 cm^{-1} (ester C=O); uv (95% EtOH), series of weak maxima (ε 99–193) in the region 240–270 mμ; nmr (CCl_4) δ 7.0–7.4 (5 H m, aryl CH), 5.03 (1 H sextet, J = 6.5 Hz, CHO), 2.4–3.2 (2 H m, benzylic CH_2), 1.90 (3 H s, CH_3CO), and 1.17 (3 H d, J = 6.5 Hz, CH_3); mass spectrum m/e (rel intensity) 118 (98), 117 (24), 91 (66), 65 (24), and 43 (100). A collected (glpc) sample of the amide **37** was identified from its spectral properties: ir (CCl_4) 1650 cm^{-1} (amide C=O); nmr (CCl_4) δ 3.1–4.2 (2 H broad, CHN), 1.97 (3 H s, CH_3CO), and 1.27 (12 H d, J = 7 Hz, CH_3).

Although we were able to generate an ethereal solution of the magnesium enolate of phenylacetone by the addition of 880 mg (5.0 mmol) of the enol acetate **18** in 3 ml of Et_2O to 8.3 ml of a cold (0–5°) ethereal solution containing 5.3 mmol of Me_2Mg, an attempt to produce a comparable enolate solution by the addition of 5.00 g (28.4 mmol) of the enol acetate to 30 ml of an ethereal solution of MeMgI (from 11.9 g or 85 mmol of MeI and 2.02 g or 84 mg-atoms of Mg) was complicated by a side reaction. After the solution had been stirred at 25° for 6 hr, it was partitioned between dilute aqueous HCl and Et_2O and the organic layer was dried and concentrated, resulting in the separation of 1.38 g (24%) of the crude diol **38**, mp 95–100°. Recrystallization from Et_2O–hexane afforded the pure diol **38** as white crystals: mp 105–107°; ir ($CHCl_3$) 3590 and 3460 cm^{-} (OH); nmr ($CDCl_3$) δ 7.0–7.7 (5 H m, aryl CH), 4.47 (2 H, s, OH), 2.96 (1 H s, benzylic CH), and two 6 H singlets at 1.41 and 1.19 [two $(CH_3)_2C$ groups].

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Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.81; H, 9.76.

A magnesium enolate solution was also obtained from an ethereal solution of the lithium enolate **19**, formed by reaction of 738 mg (3.6 mmol) of the silyl ether **11** with 4.0 mmol of MeLi in 2.7 ml of Et_2O for 60 min. The resulting solution was treated with 0.8 ml of a solution containing 1.9 mmol of $MgBr_2$ in an Et_2O–PhH mixture (1:1, v/v).

A solution of the zinc enolate of phenylacetone was obtained from a solution of the lithium enolate **19** (from 1.650 g or 8.0 mmol of the silyl ether **11** and 8.25 mmol of MeLi) in 5.0 ml of DME. To the solution was added 6.0 ml of an Et_2O solution containing 4.25 mmol of anhydrous $ZnCl_2$. A white precipitate (primarily LiCl) separated from the DME–Et_2O solution on standing. Analyses of the precipitate and the supernatant liquid gave the following results: precipitate, 1.2 mmol of Cl^-, 1.4 mmol of Li^+, and 0.1 mmol of Zn^{2+}; solution, 4.2 mmol of Zn^{2+}, 6.8 mmol of Cl^-, and 8.0 mmol of Li^+. When a comparable solution was prepared and immediately concentrated under reduced pressure to remove the bulk of the Et_2O, no LiCl precipitated from the DME solution.

In a similar experiment the lithium enolate **19**, from 1.331 g (7.6 mmol) of the enol acetate **18** and 16.5 mmol of MeLi, in 6.0 ml of DME was treated with 11.0 ml of an Et_2O solution containing 8.05 mmol of anhydrous $ZnCl_2$. The precipitate contained 0.2 mmol of Zn^{2+}, 6.0 mmol of Cl^-, and 7.8 mmol of Li^+ and the solution contained 8.1 mmol of Zn^{2+}, 9.7 mmol of Cl^-, and 12.0 mmol of Li^+. Quenching an aliquot of the solution followed by glpc analysis indicated that 92% of the ketone **24** was in the solution.

Reaction of the Potassium Enolate of Cyclohexanone with Ethyl Chloroformate.[18]—A solution of triphenylmethylpotassium, prepared[19] from 7.82 g (0.20 g-atom) of potassium and 53.8 g (0.22 mol) of Ph_3CH in 120 ml of DME, was treated with 17.27 g (0.176 mol) of cyclohexanone. The resulting suspension of the potassium enolate was added, dropwise and with stirring, to a solution of 20.6 g (0.19 mol) of $ClCO_2Et$ in 50 ml of DME. The mixture was stirred at ambient temperature for 1 hr and then partitioned between Et_2O and H_2O. The organic phase was dried, concentrated, and distilled to separate early fractions, bp 50–78° (9 mm), containing (glpc, Carbowax 20 M on Chromosorb P) mixtures of cyclohexanone (12.6 min) and the enol carbonate **33** (41.8 min), and 11.3 g (39%) of a fraction, bp 79–81° (9 mm) [lit.[20] bp 108–110° (20 mm)], containing >96% of the enol carbonate **33**: ir (CCl_4) 1760 (enol ester C=O) and 1690 cm^{-1} (enol C=C); nmr (CCl_4) δ 5.3–5.6 (1 H m, vinyl CH), 4.22 (2 H q, J = 7.5 Hz, OCH_2), 1.5–2.5 (8 H m, aliphatic CH), and 1.33 (3 H t, J = 7.5 Hz, ethoxyl CH_3); mass spectrum M^+ at m/e 170 with abundant fragment peaks at m/e 98, 97, 83, 70, 55, and 41.

Registry No.—**6**, 37160-45-5; **9**, 37160-46-6; **10**, 37160-47-7; **12**, 37406-76-1; **13**, 37160-48-8; **15**, 21300-30-1; **17**, 35249-09-3; **19**, 37392-64-6; **21**, 37392-65-7; **22a**, 933-06-2; **23**, 37160-52-4; **25**, 37392-66-8; **27a**, 37413-04-0; **27b**, 37413-05-1; **28**, 37160-53-5; **36a**, 698-87-3; **38**, 37406-77-2.

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Cycloadditions of Benzyne with Cyclic Olefins. Competition between 2 + 4, Ene, and 2 + 2 Reaction Pathways[1]

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The course of benzyne reaction with six- to eight-membered ring polyenes is examined and the factors which control the relative partitioning between 2 + 4, 2 + 2, or ene cycloaddition are delineated. The relative amounts of products derived from 2 + 4 or ene reaction were observed to be sensitive to conformational features of the cyclic olefins. This behavior is consistent with the known concerted character of benzyne 2 + 4 cycloadditions. Arguments are advanced supporting concerted character for the ene addition.

As a synthetic reagent *o*-benzyne occupies a position of particular utility.[2] It behaves essentially as a reactive ethylenic chromophore and the observed stereochemistry of reaction products derived from $2_s + 2_s$ or $2_s + 4_s$ cycloadditions are consistent with predictions from orbital symmetry rules.[3] Therefore it is not surprising that approximate molecular orbital calculations predict a symmetric singlet *o*-benzyne ground state.

It should be mentioned that in contrast to most reactive olefins, benzyne participates readily in the ene cycloaddition reaction.[5] The outcome of benzyne cycloadditions can be controlled by a judicious choice of coreactants. A variety of enamines react with *o*-benzyne to give primarily 2 + 2 addition products (eq 1).[6] 2-Methylvinyl acetate or cyclohexene each give only ene reactions (eq 2),[7] and cyclopentadiene reacts entirely *via* 2 + 4 cycloaddition (eq 3).[8] However, there are many examples where products from all three reaction pathways can simultaneously be observed.[2] In view of the fact that much attention has been given to the reaction of benzyne *via* 2 + 2 and 2 + 4 cycloadditions,[3,7a,9] it is surprising to find that there is a paucity of discussion in the literature on the relative partitioning of benzyne between the three primary reaction paths.[10] We have previously noted

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