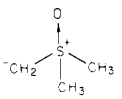
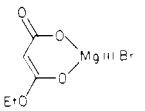
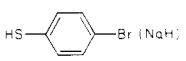
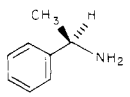
Table I. Treatment of 5 or 6 with Some Nucleophiles

nucleophiles	product[a]	mp, °C	$[\alpha]^{25}_D$, deg ($CHCl_3$)	% yield[b]
	8a[c]	110-111	-19.08 (c 1.09)	94.0
	9[c]	110-111	+19.11 (c 1.10)	94.4
	8b[d]	oil	+5.90 (c 2.03)	79.1
	8c[c]	oil	-9.95 (c 1.19)	98.7
	8d[c]	oil	+57.66 (c 1.07)	93.3

[a] Satisfactory spectral and analytical data were obtained for all products. [b] Isolated yield. [c] For the experimental procedure see ref 1. [d] To an in situ reagent[6] obtained from isopropylmagnesium bromide (5.1 mmol) and ethyl hydrogen malonate (2.5 mmol) in THF (5 mL) was added compound 5 (1 mmol) in THF (5 mL) at 0 °C, and then the mixture was stirred at room temperature overnight.[7]

It was confirmed by the ^1H NMR (100 MHz) analysis of products **8a-d** that no epimerization occurred at all during the transformation from **4** into **8**. On the ^1H NMR chart of the epimerized product, **10** or **11**, prepared under basic conditions at 50 °C (Scheme IV), signals (δ 1.08, 1.10, J = 7 Hz each) assignable to the methyl protons at C-4 were observed as two doublets. On the other hand, the ^1H NMR spectra of **8** and **12** formed under mild basic conditions showed a sharp doublet signal due to the methyl protons at C-4.

Thus, these products **8a-d** and **9** should be useful as "bifunctional chiral synthons"[8] for total synthesis of the optically active Prelog-Djerassi lactonic acid,[3b,9] methynolide,[10] 6-deoxyerythronolide B,[11] picromycin,[12] narbomycin,[13] and monensin.[14]

So far, the highly selective transformation of enantiotopic groups of the *meso*-2,4-dimethylglutaric acid derivative was performed exclusively by a special enzyme or a few microorganisms.[8] Our novel findings provide the first example of a highly selective chemical procedure of this type which is also practical.

Registry No. *meso*-**1**, 3891-70-1; (±)-**2**, 3891-69-8; *meso*-**3**, 4295-92-5; (-)-**4**, 83966-50-1; (-)-**5**, 83966-51-2; (-)-**6**, 84024-99-7; **8a**, 83966-55-6; **8b**, 83966-56-7; **8c**, 83983-94-2; **8d**, 83966-57-8; **9**, 83966-52-3; **10**, 83966-58-9; **11**, 83966-59-0; **12**, 83966-60-3; 4-(*R*)-MCTT, 80963-80-0; piperidine, 110-89-4; dimethylsulfoxonium methylide, 5367-24-8; bromomagnesium ethyl hydrogen malonate, 83966-54-5; 4-bromobenzenethiol, 106-53-6; (*R*)-α-methylbenzylamine, 3886-69-9; isopropylmagnesium bromide, 920-39-8; ethyl hydrogen malonate, 1071-46-1; (±)-(*R**,*S**)-2,4-dimethyl-5-oxa-5-piperidinylpentanoic acid, 83966-53-4.

Supplementary Material Available: Crystallographic details, tables of atomic positional and thermal parameters, and perspective views for **5** and **6** (10 pages). Ordering information is given on any current masthead page.

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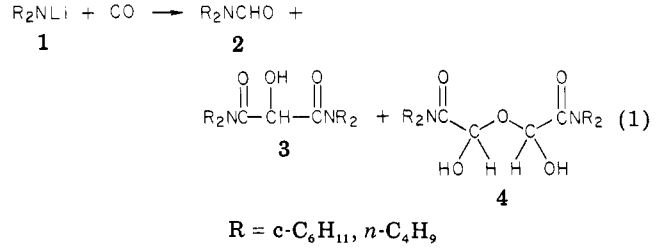
Insertion of Carbon Monoxide into Lithium-Nitrogen Bonds. One-Pot Synthesis of Dialkylformamides and Dialkylglyoxylamides[1]

Summary: Lithium dialkylamides react with CO to afford dialkylformamides **2**, tetralkylhydroxymalonamides **3**, and dialkylglyoxylamides **4**. Reaction conditions are described to produce **2** or **4** in good yields.

Sir: Continuing our investigations[2-4] on the carbon monoxide insertion into organolithium reagents and seeking for new modes of CO activation, we now report the usefulness of the reaction of lithium dialkylamides (**1**)[5] with CO to produce dialkylformamides **2** or dialkylglyoxylamides (hemihydrate) **4** in good yields (eq 1). The other reaction product which is obtained in varying yields is the tetralkylhydroxymalonamide **3**.



R = c-C_6H_{11}, *n*-C_4H_9

Previous studies of insertion of CO into N-Li bonds are scarce[6-8] and report contradictory results.[8] A common

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Table I. Reaction of Lithium Dicyclohexylamide with Carbon Monoxide (1 atm) in THF[a,b]

temp, °C	$t_{1/2}$,[c] min	% yield 2	3	4
-95		57.0	4.0	0.5
-78	1.2	21.0	28.0	34.5
0	3.8	24.0		41.5
20[d]	1.0	30.5		0.5
50[d]	1.4	44.5	1.0	

[a] The yields represent percent conversion. [b] *N,N*-Dicyclohexylhydroxyacetamide is produced in varying yields. [c] Measured by CO absorption. [d] *N,N,N',N'*-Tetracyclohexyloxalamide is also found.

Table II. Reaction of Lithium Dicyclohexylamide with Carbon Monoxide (1 atm) at 0 °C[a]

solvent	$t_{1/2}$,[b] min	% yield 2	3	4
hexane	19.5	24.5	45.0	10.0
hexane/THF (4.5:0.5)	2.7	29.0	50.5	4.0
hexane/THF (1:1)	1.9	39.5	30.0	18.0
THF[c]	3.8	24.0		41.5
THF + LiCl[d] (14 mmol)	2.3	33.8	0.5	33.1
THF + LiBr (7 mmol)	13.4	95.8		4.2
THF + cyclohexylamine (5.5 mmol)	5.8	68.5		27.5
THF/Dabco (3.5 mmol)	3.4	58.5		32.5
THF/HMPT[e] (4:1)	3.5	16.0	15.0	51.5
THF/HMPT (1:1)	4.7	7.0	1.0	85.5

[a] The yields represent percent conversion. [b] Measured by CO absorption. *N,N*-Dicyclohexylhydroxyacetamide is is also obtained in varying yields: [c] 20%, [d] 28%, and [e] 12%; in all the other cases <7%.

feature of those papers is the limited synthetic utility of the reaction due to the difficulty in obtaining suitable yields of the dialkylformamides because of the competing secondary reaction of the intermediate lithium carbamoyl.

We have investigated the reaction in detail and found conditions which give **2** or **4** in satisfactory yields. Table I shows a typical, irregular temperature effect on the reaction of lithium dicyclohexylamide. Since no obvious trend was observed, 0 °C was chosen as the most convenient working temperature. Table II gathers the solvent effects on the same reaction. It can be observed that a higher yield of **2** is obtained in THF with some LiBr added. It is evident that **2** arises from hydrolysis of the lithium carbamoyl **5** formed by insertion of CO into the N–Li bond (eq 2). The synthetic utility of **5** has been shown recently[9]

$$R_2NLi + CO \longrightarrow \left[R_2NC(=O)Li\right] \quad (2)$$

5

through its reaction with a variety of electrophiles. The present method of preparation is simpler than others previously reported,[9-11] and the yields are comparable or better.

Nevertheless, more interesting is the fact that the more difficult to prepare dialkylglyoxylamides **4** can be produced in good yield by a one-pot procedure.[12] Table II shows that, in the case of lithium dicyclohexylamide, 85.5% is converted to **4** by reaction with CO in THF/HMPT. For R = *n*-C_4H_9 a similar solvent study revealed that among the pure solvents THF gives the best results, and a systematic study of THF/HMPT mixtures shows again that the yield of **4** (R = *n*-C_4H_9) increases with the HMPT content in the solvent to reach almost a quantitative conversion in 1:1 THF/HMPT.

When **5** is generated by other methods[9-11] that do not introduce CO, neither **3** nor **4** is found after hydrolysis even after the reaction mixtures are **4** to stand for several hours. This suggests that the anionic precursors of those compounds are formed by a further addition of CO to **5** (eq 3). The fact that the yield of **4** increases from -95 to 0

$$[5] + CO \longrightarrow \left[R_2NC(OLi)=C=O \rightleftharpoons R_2NC(=O)-C(=O)Li\right] \quad (3)$$

6

$$[6] + [5] \longrightarrow [7] \xrightarrow{H_2O} \mathbf{3} \quad (4)$$

$$2[6] \xrightarrow{H_2O} \mathbf{4} \quad (5)$$

°C is likely due to the reaction of **5** with CO to give a second adduct, **6**, which partly adds more **5** to give the dianion of **3** (**7**, eq 4) or hydrolyzes to **4** (eq 5).

Other lithium amides are being studied to define the scope of this potentially most useful process (e.g., lithium morpholyl and di-*n*-pentylamides afford an unoptimized conversion to **4** greater than 80% in a 1:1 THF/HMPT solution).

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Registry No. **1** (R = c-C_6H_{11}), 4111-55-1; **1** (R = *n*-C_4H_9), 25440-26-0; **2** (R = c-C_6H_{11}), 22699-63-4; **2** (R = *n*-C_4H_9), 761-65-9; **3** (R = c-C_6H_{11}), 82024-47-3; **3** (R = *n*-C_4H_9), 79251-71-1; **4** (R = c-C_6H_{11}), 83862-72-0; **4** (R = *n*-C_4H_9), 83862-73-1; CO, 630-08-0.

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(12) Standard procedure: A stirred solution of 0.75 g of **1** (R = c-C_6H_{11})[5] dissolved in 2.0 mL of THF and 2.0 mL of HMPT at 0 °C was exposed to CO (ca. 900 mmHg). When gas absorption had ceased (ca. 15 min), the remaining CO was evacuated and the reaction mixture hydrolyzed with 30 mL of water. A standard workup[3] afforded 670 mg of **4**, mp 115-117 °C (hexane). **4** was characterized by X-ray diffraction studies[13] and IR, NMR, and mass spectra.
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Ring Formation by Base-Dependent Isomerizations of Epoxybenzyl Ethers

Summary: Selective deprotonation of benzyl ethers with lithio-2,4-dimethylpiperidide allows for intramolecular S_N2 attack at a proximal epoxide, generating oxygen-containing heterocycles. Circumstances for regioselective isomerizations of oxiranes to allylic alcohols are discussed.

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