

in three steps the same phenethylamide **14b** generated previously in four steps by Scheme II. Other examples of this double-joining reaction should be equally feasible.

The work described herein thus offers a conceptually new route to benzylisoquinoline alkaloids. The generality of the reaction of 2-lithiooxazoles and oxazolines with aromatic aldehydes as carbon electrophiles has been substantiated, and the hydrogenolytic dismantling of these heterocyclic rings has been demonstrated to be a process of routine applicability.¹⁴

Acknowledgment. We gratefully acknowledge the Health Research and Services Foundation (HRSF) of Pittsburgh, PA, and the National Institutes of Health (Grant No. R01 HL20579-03) for support of these investigations.

Registry No. **11a**, 73663-56-6; **11b**, 73680-43-0; **11c**, 73663-57-7; **13a**, 73663-58-8; **14a**, 139-76-4; **14b**, 42971-27-7; **15a**, 58-74-2; **18** (isomer 1), 73663-59-9; **18** (isomer 2), 73663-60-2; 5-(3,4-dimethoxyphenyl)oxazole, 73663-61-3; 3,4-dimethoxybenzaldehyde, 120-14-9; methyl isocyanide, 593-75-9; (*R*,R**)-2-[(3,4-methylenedioxyphenyl)acetoxymethyl]-5-(3,4-methylenedioxyphenyl)-4,5-dihydrooxazole, 73663-62-4; (*R*,S**)-2-[(3,4-methylenedioxyphenyl)acetoxymethyl]-5-(3,4-methylenedioxyphenyl)-4,5-dihydrooxazole, 73663-63-5.

Supplementary Material Available: Experimental procedures for compounds **11a**, **13a**, **14a**, **14b**, and **18** (5 pages). Ordering information is given on any current masthead page.

(14) All new compounds reported had spectral properties and high-resolution mass spectral data for the molecular ion fully compatible with the assigned structures.

(15) Fellow of the Alfred P. Sloan Foundation.

Alan P. Kozikowski,*¹⁵ Anthony Ames

Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260

Remarkable Solvent Control of Functional Group Selectivity in Complex Metal Hydride Reductions

Summary: Lithium aluminum hydride in ethyl ether reduces alkyl tosylates to the corresponding alkanes rapidly and selectively in the presence of alkyl iodides and bromides without concurrent attack on halogen, whereas in diglyme the reactivity order is reversed, alkyl iodides and bromides being reduced selectively without significant attack on alkyl tosylates.

Sir: Since the discovery of sodium borohydride¹ and lithium aluminum hydride² (LiAlH₄), a number of modified and highly selective reducing agents have evolved, largely by the introduction of various substituents in the parent complex ion.³ Unfortunately, very little attention⁴ has been devoted to the study of using solvents to control the reactivity as well as the functional group selectivity of complex metal hydrides. The lack of such data is mainly attributed to the high reactivity associated with the com-

Table I. Reaction of Lithium Aluminum Hydride with *n*-Octyl Derivatives in Representative Ethereal Solvents at 25 °C^a

| compd | solvent | % reduction ^b | | | | |
|--------------------------|---------|--------------------------|-------|-------|-------|--------|
| | | 0.25 h | 0.5 h | 1.0 h | 6.0 h | 24.0 h |
| <i>n</i> -octyl tosylate | EE | 88 | 96 | 98 | | |
| | THF | 79 | 85 | 96 | | |
| | MG | 60 | 69 | 78 | 100 | |
| | DG | 39 | 61 | 72 | 91 | |
| <i>n</i> -octyl iodide | EE | | 9 | 22 | | 90 |
| | THF | 99 | 100 | | | |
| | MG | 94 | 99 | 99 | | |
| | DG | 97 | 98 | 98 | | |
| <i>n</i> -octyl bromide | EE | | 8 | 16 | 53 | 77 |
| | THF | 84 | 97 | 99 | | |
| | MG | 84 | 97 | 100 | | |
| | DG | 92 | 100 | | | |
| <i>n</i> -octyl chloride | EE | 0 | 0 | 0 | 4 | 20 |
| | THF | 0 | 0 | 4 | 37 | 73 |
| | MG | 0 | 4 | 9 | 35 | 70 |
| | DG | 0 | 7 | 15 | 58 | 87 |

^a Solutions were 0.25 M in both LiAlH₄ and compound.

^b Monitored by GLC by measuring the *n*-octane formed, with *n*-nonane as the internal standard.

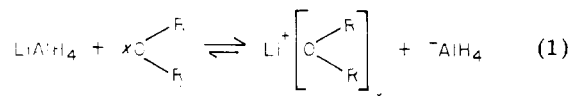
plex metal hydrides, which severely limits the choice of possible solvents for such explorations.³ As a part of an extensive study of the reactivity of various complex metal hydrides toward alkyl halides and tosylates,⁵ it was of interest to explore the influence of solvents on the reactivity of hydride reagents.

Lithium aluminum hydride was chosen as the test reagent. The rates of reduction of *n*-octyl derivatives (tosylate, iodide, bromide, and chloride) with lithium aluminum hydride in representative ethereal solvents of different solvating power (ethyl ether, THF, monoglyme, and diglyme) were examined. Reactions were run with clear solutions of the reagent in the respective solvents under identical reaction conditions (0.25 M each in LiAlH₄ and RX, 25 °C). The results are summarized in Table I.

Lithium aluminum hydride in ethyl ether (EE) reduced *n*-octyl iodide sluggishly, requiring 24 h for 90% reduction. Changing the solvent to tetrahydrofuran (THF) dramatically enhanced the rate, the reduction being essentially complete in 0.25 h! In monoglyme (MG) and diglyme (DG) the rates of reduction of *n*-octyl iodide were still faster. A similar order of solvent influence (DG > MG > THF >> EE) on the reactivity of LiAlH₄ toward alkyl bromides and chlorides was realized.

In contrast, the solvent influence on the rates of reduction of alkyl tosylates follows the order EE > THF > MG > DG, which is exactly the reverse of the order observed for alkyl halide reductions. Thus, in ethyl ether *n*-octyl tosylate was rapidly (0.5 h) and quantitatively reduced to *n*-octane. In diglyme, the corresponding reaction was sluggish, requiring 12 h for completion.

In ethereal solvents, lithium aluminum hydride can be represented as an "ion pair"⁶ (eq 1). In solvents such as



(1) Schlesinger, H. I.; Brown, H. C.; Hoekstra, H. R.; Rapp, L. R. *J. Am. Chem. Soc.* **1953**, *75*, 199-204.

(2) Finholt, A. I.; Bond, A. C., Jr.; Schlesinger, H. I. *J. Am. Chem. Soc.* **1947**, *69*, 1199-1203.

(3) For a detailed review and discussion on this subject see: (a) Brown, H. C.; Krishnamurthy, S. *Tetrahedron* **1979**, *35*, 567-607; (b) Brown, H. C.; Krishnamurthy, S. *Aldrichimica Acta* **1979**, *12*, 3-11.

(4) Jorgensen, M. J.; Thacker, A. F. *Chem. Commun.* **1968**, 973. Brown, H. C.; Ichikawa, K. *J. Am. Chem. Soc.* **1961**, *83*, 4372-4374.

(5) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 849-856.

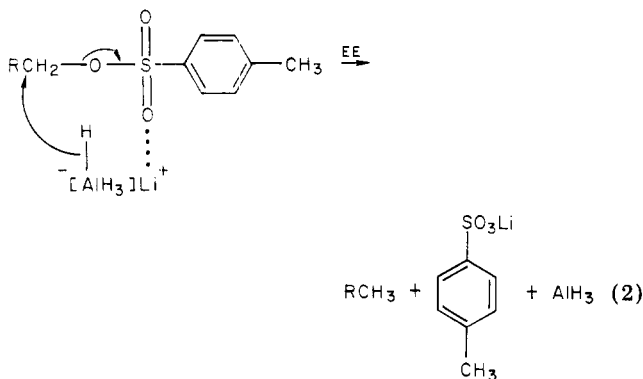
(6) (a) Köbrich, G.; Merkle, H. R.; Trapp, H. *Tetrahedron Lett.* **1965**, 969-972. (b) Brown, H. C.; Khuri, A.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1977**, *99*, 6237-6242. (c) Ashby, E. C.; Dobbs, F. R.; Hopkins, H. P., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 3158-3162.

Table II. Relative Reactivities of *n*-Octyl Tosylate and Alkyl Halides toward Lithium Aluminum Hydride at 0 °C^a

| comps used | products ^b | % yield | |
|--|---------------------------------------|-----------------|-----------------|
| | | EE ^c | DG ^d |
| <i>n</i> -octyl tosylate and <i>n</i> -heptyl iodide | <i>n</i> -octane | 100 | 1 |
| | <i>n</i> -octyl tosylate ^e | 0 | 99 |
| | <i>n</i> -heptane | 2 | 100 |
| | <i>n</i> -heptyl iodide | 98 | 0 |
| <i>n</i> -octyl tosylate and <i>n</i> -heptyl bromide | <i>n</i> -octane | 99 | 13 ^f |
| | <i>n</i> -octyl tosylate ^e | 1 | 87 ^f |
| | <i>n</i> -heptane | <1 | 85 ^f |
| | <i>n</i> -heptyl bromide | >99 | 15 ^f |

^a Solutions of LiAlH₄ in ethereal solvents were added to equimolar mixtures of tosylate and halide and stirred for 1 h. ^b Determined by GLC. ^c LiAlH₄/RX = 1.5. ^d LiAlH₄/RX = 1.0. ^e Not determined directly; estimated by difference. ^f Lowering the temperature to -23 °C increased the selectivity of ROTs/RX to 8/92.

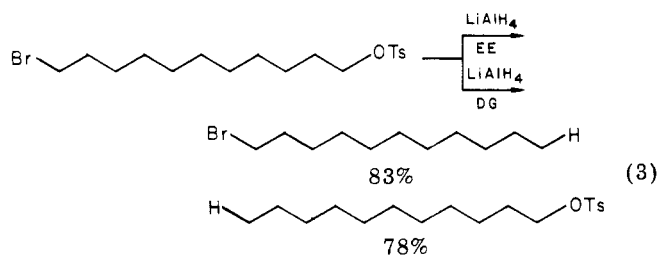
ethyl ether, the lithium ion of LiAlH₄ is poorly solvated. However, in solvents such as tetrahydrofuran, monoglyme, and diglyme, lithium ion is strongly solvated, forming solvent-separated ions, thereby dramatically enhancing the nucleophilicity of tetrahydroaluminate, resulting in rapid reduction of alkyl halides. The high reactivity of LiAlH₄ toward alkyl tosylates in weakly solvating media such as ethyl ether can be attributed to the complexation of the lithium ion with the tosylate group, which increases the leaving-group ability⁷ of that group (eq 2).



The relative reactivity of alkyl tosylates vs. alkyl iodides and bromides toward LiAlH₄ was determined by competition experiments in EE and DG. Results summarized in Table II clearly indicate that in ethyl ether alkyl tosylates can be rapidly and selectively (>99%) reduced in the presence of alkyl iodides and bromides (≤2% attack). In diglyme it is possible to selectively reduce alkyl iodides and bromides without significant attack on alkyl tosylates.

It was desirable to test the applicability of these observations in organic synthetic transformations. Reduction of 11-bromoundecyl tosylate, a difunctional molecule, was examined in EE and DG. In EE, the tosylate group was selectively reduced, yielding *n*-undecyl bromide in 83% isolated yield (95% by GLC). In DG, the reagent selectively reduced the bromo substituent, yielding *n*-undecyl tosylate in 78% yield (eq 3).

In conclusion, this work provides the first clear documentation that the solvent can be used as an effective tool to modify chemoselectivity and reactivity of the complex metal hydride. Further, by judiciously changing the solvents, it should be possible to use the same reagent to



selectively reduce various different functional groups. Recently, a number of complex borohydrides and aluminohydrides with various substituents in the complex ion have been synthesized. Some of these are soluble in a wide variety of solvents. We plan to explore the effectiveness of solvents to control the functional group selectivity of these new reagents.

Acknowledgment. I thank Professor Herbert C. Brown for his stimulating discussions. Financial support of this study by the U.S. Army Research Office through Grants DA31-124 ARO(D) and DAAG-29-76-G-0218 is gratefully acknowledged.

Registry No. *n*-Octyl iodide, 629-27-6; lithium aluminum hydride, 16853-85-3; 11-bromoundecyl tosylate, 66605-81-0; *n*-undecyl bromide, 693-67-4; *n*-undecyl tosylate, 41240-51-1; *n*-octyl tosylate, 3386-35-4; *n*-octyl bromide, 111-83-1; *n*-octyl chloride, 111-85-3; *n*-heptyl iodide, 4282-40-0; *n*-heptyl bromide, 629-04-9; *n*-octane, 111-65-9; *n*-heptane, 142-82-5.

(8) Present address: Research Laboratories, Eastman Kodak Company, Rochester, NY 14650.

S. Krishnamurthy⁸

Richard B. Wetherill Laboratory
Purdue University
West Lafayette, Indiana 47907
Received March 10, 1980

Synthetic Applications of Phenylselenenyl Chloride Additions. A Simple 1,3-Enone Transposition Sequence

Summary: The regiospecific addition of phenylselenenyl chloride to allylic alcohols is used as the key step in a simple 1,3-enone transposition sequence.

Sir: In a previous study we examined the scope and limitations of phenylselenenyl chloride additions to simple olefins.¹ During the course of our investigations we observed that additions of PhSeCl to allylic alcohols generally proceed with high regio- and stereoselectivity. For example, cyclohexenol (2, R = R' = H) reacts with PhSeCl to form only one of four possible regio- and stereoisomers² (vide infra). In this communication we wish to report that (a) the regiospecificity of this addition appears to be quite general and that (b) this reaction can be used as the key step in the general 1,3-enone transposition sequence shown in eq 1.³ The results of our study are illustrated in Scheme I.

(1) Liotta, D.; Zima, G. *Tetrahedron Lett.* 1978, 4977.

(2) PhSeCl additions to allylic ethers apparently proceed in a similar fashion. See: Masaki, Y.; Sakuma, K.; Kaji, K. *Chem. Lett.* 1979, 1235.

(3) For some examples of 1,3-enone transpositions as well as 1,3-alkylative enone transpositions, see: (a) Wharton, P. S.; Bohlen, D. H. *J. Org. Chem.* 1961, 26, 3615; (b) Wharton, P. S. *Ibid.* 1961, 26, 4781; (c) Trost, B. M.; Stanton, J. L. *J. Am. Chem. Soc.* 1975, 97, 4018; (d) Trost, B. M.; Hiroi, K.; Holy, N. *Ibid.* 1975, 97, 5873; (e) Still, W. C. *J. Am. Chem. Soc.* 1977, 99, 4836; (f) Buchi, G.; Egger, B. *J. Org. Chem.* 1971, 36, 2021; (g) Zimmerman, H. E.; Little, R. D. *J. Am. Chem. Soc.* 1974, 96, 4623.

(7) (a) Kraus, W.; Chassin, C.; Chassin, R. *Tetrahedron* 1969, 25, 3681-3692. (b) Kraus, W.; Chassin, C. *Tetrahedron Lett.* 1970, 1113-1116.