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).

Acknowledgment. We are deeply thankful to the National Research Council of Argentina (CONICET), to the Science and Technology Secretariat (SUBCYT), and to the Organization of American States (OAS) for financial support. UMYMFOR (FCEN-CONICET) is acknowledged for the spectroscopic determinations.

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.

(7) Jutzi, P.; Schroeder, F. W. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 339.
(8) Rautenstrauch, V.; Joyeaux, M. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 83.
(9) Fletcher, A. S.; Smith, K.; Swaminathan, K. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1881.
(10) Schollkopf, V. S.; Beckhaus, H. *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 293. Banhidai, B.; Schollkopf, V. S. *Ibid.* **1973**, *12*, 836.
(11) Tsuda, T.; Miwa, M.; Saegusa, T. *J. Org. Chem.* **1979**, *44*, 3734.

(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.
(13) Nudelman, N. S., Pérez, D.; Galloy, J.; Watson, W. H., submitted for publication in *Acta Crystallogr.*

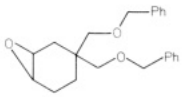
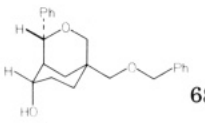
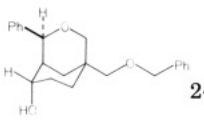
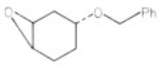
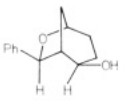
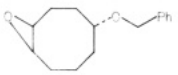
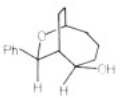
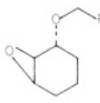
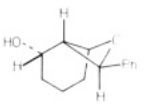
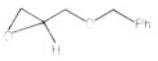
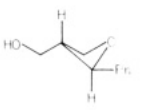
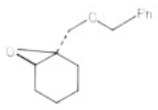
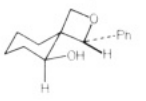
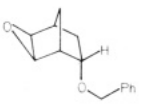
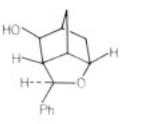
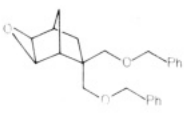
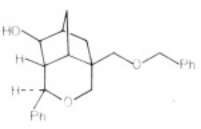
N. Sbarbati Nudelman,* Daniel Pérez
Depto. de Quimica Orgánica
Facultad de Ciencias Exactas y Naturales
Universidad de Buenos Aires
Pab. II, P. 3, Ciudad Universitaria
1428 Buenos Aires, Argentina
Received July 7, 1982

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.

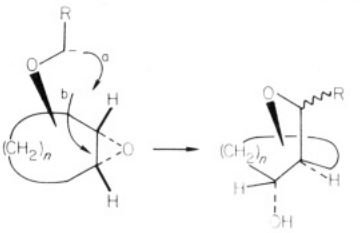
0022-3263/83/1948-0134$01.50/0

Table I

entry	epoxides	rctn times, h	products	% yield
1		4		94
				68%
				24%
2		2		95
3		12		71
4		2		85
5		2		71
6		2		72
7		7		80
8		48		50

Sir: The increasing importance of the oxirane ring as a key element in development of new methodologies and complex synthetic strategies offers recognition of the degree of regio- and stereocontrol in reactions of this functionality as well as its ease of preparation.[1,2] Considerable attention is focused on the isomerization of epoxides to allylic alcohols,[3] and, in fact, the reaction of oxiranes with strong bases constitutes a well-known method for this transformation.[4] Our efforts have studied the opportunity for a directed, intramolecular opening of the oxirane ring by an appropriately positioned, highly reactive carbanion generated by strong bases, with formation of a new carbon–carbon bond and syntheses of oxygen-containing heterocycles.

A generalized scheme is illustrated in eq 1, and results



(1)

are compiled in Table I.[5] Significant geometrical constraints imposed by the oxirane ring demonstrate rigorous requirements of nucleophilic disposition with backside collinear displacement. These considerations were recognized by Eschenmoser[6] and further explored in elegant studies by Stork, featuring epoxynitrile cyclizations.[7,8] A particular concern in our work focused on competing opportunities for isomerization to allylic alcohols in a series of cis-disubstituted cycloalkane epoxides, a process that also features stringent geometrical requirements of a syn β elimination from a coordination site on the more hindered side of the oxirane.[9] However, a number of side reactions resulting from α elimination and formation of carbenoid intermediates are also well-known for epoxides of this type.[10]

For our study, a number of oxiranes bearing a benzyloxy substituent elsewhere in the molecule were obtained via oxidation of their corresponding alkenes.[11] Whenever mixtures of *cis*- and *trans*-epoxide isomers were encountered, these were separated and individually submitted to reaction conditions with strong bases. Two sets of conditions were employed. The first utilized lithio-2,6-dimethylpiperidide (3 equiv) in dry tetrahydrofuran and hexamethylphosphoric triamide[12] (HMPA, 3 equiv) with introduction of epoxide at −78 °C (stirring for 30 min), warming to 22 °C, and continued stirring at room temperature until reactions were complete. In the second case, a 0.5 M stock solution of lithium diethylamide was prepared in 50% ether–benzene.[13] Aliquots of amide (3 equiv) were added to a toluene solution of the epoxide-containing HMPA (3 equiv)[12] at −78 °C with warming to room temperature as before.

The success of these reactions was profoundly affected by the choice of base. As summarized in Table I, use of the more sterically demanding lithio-2,6-dimethylpiperidide for starting materials bearing a trans relation-

(1) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1378. Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Viti, S. M. *J. Org. Chem.* **1982**, *47*, 1380 and references therein. For an excellent discussion, see: Kishi, Y. *Aldrichimica Acta* **1980**, *13*, 23.

(2) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. Martin, V. S.; Woodward, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *Ibid.* **1981**, *103*, 6237. Mihelich, E. D.; O'Connor, D. E.; Daniels, K.; Eickhoff, D. J. *Ibid.* **1981**, *103*, 7690.

(3) For recent methods: Yamamoto, H.; Nozaki, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 169. Whitesell, J. K.; Felman, S. W. *J. Org. Chem.* **1980**, *45*, 755. Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1979**, *101*, 2738. Miyoshi, N.; Kondo, K.; Murai, S.; Sonoda, N. *Chem. Lett.* **1979**, 909.

(4) For a comprehensive review: Crandall, J. K.; Apparu, M. *Org. React. (NY)* **1983**, *29*, in press.

(5) All yields are reported for purified samples, characterized by infrared, nuclear magnetic resonance, and mass spectral data. The ^{1}H NMR were recorded on 220-MHz and 360-MHz instruments in $CDCl_3$ (0.1% Me_4Si) solutions. See supplementary material.

(6) Tenud, L.; Farooq, S.; Seibl, J.; Eschenmoser, A. *Helv. Chim. Acta* **1970**, *53*, 2059.

(7) Stork, G.; Cohen, ,J. F. *J. Am. Chem. Soc.* **1974**, *96*, 5270.

(8) For an epoxy sulfone cyclization: Fischli, A.; Branca, Q.; Daly, J. *Helv. Chim. Acta* **1976**, *59*, 2443 and references therein.

(9) Thummel, R. P.; Rickborn, B. *J. Am. Chem. Soc.* **1970**, *92*, 2064.

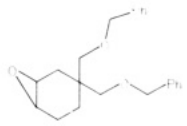
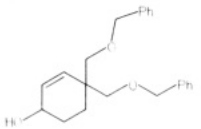
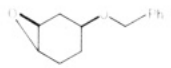
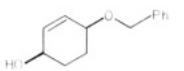
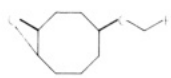
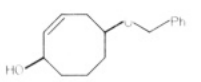
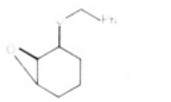
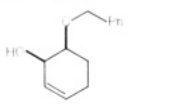
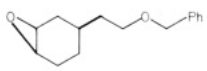
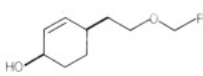
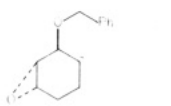
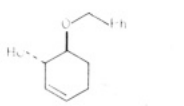
(10) For examples: Cope, A. C.; Lee, H. H.; Petree, H. E. *J. Am. Chem. Soc.* **1958**, *80*, 2849. Crandall, J. K.; Crawley, L. C.; Banks, D. B.; Lin, L. C. *J. Org. Chem.* **1971**, *36*, 510.

(11) Epoxides were generated with *m*-chloroperbenzoic acid or by aqueous *tert*-butyl hypochlorite with subsequent treatment of chlorohydrins with sodium hydride.

(12) The presence of HMPA in cyclizations was necessary for clean conversions. However, in cases with lithium diethylamide, use of HMPA accelerated reactions while also affording small quantities of side products (5–10%). In the most favorable situations, HMPA with $LiNEt_2$ led predominantly to cyclization products (Table I, entries 4, 7, 8). Exclusion of HMPA gave more selective conversion to allylic alcohols in slow reactions that often failed to proceed to completion. The quantity of HMPA is crucial, see: Apparu, M.; Barrelle, M. *Tetrahedron* **1978**, *34*, 1541, 1691.

(13) Ether is necessary to afford solubility of $LiNEt_2$.

Table II

entry	epoxides	rctn times, h	products	% yield
1		12		82
2		2		87
3		12		71
4		12 [a]		60
5		3 [a]		81 [b]
6		12 [a]		47

[a] No HMPA. [b] The *trans*-epoxide isomer is recovered unchanged.

ship of epoxide and benzyloxy substituent led to deprotonation at the benzylic position and nucleophilic opening of epoxides to afford oxetanes, tetrahydrofurans, and tetrahydropyrans with considerable stereocontrol observed at the new asymmetric benzylic carbon. The phenyl ring prefers orientations that minimize steric interactions. Closure to oxetanes is especially facile, even in cases where displacement is directed at a fully substituted carbon (entry 6). Formation of allylic alcohols could not be confirmed under these conditions. The cis isomers generally led to complete destruction of starting material without isolable products.[14]

A different reaction pathway is available by use of lithium diethylamide as illustrated in Table II.[5] In these cases cyclizations were generally not observed.[12] Clean transformations to allylic alcohols were obtained from cis isomers (entries 1–5), whereas trans compounds usually gave very poor yields of allylic alcohols with numerous side products and decomposition. In cases where cyclization is not feasible (entry 5: *trans*-epoxide gave a complex mixture upon treatment with lithio-2,6-dimethylpiperidide) allylic alcohols may be obtained in good yield from the cis isomer. High regioselectivity is a notable characteristic in each isomerization with the new double bond formed upon site-selective deprotonation apparently directed by base chelation with the benzylic ether.[15]

Further applications of these results for stereocontrolled syntheses of heterocyclic natural products are under investigation.

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(14) In all cases, our results provide the "favored" exo–tet mode of ring closure as summarized by Baldwin's observations (Baldwin, J. E. *Chem. Commun.* **1976**, 734, 738).

(15) For other examples: Still, W. C.; Lewis, A. J.; Goldsmith, D. *Tetrahedron Lett.* **1971**, 1421. Teutsch, G.; Bucourt, R. *Chem. Commun.* **1974**, 763.

Supplementary Material Available: A listing of ^{1}H NMR data for the products (4 pages). Ordering information is given on any current masthead page.

D. R. Williams,* Jonathan Grote
Department of Chemistry
Indiana University
Bloomington, Indiana 47405
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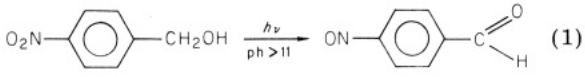
Photoredox Chemistry of *m*- and *p*-Nitrobenzyl Alcohols in Aqueous Solution. Observation of Novel Catalysis by the Hydronium and Hydroxide Ions in These Photoreactions

Summary: *p*-Nitrobenzyl alcohol is found to undergo a hydroxide ion catalyzed photoredox reaction (eq 1), while *m*-nitrobenzyl alcohol undergoes a water and hydronium ion catalyzed process (eq 3).

Sir: A recent report by Wubbels and Celander[1] on the specific- and general-base catalysis in a photochemical Smiles rearrangement prompts us to present our results on the observed catalytic phenomena in the aqueous solution photochemistry of *m*- and *p*-nitrobenzyl alcohols. We employ the definition of a photochemical catalyst (as defined by Wubbels)[1] as being a substance that appears in the quantum yield expression to a power higher than it appears in the stoichiometry.[2]

Irradiation[3] of *p*-nitrobenzyl alcohol (**1**) in aqueous sodium hydroxide at a pH >11 resulted in the formation of *p*-nitrosobenzaldehyde (**2**; eq 1) as the only observed



(1)

1 **2**

product in low-conversion experiments (i.e., <30% loss of the substrate). No reaction was observed when an identical solution was kept in the dark at room temperature. All spectroscopic data[4] (UV, ^{1}H NMR, IR, and MS) are consistent with the proposed structure of the product, which exists as its nitroso dimer.[5]

Relative quantum yields (Φ/Φ^0), where Φ^0 is the yield in 1.0 M (pH 14) NaOH, were measured as a function of pH. The results are shown in Figure 1. The efficiency of the photoreaction was found to depend strongly on the hydroxide ion concentration. Thus, under the above definition, this photoreaction is hydroxide ion catalyzed.

(1) Wubbels, G. G.; Celander, D. W. *J. Am. chem. Soc.* **1981**, *103*, 7669.

(2) As noted by Wubbels,[1] the definition could be qualified by specifying a particular reactive state as the starting state. This would exclude sensitizers as being "catalysts" in photochemical reactions.

(3) A typical experiment involves dissolving 100 mg of the substrate in 140 mL of aqueous sodium hydroxide (~6% CH_3CN, v/v) and irradiating in a Rayonet RPR 100 reactor (254- or 300-nm lamps) for 6 h, with internal cooling and continuous purging of the solution with a stream of argon. Workup involves saturating the solution with NaCl before CH_2Cl_2 extraction. The extent of conversion of the substrate to **2** could be monitored by integrating the aldehyde proton of **2** relative to the methylene protons of **1** in the ^{1}H NMR spectrum.

(4) Yellow solid, mp 185–187 °C; UV (95% EtOH) λ_{max} 340 nm (log ϵ 4.08); ^{1}H NMR ($CDCl_3$) δ 7.9–8.6 (two sets of superimposed AA′BB′ protons, 8 H), 10.1, 10.2 (two nonequivalent formyl protons, 2 H); IR ($CHCl_3$) 2740 (w), 2840 (w), 1710 (s), 1600 (m), 1460 (m), 1230 (m), 1180 cm^{-1}(s); mass spectrum, *m/e* 254 ($M^+ - 16$).

(5) A large number of nitroso compounds are known to exist as their nitroso dimers. See, for example: Luttke, W.; Gowenlock, B. G. *Q. Rev., Chem. Soc.* **1958**, *12*, 321.

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