(d, J = 8.5 Hz, H-1), 4.65 (s, H-5), 3.90 (s, OMe).[12b] The IR, NMR, and mass spectra of **14** were indistinguishable from those of authentic (−)-noroxycodone.

Intramolecular oxidative coupling of the triphenolic benzyltetrahydroisoquinoline **5** with $VOCl_3$ thus provides biomimetic access to the morphinandienone system in significantly improved yields[3,5] and leads to short synthetic pathways to the 2-hydroxy- and 14-hydroxymorphinans (five steps and seven steps from **5**, respectively). We are currently investigating the conversion of **5** to codeine itself, the successful completion of which would represent one of the more efficient total syntheses of codeine and morphine on record.

Acknowledgment. This work was supported by Public Health Service Grant DA 01962 from the National Institute on Drug Abuse. We thank Mallinckrodt, Inc. for providing us with generous samples of authentic codeine and noroxycodone, and Ms. Ingeborga Holak for preparing and carrying out the initial oxidation experiments with triphenol **5**.

Registry No. (±)-**5**, 79043-20-2; (±)-**6**, 79043-21-3; (±)-**7**, 79043-22-4; (±)-**8**, 79043-23-5; (±)-**9**, 79043-24-6; (±)-**10**, 79043-25-7; (±)-**11**, 79043-26-8; (±)-**12**, 79057-55-9; (±)-**13**, 79057-56-0; (±)-**14**, 79043-27-9; 3,5-bis(benzyloxy)-4-methoxybenzeneacetic acid, 54186-42-4; 4-hydroxy-3-methoxyphenethylamine, 554-52-9; 5-chloro-1-phenyltetrazole, 14210-25-4.

Martin A. Schwartz,* Michael F. Zoda
Department of Chemistry
The Florida State University
Tallahassee, Florida 32306
Received June 30, 1981

Carbonylation of Aryllithium Reagents in the Presence of Alkyl Halides: One-Pot Synthesis of Diarylalkylcarbinols and Derivatives[1]

Summary: The carbonylation of ArLi (Ar = Ph, *o*-anisyl) in the presence of alkyl bromides affords diarylalkylcarbinols in good yields. The reaction may be used to obtain alcohols functionalized in the alkyl chain; it can also be adapted to afford substituted tetrahydrofurans.

Sir: Although several mechanistic studies and synthetic applications of alkali aromatic ketyls[2] have been recently published, no further research on the mechanism of the reaction of phenyllithium with carbon monoxide have been reported since the work of one of us with Whitesides et al.[3] At that time, an unattractive feature of the reaction was the formation of several products. Nevertheless, reaction conditions have recently been developed for the preparation of α,α-diphenylacetophenone (94% yield).[4] We now report the high-yield production of diarylalkylcarbinols by this reaction. Besides their synthetic interest, these experiments are mechanistically relevant since they provide experimental evidence for the intermediacy of benzoyllithium: "the most important mechanistic question still unresolved"[3] in 1973.

Table I. Preparation of Diphenylalkylcarbinols[a]

RBr	% yield 3	4	others
n-C_4H_9Br	80	15	
n-C_3H_7Br	74	21	
n-$C_{12}H_{25}Br$	65	17	
i-C_3H_7Br	28	42	15[b]
t-C_4H_9Br	20	38	22[c]

[a] The yields represent the percent conversion. In all cases the compounds were identified by spectroscopic methods and confirmed by independent synthesis. [b] 1,1-Diphenyl-2-methyl-*n*-propyl isopropyl ether. [c] 1,1-Diphenyl-2-methyl-*n*-propyl *tert*-butyl ether and benzhydryl *tert*-butyl ether.

Diphenylalkylcarbinols are easily formed by adding the appropriate alkyl bromide to a solution of phenyllithium (prepared as previously described)[4] in THF at −78 °C and exposing the mixture to carbon monoxide (1 atm pressure). Fast gas absorption occurs, which ceases within 10 min. The reaction mixture is quenched with a saturated solution of ammonium chloride. Extraction with ligroin yield a mixture of products **3** and **4** (eq 1).

$$\underset{\mathbf{1}}{PhLi} + \underset{\mathbf{2}}{RBr} + CO \rightarrow \underset{\mathbf{3}}{Ph_2RCOH} + \underset{\mathbf{4}}{PhC(O)C(OH)HPh} \quad (1)$$

The results obtained for different alkyl bromides are shown in Table I. As can be observed, better yields are given by primary alkyl bromides. The lower yield of R = n-$C_{12}H_{25}$ is probably due to its smaller solubility in THF.[5] The products from secondary and tertiary alkyl bromides contain mixed-ether byproducts. Some of these ethers are difficult to prepare by other methods, and further efforts will be made to find suitable conditions for their formation in higher yields. The reaction described in eq 1 is highly dependent on the ratio of reagents. If the ratio, r = [1]/[2], is bigger than 1/3, more **4** is produced, and, therefore, the yield of **3** diminishes [58% (r = 1), 69% (r = 0.5)]. If the ratio is smaller, the yield of **3** also decreases [48% (r = 0.2)], due to the competing formation of alkylbenzene (Wurtz coupling). More reactive halides such as benzyl, vinyl, or allyl and alkyl iodides react with **1** at −78 °C.

An additional interesting feature of this reaction is the nonreactivity of alkyl chlorides. When alkyl chlorides are used instead of bromides, the same several products are formed as in the reaction of phenyllithium with CO *in the absence* of alkyl chlorides. The mechanistic reason for such differential reactivity of these halides is not clear to us, but it offers an useful way of preparing carbinols functionalized in the alkyl chain. Thus, if the reaction is carried out with R = $CH_2CH_2CH_2Cl$, 4-chloro-1,1-diphenyl-*n*-butanol (**6**) is produced in 48% yield[6] (eq 2). The product may be isolated by column chromatography or distillation at reduced pressure.

$$\underset{\mathbf{1}}{PhLi} + \underset{\mathbf{5}}{BrCH_2CH_2CH_2Cl} + CO \rightarrow \underset{\mathbf{6}}{Ph_2C(OH)(CH_2)_3Cl} + \mathbf{4} \quad (2)$$

The described one-pot preparation of **6** gives better yields than the previously reported several-step synthesis.[7]

(1) Presented in part at the XV Argentine Chemical Symposium, Tucumán, 1980.
(2) (a) C. G. Screttas and M. M. Screttas, *J. Org. Chem.*, **46**, 993 (1981); (b) S. M. Rosenfeld, *Tetrahedron Lett.*, 2655 (1978); (c) J. G. Smith and D. J. Mitchell, *J. Am. Chem. Soc.*, **99**, 5045 (1977); (d) H. W. Wang, G. Levin, and M. Szwarc, *ibid.*, **99**, 5056 (1977); (e) J. F. Garst and C. D. Smith, **ibid.**, **98**, 1520 (1976).
(3) L. S. Trzupek, T. L. Newirth, E. G. Kelly, N. S. Nudelman, and G. M. Whitesides, *J. Am. Chem. Soc.*, **95**, 8118 (1973).
(4) N. S. Nudelman and A. A. Vitale, *Org. Prep. Proced.* **13**, 144 (1981).
(5) In fact, if a 0.5 M solution of PhLi is used, a 50% yield of **3** and 29% yield of **4** are produced. When [PhLi] = 0.3 M (keeping the reagent ratio at 1:3), the yields reported in Table I are obtained.
(6) In this case the best yield is obtained by using a 0.1 M solution of phenyllithium and keeping r = $^1/_3$.

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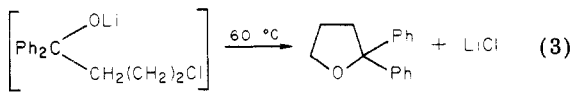
These types of alcohols are intermediates in the preparation of amino alcohols of known pharmacologic activity. Thus, if **6** is allowed to react with piperidine, 1,1-diphenyl-4-piperidylbutanol (an anesthesic) is obtained.[8c] *cis*-2,6-dimethyl-α,α-diphenylpiperidinebutanol (antiarhythmic) may be prepared in a similar way.[9]

Finally, the reaction may be easily extended to produce substituted tetrahydrofurans (eq 3). Thus, the reaction

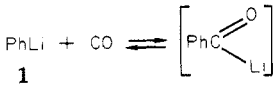


(3)

between **1** and **5** is carried out in the described way, but the reaction mixture is not quenched by water. Instead, the solvent is distilled off by heating at 60 °C. From the residue is obtained **7** in a 45% yield. Presumably, the intramolecular Williamson reaction shown in eq 3 takes place. This one-pot preparation of **7** is shorter than Hamaguchi's[10] and of similar yield (39%).

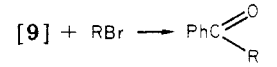
In an effort to establish the extent of the proposed method, the reaction of *o*-anisyllithium (**8**) plus *n*-butyl bromide with CO was also studied. The only reaction product is di-*o*-anisylbutylcarbinol (62% yield), containing some recovered anisole. It had been previously found that the reaction between **8** and CO is incomplete[11] and a different reaction mechanism was proposed.[12]

As mentioned above, the reaction of eq 1 has additional mechanistic relevance. A reasonable mechanism for the formation of **3** involves the intermediacy of *benzoyllithium* (**9**). An alternative pathway is the initial formation of the



(4)

1 9



(5)

10

$$10 + 1 \rightarrow 3 \quad (6)$$

benzophenone dianion (**11**) and its subsequent reaction with **2**. However, **11** does not produce **3** under the described reaction conditions; therefore, it can be reasonably excluded as an intermediate. This result, together with the complete absence of benzophenone among the reaction products, must be considered strong evidence that **9** is a major intermediate in the reaction of **1** with CO.[13]

This new reaction as well as other previously reported carbonylations of lithium amides[14] demonstrates the synthetic potential of the uncatalyzed carbonylation of organolithium reagents and suggests additional ways in which free carbon monoxide might be used in synthesis.[15]

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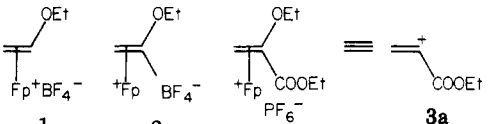
Registry No. 1, 591-51-5; 2 (R = *n*-C_4H_9), 109-65-9; 2 (R = *n*-C_3H_7), 106-94-5; 2 (R = *n*-$C_{12}H_{25}$), 143-15-7; 2 (R = *i*-C_3H_7), 75-26-3; 2 (R = *t*-C_4H_9), 507-19-7; 3 (R = *n*-C_4H_9), 5384-63-4; 3 (R = *n*-C_3H_7, 5331-17-9; 3 (R = *n*-$C_{12}H_{25}$), 79044-19-2; 3 (R = *i*-C_6H_7), 37951-09-0; 3 (R = *t*-C_4H_9), 1657-60-9; 4, 119-53-9; 5, 109-70-6; 6, 59855-97-9; 7, 887-15-0; 8, 31600-86-9; di-*o*-anisylbutylcarbinol, 79044-20-5; 1,1-diphenyl-2-methyl-*n*-propyl isopropyl ether, 79044-21-6; 1,1-diphenyl-2-methyl-*n*-propyl *tert*-butyl ether, 79044-22-7; benzhydryl *tert*-butyl ether, 28567-35-3.

N. Sbarbati Nudelman,* Arturo A. Vitale
Depto. de Química Orgánica
Facultad de Ciencias Exactas
Universidad de Buenos Aires
Pab. II, P. 3, Ciudad Universitaria
1428 Buenos Aires, Argentina
Received June 30, 1981

α-Acrylic Ester Cation Equivalent. Application in the Synthesis of α-Methylene γ-Lactones

Summary: The complex cation **3** serves as an α-acrylic ester cation in the conversion of cyclohexanone lithium enolate to the *cis*- and *trans*-α-methylene γ-lactones **10** and **11**.

Sir: We recently described the use of Fp–vinyl ether complexes **1** and **2** (Fp = $C_5H_5Fe(CO)_2$) as vinyl cation equivalents for vinylation[1] and isopropenylation[2] of cyclohexanone enolates. In order to further extend the synthetic utility of such complexes, we have sought to prepare further functionalized members of this class. One such substance (**3**) would, by analogy with the reactions



1 2 3 3a

of **1** and **2**, be expected to behave as an α-acrylic ester cation equivalent (**3a**). We now report the preparation of **3** and its use in the conversion of cyclohexanone to the α-methylene γ-lactones **10** and **11**. The wide occurrence of this functionality among biologically active terpenoid materials has made it an important synthetic objective and led to the development of a number of routes for its construction.[3] However, most of these involve sequences which utilize a preformed γ-lactone as the starting material.[3b]

Complex **3** is readily prepared in two steps from ethyl α-bromopyruvate diethyl ketal.[4] On metalation of this

(7) A total yield of 30% of **6** is obtained by the successive conversion of **5** to the cyano derivative[8a] and to the ethyl γ-chlorobutirate[8b] and its subsequent reaction with PhLi.[8c]

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(4) IR (CH_2Cl_2) 1750 cm^{-1}; NMR (CCl_4) δ 4.27 (q, 2, $COOCH_2Me$), 3.56 (m, 4, OCH_2Me), 3.56 (s, 2, CH_2Br), 1.30 (m, CH_3).

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