Table II. Synthesis of 2 from 1 and 5[a]

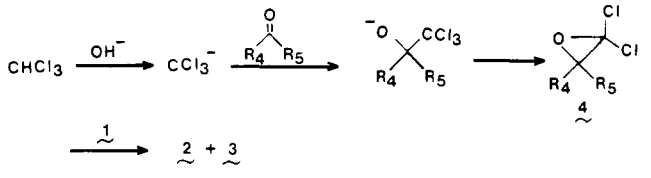
		yield ratio[b]	
	R_1	2	3
a	n-C_3H_7	85	15
b	i-C_3H_7	82 (60)	18
e	t-C_4H_9	90 (71)	10
g	Ph	85 (52)	15
h	$C(CH_3)_2CH_2OH$	90 (51)	10

[a] A 50% excess of 5 was used. Reactions were complete in 7 h. [b] Numbers in parentheses are yields of pure 2.

Recrystallization from pentane affords a 52% yield of **2b** as colorless needles: mp 82–84 °C; ^{13}C NMR ($CDCl_3$) δ 19.01 (q), 27.59 (q), 30.45 (q), 43.39 (d), 48.56 (s), 51.97 (t), 55.25 (s), 172.91 (s); mass spectrum, m/z 198 (M^+). Anal. Calcd for $C_{11}H_{20}N_2O$: C, 66.69; H, 11.12; N, 14.13. Found: C, 66.62; H, 11.19; N, 14.22.

An uncatalyzed reaction proceeds with only 12% conversion after 24 h under the same conditions. Powdered sodium hydroxide works as effectively as the aqueous solution while bromoform is less regioselective than chloroform, forming **2b** and **3b** in a 1:1 ratio from **1b**.

The generation of trichloromethide ion and its subsequent attack on carbonyl compounds are known to be very fast even at low temperature[11] while the syntheses involving dichlorocarbene require elevated temperatures to guarantee satisfactory yields.[12,13] We therefore believe the former is the reactive species and the mechanism is illustrated as follows in a simplified manner:



α-(Trichloromethyl)alkanols (e.g., **5**) which have been suggested to form the same oxirane intermediate **4** under basic conditions[14] react with **1** in similar fashion (Table II).

$$1 + \underset{5}{Me_2C(OH)(CCl_3)} \xrightarrow[50\%\ NaOH]{BTAC/CH_2Cl_2} 2 + 3$$

The piperazinones **2** are easily oxidized to their nitroxyl radicals by m-chloroperbenzoic acid in CH_2Cl_2[15] and reduced to the corresponding piperazines by $LiAlH_4$ in refluxing THF. The experimental details will be published later in a full paper.

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Registry No. **1a**, 72622-72-1; **1b**, 5448-29-3; **1e**, 38401-66-0; **1f**, 72622-73-2; **1g**, 5462-03-3; **1h**, 72622-74-3; **1i**, 72622-75-4; **2a**, 71044-00-3; **2b**, 71620-92-3; **2c**, 72622-76-5; **2d**, 72622-77-6; **2e**, 71764-81-3; **2f**, 72622-78-7; **2g**, 71620-94-5; **2h**, 71620-93-4; **2i**, 71764-80-2; **3a**, 71620-97-8; **3b**, 72638-40-5; **3c**, 72622-79-8; **3d**, 72622-80-1; **3e**, 72622-81-2; **3f**, 72610-24-3; **3g**, 72610-25-4; **3h**, 72610-26-5; **3i**, 72610-27-6; **5**, 57-15-8; acetone, 67-64-1; cyclohexanone, 108-94-1; butanone, 78-93-3.

(11) Merz, A.; Tomohogh, R. *Chem. Ber.* **1977**, *110*, 96.
(12) Reference 6b, p 281.
(13) Secondary and primary amines do proceed, although very slowly, to formamides and isocyanides, respectively, at ice-bath temperature.
(14) (a) Reference 7. (b) Weizmann, O.; Sulzbacher, M.; Bergmann, E. *J. Am. Chem. Soc.* **1948**, *70*, 1153.
(15) Rauckman, E. J.; Rosen, G. M.; Abou-Donia, M. B. *Synth. Commun.* **1975**, *5*, 409.

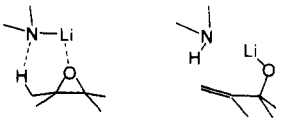
John T Lai
Research and Development Center
B. F. Goodrich Company
Brecksville, Ohio 44141
Received October 19, 1979

Asymmetric Induction. 3.[1] Enantioselective Deprotonation by Chiral Lithium Amide Bases

Summary: Optical yields as high as 31% have been observed as the result of the selectivity of a chiral base for enantiotopically related protons.

Sir: It is surprising that among the vast array of transformations that have been effected with concomitant induction of asymmetry there have been no reported cases of chiral bases showing selectivity between enantiotopic protons in prochiral molecules.[2] Of course it might be argued that a linear approach of a base along a carbon–hydrogen bond would provide but minimal opportunity for the development of discriminating interactions in the diastereomeric transition states. However, many of those transformations that are initiated by strong, anionic bases almost certainly involve complexation between the counterion of the base and the substrate, thus providing for a more ordered transition state than would be afforded by a simple, linear approach.

The rearrangement of epoxides to allylic alcohols as induced by lithium dialkylamide bases has been shown to be a process involving removal of a proton syn to the oxygen,[3] from which it may be inferred that the lithium atom is being transferred to the forming alkoxy group during deprotonation. Though it is tempting to represent this process by a cyclic, six-membered transition state, it is more likely that it involves an aggregate of the base.



We have been able to effect this rearrangement with a number of chiral, mono- and dialkyl, lithium amide bases with induction of asymmetry ranging from a low of 3% to a high of 31% ee. Table I provides a summary of our findings to date. These results represent, to the best of our knowledge,[2] the first example of enantioselective deprotonation.

It has been shown for cyclohexene oxides that deprotonation is highly selective for the syn proton that occupies the pseudoaxial orientation.[3] Thus in the present process, the enantiotopic proton selection involves a preferential reaction of the base with one of the rapidly equilibrating, enantiomeric conformations I and II.

In a typical experiment, the chiral amide base was formed from 4.4 mmol of the appropriate amine in tetra-

(1) For previous paper see: J. K. Whitesell and S. W. Felman, *J. Org. Chem.*, **42**, 1663 (1977).
(2) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions", Prentice-Hall, Englewood Cliffs, NJ, 1971; D. Valentine and J. W. Scott, *Synthesis*, 329 (1978).
(3) R. P. Thummel and B. Rickborn, *J. Am. Chem. Soc.*, **92**, 2064 (1970).

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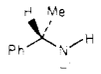
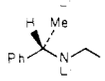
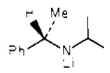
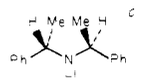
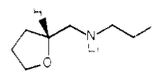
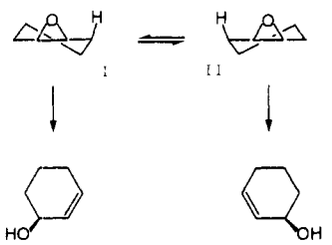
Table I

	optical[a] yield,[b] %	chem yield, %	config
	3	44	*R*
	3	51	*S*
	11	69	*R*
	9	95	*R*
 [c]	31	65	*R*
	18	76	*S*

[a] Optical yields and absolute configurations are based on $[\alpha]_D$ + 152° (*c* 5, $CHCl_3$) for optically pure H (*R*)-cyclohexenol.[4] [b] Optical yields determined from optical rotations of carefully purified, amine-free samples. [c] The base used contained approximately 20% of the meso isomer.[5]



hydrofuran solution at 0 °C under a nitrogen atmosphere by dropwise addition of 4.0 mmol of *n*-butyllithium as an approximately 2 M solution in hexane. After 20 min, cyclohexene oxide (2.0 mmol) was added, and then the reaction was warmed to and then heated at reflux for 2 h. The reaction mixture was then partitioned between ether and appropriate aqueous phases to ensure complete removal of any basic components. Vapor-phase chromatography (25% Carbowax 20M on Chromosorb G-AW) was used to purify samples for analysis. All samples were homogeneous by VPC and ^1H spectral analysis. Repeated attempts to obtain values of enantiomeric excess by using chiral shift reagents with the alcohol as well as the acetate and benzoate esters failed to provide sufficient resolution for accurate quantification. Optical yields are based on rotation values obtained on dilute chloroform solutions by using a Perkin-Elmer 151 polarimeter.

It is interesting to note that the highest levels of asymmetric induction were observed with bases where the degree of aggregation would be expected to be reduced because of steric bulk or internal solvation. Nonetheless, we have not yet been able to derive a satisfactory transition-state model to rationalize the sense of induction. We are continuing our efforts in this area, especially in the design of bases with additional internal ligation.

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Registry No. Cyclohexene oxide, 286-20-4; (*S*)-2-cyclohexen-1-ol, 6426-26-2; (*R*)-2-cyclohexen-1-ol, 3413-44-3; lithium 2(*S*),5(*S*)-dimethylpyrrolidine, 72691-77-1; lithium (*S*)-α-methylbenzenemethanamine, 20752-47-0; lithium (*S*)-*N*-ethyl-α-methylbenzenemethanamine, 72659-58-6; lithium (*S*)-*N*-isopropyl-α-methylbenzenemethanamine, 72659-59-7; lithium α(*S*),α′(*S*)-dimethyldibenzylamine, 72659-60-0; lithium (*R*)-*N*-propyl-2-furanmethanamine, 72659-61-1.

(4) R. K. Hill and J. W. Morgan, *J. Org. Chem.*, **33**, 927 (1968).
(5) C. G. Overberger, N. P. Marullo, and R. G. Hiskey, *J. Am. Chem. Soc.*, **83**, 1374 (1961).

James K. Whitesell,* Steven W. Felman

Department of Chemistry
University of Texas at Austin
Austin, Texas 78712

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