J. Org. Chem. **1985**, *50*, 1985–1987

Operations were performed as described previously.[13] The analytical scattering factors of Cromer and Waber were used;[14a] real and imaginary components of anomalous scattering for the Br and Cl atoms were included in the calculations.[14b] The hydroxyl hydrogen atoms can not be successfully refined. All other hydrogen atoms were put in calculated positions, (r_{C-H} = 0.95 Å). Details of the structure analysis and solution, in outline form, are presented in Table I.

Acknowledgment. We are grateful to the National Institutes of Health for financial support.

Registry No. **1**, 72877-50-0; **3**, 49805-30-3; **4**, 78805-80-8; **5**, 95936-41-7; **6**, 95936-42-8; **8**, 95936-43-9; **9**, 95936-44-0; benzyl bromide, 100-39-0.

Supplementary Material Available: Tables of (i) atomic coordinates, (ii) bond lengths and angles, (iii) anisotropic thermal parameters for Br and Cl atoms and isotropic thermal parameters for O, N, and C atoms, (iv) hydrogen atom positions, and (v) torsion angles (5 pages). Ordering information is given on any current masthead page. Observed and calculated structure factors are available from the authors.

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(13) Foxman, B. M. *Inorg. Chem.* **1978**, *17*, 1932. Foxman, B. M.; Mazurek, H. *Ibid.* **1979**, *18*, 113.

(14) "International Tables for X-Ray Crystallography"; Kynoch Press: Birmingham, England, 1974; Vol. IV: (a) pp 99–101, (b) pp 148–150.

Preparation of α-Oxo Amidines by the Direct Nucleophilic Acylation of Carbodiimides

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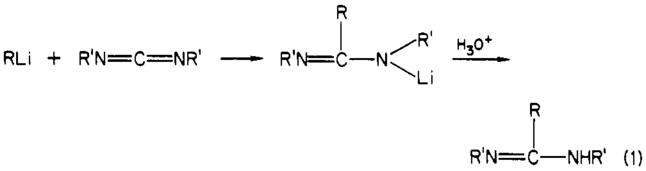
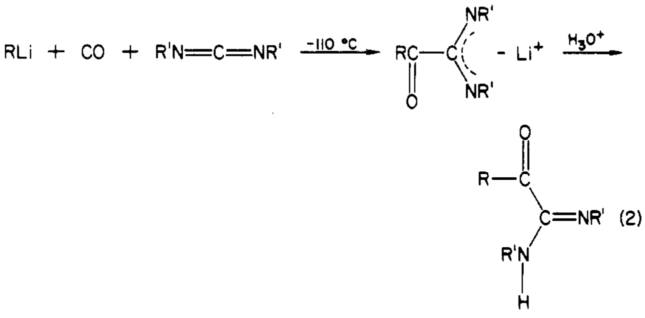
Results and Discussion

As J. Pornet and L. Miginiac have shown,[1] the alkylation and arylation of carbodiimides can be effected with Grignard and organolithium reagents to give amidines, often in good yield (eq 1). During the course of our studies of direct nucleophilic acylation of organic electrophiles with in situ generated acyllithium reagents,[2] we have studied the nucleophilic acylation of various heterocumulenes: carbon disulfide and carbonyl sulfide,[3] isocyanates, and isothiocyanates.[4] In view of the known reactivity of carbodiimides toward organometallic reagents,[1] it was of interest to see if they would react with acyllithium reagents as well. The expected products α-oxo amidines, R′C(O)-C(NR)NHR, could be of potential interest to the synthetic organic chemist.



$$\mathrm{RLi} + \mathrm{R'N{=}C{=}NR'} \longrightarrow \mathrm{R'N{=}C(R){-}N(R')Li} \xrightarrow{\mathrm{H_3O^+}} \mathrm{R'N{=}C(R){-}NHR'} \quad (1)$$

We have found that carbodiimides may be acylated by our procedure. In such reactions a 4:4:1 tetrahydrofuran/diethyl ether/pentane solvent system containing the carbodiimide is cooled to −110 °C under a nitrogen atmosphere. This solution is then saturated with carbon monoxide (at atmospheric pressure), and, while the CO stream is continued, the alkyllithium reagent solution (t- or sec-C_4H_9Li) is added very slowly at a constant rate. Under these conditions, the alkyllithium reacts with CO, not with the carbodiimide. The acyllithium reagent which is formed adds to a C=N bond of the carbodiimide. After hydrolysis with saturated aqueous ammonium chloride, the respective α-oxo amidine is produced in good yield (eq 2).



$$\mathrm{RLi} + \mathrm{CO} + \mathrm{R'N{=}C{=}NR'} \xrightarrow{-110\ ^\circ\mathrm{C}} \mathrm{RC({=}O){-}C(NR')_2^-}\ \mathrm{Li^+} \xrightarrow{\mathrm{H_3O^+}} \mathrm{RC({=}O){-}C({=}NR'){-}N(R')H} \quad (2)$$

1

These products are not very stable thermally. Satisfactory elemental analyses (±0.4%, C, H, N) could be obtained only with difficulty. When they are desired as intermediates in a synthesis, they should be used soon after they have been prepared. Their infrared spectra are characterized by bands at 1697–1700 ($\nu_{C=O}$) and 1635–1640 cm^{-1} ($\nu_{C=N}$). Their ^1H NMR spectra were consistent with the structures given.

Table I presents results obtained when *tert*- and *sec*-butyllithium were the organolithium reagents used. In contrast to these quite satisfactory results, such reactions were not successful with *n*-butyllithium. This reagent, we know, serves well in the nucleophilic acylation of other organic electrophiles,[2] hence it does react with CO under the reaction conditions used. However, the n-$C_4H_9C(O)Li$ reagent apparently reacts with dialkyl carbodiimides only very slowly at −110 °C, if at all, and in these reactions the carbodiimide was recovered in high yield. No major alternate product was formed aside from the hydrolysis product of the formal acyllithium dimer, n-$C_4H_9C(O)CH(OH)C_4H_9$-n. The lack of reaction was confirmed in an experiment in which the organic electrophile to which the n-C_4H_9Li/CO reagent was added was a 1:1 mixture of di-*n*-propylcarbodiimide and methyl isobutyrate. The only product formed (60% yield) was the α-diketone derived from nucleophilic acylation of the ester.

Direct nucleophilic acylations, using the Me_3CLi/CO and MeEtCHLi/CO in situ systems, of di-*tert*-butylcarbodiimide was unsuccessful and with diisopropylcarbodiimide only very low (<10%) product yields were obtained under our reaction conditions. Presumably adverse steric factors are operative when bulky groups are present both in the organolithium reagent and the carbodiimide.

Experimental Section

General Comments. The carbodiimides were purchased or were prepared from the corresponding thioureas by the method of Schmidt et al.[5] The organolithium reagents were purchased from ALFA-Thiokol/Ventron. The solvents were rigorously dried by using standard procedures.

IR spectra were recorded by using a Perkin-Elmer 1430 infrared spectrophotometer and NMR spectra with a JEOL FX-90X 90-MHz instrument.

Reactions of sec-C_4H_9Li/CO and t-C_4H_9Li/CO with Dialkylcarbodiimides. The reaction of the *sec*-BuLi/CO reagent

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(1) Pornet, J.; Miginiac, L. *Bull. Soc. Chim. Fr.* **1974**, 994.

(2) For a review of our early results see: Seyferth, D.; Weinstein, R. M.; Wang, W.-L.; Hui, R. C.; Archer, C. M. *Isr. J. Chem.* **1984**, *24*, 167.

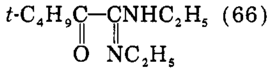
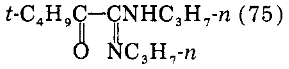
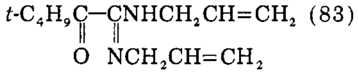
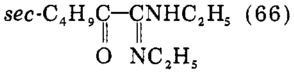
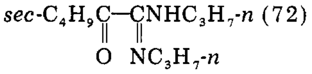
(3) Seyferth, D.; Hui, R. C. *Tetrahedron Lett.* **1984**, *25*, 2623.

(4) Seyferth, D.; Hui, R. C. *Tetrahedron Lett.* **1984**, *25*, 5251.

(5) Schmidt, E.; Hitzler, F.; Lahde, E. *Ber. Deutsch. Chem. Ges.* **1938**, *71*, 1933.

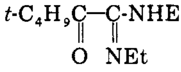
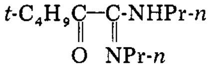
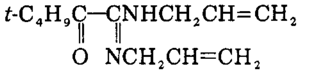
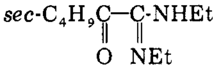
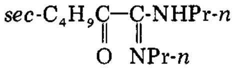
0022-3263/85/1950-1985$01.50/0 © 1985 American Chemical Society

Table I. Direct Nucleophilic Acylation of Carbodiimides

R in RLi (mmol)	R′ in R′N=C=NR′ (mmol)	product (% yield)
$t\text{-}C_4H_9$ (9.15)[a]	C_2H_5 (9.18)	 $t\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NC_2H_5}}{C}NHC_2H_5$ (66)
$t\text{-}C_4H_9$ (8.40)[a]	$n\text{-}C_3H_7$ (8.57)	 $t\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NC_3H_7\text{-}n}}{C}NHC_3H_7\text{-}n$ (75)
$t\text{-}C_4H_9$ (8.19)[a]	$CH_2CH{=}CH$ (8.20)	 $t\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NCH_2CH=CH_2}}{C}NHCH_2CH{=}CH_2$ (83)
$sec\text{-}C_4H_9$ (9.0)[b]	C_2H_5 (9.10)	 $sec\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NC_2H_5}}{C}NHC_2H_5$ (66)
$sec\text{-}C_4H_9$ (8.53)[b]	$n\text{-}C_3H_7$ (8.60)	 $sec\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NC_3H_7\text{-}n}}{C}NHC_3H_7\text{-}n$ (72)

[a] 2.10 N in pentane; addition rate 0.24 mL/min. [b] 1.55 N in pentane; addition rate 0.35 mL/min.

Table II. α-Oxo Amidines

compound	anal. found (calcd) C	H	N	IR, cm^{-1} $\nu_{C=O}$	$\nu_{C=N}$	^{1}H NMR (90 MHz, CDCl$_3$), δ
 $t\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NEt}}{C}\text{-NHEt}$	65.21 (65.18)	10.92 (10.94)	15.15 (15.20)	1697	1640	1.10–1.21 (m, 15 H, 2 CH_2CH_3, CMe_3), 2.90–3.50 (m, 4 H, NCH_2CH_3, $NHCH_2CH_3$), 4.5 (br s, 1 H, NH)
 $t\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NPr\text{-}n}}{C}\text{-NHPr-}n$	68.16 (67.88)	11.40 (11.39)	13.19 (13.19)	1700	1640	0.82–0.98 (t, J = 7.0 Hz, 6 H, 2 CH_2CH_3), 1.23 (s, 9 H, CMe_3), 1.3–1.7 (m, 4 H, $NCH_2CH_2CH_3$, $NHCH_2CH_2CH_3$), 2.8–3.0 (m, 4 H, $NCH_2CH_2CH_3$, $NHCH_2CH_2CH_3$), 3.9 (1 H, br s, NH)
 $t\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NCH_2CH=CH_2}}{C}NHCH_2CH{=}CH_2$	68.47 (69.19)	9.65 (9.68)	13.61 (13.45)	1700	1640	1.21 (s, 9 H, CMe_3), 3.6–3.7 (m, 4 H, NCH_2, $NHCH_2$, $NHCH_2$), 4.5 (1 H, br s, NH), 5.0–5.2 (m, 4 H, 2 $=CH_2$), 5.9 (m, 2 H, 2 $CH_2CH{=}CH_2$)
 $sec\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NEt}}{C}\text{-NHEt}$	65.22 (65.18)	10.87 (10.94)	15.22 (15.20)	1700	1635	0.8–1.6 (m, 14 H, $(C_2H_5)(CH_3)$-(CH)C(O), $NHCH_2CH_3$, NCH_2CH_3), 3.1–3.4 (s m, 5 H, (CH)C(O), NCH_2, $NHCH_2$), 4.4 (br s, 1 H, NH)
 $sec\text{-}C_4H_9\underset{\substack{\| \\ O}}{C}-\underset{\substack{\| \\ NPr\text{-}n}}{C}\text{-NHPr-}n$	67.63 (67.88)	11.38 (11.39)	13.86 (13.19)	1700	1640	0.80–1.7 (m, 18 H, (C_2H_5)-(CH_3)(CH)C(O), 2 $CH_2CH_2CH_3$), 3.1–3.4 (m, 5 H, (CH)C(O), NCH_2, $NHCH_2$), 5.2 (br s, 1 H, NH)

with di-*n*-propylcarbodiimide is described in order to illustrate the procedure used.

A 500-mL, oven-dried three-necked, round-bottomed flask was fitted with a mechanical stirring assembly, a Claisen adapter that held a gas outlet tube and a low temperature (pentane) thermometer, and, in the third neck, a rubber septum that held a coarse-fritted gas dispersion tube and a syringe needle. The latter was connected via polyethylene tubing to an Orion Research Inc. Model 341 syringe pump. The flask was flushed out with dry nitrogen and charged with 133 mL each of dry tetrahydrofuran and diethyl ether, 33 mL of dry pentane, and 1.08 g (8.6 mmol) of di-*n*-propylcarbodiimide. The solution was cooled to −110 °C (liquid-nitrogen-filled Dewar flask that could be raised or lowered by means of a Lab-Jack), and then a stream of carbon monoxide (directly from the gas cylinder, without further purification) was bubbled through it for 15 min. Subsequently, while the CO stream was continued, *sec*-butyllithium (5.5 mL of a 1.55 N solution in pentane) was added at a rate of 0.35 mL/min by means of the syringe pump. A pale, yellow-green solution was formed. This solution was kept at −110 ± 5 °C for 2 h and then slowly warmed to room temperature; during these operations the CO stream was continued. Subsequently, 75 mL of saturated ammonium chloride solution was added to the reaction mixture. The aqueous layer was separated and extracted with diethyl ether. The combined organic phases were dried over anhydrous $MgSO_4$. The solvents then were removed by distillation at 15–20 mmHg. The liquid residue was analyzed by GLC (6 ft × $^1/_4$ in. SE-30 silicone rubber gum on Chromosorb P, 100–275 °C column temperature, programmed heating 6 °C/min; *n*-decane internal standard) to show the presence of one main product in 72% yield (6.20 mmol). This product was identified as $C_2H_5(CH_3)CHC(O)C(NHPr\text{-}n)({=}NPr\text{-}n)$ on the basis of its analysis and IR and proton NMR spectra (Table II).

All other experiments listed in Table I were carried out by using this procedure. This procedure was not successful when applied to reactions of the $n\text{-}C_4H_9Li/CO$ reagent with EtN=C=NEt or *n*-PrN=C=NPr-*n*. In each case there was a quantitative recovery of the carbodiimide on workup. Reactions at −78 °C were equally unsuccessful.

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Science Foundation for support of this work.

Registry No. *t*-BuC(O)C(NHEt)=NEt, 96110-18-8; *t*-BuC(O)C(NHPr)=NPr, 96110-19-9; *t*-BuC(O)C(NHCH$_2$CH=CH$_2$)=NCH$_2$CH=CH$_2$, 96110-20-2; *sec*-BuC(O)C(NHEt)=NHEt,

96110-21-3; *sec*-BuC(O)C(NHPr)=NHPr, 96110-22-4; EtN=C=NEt, 693-29-8; PrN=C=NPr, 821-79-4; CH_2=$CHCH_2N$=C=NCH_2CH=CH_2, 693-50-5; *t*-BuLi, 594-19-4; *sec*-BuLi, 598-30-1; CO, 630-08-0.

Ortho Allylation of Benzyl Alcohols

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Received October 2, 1984

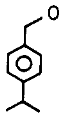
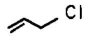
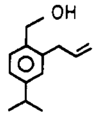
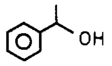
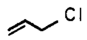
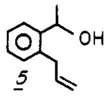
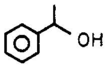
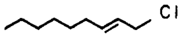
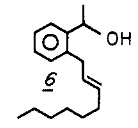
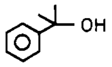
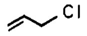
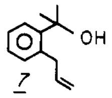
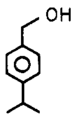
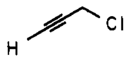
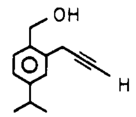
A variety of different activating groups[4,5] have been used to direct ortho lithiation of an aromatic ring. While methylation, silylation, and hydroxyalkylation of the resultant aryllithium species are straightforward, alkylation is usually not. We report herein a brief study that has led to an efficient procedure for the ortho allylation of benzyl alcohols.

This investigation was motivated by our need to attach a long-chain alkyl moiety ortho to a functional group that could become a methyl ketone. It was already known[6] that benzyl alcohols are readily ortho lithiated. While efficiency of ortho lithiation could be demonstrated in our hands by quantitative methylation, attempted alkylation with longer chain alkylating agents (chlorides, bromides, iodides, tosylates) gave low conversion.[7]

After some experimentation in other directions, we essayed formation of a mixed cuprate,[8] using the benzylic lithium alkoxide as one of the ligands on copper. While we have no evidence that such a species in fact is formed, we have found that addition of 0.5 mol equivalent of $Cu_2(CN)_2$ to the lithiated benzyl alcohol followed by an allylic halide effects quantitative (TLC) conversion to the monoallylated product (Table I).

The procedure has limitations. The product allylbenzenes are exceptionally prone toward autoxidation, especially in the presence of Cu(II) during aqueous workup.[9] The acetylenic product from alkylation with propargyl bromide partially isomerizes to the allene during isolation. Nevertheless, this procedure, proceeding directly from commercially available benzyl alcohols, could be the method of choice for the preparation of many simple alkylated benzene derivatives.[10]

Table I

starting alcohol	alkylating agent	product	% yield^a
 1		 4	67
 2		 5	87
 2		 6	60
 3		 7	53
 1		 8	56^b

^{a} Yield of material isolated by column chromatography and fully characterized. ^{b} A 3:1 mixture of acetylene to allene was isolated.

Experimental Section

General Procedures. ^1H and ^{13}C NMR spectra were determined on a Bruker WM-250 spectrometer as solutions in $CDCl_3$. Chemical shifts are reported in δ units downfield from the internal reference tetramethylsilane. The couplings (J) are in hertz (Hz). Carbon multiplicities were assigned by a J-modulated spin echo technique. The infrared (IR) spectra were determined on a Perkin-Elmer 180 spectrometer as solutions in CCl_4 and are reported in reciprocal centimeters (cm^{-1}). Mass spectra (MS) were taken at 70 eV on a DuPont 21-492B mass spectrometer and are reported as mass per unit charge (m/z), with intensities (as a percentage of the peak of greatest ion current having $m/z \geq 100$) in parentheses. Organic chemicals were purchased from Aldrich Chemical Co. *n*-Butyllithium was obtained from Alfa Inorganics and was titrated before use. Cuprous cyanide was azeotropically dried with toluene. The solvent mixtures used for chromatography (e.g., 5% ethyl acetate/hexane) are volume/volume mixtures. R_f values indicated refer to thin-layer chromatography on Analtech 2.5 × 10 cm, 250-μm analytical plates coated with silica gel GF. Column chromatography was carried out with TLC-mesh silica

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[2] Undergraduate Research Participant, University of Delaware.

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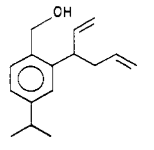
(4) For a detailed review of aromatic metalation, see: Gschwend, H. W.; Rodriguez, H. R. *Org. React. (N.Y.)* **1979**, *26*, 1.

(5) For more recent developments in aromatic metalation, see: Mills, R. J.; Snieckus, V. *J. Org. Chem.* **1984**, *49*, 737 and references cited therein.

(6) Meyer, N.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 521.

(7) Attempted alkylation with allyl bromide gave partial conversion to what was apparently (^1H NMR) i, the product of allylation followed by proton transfer.



i

(8) Other investigators have also noted the beneficial effects of Cu(I) on some such alkylations: (a) Ziegler, F. E.; Fowler, K. W. *J. Org. Chem.* **1976**, *41*, 1564. (b) Comins, D. L.; Brown, J. D.; Mantlo, N. B. *Tetrahedron Lett.* **1982**, *23*, 3979.

(9) Use of a mildly reductive workup might minimize this autoxidation.

(10) For an alternative synthetic approach to ortho-allylated benzyl alcohols, see: Semmelhack, M. F.; Zask, A. *J. Am. Chem. Soc.* **1983**, *105*, 2034.

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