Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.96; H, 10.00.

b. From Cycloheptanone Tosylhydrazone Sodium Salt and Styrene. A mixture of 1.0 g (3.4 mmol) of cycloheptanone tosylhydrazone sodium salt, 4.5 g (43 mmol) of styrene, and 30 ml of diglyme was heated at 125° for 1 hr. After cooling, the mixture was added to 150 ml of water and extracted with three 25-ml portions of pentane. The pentane extracts were concentrated and the excess styrene was removed under vacuum at 0.5 mm. The residue was then chromatographed over alumina (grade III, basic, pentane). The yield of 1-phenylspiro[2.6]nonane was 0.45 g (67%). This sample was identical with that prepared above.

Rearrangement Rates of 4 and 5. A solution of **4** or **5** (0.10 g) was dissolved in 1.3 ml of $CDCl_3$ containing 1% TMS. The solution was divided and placed into three nmr tubes. These solutions were then degassed (at least five freeze–pump–thaw cycles each) and sealed under vacuum. They were heated in a water bath whose temperature was controlled to 0.05°. At intervals, a tube was removed and quenched in ice–water. An nmr spectrum was obtained. The relative concentration of **4** or **5** was determined by integrating the signal at 0.60 or 1.21 ppm, respectively, *vs.* the internal standard, TMS. The ratio of **4** or **5** to TMS could be determined with a reproducibility of *ca.* 4%. The kinetic data are in Table I. The rate constants were determined by a least-squares method.

Mechanism of Reaction of Carbon Monoxide with Phenyllithium[1]

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Abstract: The product mixtures obtained by reaction between phenyllithium and carbon monoxide in diethyl ether, followed by hydrolysis, include benzophenone (**1**), α,α-diphenylacetophenone (**2**), benzil (**3**), α,α-diphenyl-α-hydroxyacetophenone (**4**), benzpinacol (**5**), α-hydroxyacetophenone (**6**), 1,3,3-triphenylpropane-1,2-dione (**7**), 1,3,3-triphenylpropan-1-one-2,3-diol (**8**), and benzhydrol (**9**). Compounds **1**, **2**, **6**, **7**, and **8** are produced in significant yields; **3**, **4**, **5**, and **9** are produced in trace quantities. Spectroscopic studies establish dilithium benzophenone dianion (**18**) as the first long-lived intermediate formed in this reaction; qualitative correlations between the basicity of a number of organolithium reagents and their reactivity toward carbon monoxide suggests, but does not prove, that benzoyllithium is a precursor of **18**. Labeling experiments indicate that the products ultimately isolated following hydrolysis of the reaction mixture are derived from at least two pathways which compete for the initially formed **18**. One involves combination of **18** with 1 equiv of phenyllithium and 1 equiv of carbon monoxide, followed by elimination of 1 equiv of lithium oxide, yielding **17**, the lithium enolate of **2**; a second involves combination of **18** with 1 equiv of phenyllithium and 2 equiv of carbon monoxide, yielding **22**, the trilithium trianion of **8**. Hydrolysis of **17** yields **2** directly. Hydrolysis of **22** yields **8**; reverse aldol reactions involving **8** or its precursors generate **1** and **6**. The mechanism proposed to account for the major products of the reaction of phenyllithium and carbon monoxide is outlined in Scheme III. On the basis of this scheme, plausible paths to the minor products of the reaction are proposed.

The addition of nucleophiles to carbon monoxide, activated by coordination to metal ions, forms the basis for a thoroughly explored and useful class of reactions. Transformations related to the hydroformylation process,[4] additions of organolithium reagents to metal carbonyls,[5] carbonylation of mercury(II) salts,[6] organoboranes,[7] and organocopper reagents,[8] metal-catalyzed oxidative coupling of amines with carbon monoxide,[9] and metal-catalyzed oxidation of carbon monoxide in aqueous solution,[10] each involve the attack of formally anionic groups on metal-coordinated carbon monoxide. Acylmetallic compounds have either been inferred or identified as intermediates in many of these reactions, and this class of substance provides the foundation for discussions of their mechanisms.[4,5]

The reactions of nucleophiles with free or weakly coordinated carbon monoxide are less well understood. Base-catalyzed carbonylation of alcohols and amines,[11,12] and the reactions of organolithium,[13]

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[2] National Science Foundation Trainee, 1968–1969.

[3] Fellow of the Consejo Nacional de Investigaciones Cientificas y Technicas, 1965–1966.

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[5] E. O. Fischer, and A. Maasböl, *Chem. Ber.*, 100, 2445 (1967); M. Ryang, I. Rhee, and S. Tsutsumi, *Bull. Chem. Soc. Jap.*, 37, 341 (1964); S. K. Myeong, Y. Sawa, M. Ryang, and S. Tsutsumi, *ibid.*, **38**, 330 (1965); W. F. Edgell, M. T. Yang, B. J. Bulkin, R. Bayer, and N. Koizumi, *J. Amer. Chem. Soc.*, 87, 3080 (1965); D. J. Darensbourg, and M. Y. Darensbourg, *Inorg. Chem.*, **9**, 1691 (1970); M. Ryang, *Organometal. Chem. Rev., Sect. A*, 5, 67 (1970), and references cited in each.

[6] W. Schoeller, W. Schrauth, and W. Essers, *Chem. Ber.*, **46**, 2864 (1913); T. C. W. Mak and J. Trotter, *J. Chem. Soc.*, 3243 (1962); J. M. Davidson, *J. Chem. Soc. A*, 193 (1969).

[7] M. E. D. Hillman, *J. Amer. Chem. Soc.*, **84**, 4715 (1962); H. C. Brown, *Accounts Chem. Res.*, 2, 65 (1969).

[8] J. Schwartz, *Tetrahedron Lett.*, 2803 (1972).

[9] W. Brackman, *Discuss. Faraday Soc.*, No. 46, 122 (1968); K. Kondo, N. Sonoda, and S. Tsutsumi, *Chem. Lett.*, 373 (1972).

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[11] For examples, see H. Winteler, A. Bieler, and A. Guyer, *Helv. Chim. Acta*, 37, 2370 (1954); J. Gjaldback, *Acta Chem. Scand.*, 2, 683 (1948); R. Nast and P. Dilly, *Angew. Chem., Int. Ed. Engl.*, **6**, 357 (1967).

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[13] M. Ryang and S. Tsutsumi, *Bull. Chem. Soc. Jap.*, 34, 1341

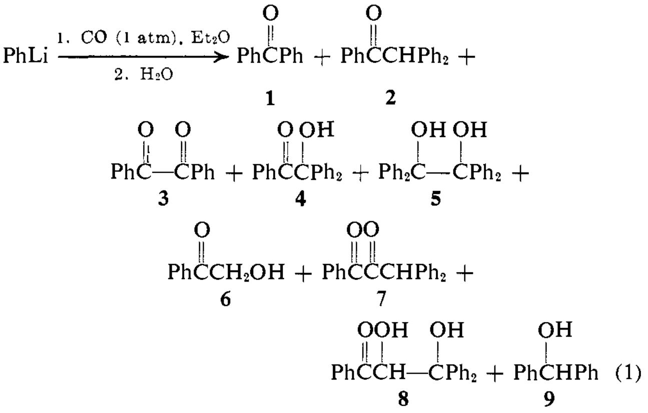
-magnesium,[14–17] -sodium,[18,19] and -zinc[20] reagents with carbon monoxide require nucleophilic attack on carbon monoxide in the absence of the obvious activation provided by coordinating transition metal ions. Stable acyl derivatives of group Ia and IIa metal ions are not well-characterized entities, although they have been implicated in reactions between carbon monoxide and *tert*-butyllithium,[21] trimethylsilyllithium,[22] and various lithium amides.[23,24]

The work reported in this paper was initiated in the hope that a study of the reaction of carbon monoxide with phenyllithium would provide evidence bearing both on the stability of acyllithium compounds and on the mechanisms of the reactions between organometallic derivatives of group Ia and IIa metal ions and that it might suggest new approaches to the generation of nucleophilic acyl groups.[25] In fact, no evidence for long-lived acyllithium compounds as intermediates in this reaction has been obtained, although the existence of these substances as transitory intermediates is suggested by certain of the data that follow. Nonetheless, these data establish the basic sequences followed in the reaction between phenyllithium and carbon monoxide, outline a number of interesting transformations involving benzophenone ketyl, benzophenone dianion, and related materials, and suggest new ways in which carbon monoxide might be used in synthesis.

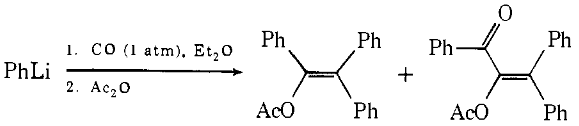
Results

Products. At −78°, phenyllithium in diethyl ether solution reacts over *ca.* 6 hr with carbon monoxide at 1 atm pressure; reaction at 0° is complete in 3–4 hr. The phenyllithium solutions used in most of the reactions in this study were obtained by reaction of bromobenzene with lithium metal and contained lithium bromide;[26] the reactions of these solutions with carbon monoxide were homogeneous throughout. Carbonylation of analogous lithium halide free solutions of phenyllithium, prepared by transmetallation of diphenylmercury(II) with lithium metal[27] or by metal–halogen exchange between *n*-butyllithium and iodobenzene in pentane solution,[28] gave similar product distributions but were heterogeneous in the latter stages of reaction. The quantity of carbon monoxide absorbed when the reactions were allowed to proceed to completion varied with reaction conditions, but typically *ca.* 0.8–1.0 equiv of carbon monoxide was consumed per equivalent of phenyllithium.

Hydrolysis and glpc analysis of the reaction mixtures led to identification of a number of products: benzophenone (**1**), α,α-diphenylacetophenone (**2**), benzil (**3**), α,α-diphenyl-α-hydroxyacetophenone (**4**), and traces of benzpinacol (**5**) and benzhydrol (**9**). Careful thin-layer chromatography of the nonvolatile products of the hydrolysis permitted isolation of α-hydroxyacetophenone (**6**) and two compounds assigned the structures 1,2,3-triphenyl-1,2-propanedione (**7**) and 1,3,3-triphenyl-2,3-dihydroxy-1-propanone (**8**) on the basis of evidence outlined below. Certain of these products, or their analogs, have been reported in previous investigations of the reactions of carbon monoxide with main group organometallics.[13–22] If reaction mixtures are quenched with acetic anhydride before hydrolysis, only two major products are isolated: 1-acetoxy-1,2,2-triphenylethylene (**10**) and 1-benzoyl-1-acetoxy-2,2-diphenylethylene (**11**). The combined yield of these materials is approximately 50–60%: **10** dominates at room temperature, **11** at low temperature.



$$\mathrm{PhLi} \xrightarrow[2.\ \mathrm{H_2O}]{1.\ \mathrm{CO\ (1\ atm),\ Et_2O}} \underset{\mathbf{1}}{\mathrm{Ph\overset{O}{\overset{\|}{C}}Ph}} + \underset{\mathbf{2}}{\mathrm{Ph\overset{O}{\overset{\|}{C}}CHPh_2}} + \underset{\mathbf{3}}{\mathrm{Ph\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}Ph}} + \underset{\mathbf{4}}{\mathrm{Ph\overset{O}{\overset{\|}{C}}\overset{OH}{\overset{|}{C}}Ph_2}} + \underset{\mathbf{5}}{\mathrm{Ph_2\overset{OH}{\overset{|}{C}}{-}\overset{OH}{\overset{|}{C}}Ph_2}} + \underset{\mathbf{6}}{\mathrm{Ph\overset{O}{\overset{\|}{C}}CH_2OH}} + \underset{\mathbf{7}}{\mathrm{Ph\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}CHPh_2}} + \underset{\mathbf{8}}{\mathrm{Ph\overset{O}{\overset{\|}{C}}\overset{OH}{\overset{|}{C}}H{-}\overset{OH}{\overset{|}{C}}Ph_2}} + \underset{\mathbf{9}}{\mathrm{Ph\overset{OH}{\overset{|}{C}}HPh}} \quad (1)$$



10 **11**

An authentic sample of compound **7** was prepared using a scheme based on the directed aldol reaction[29] and in low yield by oxidation of 1,3,3-triphenyl-1-propene with potassium permanganate in acetic anhydride (Scheme I).[30] This substance could most conveniently be obtained by the hydrolysis of the **11**, isolated on quenching the reaction of phenyllithium and carbon monoxide at room temperature with acetic anhydride. We were not successful in preparing a sample of compound **8** by independent synthesis because of the ease with which this compound undergoes a reverse

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(1961); **35**, 1121 (1962); *Trans. N. Y. Acad. Sci.*, 27, 724 (1965); *Nippon Kagaku Zasshi*, 82, 880 (1961); *Chem. Abstr.*, **58**, 12587b (1963).

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[17] M. Ryang and S. Tsutsumi, *Nippon Kagaku Zasshi*, 82, 878 (1961); *Chem. Abstr.*, **58**, 11387 (1963).

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[19] G. Wittig, L. Gonsior, and H. Vogel, *Justus Liebigs Ann. Chem.*, **688**, 1 (1965).

[20] M. W. Rathke and H. Yu, *J. Org. Chem.*, 37, 1732 (1972).

[21] P. Jutzi and F. W. Schröder, *J. Organometal. Chem.*, 24, 1 (1970).

[22] P. Jutzi and F. W. Schröder, *ibid.*, 24, C43 (1970).

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[24] The structurally related lithium aldimines are stable at low temperatures: H. M. Walborsky and G. E. Niznik, *J. Amer. Chem. Soc.*, **91**, 7778 (1969); H. M. Walborsky, W. H. Morrison, III, and G. E. Niznik, *ibid.*, **92**, 6675 (1970).

[25] D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **8**, 639 (1969).

[26] H. Gilman, E. A. Zoellner, and W. M. Selby, *J. Amer. Chem. Soc.*, **55**, 1252 (1933).

[27] G. Wittig, F. J. Meyer, and G. Lange, *Justus Liebigs Ann. Chem.*, **571**, 167 (1951).

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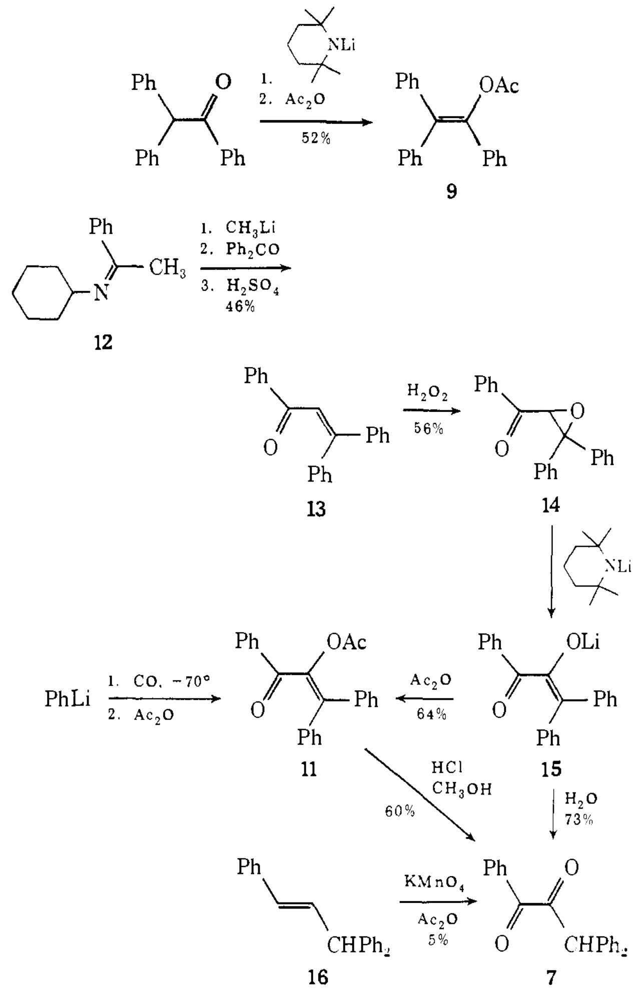
[29] H. Reiff in "Newer Methods of Preparative Organic Chemistry," Vol. VI, W. Foerst, Ed., Academic Press, New York, N. Y., 1971, p 48 ff.

[30] K. B. Sharpless, R. F. Lauer, O. Repic, A. Y. Teranishi, and D. R. Williams, *J. Amer. Chem. Soc.*, **93**, 3303 (1971).

Scheme I. Synthesis of Authentic Samples of Products



aldol reaction;[31] nonetheless, the spectral characteristics of this substance, combined with its origin and chemistry, leave no doubt concerning the essential elements of its structure. Its nmr spectrum shows two distinct OH resonances, one broad at δ 5.6, one sharp at δ 3.8, and one aliphatic CH singlet at δ 3.12, in addition to aromatic absorptions; the presence of the hydroxyl is confirmed by its infrared spectrum. The mass spectrum of **8** (70 eV) has no detectable parent ion but displays prominent peaks at 183 (Ph_2COH^+), 182 ($Ph_2CO\cdot^+$), and 105 ($PhCO^+$). The one puzzling feature of the spectral data for this substance is a carbonyl infrared absorption at 1710 cm^{-1}. The unexpectedly high frequency of this absorption may be due to a preference of **8** for a conformation in which a carbonyl C-1 is twisted out of conjugation with the geminal phenyl group or, less probably, to the existence of **8** in the tautomeric form having the carbonyl group at C-2 and a hydroxyl at C-1.

Table I lists representative product yields observed in the reaction of phenyllithium with carbon monoxide in ether. Yields of **1–5** in the first four entries in the table were obtained using unexceptional glpc techniques. The yields of **1** and **6** in the last entry were obtained by isotopic dilution, using a combination of tlc and mass spectroscopic techniques. Compounds **6**, **7**, and **8** could not be assayed directly by any glpc technique we were able to devise. Instead, phenyl-d_5-lithium was allowed to react to completion with carbon monoxide, and the reaction mixture was hydrolyzed. Known quantities of nondeuterated **1**, **6**, **7**, and **8** were added to the reaction mixture, and the resulting mixture of deuterated and nondeuterated materials was separated by preparative tlc. The yields of products in the reaction of the phenyl-d_5-lithium with carbon monoxide were estimated on the basis of the results of mass spectral analysis of the isotopic composition of these mixtures. The difference in the yields of **1** observed at −70° using glpc and isotopic dilution analyses is easily rationalized on the assumption that **8** decomposes in part to **1** in the glpc injection port (*vide infra*).

Table I. Product Yields (%) from the Reaction of Phenyllithium with Carbon Monoxide in Diethyl Ether[a]

Temp, °C	1	2	3	4	5[b]	6[c]	7[c]	8[c]
25	2	65	0	9				
0	16	43	1	1	3			
−20	31	4	0	0				
−70	47	6	0	0				
−70	26[d]	7	0	0	0	11[d]	7[d]	40[d]

[a] Phenyllithium solutions had concentrations between ~0.5 and ~1.0 *N* and contained ~1 equiv of lithium bromide per equiv of phenyllithium. Blank entries were those not measured. Yields were determined by glpc, except when noted otherwise. [b] Determined as benzpinacol, following acid-catalyzed pinacol rearrangement. [c] Analyses for **6**, **7**, and **8** were only carried out in the experiment listed in the last row of this table. [d] Obtained using isotopic dilution techniques; see the text for a discussion.

The necessity for using isotopic dilution techniques to determine yields of **6**, **7**, and **8** rendered product distribution studies too laborious to be a practical method of approaching a study of the mechanism of this reaction. Further, product distributions were difficult to reproduce in detail, and product balances greater than 80% were achieved only under special circumstances. Nonetheless, two qualitative features of the observed product distributions are experimentally significant and pertinent to the mechanistic discussions that follow. First, the yields of **1** and **2** vary in a reproducible way with temperature: **2** dominates at room temperature; **1** dominates at low temperature. Second, the yields of **1–5** (and presumably **6–8**) are relatively insensitive to changes in reaction conditions other than temperature: addition of dimethoxyethane (DME) or *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) to these ethereal reaction solutions results in an increase in the yield of benzil (**3**) to *ca.* 10% with decreases of the same magnitude in the yields of **1** and **2**; substituting solutions of lithium halide free phenyllithium for the lithium halide-containing solutions usually used or changing the concentration of phenyl-

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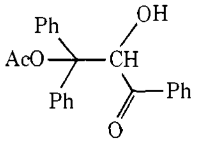
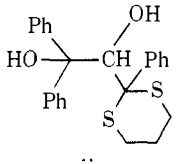
[31] Compounds i and ii were prepared in attempts to synthesize



i

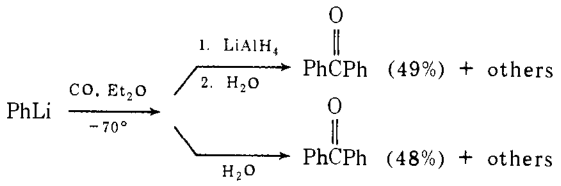


ii

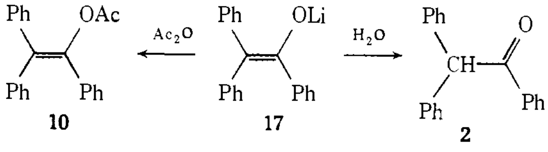
9. Efforts to remove the protecting groups from these substances under a variety of conditions led only to fragmentation to **1**, **6**, and other products. Details of these procedures and of other attempted routes to **8** may be found in the Ph.D. Thesis of T. L. Newirth, Massachusetts Institute of Technology, Cambridge, Mass., 1971.

lithium by a factor of 5, resulted only in small changes in yields. In no cases were new products detected.

In an effort to establish the fate of the phenyl groups that do not appear among the characterized products of the reaction, several reaction mixtures were explicitly examined for the presence of a number of compounds which might plausibly have been produced. Careful analyses of representative reaction mixtures demonstrated that benzene, benzoic acid, benzaldehyde, benzyl alcohol, biphenyl, triphenylmethane, triphenylcarbinol, and 1,1,2-triphenylethane-1,2-diol were not produced in detectable quantity. The observation that triphenylcarbinol is *not* a reaction product is of particular mechanistic significance. Since phenyllithium reacts readily with benzophenone, yielding triphenylcarbinol, under the conditions of these reactions, *the absence of triphenylcarbinol as a product indicates that benzophenone does not appear in the reaction mixture until phenyllithium has been completely consumed.* This conclusion was strengthened and extended by determining indirectly the quantity of benzophenone present in solution on completion of the reaction between phenyllithium and carbon monoxide *before* hydrolysis. An aliquot of a reaction solution that had been allowed to react to completion with carbon monoxide at room temperature was treated with lithium aluminum hydride, then hydrolyzed. The yield of benzophenone observed in the hydrolyzed solution was indistinguishable from that observed in a second aliquot of the original reaction mixture that had not been treated with lithium aluminum hydride. Since any benzophenone present before hydrolysis would have been reduced to benzhydrol by $LiAlH_4$, this experiment establishes that the benzophenone observed as a product in these reactions is not present in the reaction mixture before hydrolysis.



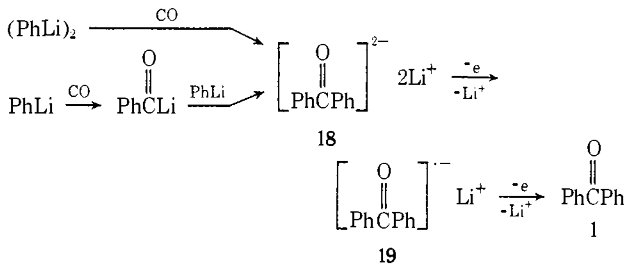
One additional useful datum can be derived from studies of the products of the reaction; *viz*, since 1,2,2-triphenyl-1-acetoxyethylene (**10**) replaces **2** in room temperature reaction mixtures quenched with acetic anhydride, the immediate precursor of **2** before hydrolysis is probably the corresponding lithium enolate **17**.



Similarly, the observation that **1**, **6**, and **7** are replaced by **11** on treatment of product mixtures obtained at low temperature suggests that these materials share a common precursor. Confirming this suggestion and identifying the structure of the precursor is one focus of the work that follows.

Dilithium Benzophenone Dianion (18) and Lithium Benzophenone Ketyl (19). The first substantial evidence concerning the nature of the intermediates in the reaction of phenyllithium and carbon monoxide emerged from spectroscopic studies of the striking color changes that characterize the reaction. Contact of carbon monoxide with phenyllithium in diethyl ether or ether–DME solutions produces an immediate intense red coloration in the solution, which persists throughout the greater part of the reaction. The final stages of reaction are characterized by a transition of the solution color from red to greenish brown.

Our initial attempts to identify the substance(s) responsible for the red color were guided by the hypothesis that benzophenone and other products containing diphenylmethyl moieties might be derived in some fashion from dilithium benzophenone dianion (**18**),



which forms deep red-purple solutions in ether solution, or from lithium benzophenone ketyl (**19**). In principle, carbon monoxide insertion into a phenyllithium dimer would yield **18**; alternatively, carbon monoxide insertion into phenyllithium monomer could yield a transitory benzoyllithium species which could be converted into **18** by reaction with a second molecule of phenyllithium.[32] One-electron oxidation could convert **18** to **19** and ultimately to benzophenone. In order to test this hypothesis, it was clearly necessary to have available authentic samples of **18** and **19**. Although both **18** and **19** have been thoroughly studied in other circumstances, the techniques used for preparation of these species, and for their characterization and identification under the reaction conditions encountered in these studies, were not entirely straightforward and are outlined here.

Solutions of dilithium benzophenone dianion in DME were prepared by reduction of benzophenone with an excess of lithium dispersion.[33,34] Solutions of **19** in DME were obtained by reduction of 1 equiv of benzophenone with 1 equiv of lithium dispersion,[35–38] or by reaction of benzpinacol with excess methyl- or phenyllithium. Preparation of these materials in diethyl ether solution were carried out using similar

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(32) The state of aggregation of phenyllithium under the conditions of these experiments is unknown. Vapor-phase osmometry indicates that halide-free phenyllithium is dimeric in ether [P. West and R. Waack, *J. Amer. Chem. Soc.*, **89**, 4395 (1967); see also G. E. Hartwell and A. Allerhand, *ibid.*, **93**, 4415 (1971)]; lithium nmr studies suggest that it is monomeric [J. A. Ladd and J. Parker, *J. Organometal. Chem.*, **28**, 1 (1971)]. Regardless, lithium halides and lithium ethoxides are incorporated into alkyllithium clusters: L. M. Seitz and T. L. Brown, *J. Amer. Chem. Soc.*, **88**, 2174 (1966); D. P. Novak and T. L. Brown, *ibid.*, **94**, 3793 (1972).

(33) A. Le Berre and P. Goasguen, *Bull. Soc. Chim. Fr.*, 1838 (1963).

(34) For alternative procedures, see (a) S. Selman and J. F. Eastham, *J. Org. Chem.*, 30, 3804 (1965); (b) E. L. Anderson and J. E. Casey, Jr., *ibid.*, 30, 3959 (1965), and references cited in each. A less convenient process, based on experiments described by A. Maercker and J. D. Roberts [*J. Amer. Chem. Soc.*, **88**, 1742 (1966)], involves reaction of dipotassium benzophenone dianion with anhydrous lithium bromide.

(35) W. Schlenk and A. Thal, *Chem. Ber.*, **46**, 2840 (1913).

(36) W. E. Bachmann, *J. Amer. Chem. Soc.*, **55**, 1179 (1933).

(37) N. Hirota in "Radical Ions," E. T. Kaiser and L. Kevan, Ed., Interscience, New York, N. Y., 1968, p 53 ff.

(38) B. J. McClelland, *Chem. Rev.*, **64**, 301 (1964); see also M. Szwarc, *Progr. Phys. Org. Chem.*, **6**, 323 (1968).

Table II. Representative Analyses of Product Mixtures Obtained on Oxidation or Hydrolysis of Solutions of $(Ph_2CO)^-M^+$ and $(Ph_2CO)^{2-}2M^+$

Compound	Concn, *M*	Solvent	Method of preparation	Quenching agent	Yield,[a] %	
					Ph_2CO	Ph_2CHOH
Ph_2COLi_2	0.067	DME	*b*	aq KOH[c]	1	90
				O_2	90	0
Ph_2COLi	0.022	DME	*d*	aq KOH[c]	47	49
				O_2	100	0
Ph_2COLi_2	0.0065	Et_2O	*b*	H_2O	0	70
				O_2	74	0
Ph_2COLi	0.012[f]	Et_2O	*d*	CH_3OH—KOH[e]	53	47
				O_2	100	0
Ph_2CONa_2	0.067	Et_2O	*b*	aq KOH[c]	1	100
				O_2	95	0
Ph_2CONa	0.20[f]	Et_2O	*b*	aq KOH[c]	47	41
				O_2	91	0

[a] Yields are based on either starting benzophenone or benzpinacol and are precise to ±5%. [b] Prepared by reaction of Ph_2CO with a dispersion of alkali metal. [c] The pH of these solutions was *ca.* 13. [d] Prepared by reaction of 2 equiv of methyllithium with 1 equiv of benzpinacol. [e] Saturated methanolic KOH. [f] Some fraction of these ketyls may have been insoluble under the reaction conditions; these concentrations should be taken as upper limits (*cf.* footnote 39).

techniques, although the low solubilities of **18** and **19** in this solvent make their solutions particularly susceptible to accidental hydrolysis or oxidation.[39]

Solutions were analyzed for **18** and **19** by taking advantage of the characteristic behavior of these materials on oxidation and hydrolysis. Both dilithium benzophenone dianion and lithium benzophenone ketyl are oxidized to benzophenone by molecular oxygen.[33,34] Hydrolysis of dilithium benzophenone dianion yields benzhydrol; hydrolysis of benzophenone ketyl with aqueous base (pH >13) yields a 1:1 mixture of benzophenone and benzhydrol. Thus, in principle, comparison of the yields of benzophenone and benzhydrol obtained on oxidation and hydrolysis of aliquots of a solution containing **18** and **19** should provide a straightforward method of determining the concentrations of these species: the yield of benzophenone obtained on oxidation of the solution would reflect the combined quantities of **18** and **19** present; the yield of benzhydrol obtained on alkaline hydrolysis would correspond to one-half the quantity of **19** present. This analytical technique suffers, however, from two ambiguities. First, the extent to which the ketyl **19** is dimerized in solution, particularly at the relatively high concentrations used in this work, is unclear;[40] thus, the yield of benzhydrol obtained on basic hydrolysis is probably best considered a measure of the *total* quantity of monomeric and dimeric **19** rather than a direct measure of monomeric **19** alone. Second, since it has not been possible to prepare samples of either **18** or **19** unambiguously, it has not been possible to prove that either hydrolysis or oxidation lead *quantitatively* to the indicated products. Thus the concentrations for **18** and **19** inferred from these analyses should be taken as minimum values. Nonetheless, several experimental observations suggest that determination of the relative yields of benzophenone and benzhydrol obtained following hydrolysis and oxidation of a solution containing **18** and **19** does in fact provide a reasonably accurate method for determining the concentrations of these compounds. First, the yields of benzophenone and benzhydrol observed on oxidation or hydrolysis of solutions of **18** and **19** prepared by reduction of benzophenone with appropriate quantities of lithium metal account for 85–100% of the starting material (Table II). Further, the product balances obtained on hydrolysis and oxidation of aliquots of a common solution agree well. Thus, it appears that both reactions take place in high yield. Second, the ratio of benzhydrol to benzophenone obtained on hydrolysis of solutions ostensibly containing benzophenone dianion is <0.01, while this ratio for solutions ostensibly containing benzophenone ketyl ranges from 0.87–0.95, in reasonable agreement with the expected value of 1.00. Third, the spectroscopic examinations described below establish that reduction of benzophenone with 1 equiv of lithium yields a solution which contains benzophenone ketyl but little if any benzophenone dianion and that continued reduction using an excess of lithium yields solutions containing benzophenone dianion but little benzophenone ketyl. Taken together, these results indicate that reduction of even high concentrations of benzophenone with appropriate quantities of lithium metal in ethereal solvents yields solutions containing **18** and **19** in good yield, uncontaminated by important quantities of other materials, and that comparison of the yields

$$Ph_2CO \xleftarrow{O_2} \mathbf{18} \xrightarrow{H_2O} Ph_2CHOH$$

$$Ph_2CO \xleftarrow{O_2} \mathbf{19} \xrightarrow[\text{pH} > 13]{H_2O} 0.5Ph_2CO + 0.5Ph_2CHOH$$

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(39) Solubility of both **18** and **19** in ethereal solvents is limited: **18** appears to precipitate from solutions of DME at ambient temperatures at concentrations $\gtrsim 0.067$ *M*, and from solutions of Et_2O at concentrations $\gtrsim 0.0065$ *M*; the limiting solubility of **19** in DME is $\gtrsim 0.06$ *M*; in Et_2O it is $\gtrsim 0.003$ *M*.

(40) Although **19** is apparently monomeric in dioxane solution at 10^{-3}–10^{-4} *M* concentrations,[41] its visible absorption in diethyl ether shows significant deviations from Beer's law.[42] No benzpinacol is observed on hydrolysis of **19** under basic conditions, in agreement with earlier work;[35,36] nonetheless, because benzpinacol is rapidly cleaved to benzophenone and benzhydrol by base, this observation is not useful in determining an equilibrium constant for dimer formation.[36,38]

(41) H. V. Carter, B. J. McClelland, and E. Warhurst, *Trans. Faraday Soc.*, **56**, 455 (1960); for related studies of sodium benzophenone ketyl, see D. J. Morantz and E. Warhurst, *ibid.*, **51**, 1375 (1955); N. Hirota and S. I. Weissman, *J. Amer. Chem. Soc.*, **86**, 2538 (1964). See also D. H. Eargle, Jr., and R. Emrich, *J. Org. Chem.*, **35**, 3744 (1970), for an interpretation of the ir spectrum of **19** in DME.

(42) H. E. Bent and A. J. Harrison, *J. Amer. Chem. Soc.*, **66**, 969 (1944). The visible spectrum of sodium benzophenone ketyl obeys Beer's law at $\sim 10^{-4}$ *M* in DME but deviates in diethyl ether; the equilibrium constant for dimerization in the latter solvent is $\sim 10^3$ l. mol^{-1}: J. Garst, D. Walmsley, C. Hewitt, W. Richards, and E. Zabolotny, *ibid.*, **86**, 412 (1964). Magnetic susceptibility measurements indicate that sodium benzophenone ketyl is >99% associated to a diamagnetic form in benzene: R. N. Doescher and G. W. Wheland, *ibid.*, **56**, 2011 (1934).

Table III. Absorption Maxima and Extinction Coefficients for Organometallic Species

Compound	Method of preparation	Solvent[a]	λ_{max}, nm	ϵ
$PhCOC(OLi){=}CPh_2$ (**15**)	 $Ph_2C(O)CHCOPh$ + LiTMP	Et_2O	417	
		DME	437	
$Ph_2C{=}C(OLi)Ph$ (**17**)	$Ph_2C{=}C(OAc)Ph + PhLi$[c]	DME	288	440,000
Ph_2COLi_2 (**18**)	Ph_2CO + Li	Et_2O	494	25,000
		DME	535	
Ph_2COLi (**19**)	$(Ph_2COH)_2 + PhLi$[c]	Et_2O	600	
		DME	634	
$PhC(OLi){=}C(OLi)C(CH_3)_3$ (**20**)	$PhCOCOC(CH_3)_3$ + excess lithium	DME	300	
Ph_3CLi	$Ph_3CH + PhLi$[c]	DME	435	*b*

[a] Solutions were 0.1 *N* in phenyllithium. [b] The literature values for the extinction coefficient of trityllithium in tetrahydrofuran is log ϵ 3.97 (425 nm).[44] [c] The phenyllithium used was that present in the solvent.

of benzophenone and benzhydrol obtained on oxidation and hydrolysis of these solutions provides a practical method of analyzing for these substances.

Spectroscopic Studies. The procedures described were used to prepare samples of **18** and **19** whose uv and visible spectra could be compared with those from solutions obtained on reaction of phenyllithium with carbon monoxide. The spectra of **18** and **19** are strongly dependent on concentration, on the nature and concentration of associated metal ions, and on the polarity of the solvent.[37,38,42,43] In order to obtain spectra of **18** and **19** that could be compared directly with spectra taken in the initial stages of reactions between phenyllithium and carbon monoxide, we carried out spectroscopic studies of authentic solutions of **18** and **19** in ethereal solutions containing approximately 0.1 *M* phenyllithium. The use of phenyllithium solution as solvent has the additional practical advantage of minimizing the effects of adventious traces of oxygen or water on the spectra of the benzophenone ketyls and dianions by acting as a scavenger for materials which would react with these organometallic reagents. The spectrum of phenyllithium itself does not interfere with those of the compounds of interest at wavelengths longer than approximately 300 nm. Visible spectra for dilithium benzophenone dianion and lithium benzophenone ketyl in 0.1 *M* solutions of phenyllithium in DME are given in Figure 1. The spectra of **18** were obtained with solutions prepared by dilution of concentrated stock solution to $\sim 10^{-3}$ *M;* the spectra of **19** were obtained from solutions prepared by a similar dilution procedure or directly by reaction of benzpinacol with phenyllithium solution in the cuvette. For comparison, this figure also gives spectra of several compounds that either are themselves formed in significant concentration during the reaction (the lithium enolates of α,α-diphenylacetophenone (**17**) and 1,1,3-triphenylpropane-1,2-dione (**15**)) or that are spectroscopic models for compounds that are formed during the reaction (the dilithium dianion of 1-phenyl-3,3-dimethylbutane-1,2-dione (**20**) which is used as a model for the trilithium salt of **8**, $Ph_2C(OLi)C(OLi){=}C(OLi)Ph$ (**22**) (*vide infra*)).[44] Absorption maxima and extinction coefficients (when estimated) obtained from these spectra are summarized in Table III.

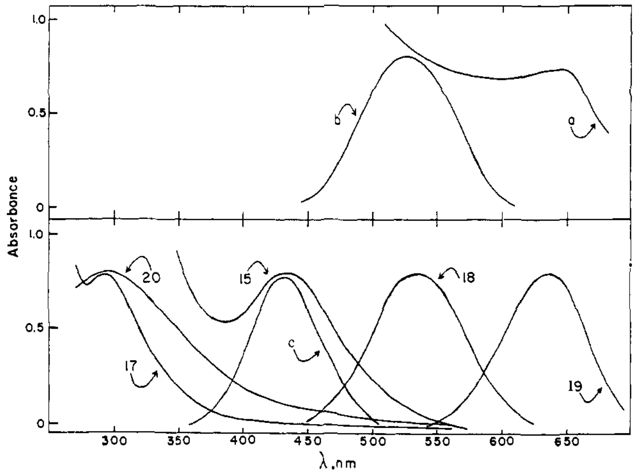

Figure 1. Ultraviolet–visible spectra of organometallic species in DME solution: (a) the reaction mixture obtained by adding phenyllithium to an excess of carbon monoxide dissolved in DME; (b) the reaction mixture obtained by adding carbon monoxide to a large excess of phenyllithium dissolved in DME; (c) Ph_3CLi; (**15**) $PhCOC(OLi){=}CPh_2$; (**17**) $Ph_2C{=}C(OLi)Ph$; (**20**) $PhC(OLi){=}C(OLi)C(CH_3)_3$; (**18**) Ph_2COLi_2; (**19**) Ph_2COLi. Since only the absorption maxima and peak shapes could be determined with any accuracy from these spectra, they are not drawn to scale, and the absorbances of the various spectra are arbitrary.

These spectra were compared with spectra of solutions obtained by reaction of phenyllithium and carbon monoxide under conditions approximating those obtaining during the product studies summarized in Table I. Addition of 0.16 μmol of carbon monoxide to 4 ml of 0.1 *N* ethereal phenyllithium solution in a Pyrex cuvette at room temperature produced the red coloration characteristic of the initial stages of the large scale reactions (Figure 2, curve b); a precisely analogous reaction carried out in DME yielded the spectrum shown in Figure 1, curve b. The similarity of the peak shapes and absorption maxima of the light absorbing material produced in these experiments and of authentic dilithium benzophenone dianion **18** strongly suggests that the compound formed initially in the reaction of

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(43) For a study of the influence of lithium bromide on the spectrum of lithium benzophenone ketyl, see D. G. Powell and E. Warhurst, *Trans. Faraday Soc.*, **58**, 953 (1962).

(44) Compound 17 was prepared by reaction of 1,2,2-triphenyl-1-acetoxyethylene (10) with phenyllithium in the cuvette. Lithium 1,1-diphenyl ethoxide formed as the other product of this reaction is transparent in the spectral region of interest. Compound 20 was prepared by reduction of 1-phenyl-3,3-dimethylbutane-2,3-dione (21) with excess lithium dispersion in DME (see the Experimental Section). Compound 15 was obtained by reaction of 1,1-diphenyl-2-benzoylethylene oxide with lithium 2,2,6,6-tetramethylpiperidide (LiTMP).[45] The spectrum of lithium triphenylmethide, prepared according to the procedure of R. Waack and M. Doran, *J. Amer. Chem. Soc.*, **85**, 1651 (1963), is also included in Figure 1.

(45) R. A. Olofson and C. M. Dougherty, *J. Amer. Chem. Soc.*, **95**, 583 (1973).

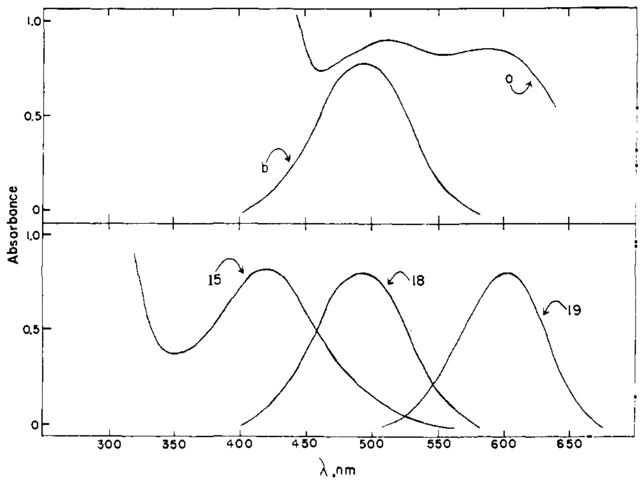


Figure 2. Ultraviolet-visible spectra of organometallic species in diethyl ether solution: (a) the reaction mixture obtained by adding phenyllithium to an excess of carbon monoxide dissolved in ether; (b) the reaction mixture obtained by adding carbon monoxide to a large excess of phenyllithium dissolved in ether; (**15**) $PhCOC(OLi){=}CPh_2$; (**18**) Ph_2COLi_2; (**19**) Ph_2COLi. The absorbances of the spectra are arbitrary.

phenyllithium and carbon monoxide is in fact dilithium benzophenone dianion; none of the other compounds examined (**15**, **17**, or **20**) overlapped the absorption region for this dianion sufficiently to hamper its identification. Comparison of the absorptivity observed in the solution resulting from reaction of phenyllithium and carbon monoxide with that estimated from the extinction coefficient of **18**, determined independently, and the quantity of carbon monoxide used in the reaction indicates that the amount of **18** formed accounts for ~50% of the carbon monoxide added.

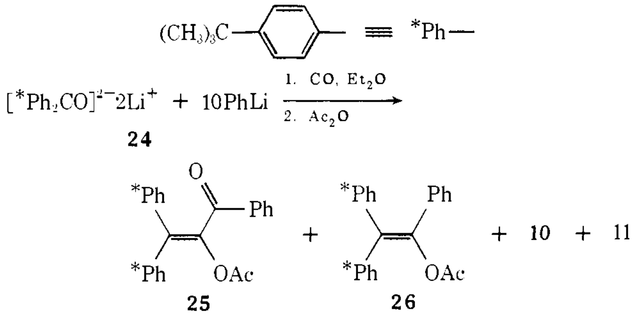
In an effort to generate spectra characteristic of the compounds present late in the reaction between carbon monoxide and phenyllithium, a small quantity of phenyllithium was added to cuvettes containing DME or ether saturated with carbon monoxide (Figure 1, curve a and Figure 2, curve a, respectively). The maxima of two prominent long wavelength bands observed in the visible spectrum in ether correspond roughly to those of **18** and **19**; under these conditions spectra characteristic of **17** and **22** were obscured by overlap and possibly by other species in solution. The spectrum in DME is not simply interpreted. Estimates of the conversions of phenyllithium **18** and **19** under these conditions, if indeed these were the compounds responsible in the region between 450 and 650 nm, would not be significant, since impurities present in the ether solution before addition of phenyllithium destroyed appreciable quantities of the initially formed organometallic materials. Control experiments established that neither **18** nor **19** reacted with phenyllithium in these or more concentrated solutions.

To lend further support to the contention that **18** is present in reacting mixtures of phenyllithium and carbon monoxide, a 1 *M* solution of phenyllithium was stirred under 1 atm of carbon monoxide for 20 min and then quenched by addition of NaOD in D_2O. Analysis by glpc and mass spectral analysis after the usual workup indicated the presence of 0.8% benzhydrol, containing >0.8 deuterium atoms per molecule.

The important conclusion from these spectroscopic experiments is that dilithium benzophenone dianion **18** is formed at the outset of the reaction of phenyllithium with carbon monoxide. Lithium benzophenone ketyl may be present in the reaction mixture late in the reaction.

Reactions of Dilithium Benzophenone Dianion with Carbon Monoxide in the Presence of Phenyllithium. Although these spectroscopic studies implicate dilithium benzophenone dianion as the principal substance generated in the initial stage of these reactions, it remained to establish the role of this compound in the formation of the products actually isolated as their conclusion. In particular, it was important to know whether the lithium enolate of α,α-diphenylacetophenone (**17**) observed as the major reaction product at room temperature was derived from **18** or from phenyllithium by some reaction path not involving **18** and to determine whether **18** could plausibly give rise to benzophenone, the major low-temperature product, under the reaction conditions used in this work.

It was possible to establish by simple labeling experiments that the benzophenone moiety of benzophenone dianion was incorporated into both high- and low-temperature products on reaction with phenyllithium and carbon monoxide. For this purpose, we used 4,4′-di-*tert*-butylbenzophenone (**23**) as the labeled benzophenone rather than ^2H- or ^{14}C-labeled material, because the dilithium dianion, **24**, of this substituted benzophenone was much more soluble in ethereal solvents, and hence easier to prepare and manipulate, than was dilithium benzophenone dianion itself. Reaction of **24** with carbon monoxide in the presence of a tenfold excess of phenyllithium, followed by quenching of the reaction mixture with acetic anhydride, led to substantial incorporations (~60%) of the labeled benzophenone moiety into the products **25** and **26**, the expected analogs of **10** and **11**;[46] yields of **10**, **11**, **25**, and **26** obtained in several reactions are summarized in Table IV. An authentic sample of **26** was prepared by substitution of 4,4′-di-*tert*-butylbenzophenone for benzophenone in the procedures summarized in Scheme I; authentic **25** was synthesized by the procedure outlined in Scheme II.



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[46] To establish that these results were independent of the method of labeling the reaction partners, similar although less accurate studies were carried out involving ethereal solutions containing 1 equiv of dilithium benzophenone dianion and 5 equiv of *p*-ethylphenyllithium. Exposure of these solutions to carbon monoxide, followed by hydrolysis, led to α,α-diphenyl-*p*-ethylacetophenone (iii) in 24% yield,

$$[Ph_2C{=}O]^{2-}2Li^+ + 5LiPh\text{-}p\text{-}Et \xrightarrow{CO} \xrightarrow{H_2O} \underset{\text{iii}}{Ph_2CHCOPh\text{-}p\text{-}Et} + \text{other products}$$

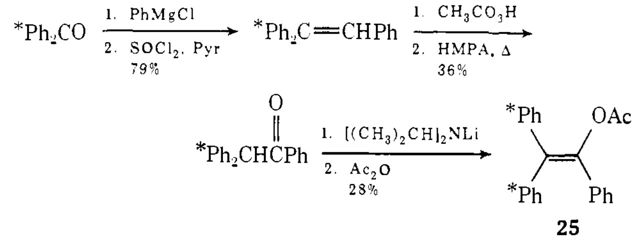
based on **18**.

Table IV. Products Observed Following an Acetic Anhydride Quench of Product Mixtures from Reactions of Dilithium 4,4′-Di-*tert*-butylbenzophenone Dianion (**24**), Phenyllithium, and Carbon Monoxide

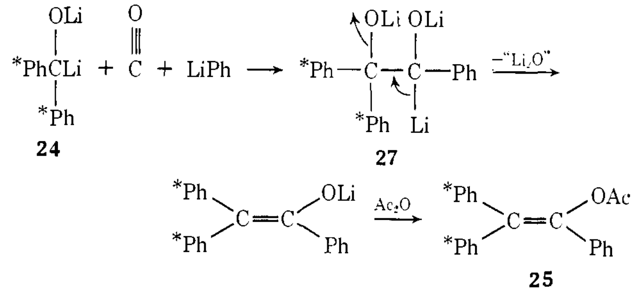
PhLi (concn, *M*)	**24** (concn, *M*)	Temp, °C	Yield,[a] % **10**	**11**	**25**	**26**
0.50	0	25	39	14	0	0
0.25	0.05	25	32	16	7 (36)[b]	
0.50	0.05	25	34	16	6 (62)[b]	Trace
0.50	0	−78	0	60	0	0
0.25	0.05	−78	0	44	0	4 (20)[b]
0.50	0.05	−78	0	47	0	6 (59)[b]

[a] Yields were determined by glpc and are based on phenyllithium unless noted. [b] Yield based on **24**.

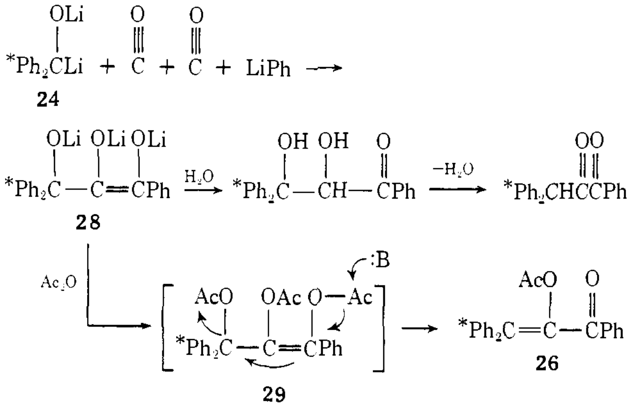
Scheme II. Synthesis of **25**

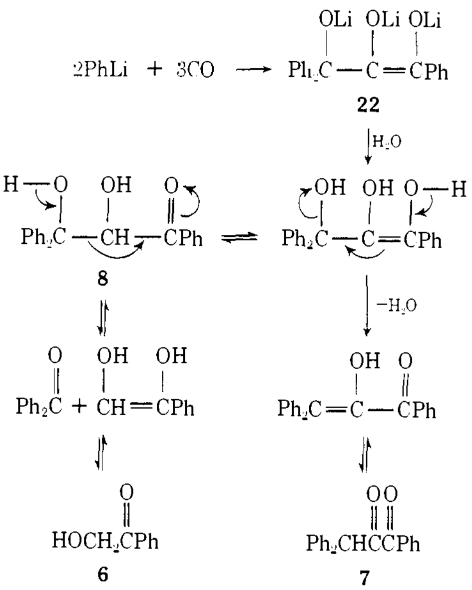


A plausible reaction sequence for the transformation of **24** to **25** involves initial transformation to an intermediate **27**, either by insertion of carbon monoxide into a mixed organolithium cluster containing units of both phenyllithium and dianion **24** in a manner analogous to that suggested for formation of **18**, by nucleophilic addition of **24** to an initially formed benzoyllithium, or by nucleophilic reaction of phenyllithium with an adduct of **24** and carbon monoxide.[47] Elimination of the elements of lithium oxide from **27** would yield the lithium enolate of **25**.[49]



The mechanism for conversion of the diarylmethylene moiety of **24** to **26** is clearly more complex than that for the transformation of **24** to **25**. Combination of 1 equiv of dianion **24**, 2 equiv of carbon monoxide, and 1 equiv of phenyllithium in a process analogous to that required to form **27** would generate the trianion **28**, the labeled analog of **22**. Acylation of this substance with acetic anhydride, followed by loss of the oxygen originally present in **24**, would in turn yield **26**. Since the acetoxy group required to leave in this last step is activated toward heterolysis by two adjacent phenyl groups and one oxygen-substituted β-styryl moiety, sufficiently rapid conversion of **29** to **26** to preclude isolation of **29** would not be surprising; however, alternative schemes for conversion of **28** to **26** involving, *e.g.*, monoacylation of the oxygen derived from **27** followed by rapid loss of acetate ion, can of course also be written. We have no direct evidence for **29** or related species in these reactions, but the postulation of **28** as an intermediate is immediately compatible with the formation of compounds **1**, **6**, **7**, and **8** as hydrolysis products from the reaction of phenyllithium and carbon monoxide by protonation, dehydration, and reverse aldol reactions, starting from the analogous trianion **22**. The difference in the observed yields of **1** and **6** from the reaction presumably reflects the sensitivity of **6** to the conditions encountered during the hydrolytic workup.





Thus, examination of products derived from reactions of the labeled dilithium diaryl ketone dianion **24** with phenyllithium and carbon monoxide fully supports the hypothesis that dilithium benzophenone **18** is an intermediate in the reaction of phenyllithium and carbon monoxide and provides a unifying mechanistic rationalization for most of the products of this reaction based on conversion of **18** to intermediates having structures **17** and **22**.

Oxidation of Dilithium Benzophenone and Lithium

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(47) The ability of disodium benzophenone dianion to act as a nucleophile toward carbon is well established;[34a,48] the reactivity of **18** should be similar.

(48) H. E. Zaugg and R. J. Michaels, *J. Org. Chem.*, 33, 2167 (1968).

(49) Attempts to prepare an authentic sample of **27** were not successful. Nonetheless, reduction of α,α-diphenyl-α-hydroxyacetophenone (**4**) with excess dilithium benzophenone dianion did yield **2** (∼70%) after hydrolysis. Thus it apparently is possible to eliminate lithium oxide from a species resembling **27** under reducing conditions. A similar elimination of lithium oxide is proposed to occur during formation of 1,2-di-*tert*-butylethylene from the reaction of *tert*-butyllithium with *tert*-butylethylene oxide; *cf.* J. K. Crandall and L. H. C. Lin, *J. Amer. Chem. Soc.*, 89, 4527 (1967).

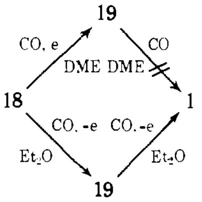
Benzophenone Ketyl by Carbon Monoxide. Benzpinacol (**5**) and benzil (**3**) are the sole isolated products of the reaction of phenyllithium and carbon monoxide not easily generated from **17** or **22**. One possible rationalization for the formation of **5** rests on the demonstration that carbon monoxide is a sufficiently strong oxidizing agent to convert benzophenone dianion to benzophenone ketyl (and benzophenone ketyl ultimately to benzophenone). Carbon monoxide is an effective one-electron oxidant toward a variety of aromatic radical ions and dianions,[50] toward metallic potassium,[51] and toward solutions of potassium in ammonia,[52] yielding in each case substances that can be derived from a hypothetical "alkali metal carbonyl" $M^+CO\cdot$

Chemical and spectroscopic data demonstrate that carbon monoxide is also capable of oxidizing **18** and **19**; the nature of the products derived from the carbon monoxide was not established in these experiments. Thus, Table V summarizes the yields of benzophenone and benzhydrol observed following hydrolysis of solutions of **18** and **19** that had been allowed to react to

Table V. Yields of Benzophenone and Benzyhydrol Obtained by Oxidation of Dilithium Benzophenone Dianion (**18**) and Lithium Benzophenone Ketyl (**19**) with Carbon Monoxide, Followed by Hydrolysis[a]

Compound (concn, *M*)	Solvent	Product (% yield) Ph_2CO	Ph_2CHOH
18 (0.06)	DME	50	45
18 (0.004)	Et_2O	20	6
19 (0.05)	DME	52	38
19 (0.003)	Et_2O	95	0

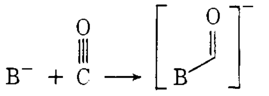
[a] Yields are based on the initial concentration of **18** or **19**. The fate of the organic moieties not detected as benzophenone or benzhydrol in these experiments was not established.



completion with carbon monoxide under conditions approximating those utilized for the reactions of carbon monoxide with phenyllithium. The observation of approximately equal yields of benzophenone and benzhydrol, characteristic of **19**, after reaction and hydrolysis of either **18** or **19** with carbon monoxide in DME contrasts with the detection of benzophenone alone after reaction and hydrolysis of these substances in diethyl ether. The inference from these experiments is that carbon monoxide will oxidize **18** to **19** in either DME or ether but will oxidize **19** to benzophenone at a significant rate only in ether; this inference is in qualitative accord with the supposition that **19** should be less strongly reducing in the more strongly solvating DME than in the less basic ether.

Qualitatively similar conclusions were reached on examination of the changes induced in the visible spectra of solutions of **18** in ether and DME following exposure to carbon monoxide. In DME, this exposure results in disappearance of the band due to **18** and appearance of a band at 634 nm attributable to **19**; in ether, addition of carbon monoxide results in complete bleaching, with the only new peak appearing at ∽350 nm (benzophenone).

Reactions with Other Organometallic Reagents. We have examined briefly the reactivity of several other types of organometallic reagents toward carbon monoxide. These experiments, together with results obtained by others, indicate qualitatively that only derivatives of strongly basic anions will react with carbon monoxide under conditions similar to those used in the work described in this paper. Thus, *tert*-butyllithium,[21] phenyllithium, *n*-butyllithium,[53] methyllithium, trimethylsilyllithium,[22] and cyclopropyllithium[53] readily absorb carbon monoxide, as do dimsyl sodium and several lithium amides;[23] the less basic lithium phenylacetylide, lithium *n*-butylacetylide, lithium diphenylamide, lithium cyclopentadienide,[13] and lithium diphenyl phosphide appear not to react. These data suggest that in classifying anions according to their reactivity toward carbon monoxide it may be heuristically valuable to consider these reactions as proceeding through acyl anions (**30**) whether or not



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substances of this class are true intermediates. Values for pK_b's of species containing the acyl anion moiety are not well-established, although that of $CH_3O_2C^-$ (**30**, B = OCH_3) has been estimated to be *ca.* 35;[54] this value seems consistent with what little is known about the chemistry of acyl anions. These organolithium reagents that have so far been found to react with carbon monoxide all are derivatives of anions having pK_b's of this magnitude or greater, while those that have proved unreactive are characterized by pK_b's that are smaller.[55] Thus, it may prove possible to predict the facility of addition of organic anions to carbon monoxide on the basis of their basicity relative to that of the appropriate acyl anion **30**.

Discussion

Three principal kinds of data bear on the mechanism of the reaction of phenyllithium with carbon monoxide. First, spectroscopic studies indicate that dilithium benzophenone dianion is formed in the early stages of the reaction. Second, examination of the products of reactions of carbon monoxide with a mixture of labeled

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(50) W. Büchner, *Chem. Ber.*, **99**, 1485 (1966).

(51) W. Büchner and E. A. C. Lucken, *Helv. Chim. Acta*, **47**, 2113 (1964); W. F. Sager, A. Fatiadi, P. C. Parks, D. G. White, and T. P. Perros, *J. Inorg. Nucl. Chem.*, **25**, 187 (1963).

(52) W. Büchner, *Helv. Chim. Acta*, **46**, 2111 (1963), and references cited therein.

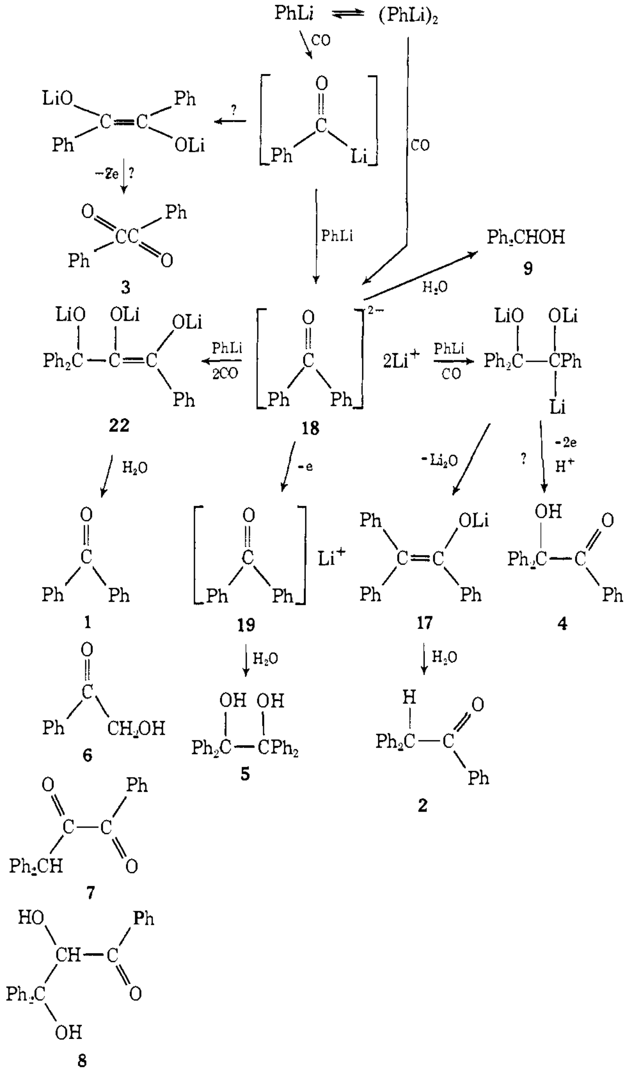
(53) E. G. Kelly, Ph.D. Thesis, Massachusetts Institute of Technology, Cambridge, Mass., 1968. The major products from the reaction of *n*-butyllithium with carbon monoxide in hexane resemble those produced from phenyllithium, *viz.* dibutyl ketone (3–6%), 6-butyldecan-5-one (60–70%), and 7-butylundecane-5,6-dione (10%).

(54) K. P. Butin, I. P. Beletskaya, A. N. Kashin, and O. A. Reutov, *J. Organometal. Chem.*, **10**, 197 (1967).

(55) For discussions of the pK_a's of weak organic acids, see H. F. Ebel in "Methoden der Organischen Chemie," (Houben-Weyl), Vol. 13/1, 4th ed, Georg Thieme Verlag, Stuttgart, 1970, p 27 ff; J. R. Jones, *Quart. Rev., Chem. Soc.*, **25**, 365 (1971); D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, Chapter 1.

dilithium benzophenone dianion and phenyllithium establishes that the diarylmethylene moiety of the former is effectively incorporated into products characteristic of the reaction of carbon monoxide with phenyllithium. Third, examination of the influence of temperature and reaction composition on the distribution of products indicates that at least two related processes compete in these reaction mixtures: one, taking place at room temperature, converts 3 equiv of phenyllithium and 2 equiv of carbon monoxide to the lithium enolate of α,α-diphenylacetophenone (**17**); a second, dominating at −78°, involves 3 equiv of phenyllithium and 3 equiv of carbon monoxide and generates the trilithium trianion **22**. The products of the reaction isolated following quenching with water or acetic anhydride are derived in straightforward ways from **17** and **22**. The mechanism implied by these data is summarized in Scheme III, together with speculations concerning the derivation of certain of the minor products and the structures of undetected intermediates between established structures.

Scheme III. Summarizing Reaction Sequence for the Conversion of Phenyllithium and Carbon Monoxide to Products



The complexity of this mechanism, and of the resulting product mixtures, suggests that many of the various intermediates formed during the course of the reaction take part in further reactions with carbon monoxide and one another at rates that are comparable with or faster than the initial rate of formation of dilithium benzophenone dianion **18**. In particular, our inability to generate more than traces (*ca.* 1%) of benzhydrol on hydrolysis of reactive mixtures that have absorbed only small quantities of carbon monoxide indicates that the concentration of **18** is never high and that its subsequent reactions with carbon monoxide and phenyllithium (or benzoyllithium, whichever is actually involved) are faster than its formation. Further, since the particular combinations of benzophenone dianion, carbon monoxide, and phenyllithium shown in Scheme III are certainly not the only ones that can be written, the low product yields observed under many conditions may result from condensations of these materials in different combinations to yield higher molecular weight products. The factors influencing the partitioning of intermediates between the reaction paths so far identified have not been established. One attempt to test the hypothesis that the relative importance of the low- and high-temperature paths for the reaction reflected the concentration of carbon monoxide in solution by studying the reaction at high carbon monoxide pressure was frustrated by a drop in the product balance; further studies have not been carried out.

The most important mechanistic question still unresolved concerning this reaction is the importance of benzoyllithium in these transformations. Qualitative correlation of the reactivity toward carbon monoxide of a number of organolithium reagents with their basicity is compatible with, but does not demand, production of transitory acyllithium compounds as the first intermediate in these reactions; the plausibility of these materials as intermediates is increased by previous work in which they have also been implicated.[21,24] Nonetheless, there is no unambiguous method of distinguishing between, *e.g.*, conversion of monomeric phenyllithium to dilithium benzophenone dianion **18** by way of benzoyllithium and conversion of dimeric phenyllithium to **18** by a concerted insertion of carbon monoxide into an aggregate; similarly, there is presently no way of deciding whether or not transformations of **18** to **22** or **17** involve benzoyllithium.

In a more general vein, the reaction of organic anions with carbon monoxide would seem to hold promise as a method of generating a number of unusual types of organic anions—especially dilithium dianions of symmetrical ketones and possibly acyllithium reagents-provided that ways can be devised to inhibit the condensation reactions that lead to formation of the mechanistically significant but synthetically unappealing types of products encountered in these studies.

Experimental Section

General Methods. Reactions involving organometallic reagents were carried out using standard techniques for manipulation of oxygen and water-sensitive compounds.[56] Melting points were determined using a Thomas-Hoover capillary melting point apparatus and are uncorrected. Boiling points are uncorrected. Nmr spectra were run on Varian A-60 or Varian T-60 spectrometers; chemical shifts are reported in ppm downfield from TMS and coupling constants in Hz. Infrared spectra were taken in sodium chloride cells using a Perkin-Elmer Model 237B grating spectrophotometer. Ultraviolet spectra were determined on a Cary 14

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(56) D. F. Shriver, "The Manipulation of Air-sensitive Compounds," McGraw-Hill, New York, N. Y., 1969, Chapter 7.

spectrophotometer. Mass spectra were determined on a Hitachi-Perkin-Elmer RMU-6D or RMU-6E mass spectrometer. Glpc analyses were performed on F & M Model 810 instruments equipped with flame ionization detectors and Disc integrators. Analytical thin-layer chromatography (tlc) was performed using Bakerflex prepared analytical plates coated with silica gel 1B-F or 2B-F. Preparative tlc plates were either Analtech plates precoated with silica gel GF or home-made plates coated with Merck Silica gel PF-254. Diethyl ether was distilled from lithium aluminum hydride or calcium hydride under a nitrogen atmosphere immediately before use; 1,2-dimethoxyethane (DME), tetrahydrofuran (THF), and benzene were purified by distillation under nitrogen from dark purple solutions or suspensions of disodium benzophenone dianion. Hexane was treated with concentrated sulfuric acid, washed with water, dried ($CaCl_2$), and distilled from a suspension of disodium benzophenone dianion under nitrogen. Carbon monoxide (C. P., Matheson) was routinely passed through a column of calcium sulfate before use. However, no significant changes in product yields were observed using carbon monoxide passed over calcium sulfate, passed through a solution of disodium benzophenone dianion in DME, or taken directly from the cylinder without treatment. Glpc analyses for compounds **1** and **2** were carried out using an 8-ft column packed with 5% DEGS on Chromosorb W or a 2-ft column packed with 5% Carbowax 20M on 80–100 mesh Chromosorb P using *n*-alkanes as internal standards. Analyses of **3**, **4**, and **5** were carried out using a 2-ft column packed with 5% SE-30 on 80–100 mesh Chromosorb P using eicosane as an internal standard. Analyses for **10**, **11**, **25**, and **26** were carried out with either a 4-ft or 8-ft column packed with 3% OV-17 on 80–100 mesh Chromosorb Q using dotriacontane as an internal standard. Benzhydrol was analyzed on a 4-ft, 5% Carbowax 20M on Chromosorb W column using octacosane as internal standard. Phenyllithium was prepared using standard procedures; *n*-butyllithium in hexane was purchased from the Foote Mineral Corp. Concentrations of organolithium reagents were determined using a double titration method.[57] Organolithium reagent solutions were discarded when the concentration of residual base in these analyses exceeded 10% of that organolithium reagent; however, residual base titer had no obvious influence on product distributions. Microanalyses were performed by Midwest Microlabs, Inc.

α,α-Diphenyl-α-hydroxyacetophenone (4), prepared in 18% yield according to the procedure of Greene and Zook, had mp 84–85° [lit.[58] mp 84.5–85°].

α-Hydroxyacetophenone (6), prepared in 30% yield by the procedure of Tsuji,[59] had mp 84–85°.

1,3,3-Triphenyl-1-propene (16). Benzyltriphenylphosphonium chloride (4.3 g, 15 mmol) in 50 ml of ether was added to a dry, 200-ml, three-necked flask equipped with a condenser, dropping funnel, and nitrogen inlet tube. *n*-Butyllithium (10 ml, 1.5 *N*, 15 mmol) was added slowly to the vigorously stirred solution and the resulting orange mixture was allowed to stir at 25° for 3 hr. To this solution was added 3.8 g (20 mmol) of α,α-diphenylacetaldehyde in ether. The resulting mixture was allowed to reflux overnight, yielding an almost colorless solution and a white precipitate. The mixture was hydrolyzed and the white precipitate was separated by filtration and washed with ether. The combined ether layer was concentrated and passed through a silica gel G column (2 × 8 cm) eluting with 2:1 hexane:methylene chloride to yield 0.8 g (19%) of 1,3,3-triphenyl-1-propene as a white crystalline solid having mp 93.5–95.5° [lit.[60] mp 98–99°]: ir ($CHCl_3$) 3050, 2870, 1600, 1450, 970 (trans olefin) cm^{-1}; nmr ($CDCl_3$) δ 7.2–7.4 (m, 15), 6.4–6.8 (m, 2), and 4.9 (d, 1, $J = 7$ Hz).

1,3,3-Triphenyl-1,2-propanedione (7) was prepared in low yield by the procedure of Sharpless, *et al.*;[30] 0.66 g (2.44 mmol) of 1,3,3-triphenyl-1-propene in 10 ml of DME was added slowly to a stirring solution of 1.58 g (9.76 mmol) of potassium permanganate in 15 ml of 99.9% acetic anhydride, kept at 0° by immersion in an ice bath. The solution was allowed to stir at 0° for 1.5 hr and was then hydrolyzed and titrated with a saturated sodium bisulfite solution to destroy excess permanganate. Ether was added and the solution was washed with *ca.* 10 volumes of water, and three 20-ml portions of 10% potassium hydroxide. The ether was dried ($MgSO_4$) and concentrated to yield a yellow oil. Isolation of the yellow component using preparative tlc coated with 2 mm of silica gel PF-254, using 2:1 methylene chloride:benzene as an eluent afforded the desired product as an oil: ir ($CHCl_3$) 3030, 2900, 1715, 1670, 1600, 1500, 1450, 1100 cm^{-1}; nmr ($CDCl_3$) δ 7.1–8.0 (m, 15), 6.0 (s, 1); mass spectrum (70 eV) (rel intensity) 300 (6.4, M$^+$), 167 (36), 105 (100), 77 (47); calcd mol wt for $C_{21}H_{16}O_2$ 300.1150, found 300.1149.

Hydrolysis of **17** afforded **7** in better yield. A 50-ml round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and No-Air stopper was charged with 0.77 g (5.5 mmol) of 2,2,6,6-tetramethylpiperidine and 15 ml of THF. The flask was swept with nitrogen and cooled to 0°. Methyllithium (2.2 ml of a 2.4 *N* ether solution, 5.2 mmol) was added to the solution by syringe. The reaction mixture was stirred for 10 min, and a solution of 1.5 g of **14** (5 mmol) in 25 ml of THF was added by cannula. The resulting deep red solution was stirred at 0° for 30 min and 10 ml of a saturated aqueous solution of ammonium chloride was added by syringe. After the reaction mixture had stirred for 10 min, an additional 20 ml of water was added and stirring was continued for an additional 20 min. The layers were separated, the aqueous layer was extracted with 30 ml of ether, and the organic layers were combined, dried (Na_2SO_4), and concentrated by rotary evaporation. The orange oil remaining was distilled through a short-path still to yield 1.1 g (3.7 mmol, 73%) of **7** as a yellow oil, bp 155° (0.15 Torr).

The most convenient procedure for the preparation of **7** involved hydrolysis of **11**, isolated from an acetic anhydride quench of the low temperature reaction of phenyllithium with carbon monoxide. Typically, a solution of 1.5 g (4.4 mmol) of **11** in 50 ml of methanol was treated with 0.5 ml of concentrated hydrochloric acid. The solution was allowed to reflux for 4 hr and was then saturated with sodium chloride. The organic products were extracted with three 30-ml portions of ether. The combined ether phase was washed with aqueous sodium bicarbonate solution, water, and aqueous sodium chloride solution, dried ($MgSO_4$), and concentrated to give 1.33 g of a crude yellow oil. Compound **7** was isolated in 60% yield from this oil by preparative tlc.

1,1,2-Triphenylethane-1,2-diol. α,α-Diphenyl-α-hydroxyacetophenone (0.28 g, 0.97 mmol) in 3 ml of ethyl ether was added slowly with stirring to lithium aluminum hydride (0.138 g, 3.65 mmol) in 15 ml of ethyl ether under nitrogen at room temperature. After 15 min, the reaction was quenched by the slow addition of ethyl acetate. Several milliliters of ethyl ether was added, followed by several milliliters of water. The organic layer was separated and dried (Na_2SO_4). The solvent was removed, leaving a solid which was recrystallized from absolute ethanol giving 0.20 g (72%) of 1,1,2-triphenylethane-1,2-diol, having mp 165–166° [lit.[61] mp 168°].

1,2,2-Triphenyl-1-acetoxyethylene (10) was prepared from **2** by the method of House and Trost[62] in 65% yield or in 52% yield by a procedure analogous to that described for **25** (except that LiTMP was used in place of lithium diisopropylamide): mp 104–105°; nmr (CCl_4) δ 7.2 (m, 15), and 1.85 (s, 3); ir (CCl_4) 3030, 2915, 1760, 1600, 1500, 1440, 1360, 1205, 1170, 1050, 1020, 730, 690 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 314 (16, M$^+$), 273 (22), 272 (100), 165 (34), 105 (29).

Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.78; H, 5.93.

1,1,3-Triphenyl-2-acetoxy-prop-2-en-3-one (11) was isolated as the major product on quenching the mixture obtained by reaction between phenyllithium and carbon monoxide at $-70°$ with acetic anhydride. An ether solution of 30 ml of phenyllithium (0.805 *N*, 25 mmol) was allowed to stir under an atmosphere of carbon monoxide at $-70°$ until reaction was complete. Freshly distilled acetic anhydride (10.2 g, 100 mmol) was added by syringe to the vigorously stirring solution. The solvent was removed *in vacuo* (1.0 Torr) leaving a white solid which was filtered and recrystallized from ethanol to give 1.34 g (48%) of a white crystalline solid, 1,3,3-triphenyl-2-acetoxy-2-propen-1-one (**11**): mp 140.5–142°; ir ($CHCl_3$) 3025, 3010, 1755, 1655 m, 1600, 1575, 1500, 1450, 1375, 1330, 1270, 1180, 1150, 1020, 980, 950, 880 cm^{-1}; nmr ($CDCl_3$) δ 7.0–7.95 (m, 15), and 2.1 (s, 3).

Anal. Calcd for $C_{23}H_{18}O_3$: C, 80.68; H, 5.30. Found: C, 80.42; H, 5.44.

This material was also synthesized by a route analogous to that described for **26**.

***N*-(1-Phenylethylidene)cyclohexylamine (12)** was prepared by the

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(57) G. M. Whitesides, C. P. Casey, and J. K. Krieger, *J. Amer. Chem. Soc.*, **93**, 1379 (1971), and references cited therein.

(58) J. L. Greene and H. D. Zook, *ibid.*, 80, 3629 (1958).

(59) T. Tsuji, *Tetrahedron Lett.*, 2413 (1966).

(60) J. H. Burckhalter and S. H. Johnson, Jr., *J. Amer. Chem. Soc.*, 73, 4830 (1951).

(61) C. A. Guthrie, E. Y. Spencer, and G. F. Wright, *Can. J. Chem.*, **35**, 873 (1957).

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

method of Norton.[63] Acetophenone (18 g, 0.15 mol), 17.4 ml of cyclohexylamine (15 g, 0.15 mol), and 10 ml of benzene were placed in a 50-ml round-bottomed flask equipped with a Dean-Stark trap, reflux condenser, Teflon-coated magnetic stirring bar, and outlet to a bubbler. The apparatus was swept with nitrogen and the reaction mixture refluxed for 16 hr with continuous removal of water and then concentrated at 12 Torr to remove all material boiling below 98°. The pot residue was distilled trap-to-trap at 1 Torr to yield 18 g of a clear liquid (90 mmol, 67%): nmr (CCl_4) δ 1.57 (b, 10), 1.87 (s, 3), 3.47 (b, 1), 7.30–7.67 (m, 5). This material was not purified further.

1,3,3-Triphenylprop-2-en-1-one (13) was prepared by a procedure analogous to that described below for 1-phenyl-3,3-di(*tert*-butylphenyl)prop-2-en-1-one: mp 84–85° [lit.[64] mp 86–87°]; nmr ($CDCl_3$) δ 7.13 (s, 1), 7.27–8.00 (m, 15).

1,1-Diphenyl-2-benzoylethylene oxide (14) was prepared using the procedure of House:[65] mp 115–119° [lit.[65] mp 123.5–124.5°], nmr ($CDCl_3$) δ 4.70 (s, 1), 7.23–8.00 (m, 15).

1-Bromo-4-*tert*-butylbenzene. In a 500-ml, three-necked, round bottomed flask equipped with a Teflon-coated magnetic stirring bar, a reflux condenser, addition funnel, and a gas outlet tube connected to a bubbler was placed 100 g of *tert*-butylbenzene (0.75 mol). The addition funnel was charged with 38.5 ml of bromine (120 g, 0.75 mol), and the bromine was added to the stirred reaction mixture at a fairly rapid rate. Evolution of hydrogen bromide proceeded for *ca.* 2 hr, at which time the reaction mixture was irradiated with a flood lamp and was stirred for an additional 48 hr. The red reaction mixture was washed with 100 ml of 10% aqueous sodium bisulfite solution, 100 ml of water, 100 ml of 10% aqueous sodium bicarbonate solution, and an additional 100 ml of water. The cloudy yellow organic liquid was dissolved in 300 ml of ether, dried ($MgSO_4$), and concentrated and the resulting liquid distilled at aspirator vacuum to yield 90 g of product (0.42 mol, 56%): bp 108° (14 Torr), lit.[66] bp 230°, nmr (CCl_4) δ 1.42 (s, 9), 7.03 (q, 4).

4,4′-Di-*tert*-butylbenzophenone (23). The procedure used for the preparation of **23** was modeled on that described by Jorgenson.[67] In a flame-dried, 500-ml, three-necked, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar, a reflux condenser, an addition funnel, and No-Air stoppers was placed 1.5 g of lithium hydride (0.19 mol) and 50 ml of dimethoxyethane, freshly distilled from sodium benzophenone ketyl. The reaction vessel was swept with nitrogen, and a solution of 20 g of 4-*tert*-butylbenzoic acid (0.11 mol) in 80 ml of freshly distilled dimethoxyethane was added through the addition funnel. After addition was complete, the reaction mixture was refluxed for 6 hr, then cooled. To the cooled (0°) slurry of lithium carboxylate was added slowly by cannula 110 ml of a 1.14 *N* solution of 4-*tert*-butylphenyllithium in ether, in turn prepared from 1-bromo-4-*tert*-butylbenzene using unexceptional procedures. Most of the solid material present in the reaction mixture dissolved in the course of the addition. After all the lithium reagent had been added, the reaction mixture was stirred for 1 hr at room temperature, and was then quenched by transferring the solution by cannula to a well-stirred solution of ice water (500 ml) in a 1-l. erlenmeyer flask. The organic layer was separated, washed with two 100-ml portions of 1 *N* sodium hydroxide solution, dried ($MgSO_4$), and concentrated on a rotary evaporator to yield a white crystalline solid, which on recrystallization from hexane gave 26.0 g of **23** (0.88 mol, 79%): mp 132–133°; nmr (CCl_4) δ 1.37 (s, 18), 7.43 (q, 8); ir (CCl_4) 1675 cm^{-1} (C=O).

Anal. Calcd for $C_{21}H_{26}O$: C, 85.71; H, 8.84. Found: C, 85.44; H, 8.92.

Benzylmagnesium chloride was prepared using a modified version of the procedure described by Adkins and Zartman.[68] In a 250-ml, three-necked, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar, reflux condenser, and No-Air stoppers was placed 2.0 g of magnesium turnings and 100 ml of freshly distilled ether. Benzyl chloride (10 g, 79 mmol) was added to the well-stirred mixture by syringe; the benzyl chloride was added in 1 ml portions at the beginning of the reaction; once the reaction had initiated, it was added at such a rate that refluxing was maintained at a steady level. The pale green solution was stirred 1 additional hr and then transferred by cannula to a flame-dried storage flask. Titration against 2-butanol, using 1,10-phenanthroline as an indicator,[69] yielded a value of 0.67 *M* for the 105 ml of benzylmagnesium chloride solution (*ca.* 89%).

1,1-Di(4-*tert*-butylphenyl)-2-phenylethanol (31) was synthesized by a procedure analogous to that described by Adkins and Zartman.[68] To a solution of 105 ml of 0.67 *M* benzylmagnesium chloride in ether (70 mmol) in a 250-ml, three-necked, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar, a reflux condenser, and No-Air stoppers was added by cannula a solution of 20.6 g of **23** (70 mmol) in 100 ml of ether. Each drop of ketone turned a deep purple as it struck the solution of Grignard reagent, the color faded with stirring. After addition was complete, the reaction mixture was stirred for an additional 0.5 hr. The solution was transferred by cannula to 50 ml of stirred ice water. To the resulting slurry was added 35 ml of cold 20% sulfuric acid. The organic layer was separated, the aqueous layer extracted with two 50-ml portions of ether, and the organic layers combined, dried ($MgSO_4$), and concentrated to yield 25.5 g (94%) of crude **31**: mp 109–110° after recrystallization from hexane; nmr (CCl_4) δ 1.23 (s, 18), 1.93 (s, 2), 3.40 (s, 1), 6.72–7.02 (m, 5), 7.17 (s, 8).

Anal. Calcd for $C_{28}H_{34}O$: C, 87.04; H, 8.80. Found: C, 86.98; H, 9.06.

1,1-Di(4-*tert*-butylphenyl)-2-phenylethylene (32) was prepared by thionyl chloride–pyridine dehydration of **31** according to a procedure modeled on that of Newman.[70] In a 250-ml erlenmeyer flask equipped with a Teflon-coated magnetic stirring bar was placed 25.5 g (66 mmol) of crude **31** and 150 ml of pyridine, freshly distilled from barium oxide. The reaction mixture was swept with nitrogen, and the flask capped with a No-Air stopper and cooled in an ice bath. Thionyl chloride (10 g, 80 mmol) was added slowly to the stirred mixture by syringe. The mixture was stirred for 1 hr, poured into 400 ml of water, and extracted with three 50-ml portions of ether. The combined ether extracts were washed with three 50-ml portions of 10% aqueous hydrochloric acid and three 50-ml portions of water. The organic material was dried ($MgSO_4$) and concentrated to yield 20.5 g (84%) of crude **32** as a pale yellow solid. Recrystallization from hexane yielded large white crystals: mp 78–81°; nmr (CCl_4) δ 1.21 (s, 9), 6.72–7.23 (m, 14).

Anal. Calcd for $C_{28}H_{32}$: C, 91.30; H, 8.69. Found: C, 91.14; H, 8.76.

1-Phenyl-2,2-di(4-*tert*-butylphenyl)-2-acetoxyethan-1-ol (33). Crude **32** (20.5 g, 56 mmol), 125 ml of chloroform, and 0.5 g of sodium acetate trihydrate were placed in a 250-ml erlenmeyer flask with a Teflon-coated magnetic stirring bar. The mixture was cooled in an ice bath, stirred, and 7.4 ml of 40% peracetic acid (56 mmol) was added. The ice bath was removed after 1 hr; the mixture was stirred for 60 hr, poured into 200 ml of ice water, and extracted with two 50-ml portions of chloroform. The combined organic layers were washed with 50 ml of 10% aqueous sodium carbonate and two 50-ml portions of water. The organic solution was dried ($MgSO_4$) and concentrated to yield a gummy white solid. Recrystallization from hexane yielded 12.2 g (49%) of **33**: mp 203–205°; nmr (CCl_4) δ 1.23 (s, 9), 1.35 (s, 9), 2.48 (s, 1), 7.00 (s, 8), 7.33 (s, 5); ir (CCl_4) 1755 cm^{-1} (C=O). This substance was used without further purification in the following step.

α,α-Di(4-*tert*-butylphenyl)acetophenone (34). A solution of 10.2 g of **33** in 50 ml of dry hexamethylphosphoramide was placed in a 100-ml round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and reflux condenser with an outlet to a nitrogen bubbler. The mixture was flushed with nitrogen, then stirred and heated at 210° for 3 hr. The deep red solution was cooled and poured into 400 ml of stirred ice water. The yellow solid which precipitated was isolated by suction filtration. This solid was dissolved in 200 ml of chloroform; the chloroform extracted once with 100 ml of water, dried ($MgSO_4$), and concentrated to yield a yellow solid, which on recrystallization from hexane yielded 6.6 g (74%) of **34** as white needles: mp 153–154°; nmr (CCl_4) δ 1.23 (s, 18), 5.77 (s, 1), 6.90–8.03 (m, 13); ir (CCl_4) 1700 cm^{-1} (C=O).

Anal. Calcd for $C_{28}H_{32}O$: C, 87.50; H, 8.33. Found: C, 87.21; H, 8.46.

1-Acetoxy-1-phenyl-2,2-di(4-*tert*-butylphenyl)ethylene (25). Freshly distilled diisopropylamine (1.2 ml, 0.8 g, 8 mmol) and 20

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[63] D. G. Norton, *et al.*, *J. Org. Chem.* **19**, 1054 (1954).

[64] P. L. Southwick, L. A. Pursglove, and P. Numerof, *J. Amer. Chem. Soc.*, 72, 1600 (1950).

[65] H. O. House and D. J. Reif, *ibid.*, 77, 6525 (1955).

[66] C. S. Marvel, M. B. Mueller, C. M. Himel, and J. F. Kaplan, *ibid.*, **61**, 2771 (1939).

[67] M. J. Jorgenson, *Org. React.*, **18**, 1 (1970).

[68] H. Adkins and W. Zartman, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 606.

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

[70] M. S. Newman, A. Arkell, and T. Fukunaga, *J. Amer. Chem. Soc.*, 82, 2498 (1960).

ml of ether were placed in a flame-dried, 125-ml, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and No-Air stopper. The flask was swept with nitrogen and cooled in an ice bath and 5.0 ml of a 1.6 *M* solution of methyllithium in ether was added by syringe. The mixture was stirred for 10 min, and a suspension of 3.1 g (8 mmol) of **34** in 50 ml of ether was added by cannula. The solution turned a deep yellow, and stirring was continued for 10 min. The resulting enolate solution was added by cannula to a stirred solution of 5 ml of freshly distilled acetic anhydride in 100 ml of ether in 250-ml, round-bottomed flask. This solution was treated with 100 ml of saturated aqueous sodium bicarbonate. The organic layer was separated, dried ($MgSO_4$), and concentrated to yield a yellow oil which solidified on standing overnight. This material was taken up in hot hexane and recrystallized. Unreacted ketone precipitated first; crystallization of the concentrated mother liquor yielded 1.0 g (28%) of **25**: mp 144–146°; nmr (CCl_4) δ 1.23 (s, 9), 1.33 (s, 9), 1.80 (s, 3), 6.87–7.23 (m, 13); ir (CCl_4) 1745 cm^{-1} (C=O).

Anal. Calcd for $C_{30}H_{34}O_2$: C, 84.50; H, 7.98. Found: C, 84.25; H, 8.28.

***N*-(1-Phenyl-3,3-di(4-*tert*-butylphenyl)-3-hydroxy)propylidenecyclohexylamine (35)** was synthesized by a directed Aldol condensation using a procedure similar to those described by Wittig and Hesse.[29,71] Freshly distilled diisopropylamine (5.05 g, 50 mmol) and 40 ml of freshly distilled THF were placed in a flame-dried, 300-ml, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and No-Air stopper. The reaction vessel was flushed with nitrogen and cooled to 0°, and 30 ml of a 1.6 *M* solution of methyllithium in ether was added by cannula. Evolution of methane was evident during the addition. The mixture was stirred for 10 min, and a solution of 10 g (50 mmol) of **12** in 80 ml of THF was added by cannula. This yellow solution was stirred at 0° for 10 min, cooled to −78°, and a solution of 15.1 g (50 mmol) of **23** in 80 ml of THF was added by cannula to the stirred solution. After addition was complete, the cooling bath was removed and the mixture was allowed to stand for 20 hr; it was then cooled to 0° and treated with 100 ml of water. Stirring was continued at 0° for 0.5 hr. The cold mixture was filtered to yield the ketimine **35** as a white solid. The filtrate was diluted with 50 ml of ether and the organic layer was separated, dried ($MgSO_4$), and concentrated by rotary evaporation to yield additional product. The combined crude product was used without further purification or analysis in conversion to **36**.

1,1-Di(4-*tert*-butylphenyl)-3-phenylprop-1-en-3-one (36). The hydrolysis of the crude ketimine **35** was carried out by a method analogous to that of Reiff.[29] In a 500-ml, round-bottomed flask equipped with a reflux condenser and Teflon-coated magnetic stirring bar was placed the total quantity of crude ketimine described above and 250 ml of 2 *N* sulfuric acid. This mixture was heated at reflux temperature for 2 hr. The cooled reaction mixture was extracted with two 100-ml portions of ether. The ether extracts were combined, dried ($MgSO_4$), and concentrated to yield a yellow oil. Analysis of this yellow oil by nmr and tlc indicated that it was a mixture of α,β-unsaturated ketone and β-hydroxy ketone. This crude oil was then dissolved in 150 ml of ethanol and treated with 15 ml of concentrated hydrochloric acid at reflux for 4 hr. The reaction mixture was cooled and extracted with two 100-ml portions of methylene chloride. The organic portions were combined, washed with 100 ml of saturated aqueous sodium bicarbonate, 100 ml of water, dried ($MgSO_4$), and concentrated to yield a yellow solid. Recrystallization from ethanol afforded 5.4 g (28%) of product. Treatment of the mother liquors with additional hydrochloric acid, followed by further recrystallization, yielded an additional 3.6 g of product; the total yield of **36** was 9.0 g (46%): mp 104–106°; nmr (CCl_4) δ 1.30 (s, 9), 1.37 (s, 9), 7.03–7.87 (m, 14); ir (CCl_4) 1670 cm^{-1} (C=O).

Anal. Calcd for $C_{29}H_{32}O$: C, 87.87; H, 8.08. Found: C, 87.98; H, 8.22.

1,1-Di(4-*tert*-butylphenyl)-2-benzoylethylene oxide (37) was prepared by epoxidation of **36** by a procedure modeled on that described by House and Reif.[65] In a 1-l. erlenmeyer flask equipped with a Teflon-coated magnetic stirring bar was placed 3.96 g (10 mmol) of α,β-unsaturated ketone **36** in 300 ml of absolute methanol and 50 ml of methylene chloride. To the stirred solution was added 6 ml of 6 *N* aqueous sodium hydroxide and 12 ml of 30% hydrogen peroxide. This mixture was stirred for 36 hr; additional 9-ml portions of 30% hydrogen peroxide were added at 6, 10, and 24 hr. After 36 hr, the reaction mixture was filtered to yield 3.5 g of a white solid. The filtrate was treated with an additional 9 ml of hydrogen peroxide, stirred another 12 hr, treated once again with 9 ml of hydrogen peroxide, stirred a final 12 hr, and then filtered to yield an additional 0.8 g of white solid. The solid material was combined and treated with 100 ml of ether. The insoluble solid remaining was removed by suction filtration; the filtrate was concentrated by rotary evaporation to yield 2.32 g (56%) of **37**: mp 149–151°; nmr (CCl_4) δ 1.27 (s, 9), 1.35 (s, 9), 4.35 (s, 1), 7.30 (m, 13); ir (CCl_4) 1700 cm^{-1} (C=O).

Anal. Calcd for $C_{29}H_{32}O_2$: C, 84.46; H, 7.76. Found: C, 84.39; H, 7.90.

1,1-Di(4-*tert*-butylphenyl)-2-acetoxy-3-phenylprop-1-en-3-one (26). Freshly distilled THF (20 ml) and 2,2,6,6-tetramethylpiperidine (0.42 g, 3 mmol) were placed in a flame-dried 100-ml, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and No-Air stopper. This mixture was swept with nitrogen and cooled to 0°. A solution of methyllithium in ether (1.8 ml of a 1.6 *M* solution) was added by syringe to the stirred mixture. Stirring was continued for 5 min, and a solution of 1.05 g of the substituted ethylene oxide prepared in the preceding step in 20 ml of THF was added by cannula. The deep red reaction mixture was stirred for 1 hr at 0° and 1 hr at 25° and was then quenched by addition to a stirred solution of 10 ml of acetic anhydride in 75 ml of ether. The resulting suspension was treated with 100 ml of saturated aqueous sodium bicarbonate solution and the organic layer was separated, dried ($MgSO_4$), and concentrated to give an orange oil. This oil was distilled trap-to-trap at 1 Torr to remove the last traces of acetic anhydride and 2,2,6,6-tetramethylpiperidine. The orange solid remaining was recrystallized from ethanol to yield 0.75 g (65%) of **26**: mp 168–169°; nmr (CCl_4) δ 1.13 (s, 9), 1.38 (s, 9), 2.13 (s, 3), 6.87 (m, 13); ir (CCl_4) 1760 and 1675 cm^{-1}.

Anal. Calcd for $C_{31}H_{34}O_3$: C, 81.93; H, 7.49. Found: C, 81.89; H, 7.62.

α,α-Diphenyl-*p*-ethylacetophenone. Diphenylketene[72] (9.7 g, 50 mmol) in 30 ml of ethyl ether was added slowly to a solution of *p*-ethylphenyllithium (75.0 mmol) in 120 ml of ether at room temperature with vigorous stirring. After the addition was complete, the reaction mixture was held at reflux temperature for 30 min, cooled to 0°, and hydrolyzed with 20 ml of a saturated aqueous solution of ammonium chloride. Water (30 ml) was added and the ether layer was separated. The aqueous layer was extracted with two 100-ml portions of ether. The ethereal portions were combined, washed with water, and dried ($CaCl_2$). The ether was removed, leaving a solid which was dissolved in absolute ethanol, treated with decolorizing charcoal, and recrystallized to give 1.57 g (10.5%) of white crystals: mp 102–103°; ir (CCl_4) 1690 cm^{-1} (C=O); nmr (CCl_4) δ 7.17 (m, 14, aryl-H), 5.88 (s, 1, CH), 2.50 (q, 2, J = 8 Hz, CH_2), and 1.22 (t, 3, J = 8 Hz, CH_3).

Anal. Calcd for $C_{22}H_{20}O$: C, 87.96; H, 6.71. Found: C, 87.91; H, 6.74.

3,3-Dimethyl-1-phenyl-2-hydroxy-1-butanone (38). To a solution of 3 g (15 mmol) of 2-phenyl-1,3-dithiacyclohexane in 100 ml of dry tetrahydrofuran cooled to −60° was slowly added 10 ml (15 mmol, 1.5 *N*) of *n*-butyllithium by syringe.[73] The solution was allowed to stir at −60° for 1 hr; then 1.6 g (17.5 mmol) of 2,2-dimethylpropanal was slowly added and the solution was allowed to warm to −28° over a 4-hr period. The solution was hydrolyzed and the organic layer was separated and washed with aqueous sodium chloride solution, dried (Na_2SO_4), and concentrated to give 3.5 g of a mixture of the starting thioketal and another compound. Without further purification, the 3.5 g of white solid was added to a 500-ml, round-bottomed flask containing 200 ml of 9:1 methanol:water and 3.24 g (15 mmol) of mercuric oxide. The mixture was heated to reflux under nitrogen; then 8.13 g (30 mmol) of mercuric chloride in 40 ml of the same solvent was added. The mixture was allowed to reflux under nitrogen for 4 hr. The resulting white precipitate was separated by filtration and washed with three 50-ml portions of methylene chloride. The filtrate was diluted with an equal volume of water and extracted with three 50-ml portions of methylene chloride. The combined methylene chloride phase was washed with water, aqueous ammonium acetate, and water, dried ($MgSO_4$), and concentrated to give an oil which was a mixture of benzaldehyde and another compound. The oil in *ca.* 100 ml of methylene chloride and a few drops of absolute ethanol was allowed to stir overnight with 3.5 g of pulverized calcium chloride.[74] The calcium

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[71] G. Wittig and A. Hesse, *Org. Syn.*, **50**, 66 (1970).

[72] H. Staudinger, *Chem. Ber.*, **44**, 1619 (1911).

[73] D. Seebach, *Synthesis*, 17 (1969).

[74] Isolation of **37** by adsorption on calcium chloride was suggested to us by Professor Barry Sharpless.

chloride was separated by filtration and washed with small portions of methylene chloride and then was added to a mixture of 100 ml of water and 100 ml of benzene. The benzene layer was separated, washed with aqueous sodium chloride, dried ($MgSO_4$), and concentrated to give 0.9 g (37%) of 3,3-dimethyl-1-phenyl-2-hydroxy-1-butanone: mp 33–33.5°; ir (CCl_4) 3500, 1670, 1600, cm^{-1}; nmr (CCl_4) δ 7.25–7.9 (m, 5), 4.68 (d, 1, J = 8 Hz), 3.3 (d, 1, J = 8 Hz), 0.85 (s, 9).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.97; H, 8.40.

1-Phenyl-3,3-dimethyl-1,2-butanedione. To a solution of 0.558 g (3.14 mmol) of *N*-bromosuccinimide in 60 ml of 90% aqueous acetone was added 100 mg (0.522 mmol) of 1-phenyl-3,3-dimethyl-2-hydroxy-1-butanone in 20 ml of acetone. The solution was allowed to stir for 2 hr at 25° then diluted with 30 ml of 1:1 methylene chloride:pentane and 30 ml of saturated sodium bicarbonate. The organic layer was washed with five 30-ml portions of saturated sodium bicarbonate, with saturated sodium chloride, dried ($MgSO_4$), and concentrated, yielding 0.79 g (80%) of 1-phenyl-3,3-dimethyl-1,2-butanedione as a yellow oil. The oil can be purified by preparative thin-layer chromatography using 6:1 cyclohexane:ethyl acetate as eluent. This substance has nmr (CCl_4) δ 7.3–8.0 (m, 5, aromatic), 1.3 (s, 9, $C(CH_3)_3$), and ir (CCl_4) 1725, 1695 cm^{-1}, with no OH absorption.

Small-Scale Reactions of Phenyllithium with Carbon Monoxide. A stock solution of phenyllithium was prepared by adding appropriate quantities of *n*-heptane, *n*-tetradecane, and *n*-nonadecane as internal glpc standards to a solution of phenyllithium in ether. The resulting solution was assayed by double titration, and aliquots were used for reaction with carbon monoxide. Typically, 15 ml of an *ca.* 0.5 *N* solution of phenyllithium was transferred either to a Schlenk tube containing a Teflon-covered stirring bar and connected to a gas adsorption apparatus or to a 40-ml heavy walled centrifuge tube with stirring bar capped with a No-Air stopper. The stirred solutions were exposed to carbon monoxide (in the former case from the gas absorption apparatus, in the latter from a carbon monoxide cylinder connected to the centrifuge tube through a length of Tygon tubing and hypodermic needle). When gas absorption had ceased (4 hr at 0° and 1 atm pressure, 2–3 hr at 0° and 2 atm), the resulting dark brown reaction mixture was quenched by the addition of 0.5 ml of distilled water. Saturated aqueous ammonium chloride solution (1 ml) and ether (15 ml) were added, and the ether layer was analyzed by glpc.

Isolation and Characterization of Products by Glpc. Benzophenone and benzil were identified by comparison of glpc retention times, mass spectra, and infrared spectra of collected samples with those of authentic samples. Compounds **2** and **4** were isolated by combining several hydrolyzed reaction mixtures. The solvent was removed leaving a yellow oil which was dissolved in a minimum volume of hot benzene. The solution was allowed to cool to room temperature, and the resulting crystals were collected and recrystallized from absolute ethanol to give α,α-diphenylacetophenone (**2**): mp 137.5–138.5° [lit.[75] mp 137–139°]; ir (CCl_4) 1695 cm^{-1} (C=C); nmr (CCl_4) δ 5.86 (s, 1), 7.17–8.00 (m, 15); mass spectrum (70 eV) *m/e* (rel intensity) 272 (2.4, M$^+$), 167 (30), 105 (100), 77 (14).

Anal. Calcd for $C_{20}H_{16}O$: C, 88.20; H, 5.92. Found: C, 88.12, H, 5.95.

α,α-Diphenyl-α-hydroxyacetophenone (**4**) was identified in the hexane solution by comparison of its glpc retention times on two columns (8-ft 5% DEGS on Chromosorb W at 200° and 8-ft 13% SE-52, on silanized Chromosorb W at 225°) and its tlc R_f values on two adsorbents (Silica Gel and Alumina eluting with chloroform:methylene chloride 4:1) with those of an authentic sample. Benzpincol (**5**) was assayed by treating an aliquot of the original reaction mixture with saturated aqueous ammonium chloride solution, followed by hydrochloric acid and acetic acid, and analyzing the resulting solution for benzpinacolone by glpc.

Isolation and Characterization of Products Using Preparative Thin-Layer Chromatography. Phenyllithium (50 ml, 0.6 *N*, 30.0 mmol) was allowed to stir under a carbon monoxide atmosphere at −70° for 6 hr. The resulting green reaction mixture was quenched with 2 ml of saturated aqueous ammonium chloride solution and 0.25 ml of concentrated hydrochloric acid. The ether layer was separated, dried ($MgSO_4$), and concentrated, yielding a viscous yellow oil. This oil was subjected to thin-layer chromatography (tlc). The major unidentified spot had an R_f value of 0.313 on silica gel 2B-F analytical plates using 4:1 methylene chloride:ether as eluent. This compound (**6**), identified as α-hydroxyacetophenone,[59] was isolated from a 20 × 20-cm preparative tlc plate coated with 2 mm of silica gel PF-254 using 2:1 methylene chloride:ether eluent, as a white crystalline solid: mp 84–85°; mmp 84–85°. The ir spectrum of **6** is indistinguishable from the published ir spectrum of α-hydroxyacetophenone.[76]

A second component appeared as a yellow spot having R_f 0.79 on analytical tlc silica gel 2B-F plates using methylene chloride: benzene in the ratio of 4:1 as an eluent. To isolate this substance, which was a minor product, an aliquot of the reaction mixture was sublimed (70°, 0.05 Torr) to remove benzophenone, leaving a residual yellow oil, enriched with this yellow substance, which was subjected to preparative tlc. From a 20 × 20-cm plate coated with 2 mm of silica gel PF-254, eluting with 2:1 methylene chloride:benzene, was isolated a yellow oil (**7**), which gave only one spot by analytical tlc using 4:1 methylene chloride:benzene as eluent. This substance had ir spectrum, mass spectrum, and R_f value (methylene chloride:benzene 4:1) indistinguishable from that of an authentic sample of 1,3,3-triphenyl-1,2-propanedione.

The R_f value for a third compound (**8**) was 0.47 on analytical silica gel 2B-F tlc plates using 3:1:12 benzene:ether:methylene chloride as eluent. The same solvent system was used with 20 × 20-cm plates coated with 2 mm of silica gel PF-254 to isolate a colorless oil which solidified to a white crystalline solid (**8**): mp 93.0–94.0°; ir ($CHCl_3$) 3590, 3500 (br), 3050, 2860, 1710, (C=C), 1600, 1500, 1450, 1380 cm^{-1}; nmr ($CDCl_3$) δ 7.1–7.4 (m, 15), 5.6 (s, 1), 3.8 (broad s, 1), and 3.12 (s, 1); mass spectrum (70 eV) *m/e* (rel intensity) 183 (24), 182 (18), 105 (100), 77 (65).

Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.46; H, 5.68.

Product Balance by Isotopic Dilution. An ethereal solution of phenyllithium-d_5[77] (31 ml, 0.52 *N*, 16 mmol), prepared from bromobenzene-d_5[78] and lithium wire, was allowed to stir under carbon monoxide at −70° until reaction was complete. The solution was quenched with saturated aqueous ammonium chloride solution and concentrated hydrochloric acid. To the resulting mixture was added authentic benzophenone (187 mg, 1.03 mmol), **6** (53 mg, 0.39 mmol), **7** (13 mg, 0.0434 mmol), and **8** (20 mg, 0.063 mmol). The organic layer was separated and washed with water and aqueous sodium chloride solution, dried ($MgSO_4$), and concentrated to an oil. Samples of benzophenone, **6**, **7**, and **8** were isolated from this oil for mass spectroscopic analyses using preparative tlc. Benzophenone and **14** were isolated using Analtech tlc plates precoated with 1.5 mm of silica gel GF with 2:1 methylene chloride:cyclohexane eluent. The R_f values for benzophenone and **7** under these conditions are 0.43 and 0.545, respectively. Using the same type of plate and 8:2:1 methylene chloride:benzene:ether eluent, **6** and **8** were isolated. The R_f values for **6** and **8** under these tlc conditions are 0.40 and 0.514, respectively. Isotopic analyses of each of these isolated isotopic mixtures were carried out using a nominal ionizing voltage of 15 eV. In each case, the ratios reported are the average of several spectra. For benzophenone the ratio of peak heights of the 192/182 ions was 1.94 ± 0.03. For **6** the ratio of peak heights of the 110/105 ions was 4.33 ± 0.05. For **7** the ratio of the peak heights of the 177/167 and the 110/105 ions was 8.2 ± 0.1. For **8** the ratio of the peak heights of the 110/105 ions was 33 ± 0.6. The product yields derived from these data are outlined in Table I.

Partial Reaction of Phenyllithium and Carbon Monoxide in Ether and Quench with Sodium Deuteroxide. A solution of phenyllithium in ether (5 ml, 1.0 *M*, 5 mmol) was transferred by syringe to a 25-ml, round-bottomed flask equipped with a No-Air stopper and Teflon-coated magnetic stirring bar. This reaction mixture was swept out with a stream of carbon monoxide and then stirred under an atmosphere of carbon monoxide for *ca.* 20 min. The reaction mixture was cooled in an ice bath and 5 ml of sodium deuteroxide in degassed deuterium oxide (prepared by the addition of 0.1 g of sodium to 20 ml of deuterium oxide) was added cautiously by syringe. The quenched reaction mixture was allowed to stir for *ca.* 30 min and was then diluted with 50 ml of water and 50 ml of ether. The ether layer was separated, washed with two 50-ml por-

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[75] A. C. Cope, P. A. Trumbull, and E. R. Trumbell, *J. Amer. Chem. Soc.*, 80, 2844 (1958).

[76] "The Sadtler Standard Spectra," Sadtler Research Laboratories, Philadelphia, Pa., 1970, ir prism spectrum 9770.

[77] An aliquot of phenyl-d_5-lithium was quenched with water; the resulting benzene, collected from an 8-ft 20% UC-W98 column and analyzed by mass spectroscopy, was found to be 97.3% benzene-d_5, 2.7% benzene-d_4.

[78] G. M. Whitesides and W. J. Ehmann, *J. Amer. Chem. Soc.*, 92, 5625 (1970).

tions of water, dried ($MgSO_4$), and analyzed using a coupled glpc mass spectrometer.

Reaction of Phenyllithium and Carbon Monoxide in Ether and Treatment of the Resulting Reaction Mixture with Lithium Aluminum Hydride. A solution of 14 ml of 0.6 *N* phenyllithium (8.4 mmol) in ether and 0.27 g (0.975 mmol) of eicosane in a flame-dried 40-ml centrifuge tube, equipped with a No-Air stopper and a magnetic stirring bar. was allowed to stir at −70° under an atmosphere of carbon monoxide for 4 hr. As usual, during the course of the reaction the solution first became red and then green. When the reaction was complete, one 1-ml aliquot was quenched with 1 ml of aqueous potassium hydroxide solution and another 1-ml aliquot was quenched with 1 ml of saturated ammonium chloride solution and 0.1 ml of concentrated hydrochloric acid. The remaining reaction mixture was added to a solution prepared by mixing 95 mg (2.5 mmol) of lithi umaluminum hydride ($LiAlH_4$) and 20 ml of ether, refluxing for 0.5 hr, and cooling to room temperature. The mixture was allowed to stir at 25° under nitrogen for 30 min and was then cautiously hydrolyzed with 3 ml of water. Each of the hydrolyzed solutions were analyzed for benzophenone, benzhydrol, and benzil by glpc. As controls, these reactions were repeated using 20 ml of phenyllithium (0.5 *N*, 9.9 mmol) in ether. When each of the reactions was complete, a solution of 0.15 g (0.83 mmol) of benzophenone in 5 ml of ether was added *via* a cannula to each reaction mixture. The resulting mixtures were hydrolyzed and treated with $LiAlH_4$ as described above. The hydrolyzed ether solutions were analyzed by glpc. Analysis of the glpc data indicated that the benzophenone which had been added prio rto treatment with $LiAlH_4$ had been reduced to benzhydrol.

Dilithium Benzophenone Dianion (18) from Benzophenone and Lithium. Benzophenone (1.82 g, 10 mmol) and *n*-nonadecane (0.824 g, 3.07 mmol) were dissolved in 150 ml of anhydrous DME. Lithium wire (1.0 g, 140 mg-atoms, cut into 0.25-in. pieces) or lithium dispersion was added and the mixture was allowed to stir for 1 day at room temperature under nitrogen to yield a dark red solution of **18**. Dilithium benzophenone dianion can also be prepared in ethyl ether using an analogous procedure. A pale blue precipitate of lithium benzophenone ketyl forms initially; this precipitate is subsequently reduced to a red precipitate. Vigorous stirring is required to keep the precipitates from settling.

Lithium Benzophenone Ketyl (19) from Benzophenone and Lithium. Benzophenone (0.48 g, 2.64 mmol) was dissolved in 50 ml of DME. Lithium wire (0.0187 g, 2.64 mg-atoms) was added and the mixture was allowed to stir at room temperature under nitrogen for 24 hr.

Lithium Benzophenone Ketyl (19) from Benzpinacol and Methyllithium. Benzpinacol (1.05 g, 2.87 mmol) and *n*-nonadecane (0.366 g, 1.36 mmol) were dissolved in 20 ml of DME and were slowly added to methyllithium in ethyl ether (3.90 ml, 1.62 *N*, 6.31 mmol) *via* cannula. An intense blue color formed immediately.

The Oxidation of Dilithium Benzophenone Dianion with Carbon Monoxide in Ether. Ten milliliters of an ether solution of dilithium benzophenone dianion (*ca.* 0.004 *M*), which contained a known amount of nonadecane, was transferred to a flame-dried centrifuge tube equipped with a No-Air stopper *via* cannula. The solution was exposed to carbon monoxide and stirred occasionally. After 20 min the deep red solution of **18** had turned green. An aliquot of the solution was quenched with degassed methanolic potassium hydroxide and analyzed using glpc (Table V).

The Oxidation of Lithium Benzophenone Ketyl with Carbon Monoxide in Ether. Benzpinacol (79.2 mg, 0.217 mmol), nonadecane (58.5 mg, 0.218 mmol), and *ca.* 25 ml of ether, freshly distilled from sodium benzophenone ketyl, were added to a flame-dried 40-ml centrifuge tube equipped with a No-Air stopper and a glass-covered stirring bar. To this solution methyllithium (*ca.* 0.5 mmol) was slowly added by syringe with immediate formation of a light blue precipitate. After 2 hr, this precipitate was compacted by centrifugation and the blue supernatant solution was transferred by cannula to another 40-ml centrifuge tube, which had previously been flame-dried and washed with a solution of methyllithium in ether. A 5-ml aliquot of this supernatant solution was transferred to a similarly dried centrifuge tube and was quenched with degassed methanolic potassium hydroxide. The remaining solution was allowed to react with carbon monoxide for 5 hr, during which time the clear blue solution became colorless. The colorless solution was quenched with methanolic potassium hydroxide. Analysis of both quenched solutions was carried out by glpc (Table V).

Oxidations of 18 and 19 with carbon monoxide in DME were carried out using procedures analogous to those used in ether.

Spectroscopic Studies. Solutions of lithium benzophenone ketyl were obtained by injection of known quantities of benzpinacol through a serum cap into 0.1 *N* solutions of phenyllithium contained in 1-cm Pyrex spectrophotometer cells. Solutions of trityllithium and of **17** were prepared by analogous procedures starting with triphenylmethane and **10**, respectively. Samples of dilithium benzophenone were prepared by addition of small amounts of **18** to 0.1 *N* solutions of phenyllithium contained in 1-cm Pyrex cells. Samples of **20** were prepared by reducing 74 mg of 1-phenyl-3,3-dimethyl-1,2-butanedione with excess lithium dispersion in 25 ml of DME and diluting aliquots of this stock solution approximately 1:2.5 with DME. Solutions of **15** were obtained by reaction of 1.1 equiv of **37** with 1.0 equiv of LiTMP in ether, as described in the preparation of **26**.

Samples used in studies requiring **18** or **19** in solutions free of phenyllithium were obtained by diluting concentrated solutions of these substances in closed systems using standard techniques.[42]

Experiments involving the reaction of carbon monoxide with **18**, **19**, or phenyllithium were carried out by mixing the reaction components directly in the spectrophotometer cell.

Dilithium 4,4′-Di(*tert*-butyl)benzophenone Dianion (24). In a flame-dried, 100-ml, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and a No-Air stopper was placed 0.93 g of **23** (3.2 mmol) and 60 ml of freshly distilled ether. The reaction mixture was swept with argon, and 0.40 g of freshly cut lithium wire (57 mg-atoms) was added to the reaction flask in a stream of argon. The flask was sealed with a No-Air stopper and stirred overnight. The solution turned a deep blue, then purple, and finally dark red as the reaction progressed.

Using a syringe, 20 ml of this red solution was withdrawn and added to a 50-ml erlenmeyer flask containing a Teflon-coated magnetic stirring bar. The solution was stirred in air until the red color had faded to pale green-yellow. This solution was treated with 20 ml of water; the organic layer was separated, the aqueous layer was extracted once with 10 ml of ether, and the organic portions were combined, dried ($MgSO_4$), and analyzed by glpc using tetracosane as an internal standard. Glpc analysis revealed the presence of **23** in 50% yield, with a small amount (*ca.* 10%) of the corresponding benzhydrol as well as a small amount of a higher boiling material. The authentic sample of the *tert*-butylated benzhydrol was prepared by the reduction of **23** with lithium aluminum hydride.

Using a syringe, another 20 ml of the red solution of **24** was withdrawn and was added to a well-stirred solution of 10 ml of 2 *N* potassium hydroxide solution. After stirring for 10 min, the layers were separated, the aqueous layer was extracted with 20 ml of ether, the organic portions were combined, dried ($MgSO_4$), and analyzed by glpc. Glpc analysis revealed only 4,4′-di(*tert*-butyl)benzhydrol as a product, in 88% yield.

Reaction of Phenyllithium with Carbon Monoxide in the Presence of 24. In a typical experiment, a flame-dried, 100-ml, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and No-Air stopper was charged with 0.69 g of 4,4′-di(*tert*-butyl)benzophenone (**23**) (2.5 mmol), 40 ml of freshly distilled ether, and 0.1 g of lithium wire (14 mg-atoms) in an argon atmosphere. This mixture was stirred overnight, during which time the solution turned a deep red. Into another flame-dried 100-ml, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and No-Air stopper was transferred by cannula 20 ml of a 1.25 *N* solution of phenyllithium in ether (25 mmol). To this solution was added by cannula the solution of **24** described above. This reaction mixture was stirred for 3 hr at 25° (or for 5 hr at −78°) under an atmosphere of carbon monoxide. The reaction mixture was then transferred by cannula to a stirred solution of 20 ml of acetic anhydride in 75 ml of freshly distilled ether cooled in an ice bath. The resulting suspension was washed with 100 ml of a saturated aqueous solution of sodium bicarbonate and dried (Na_2SO_4). This solution was diluted to 300 ml with ether, dotriacontane was added as an internal standard, and the reaction mixture was analyzed by glpc.

The Reaction of Dilithium Benzophenone Dianion with *p*-Ethylphenyllithium in the Presence of Carbon Monoxide. A mixture of dilithium benzophenone dianion (0.093 *M*, 1.3 mmol, 14.0 ml) in DME containing a known amount of *n*-nonadecane as an internal standard and *p*-ethylphenyllithium (0.08 *N*, 1.00 mmol, 1.25 ml) in ethyl ether was stirred under 1 atm pressure of carbon monoxide at room temperature for 2 hr. The reaction mixture was hydrolyzed with 0.2 ml of aqueous potassium hydroxide solution (pH 13), 5 ml of ether was added, and the reaction mixture was analyzed by glpc. α,α-Diphenyl-*p*-ethylacetophenone was identified by comparison of its physical properties with those of an authentic sample.

The Reduction of α,α-Diphenyl-α-hydroxyacetophenone with

Dilithium Benzophenone Dianion. Butyllithium in hexane (6.0 mmol) was added slowly to 1,2-dibromoethane (0.957 g, 5.1 mmol) in a 40-ml centrifuge tube capped with a No-Air stopper. The resulting precipitate of anhydrous lithium bromide was washed four times with 20-ml portions of pentane, dissolved in 7 ml of hot DME, and added to 2 mmol of dipotassium benzophenone dianion in 30 ml of DME containing 0.1534 g of *n*-nonadecane as internal standard in a stoppered 40-ml centrifuge tube. The solution was thoroughly mixed by shaking and the precipitate of potassium bromide separated by centrifugation. The resulting solution of dilithium benzophenone[79] was added to a solution of α,α-diphenyl-α-hydroxyacetophenone (0.0967 g, 0.336 mmol) in 10 ml of DME. The red color of dilithium benzophenone persisted after the addition. After stirring at room temperature for 2 hr, the reaction mixture was hydrolyzed with aqueous potassium hydroxide solution; the aqueous layer was separated and extracted with one 50-ml portion of ethyl ether, and the organic layers were combined and dried (Na_2SO_4). Analysis by glpc indicated the presence of α,α-diphenylacetophenone (72%) and α,α-diphenyl-α-hydroxyacetophenone (9%).

Preparation of Other Anions. Lithium phenyl acetylide and lithium butyl acetylide were prepared by reaction of the corresponding acetylene with methyllithium in ether solution. Lithium diphenyl phosphide was prepared by the reaction of diphenylphosphine with *n*-butyllithium in THF. Lithium diphenylamide was prepared by the reaction of diphenylamine with methyllithium in THF. Sodium dimsylate was prepared as described by Greenwald, Chaykovsky, and Corey.[80] All of the above were reacted with carbon monoxide at 200 psi; only sodium dimsylate took up an appreciable quantity of carbon monoxide (0.5 equiv of carbon monoxide per equivalent of dimsylate over a 24-hr period).

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(79) Solutions of **18** prepared using this procedure were analyzed for potassium by hydrolysis and treatment with lithium tetraphenylborate: *cf.* D. N. Bhattacharyya, C. L. Lee, J. Smid, and M. Szwarc, *J. Phys. Chem.*, **69**, 608 (1965). Less than 1% of the potassium originally present as dipotassium benzophenone remained in solution after addition of the lithium bromide.

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Mechanism of Oxidative Cyclization of Squalene. Evidence for Cyclization of Squalene from Either End of the Squalene Molecule in the *in Vivo* Biosynthesis of Fusidic Acid by *Fusidium coccineum*[1a]

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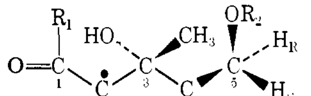
Abstract: Fusidic acid biosynthesized by *F. coccineum* from (3*RS*,5*S*)-[2-^{14}C,5-^{3}H]mevalonic acid was shown to contain 0.5 atom of tritium at the C-11β and C-12 positions. From the known mechanism of squalene formation the 0.5 atom of tritium at C-12 must have the α configuration. Our results indicate that either one of the terminal double bonds of squalene is epoxidized to an equal degree, and that the ensuing cyclization to prosterol occurs from either end of the squalene molecule. This shows that the geometrical asymmetry imparted to the squalene on the squalene synthethase is not retained during the conversion to oxidosqualene. These observations are consistent with the hypothesis of the release of squalene into a free squalene pool prior to epoxidation.

The biosynthetic steps involved in the formation of squalene from mevalonic acid (MVA) (**1a**) are now well understood.[2] Mevalonic acid is first converted to the C-5 pyrophosphate (**1b**), which undergoes in the presence of ATP a concerted decarboxylation and elimination of the C-3 tertiary hydroxyl to yield[3] isopentenyl pyrophosphate (**2**). This process involves a trans elimination of the two participating moieties.[4]



1a, R_1 = OH; R_2 = H; H_R = 5-pro-*R* hydrogen
H_S = 5-pro-*S* hydrogen
b, R_1 = OH; R_2 = pyrophosphate (PP)
c, R_1 = $NHCH(C_6H_5)_2$; R_2 = H; $\overset{\bullet}{C} \equiv {}^{14}C$; $H_S \equiv {}^3H$

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(1) (a) The results described in this paper were presented at the 9th International Congress of Biochemistry, Stockholm, 1973, Abstract 9f6, and in a series of lectures at the Bar-Ilan University, Hebrew University, Jerusalem, University of the Negev, Beer-Sheva, and the Weizmann Institute, Rehovoth, during the tenure by E. Caspi of a visiting professorship at the Bar-Ilan University in Ramat Gan, Israel. (b) Worcester Foundation for Experimental Biology. (c) Postdoctoral Fellow, 1970–1973. (d) Except for the microbial incubation experiment, the work was carried out at the Worcester Foundation for Experimental Biology. (e) Leo Pharmaceutical Products.

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