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Enantioselective Addition of Dialkylzincs to Aldehydes Using Heterogeneous Chiral Catalysts Immobilized on Alumina and Silica Gel

Kenso Soai,* Masami Watanabe, and Atsuhiro Yamamoto

Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Shinjuku, Tokyo 162, Japan

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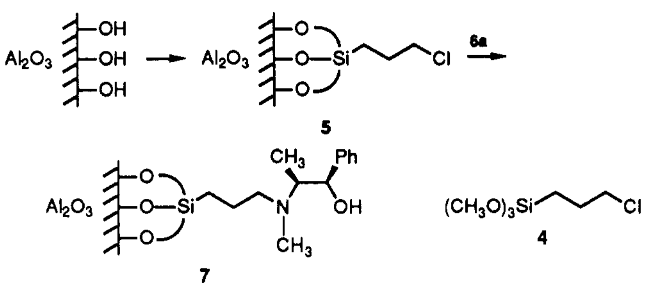
The first example of the use of alumina and silica gel as insoluble supports for the chiral catalyst in the enantioselective addition of dialkylzincs to aldehydes is described. Chiral *N*-alkylnorephedrines were immobilized on (3-chloropropyl)silyl-functionalized alumina or silica gel. Ephedrine was also immobilized on silica gel coated with chloromethylated polystyrene. Using these chiral catalysts, optically active secondary alcohols were obtained in 24-59% enantiomeric excess. The catalyst immobilized on silica gel coated with polystyrene was recycled without the loss of its enantioselectivity.

Alumina and silica gels are readily available inorganic compounds and are widely utilized as the stationary phase in chromatographic separations. They have also been utilized in organic synthesis as acidic or basic catalysts[1] and as insoluble supports for reagents.[2,3]

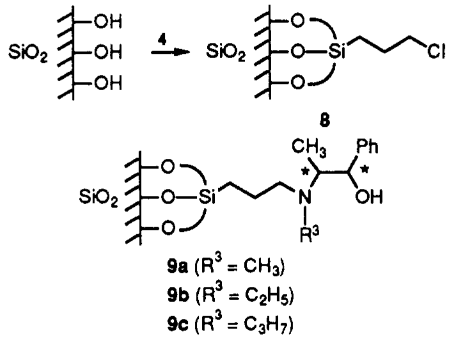
Although chiral stationary phases bonded to silica gel have been used for the chromatographic resolution of enantiomers,[4] to the best of our knowledge, no report has appeared on the use of alumina or silica gel as heterogeneous supports for chiral catalysts in asymmetric carbon-carbon bond forming reactions.

Recently, much interest has been centered on catalytic asymmetric carbon-carbon bond forming reactions.[5] We have reported the enantioselective addition of dialkylzincs to aldehydes using chiral pyrrolidinylmethanols,[6] *N,N*-dibutylnorephedrine,[7] chiral piperazine,[8] and chiral ammonium salt[9] as the chiral catalysts.[10] Recently, we reported the enantioselective addition of dialkylzincs to both aromatic and aliphatic aldehydes using polystyrene-bound chiral catalysts.[11]

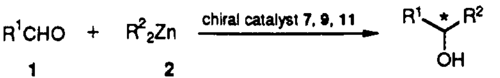
Scheme I



Scheme II



In this paper, we describe the first use of chiral catalysts immobilized on alumina and silica gel for the enantioselective addition of dialkylzincs to aldehydes (eq 1). One



$$\underset{\mathbf{1}}{R^1CHO} + \underset{\mathbf{2}}{R^2{}_2Zn} \xrightarrow{\text{chiral catalyst 7, 9, 11}} \underset{\mathbf{3}}{R^1\overset{*}{C}H(OH)R^2} \quad (1)$$

advantage of these catalysts over the soluble catalysts previously described is their easy removal from the reaction mixture by simple filtration. Furthermore, the recycling of the chiral catalyst is possible in some cases. Since both ephedrine and norephedrine are commercially available in either enantiomeric form, either enantiomer of the product could be obtained by using the appropriate enantiomer of the catalyst.

Results and Discussion

Preparation of Ephedrine Immobilized on Alumina 7. The reaction of (3-chloropropyl)trimethoxysilane (4) with alumina (Merck No. 1067) according to the literature procedure afforded 5.[2] Subsequent reaction of 5 with (1*R*,2*S*)-ephedrine (6a) in the presence of triethylamine in refluxing toluene for 20 h afforded the chiral catalyst

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[1] Reviews: Posner, G. H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 487. Hojo, M.; Masuda, R. *Yuki Gosei Kagaku Kyokaishi* **1979**, *37*, 557, 689.

[2] (a) Carpino, L.; Mansour, M. E.; Knapczyk, J. *J. Org. Chem.* **1983**, *48*, 666. (b) Carpino, L.; Mansour, E. M. E.; Cheng, C. H.; Williams, J. R.; MacDonald, R.; Knapczyk, J.; Carman, C. *Acc. Chem. Res.* **1987**, *20*, 40.

[3] (a) Leal, O.; Anderson, D. L.; Bowman, R. G.; Basolo, F.; Burwell, R. L., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 5125. (b) Tundo, P.; Venturello, P. *J. Am. Chem. Soc.* **1979**, *101*, 6606. (c) Tundo, P.; Venturello, P.; Angeletti, E. *Ibid.* **1982**, *104*, 6547. (d) Angeletti, E.; Canepa, C.; Marinetti, G.; Venturello, P. *J. Chem. Soc., Perkin Trans. 1* **1989**, 105.

[4] Yuki, Y.; Saigo, K.; Tachibana, K.; Hasegawa, M. *Chem. Lett.* **1986**, 1347. Review: Armstrong, D. W. *Anal. Chem.* **1987**, *59*, 84A.

[5] Bosnich, B. *Asymmetric Catalysis*, Martinus Nijhoff: Dordrecht, 1986.

[6] Soai, K.; Ookawa, A.; Ogawa, K.; Kaba, T. *J. Chem. Soc., Chem. Commun.* **1987**, 467; *J. Am. Chem. Soc.* **1987**, *109*, 7122.

[7] Soai, K.; Yokoyama, S.; Ebihara, K.; Hayasaka, T. *J. Chem. Soc., Chem. Commun.* **1987**, 1690.

[8] Soai, K.; Niwa, S.; Yamada, Y.; Inoue, H. *Tetrahedron Lett.* **1987**, *28*, 4841.

[9] Soai, K.; Watanabe, M. *J. Chem. Soc., Chem. Commun.* **1990**, 43.

[10] For the recent related reactions, see: Yoshioka, M.; Kawakita, T.; Ohno, M. *Tetrahedron Lett.* **1989**, *30*, 1657. Joshi, N. N.; Srebnik, M.; Brown, H. C. *Ibid.* **1989**, *30*, 5551. Oeveren, A.; Menge, W.; Feringa, B. L. *Ibid.* **1989**, *30*, 6427. Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028. Tanaka, T.; Ushio, H.; Suzuki, H. *J. Chem. Soc., Chem. Commun.* **1989**, 1700. Corey, E. J.; Hannon, F. J. *Tetrahedron Lett.* **1987**, *28*, 5233; **1987**, *28*, 5237.

[11] (a) Soai, K.; Niwa, S.; Watanabe, M. *J. Org. Chem.* **1988**, *53*, 927. (b) Soai, K.; Niwa, S.; Watanabe, M. *J. Chem. Soc., Perkin Trans. 1* **1989**, 109. See also: Itsuno, S.; Fréchet, J. M. J. *J. Org. Chem.* **1987**, *52*, 4140. Itsuno, S.; Sakurai, Y.; Ito, K.; Maruyama, T.; Nakahama, S.; Fréchet, J. M. J. *Ibid.* **1990**, *55*, 304.

[12] Pickard, R. H.; Kenyon, J. J. *J. Chem. Soc.* **1914**, 1115.

[13] Capillon, J.; Guette, J.-P. *Tetrahedron* **1987**, *26*, 3013.

[14] Oguni, N.; Omi, T.; Yamamoto, Y.; Nakamura, A. *Chem. Lett.* **1983**, 841.

0022-3263/90/1955-4832$02.50/0

Table I. Enantioselective Addition of Dialkylzincs to Aldehydes Using 7 as a Chiral Catalyst

					3				
entry[a]	R^1 in 1	R^2 in 2	temp, °C	time, days		yield, %	$[\alpha]_D$ (*c*, solvent)	% ee[b]	confign
1	C_6H_5	Et	rt	2	**a**	81	$[\alpha]^{25}$ +19.3° (5.29, $CHCl_3$)	43	*R*
2	C_6H_5	Et	0	5	**a**	79	$[\alpha]^{25}$ +26.8° (5.30, $CHCl_3$)	59	*R*
3	C_6H_5	*n*-Bu	0	5	**b**	13[c]	$[\alpha]^{25}$ +15.97° (1.39, $CHCl_3$)	40[d]	*R*
4	*p*-$CH_3C_6H_4$	Et	0	5	**c**	58	$[\alpha]^{25}$ +21.4° (4.55, C_6H_6)	55	*R*
5[e]	C_6H_5	Et	rt	3	**a**	66	$[\alpha]^{23}$ +22.8° (4.68, $CHCl_3$)	50	*R*

[a] Unless otherwise noted, the reactions were run in hexane. [b] Based on the reported values of $[\alpha]_D$ +45.45° (*c* 5.15, $CHCl_3$) for (*R*)-**3a**;[12] $[\alpha]_D$ −39.2° (C_6H_6) for (*S*)-**3c**.[13] [c] Benzyl alcohol (59%) was also obtained. [d] Based on HPLC analysis using a chiral column (Daicel Chiralcel OB, 250 mm; 254 nm UV detector). [e] Using hexane–benzene (1:1.1, v/v) as a mixed solvent.

Table II. Enantioselective Addition of Diethylzinc to Benzaldehyde Using *N*-Alkylnorephedrine Immobilized on Silica Gel 9a–c as Chiral Catalysts

				3			
entry	catalyst	temp, °C	time, days	yield, %	$[\alpha]_D$ (*c*, $CHCl_3$)	% ee[a]	confign
1	**9a**	rt	2	75	$[\alpha]^{20}$ +11.4° (5.15)	25	*R*
2	**9a**	0	5	47	$[\alpha]^{22}$ +16.7° (2.53)	37	*R*
3	**9b**	0	5	61	$[\alpha]^{24}$ −10.7° (3.75)	24	*S*
4	**9c**	0	5	59	$[\alpha]^{25}$ −13.3° (3.53)	29	*S*

[a] Based on the reported value of $[\alpha]_D$ +45.45° (*c* 5.15, $CHCl_3$) for (*R*)-**3a**.[12]

Table III. Enantioselective Addition of Dialkylzincs to Aldehydes Using Ephedrine Immobilized on Silica Gel 9a as a Heterogeneous Chiral Catalyst

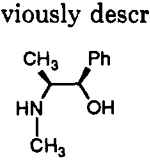
				3				
entry[a]	R^1 in 1	R^2 in 2	time, days		yield, %	$[\alpha]_D$ (*c*, solvent)	% ee[b]	confign
1	C_6H_5	Et	5	**a**	47	$[\alpha]^{22}$ +16.7° (2.53, $CHCl_3$)	37	*R*
2	C_6H_5	*n*-Pr	5	**d**	12[c]	$[\alpha]^{22}$ +13.3° (1.13, C_6H_6)	38[d]	*R*
3	2-naphthyl	Et	4	**e**	56	$[\alpha]^{26}$ +13.9° (5.00, C_6H_6)	33	*R*
4	*p*-$CH_3C_6H_4$	Et	5	**c**	33	$[\alpha]^{25}$ +15.9° (1.93, C_6H_6)	40	*R*
5[e]	C_6H_5	Et	5	**a**	69	$[\alpha]^{22}$ +17.7° (4.81, $CHCl_3$)	39	*R*

[a] Unless otherwise noted, the reactions were run in hexane at 0 °C. [b] Based on the reported values of $[\alpha]_D$ +45.45° (*c* 5.15, $CHCl_3$) for (*R*)-**3a**;[12] $[\alpha]_D^{20}$ −18.81° (C_6H_6) for (*S*)-**3e** for 44.7% ee.[14] [c] Benzyl alcohol (52%) was also obtained. [d] Based on HPLC analyses using a chiral column (Daicel Chiralcel OB) 250 mm; 254 nm UV detector. [e] Using hexane–benzene (1:1.1, v/v) as a mixed solvent.

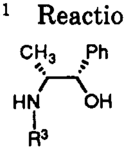
7 (Scheme I). The degree of functionalization of the alumina was determined by elemental analysis; 0.15 mmol of **6a** was immobilized on 1 g of **7**.

Enantioselective Addition of Dialkylzincs to Aldehydes Using 7 as a Heterogeneous Chiral Catalyst. We first examined the enantioselective addition of diethylzinc to benzaldehyde in the presence of **7** as a chiral catalyst. When the reaction was quenched, the catalyst was easily removed from the reaction mixture by simple filtration. The results are summarized in Table I. Reaction of benzaldehyde with diethylzinc in hexane at room temperature in the presence of **7** as a chiral catalyst afforded (*R*)-(+)-1-phenylpropanol (**3a**) in 79% chemical yield and in 59% enantiomeric excess (ee) (entry 2). The reaction using a mixed solvent of hexane–benzene (1:1.1, v/v) afforded a higher ee of (*R*)-**3a** (50% ee, entry 7) than hexane (entry 1), and the reaction run at 0 °C in hexane afforded (*R*)-**3a** of higher ee (59%) than that run at room temperature (entries 1 and 2). Reaction of dibutylzinc with benzaldehyde afforded (*R*)-(+)-1-phenylpentanol (**3b**) in 13% yield and 40% ee (entry 3).

Preparation of *N*-Alkylnorephedrines Immobilized on Silica Gel 9. *N*-Alkylnorephedrines (**6b–c**) were prepared as previously described.[11] Reaction of activated silica gel (Merck No. 7734)[2] with **4** afforded **8**. Subsequent reaction of **8** with *N*-alkylnorephedrines (**6a–c**) afforded silica gel bound *N*-alkylnorephedrines (**9a–c**) (Scheme II). The degree of the functionalization of the silica gel was determined by elemental analysis, to be 0.35–0.56 mmol of **6a–c** per gram of **9**.

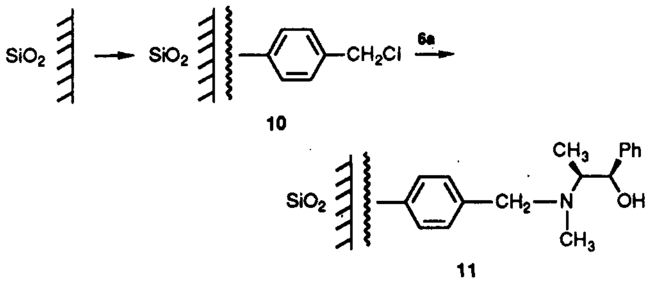


6a



6b ($R^3 = C_2H_5$)
6c ($R^3 = C_3H_7$)

Scheme III



Enantioselective Addition of Dialkylzincs to Aldehydes Using 9a–c as Catalysts. The results of the addition of diethylzinc to benzaldehyde using **9** as chiral catalysts are shown in Table II. Reaction using **9** afforded (*R*)-**3a** of 25% ee in 75% yield (entry 1). When the reaction was run at 0 °C, the ee of (*R*)-**3a** increased to 37% (entry 2). In order to investigate the effect of the catalysts structure, we examined the reaction at 0 °C using the catalysts **9b–c** with ethyl (**9b**) and *n*-propyl (**9c**) substituents on the nitrogen atom; ee's of the obtained alcohols were 24 and 29%, respectively (entries 3 and 4). Catalyst **9a** with a small methyl substituent on the nitrogen atom afforded the highest ee. We then examined the enantioselective addition of dialkylzincs to various aldehydes in hexane at 0 °C in the presence of a catalytic amount of **9a** (Table III). Aromatic aldehydes were ethylated in moderate ee's (entries 3 and 4).

Table IV. Enantioselective Addition of Diethylzinc to Aldehydes Using (1*R*,2*S*)-Ephedrine Immobilized on Silica Gel Coated with Polystyrene 11 as Chiral Catalyst

						3			
entry	R^1 in 1	solvent[a]	temp, °C	time, days		yield, %	$[\alpha]_D$ (*c*, solvent)	% ee[b]	confign
1	C_6H_5	H	0	5	**a**	56	$[\alpha]^{25}$ +16.41° (3.59, $CHCl_3$)	36	*R*
2	C_6H_5	H	rt	2	**a**	76	$[\alpha]^{25}$ +14.75° (5.13, $CHCl_3$)	32	*R*
3	C_6H_5	H-B	0	5	**a**	64	$[\alpha]^{26}$ +25.42° (4.29, $CHCl_3$)	56	*R*
4	C_6H_5	H-B	rt	3	**a**	66	$[\alpha]^{25}$ +22.17° (4.40, $CHCl_3$)	49	*R*
5[c]	C_6H_5	H-B	rt	3	**a**	78	$[\alpha]^{24}$ +22.33° (3.82, $CHCl_3$)	49	*R*
6	C_6H_5	B	rt	5	**a**	63	$[\alpha]^{24}$ +21.75° (4.23, $CHCl_3$)	48	*R*
7	C_6H_5	T	0	5	**a**	59	$[\alpha]^{25}$ +19.11° (4.35, $CHCl_3$)	42	*R*
8	*n*-C_8H_{17}	H-B	rt	5	**f**	40	$[\alpha]^{22}$ −2.99° (3.19, EtOH)	48	*R*

[a] H = hexane, B = benzene, T = toluene. [b] Based on the reported values of $[\alpha]_D$ +45.45° (*c* 5.15, $CHCl_3$) for (*R*)-**3a**;[12] $[\alpha]_D^{20}$ −6.22° (EtOH) for (*R*)-**3f**.[16] [c] Recycled 11 was used.

Preparation of Ephedrine Immobilized on Silica Gel Coated with (Chloromethyl)polystyrene 11. We synthesized a new type chiral catalyst (**11**) using silica gel coated with chloromethylated polystyrene (**10**). Copolymerization of (chloromethyl)styrene and divinylbenzene absorbed on the surface of silica gel afforded silica gel coated with chloromethylated polystyrene (**10**).[15] The subsequent reaction of **10** with (1*R*,2*S*)-**6a** afforded **11** (Scheme III). The degree of the functionalization was determined to be 0.91 mmol of **6a** per gram of **11**.

Enantioselective Addition of Dialkylzincs to Aldehydes Using 11. We performed the enantioselective addition of diethylzinc to benzaldehyde using **11** as a chiral catalyst. Both aromatic and aliphatic secondary alcohols were obtained in moderate ee's (Table IV). The ee is higher at 0 °C than room temperature (entries 1 vs 2 and 3 vs 4). Using benzene–hexane (1:1.1, v/v) as a mixed solvent, the ee of the obtained alcohol (42–56% ee) was better than in hexane (32–36% ee) (entries 1–4 and 6). This solvent effect contrasts with that of polystyrene-bound chiral catalyst[11b] where hexane affords higher enantioselectivity than toluene. Catalyst **11** was easily removed from the reaction mixture by filtration, and after treatment with alkali, the recovered **11** was successfully used again without the loss of catalytic activity and enantioselectivity (entry 5).

Conclusions. It was shown for the first time that alumina and silica gel can be utilized as supports for the chiral catalysts of the enantioselective addition of dialkylzinc reagents to aldehydes. These catalysts were easily removed from the reaction mixture by filtration. In the case of the catalyst immobilized on silica gel coated with polystyrene, ee's of the alcohols obtained were 32–56%, and the catalyst was recycled without the loss of any enantioselectivity.[17]

Experimental Section

General. Optical rotation was taken on a JASCO DIP-181 polarimeter. Bulb-to-bulb distillation was carried out with a Shibata Glass Tube Oven. Hexane, benzene, and toluene were distilled from lithium aluminum hydride. All reactions were carried out under an argon atmosphere.

Material. Diethylzinc in hexane was commercially available. Dipropylzinc and dibutylzinc were prepared according to the literature procedure[18] and were purified by distillation. Alumina (Merck No. 1067, surface area 180–200 m^2/g, diameter 60 Å) and silica gel (Merck No. 7734, surface area 500 m^2/g, diameter 60 Å) were purchased from Merck. (Chloromethyl)styrene was purified by distillation. Divinylbenzene was washed with 5% aqueous NaOH and distilled.

Preparation of (3-Chloropropyl)silyl-Functionalized Alumina 5. (3-Chloropropyl)-functionalized alumina **5** was prepared according to the literature procedure from dry (dried at 100 °C at 2 mmHg, 5 h) alumina (10 g) and (3-chloropropyl)trimethoxysilane (**4**) (1.95 mL, 10 mmol) in refluxing toluene.[2a] Compound **5** was obtained in a 10.6 g yield. Elemental analysis showed that 0.5 mmol of **4** was immobilized on 1 g of **5**. Anal. Found: C, 1.8; H, 0.6.

Preparation of (1*R*,2*S*)-Ephedrine Immobilized on Alumina 7. Catalyst **7** was prepared by the reaction of **5** (2 g) and (1*R*,2*S*)-ephedrine (**6a**) (581 mg, 1.76 mmol) in refluxing toluene for 20 h in the presence of triethylamine (1.76 mmol). After cooling, **7** was collected by filtration, washed with ether and methanol, and dried in vacuo (2 mmHg) at 40 °C for 3 h. Catalyst **7** was obtained (1.7 g). Elemental analysis showed that 0.15 mmol of **6a** was immobilized on 1 g of **7**. Anal. Found: C, 3.8; H, 0.6; N, 0.2.

Preparation of (3-Chloropropyl)silyl-Functionalized Silica Gel 8. (3-Chloropropyl)trimethoxysilane immobilized on silica gel **8** was prepared from activated silica gel[19] (6.6 g) and **4** according to the literature procedure.[2a] Compound **8** (7.08 g) was obtained. Anal. Found: C, 2.0; H, 0.5.

Preparation of *N*-Alkylnorephedrine Immobilized on Silica Gel 9a–c. Catalyst **9a** was prepared from (1*R*,2*S*)-**6a** in a manner similar to that described for the preparation of **7**. Catalysts **9b–c** were prepared from the corresponding (1*S*,2*R*)-*N*-alkylnorephedrines **6b–c** and **8** according to the procedure described for the preparation of **7**. Elemental analysis showed that 0.35–0.56 mmol of **6a–c** were immobilized on 1 g of **9a–c**, respectively. **9a**, Anal. Found: C, 8.5; H, 1.3; N, 0.8. **9b**, Anal. Found: C, 6.4; H, 1.1; N, 0.5. **9c**, Anal. Found: C, 8.6; H, 1.2; N, 0.6.

Preparation of Silica Gel Coated with (Chloromethyl)polystyrene Resin 10. Compound **10** was prepared from (chloromethyl)styrene (3 mL), divinylbenzene (0.075 mL), 2,2′-azobis(isobutyronitrile) (AIBN) (48.9 mg, 0.30 mmol), and 3.91 g of activated silica gel[19] according to the literature procedure.[15] Compound **10** (3.72 g) was obtained. Anal. Found: C, 9.3; H, 1.0.

Preparation of (1*R*,2*S*)-Ephedrine Immobilized on Silica Gel Coated with Chloromethylated Polystyrene 11. A mixture of (1*R*,2*S*)-**6a** (346 mg, 2.09 mmol), anhydrous potassium carbonate (296 mg, 2.14 mmol), and **10** (1.03 g) in toluene was refluxed for 26 h. Catalyst **11** was collected by filtration and washed successively with water, methanol, THF, THF–water, THF, and methanol. After drying in vacuo (2 mmHg) at 40 °C for 3 h, 1.12 g of **11** was obtained. Elemental analysis showed that 0.91 mmol of **6a** was immobilized on 1 g of **11**. Anal. Found: C, 19.2; H, 2.1; N, 1.3.

General Procedure for the Enantioselective Addition of Dialkylzincs to Aldehydes Using 7, 9, and 11 as Chiral Catalysts. A suspension of **7** (130 mg), **9** (100 mg), or **11** (94 mg) and aldehyde (0.98 mmol) in hexane (2 mL) was stirred at 0 °C. After 15 min, 2.2 mL of 1 M solution of dialkylzinc (2.2 mmol) was added dropwise. The resulting mixture was stirred at 0 °C

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(15) Itabashi, O.; Goto, T. *Chem. Ind. (London)* **1986**, 287. Suzuki, T. M.; Itabashi, O.; Yokoyama, T.; Kimura, T. *Anal. Sci.* **1986**, *2*, 391. Itabashi, O.; Goto, T.; Moriya, H. *Nippon Kagaku Kaishi* **1987**, 1600. Kida, S.; Hirano, S.; Ando, F.; Nonaka, H. *Ibid.* **1977**, 915.

(16) Mukaiyama, T.; Hojo, K. *Chem. Lett.* **1976**, 893.

(17) The results described in this paper were reproducible within experimental errors.

(18) Noller, C. R. *Organic Syntheses*; Wiley: New York, 1966; p 184.

(19) Fritz, J. F.; King, J. N. *Anal. Chem.* **1976**, *48*, 570.

for 5 days. The reaction was quenched with the addition of 1 M hydrochloric acid (5 mL). The catalyst was removed by filtration and washed with dichloromethane. The filtrate was extracted with dichloromethane. The combined organic layers were dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was purified by silica gel TLC (AcOEt-hexane = 1:4, v/v as eluent), and subsequent bulb-to-bulb distillation afforded optically active secondary alcohol **3**.

Recovery of Catalyst 11. The catalyst was collected from the reaction mixture by filtration and was stirred for 1 h in a mixture of THF-2 M HCl (4:1, v/v). The catalyst was filtered and washed successively with water and dioxane. Then the catalyst was stirred again in a mixture of THF-2 M aqueous NaOH (4:1, v/v). The catalyst was filtered and washed successively water, THF, and methanol. After drying in vacuo at 40 °C, the catalyst was reused in the enantioselective addition of dialkylzinc to aldehyde.

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Novel (α,β-Epoxyalkyl)lithium Reagents via the Lithiation of Organyl-Substituted Epoxides[1]

John J. Eisch* and James E. Galle

Department of Chemistry, The State University of New York at Binghamton, Binghamton, New York 13901

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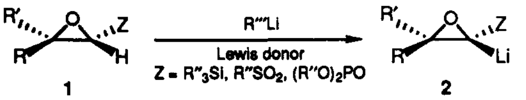
A series of epoxides bearing unsaturated organyl groups attached directly to the epoxy group was found to have sufficient kinetic acidity to undergo clean lithiation at low temperatures. Epoxides of the type $R_2\overline{C\text{—}CH(Un)O}$, where Un is aryl, vinylic, acetylenic, alkoxycarbonyl, or cyano, were smoothly converted into $R_2\overline{C\text{—}CLi(Un)O}$ by either *t*-BuLi or LDA in the temperature range of -80 to -115 °C. The resulting (α,β-epoxyalkyl)lithium reagents could be transformed into a variety of substituted epoxides, such as $R_2\overline{C\text{—}CE(Un)O}$, where E = D, R_3Si, R_3Sn, R, RCO, CO_2H, or $COH(R)_2$. In cases where Un is acyl, addition to the carbonyl, rather than lithiation, occurred preferentially. Attempted lithiations of aziridines and thiiranes led to extrusion of nitrogen and sulfur, respectively. Even the relatively stable $R_2\overline{C\text{—}CLi(Un)O}$ intermediates generated at <-90 °C underwent carbenoid-like decomposition at higher temperatures to yield isomerization and intermolecular-insertion products. Observation of these processes gives direct corroboration of reaction mechanisms proposed for the base-promoted isomerizations of epoxides.

The finding that (α,β-epoxyalkyl)lithium compounds are readily available via the lithiation of a variety of α-heterosubstituted epoxides (eq 1) has presented chemists with a versatile class of synthetic intermediates.[2] Especially for the cases where triorganylsilyl groups are involved, the resulting (α-silyl-α,β-epoxyalkyl)lithium reagents have commanded attention for the construction of carbon skeletons in a controlled, stereoselective fashion.[2a,3] The availability of such lithiated epoxides has thus enhanced considerably the already impressive potential of organosilicon reagents in organic synthesis.[4,5]



(1)

Because of the significance of (epoxyalkyl)lithium reagents **2**, we were interested to learn what other heteroatom substituents Z in **1** would also serve to acidify the α-proton and, further, whether certain organyl groups (Z = vinyl, acetylenic, aryl, acyl, alkoxycarbonyl, cyano, or alkyl) might serve a similar purpose. From previous extensive research on the base-promoted isomerizations of epoxides, there is ample evidence to support the transitory formation of α-metalloepoxides in such transformations.[6] By conducting the lithiations of a series of α-organyl-substituted epoxides at low temperatures, we hoped to generate and form synthetically useful derivatives of such labile intermediates. Some success in this endeavor would extend the availability of (epoxyalkyl)lithium reagents from solely α-heteroatom-substituted epoxides to α-organyl-substituted epoxides as well. We report here that these hopes have been largely realized.

Results

Organyl-Substituted Epoxides. In order to investigate the acidifying character of various organic groups α to the epoxide linkages (R'' in eq 2), the compounds depicted in Scheme I were subjected to the action of the 1:1 complex of *tert*-butyllithium and TMEDA at temperatures of -80 to -115 °C.[7] After a suitable interval the reaction

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(1) Part 8 of the series of publications devoted to "Functionalized Organolithium Reagents" and herewith established. Previous parts, Part 7: *J. Organomet. Chem.* **1988**, *341*, 293. Part 6: *J. Org. Chem.* **1985**, *50*, 3674. Part 5: *J. Organomet. Chem.* **1985**, *285*, 121. Part 4: *J. Org. Chem.* **1980**, *45*, 4534. Part 3: *J. Org. Chem.* **1979**, *44*, 3279. Part 2: *J. Organomet. Chem.* **1976**, 121, C10. Part 1: *J. Am. Chem. Soc.* **1976**, *98*, 4646.

(2) (a) Eisch, J. J.; Galle, J. E. *J. Organomet. Chem.* **1988**, *341*, 293. (b) Eisch, J. J.; Galle, J. E. *J. Org. Chem.* **1976**, *41*, 2615. (c) Eisch, J. J.; Galle, J. E. *J. Organomet. Chem.* **1976**, *121*, C10. (d) Eisch, J. J.; Galle, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 4646.

(3) Molander, G. A.; Mautner, K. *J. Org. Chem.* **1989**, *54*, 4042.

(4) Hudrlik, P. F. In *New Applications of Organosilicon Reagents in Organic Synthesis*; Seyferth, D.; Ed.; Elsevier: Amsterdam, 1976; pp 127-159.

(5) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: New York, 1988; p 147.

(6) Crandall, J. K.; Apparu, M. *Org. React.* **1983**, *29*, 345.

(7) An even more powerful base for kinetically controlled lithiations, lithium diisopropylamide, proved advantageous with certain substrates (such as α-cyanoalkyl epoxides) not cleanly responsive to *t*-BuLi·TMEDA.

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