diamines,[9] where the first and second pK_a's are similar. Dynamic protection of diamines using 1 equiv of 18-crown-6 appears to be subject to similar limitations.[16]

Also, one can sometimes find a solvent such that the desired monoamide precipitates from solution as it is formed (thereby taking it out of competition for acylating agent), though the aggregation-precipitation event is usually too slow to prevent manifestation of the mixing problem. Since it is almost always possible to modify the acylating moiety of the needed carboxylic acid component at will, we see no reason why the combined strategy of low reactivity, high dilution, low temperature, and excess diamine cannot be generally employed for the synthesis of monoacylated diamines. Even in cases where the low volatility of diamine makes the separation of the desired monoamide product from unreacted diamine nontrivial, one can usually work out conditions employing selective extraction and/or chromatographic procedures.

An analogous strategy to that discussed above should be applicable to the selective monosulfonylation and mono*alkyl*ation of diamines.

Experimental Section

All reagents were used as obtained from commercial sources (ACS or AR grade), with the exception of phenylacetic anhydride[17] and *N*-(phenylacetoxy)succinimide ($PhCH_2COOSu$),[18] which were prepared as described. All diamines except 4-(dimethylamino)butylamine (Pfaltz & Bauer) were purchased from Aldrich Chemical Co., were of the highest quality obtainable (generally 99+% "Gold Label"), and were stored over NaOH pellets for 24 h before use. The *N*-monoacetyl derivatives of 1,3-propanediamine and 1,4-butanediamine were synthesized from the parent diamines by using Ac_2O in water containing NaOAc according to the published procedure.[15] *N*-Acetylethylenediamine and 4-nitrophenyl acetate were from Aldrich. Reactions were qualitatively monitored by TLC on silica gel plates using MeOH-EtOAc-NH_4OH (50:50:1) as eluant, with visualization by UV or ninhydrin. In this system, monoacyl product, diacyl product, and unreacted diamine had R_f's of about 0.4-0.5, 0.8-0.9, and 0, respectively. NMR spectra were recorded on Varian EM-360 and XL-200 instruments in Me_2SO-d_6. The reaction conditions for the kinetic experiments are given in Table II. Second-order plots constructed for representative kinetic runs, in order to ensure the accuracy of the rate constant calculated from measured $t_{1/2}$ values, were found to be linear to >75% reaction. It was found necessary to make up fresh CH_2Cl_2 solutions of the diamines prior to each kinetic run, in order to obtain reproducible rates.

"Standard" Acylation Procedure. RCOCl (2 mmol) diluted in 5 mL of CH_2Cl_2 was added dropwise over 30 min to a vigorously stirred solution of 1,2-ethanediamine or 1,4-butanediamine (10 mmol) in 15 mL of CH_2Cl_2 at -78 °C (dry ice, 2-propanol). Upon completion of the addition, the reaction mixture was allowed to come to room temperature with stirring overnight and extracted with two 30-mL portions of 5% aqueous HCl. TLC indicated that this extraction procedure removed all unreacted diamine and monoacyl product and that no hydrolysis occurred in the case of RCOCl. The organic layer was taken to dryness, an accurately weighed amount (20-30 mg) of hexamethylbenzene (HMB) and Me_2SO-d_6 were added, and the ^1H NMR spectrum was recorded. The yield of diacyl product was calculated from the relative integration of sample peaks and the HMB singlet. In some cases, the acidic aqueous layer was basified with NH_4OH and thoroughly extracted with CH_2Cl_2, and the organic layer was evaporated and analyzed by ^1H NMR as above in order to calculate the yield of monoacyl product.

For reactions involving $(RCO)_2O$ rather than RCOCl, the organic layer left after extraction with 5% aqueous HCl was extracted with saturated aqueous $NaHCO_3$ (to remove RCOOH) before processing as above.

"High-Dilution" Acylation Procedure. This was the same as above, except that the acylating agent in 100 mL of CH_2Cl_2 (20 times the volume used above) was added to the diamine in 300 mL of CH_2Cl_2 with vigorous stirring over 30 min.

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Efficient Method for the Reductive Cleavage of Acetals and Ketals with $Zn(BH_4)_2/Me_3SiCl$

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The reductive cleavage of acetals and ketals to ethers is a synthetically useful method in asymmetric synthesis[1] and protective chemistry.[2] Until recently, a number of methods have been developed for this transformation involving various reagents such as $LiAlH_4$-Lewis acids,[3] Me_3SiH-Me_3SiOTf,[4] Et_3SiH-acids,[5] diisobutylaluminum hydride,[6] B_2H_6,[7] BH_2Cl,[8] $NaBH_3CN$-HCl,[9] $NaBH_4$-CF_3COOH,[10] Li/NH_3,[11] and H_2 over catalysts.[12]

In a continuation of our study to develop the reducing ability of $Zn(BH_4)_2$,[13] we have found that the use of this reagent with Me_3SiCl is very effective in the reductive cleavage of a wide variety of acetals and ketals under mild conditions. Thus, the treatment of acetals or ketals with 0.5 equiv of $Zn(BH_4)_2$ in the presence of 1.2 equiv of Me_3SiCl leads to the formation of the ethers in excellent to good yields (Table I).

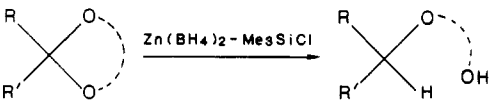

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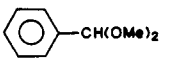
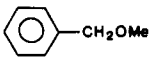
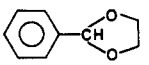
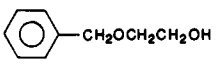
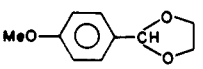
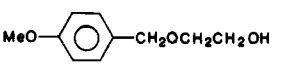
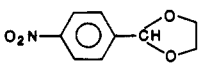
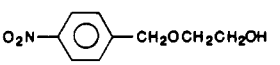
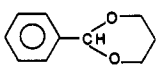
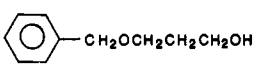
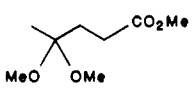
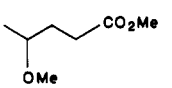
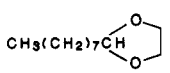
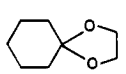
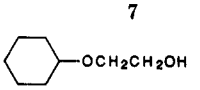
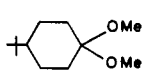
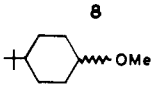
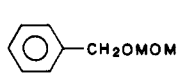
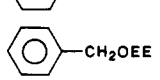
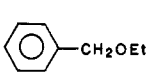
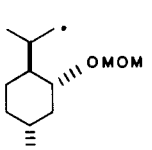
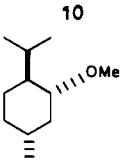
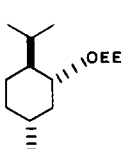
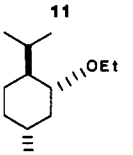
Table I. Reduction of Acetals and Ketals to Ethers with $Zn(BH_4)_2/Me_3SiCl$

run	substrate	reactn conditions:[a] temp, °C/time	product	yield,[b] %
1		25/2.5 h	 **1**	81 (100)
2		25/45 min	 **2**	86
3		0/15 min	 **3**	80
4		25/45 h[c]	 **4**	77[d]
5		25/6 h	 **5**	89
6		25/1.5 h	 **6**	90
7		25/14 h	$CH_3(CH_2)_7CH_2OCH_2CH_2OH$ **7**	97
8		25/25 h	 **8**	80
9		25/3 h	 **9**	95[e]
10		25/40 h[c]	1	90[f]
11		25/20 h[c]	 **10**	47[g]
12		25/2 h[c]	 **11**	87
13		25/2 h[c]	 **12**	92

[a] Ether as solvent, unless otherwise stated. [b] Yields represent pure isolated products: value in parentheses was determined by GLC. [c] CH_2Cl_2/Et_2O as solvent. [d] After 88% conversion. [e] Trans:cis = 59:41 determined by GLC. [f] After 98% conversion. [g] 41% of benzyl alcohol was also formed.

As can been seen in Table I, compared to the aromatic acetals the aliphatic ones require a longer reaction time (runs 7 and 8). And the nitro-substituted acetal is reduced extremely slowly (run 4). These results suggest that the reduction presumably proceeds via the resonance-stabilized carbocation intermediate formed by Me_3SiCl-promoted cleavage of acetals or ketals.

This new method has also been applied for the reductive cleavage of methoxymethyl (MOM)[14] and 1-ethoxyethyl (EE)[15] ethers, which can be regarded as acetals (runs 10–13). Both MOM and EE ethers are efficiently reduced to the corresponding methyl and ethyl ethers, respectively, in good yields except for benzyl alcohol EE ether (run 11). Since the starting MOM and EE ethers are readily available from the corresponding alcohols under relatively mild conditions,[16] this procedure will provide an alternative method for methyl or ethyl ether formation.

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It should be pointed out that in the absence of Me_3SiCl no reduction occurs. And also the combination of $NaBH_4/Me_3SiCl$ was not effective. Reduction attempts using Lewis acids ($BF_3{\cdot}OEt_2$, $ZnCl_2$) were also fruitless.

Although there are several methods available for reductive cleavage of acetals and ketals, we believe that the present method offers considerable advantages in terms of simpleness, readily available reagents, and very mild conditions.[17]

Experimental Section

Melting points and boiling points are uncorrected. Kugelrohr distillation boiling points (bp) refer to the bath temperature. ^1H NMR spectra were recorded at 100 MHz on JEOL MH-100 with Me_4Si as an internal standard. High-resolution mass spectra were obtained with a JEOL HX-100 spectrometer. GLC analyses were performed on Shimadzu GC-7A flame ionization instruments with OV-1 or SE-30 columns.

Et_2O was distilled from sodium benzophenone ketyl before use, and CH_2Cl_2 was from CaH_2. Reagents were added via dry syringes through septa.

All starting derivatives in this study were prepared by known procedures[16] and purified by distillation. All products were identified through their ^1H NMR, IR, and high-resolution mass spectra.

General Procedure of the Reductive Cleavage of Acetals and Ketals with $Zn(BH_4)_2/Me_3SiCl$. To an Et_2O or CH_2Cl_2 solution (1.4 mL) of acetal or ketal (1 mmol) at 0 °C were added successively $Zn(BH_4)_2$ (0.15 M Et_2O solution; 3.4 mL, 0.5 mmol)[18] and Me_3SiCl (1.2 mmol). When Me_3SiCl was added, a small amount of gas evolution was observed. And the mixture was stirred at 0 °C or at room temperature until completion of the reaction, as monitored by TLC or GLC analysis. During the reaction the solution gradually turned cloudy white. After the reaction was quenched by addition of dilute HCl and conventional workup, the residue was purified by flash column chromatography[19] to provide the corresponding ethers.

Benzyl methyl ether (1): bp 68 °C (18 mmHg) [lit.[20] bp 59–60 °C (12 mmHg)]; IR (neat) 1435, 1385, 1100, 740, 700 cm^{-1}; ^1H NMR (CCl_4) δ 3.27 (3 H, s), 4.34 (2 H, s), 7.18 (5 H, s); mass spectrum, m/z (M^+) calcd for $C_8H_{10}O$ 122.0732, obsd 122.0747.

2-(Benzyloxy)ethanol (2): bp 72–73 °C (1 mmHg) [lit.[3a] bp 135 °C (13 mmHg)]; IR (neat) 3400, 1450, 1355, 1105, 1060, 735, 695 cm^{-1}; ^1H NMR (CCl_4) δ 2.92 (1 H, br s), 3.50 (4 H, m), 4.42 (2 H, s), 7.19 (5 H, s); mass spectrum, m/z (M^+) calcd for $C_9H_{12}O_2$ 152.0837, obsd 152.0824.

2-[(4-Methoxyphenyl)methoxy]ethanol (3): bp 146–147 °C (4.5 mmHg) [lit.[21] bp 109 °C (0.5 mmHg)]; IR (neat) 3400, 1610, 1247, 1107, 1067, 1032, 817 cm^{-1}; ^1H NMR (CCl_4) δ 3.17 (1 H, br), 3.46 (4 H, m), 3.67 (3 H, s), 4.33 (2 H, s), 6.71 (2 H, d, J = 8 Hz), 7.11 (2 H, d, J = 8 Hz); mass spectrum, m/z (M^+) calcd for $C_{10}H_{14}O_3$ 182.0943, obsd 182.0915.

2-[(4-Nitrophenyl)methoxy]ethanol (4): mp 46.5–47 °C (from hexane–Et_2O); IR ($CHCl_3$) 3600, 1605, 1520, 1350, 1110, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.58 (1 H, br), 3.55–3.90 (4 H, m), 4.63 (2 H, s), 7.48 (2 H, d, J = 8 Hz), 8.15 (2 H, d, J = 8 Hz); mass spectrum, m/z (M^+) calcd for $C_9H_{11}NO_4$ 197.0688, obsd 197.0678.

3-(Benzyloxy)-1-propanol (5): bp 88–89 °C (0.25 mmHg) [lit.[3a] bp 110 °C (0.5 mmHg)]; IR (neat) 3400, 1450, 1365, 1090, 1070, 735, 695 cm^{-1}; ^1H NMR (CCl_4) δ 1.71 (2 H, quintet, J = 6 Hz), 2.84 (1 H, s), 3.4–3.65 (4 H, m), 4.38 (2 H, s), 7.18 (5 H, s); mass spectrum, m/z (M^+) calcd for $C_{10}H_{14}O_2$ 166.0994, obsd 166.0992.

Methyl 4-methoxypentanoate (6): bp 64–65 °C (19 mmHg) [lit.[22] bp 70–71 °C (20 mmHg)]; IR (neat) 1740, 1170, 1090 cm^{-1}; ^1H NMR (CCl_4) δ 1.09 (3 H, d, J = 6 Hz), 1.6–1.8 (2 H, m), 2.29 (2 H, t, J = 8 Hz), 3.21 (3 H, s), 3.1–3.4 (1 H, m), 3.59 (3 H, s); mass spectrum, m/z (M^+) calcd for $C_7H_{14}O_3$ 146.0943, obsd 146.0988.

2-(1-Nonyloxy)ethanol (7): bp 66–67 °C (0.4 mmHg); IR (neat) 3400, 1460, 1120, 1060 cm^{-1}; ^1H NMR (CCl_4) δ 0.90 (3 H, t, J = 6 Hz), 1.48 (12 H, br s), 1.55 (2 H, br m), 2.96 (1 H, br), 3.3–3.7 (6 H, m); mass spectrum, m/z (M^+) calcd for $C_{11}H_{24}O_2$ 188.1776, obsd 188.1798.

2-(Cyclohexyloxy)ethanol (8): bp 113–114 °C (23 mmHg) [lit.[3a] bp 100 °C (14 mmHg)]; IR (neat) 3400, 1450, 1365, 1110, 1100, 1060, cm^{-1}; ^1H NMR (CCl_4) δ 1.2–2.1 (11 H, m), 3.30 (1 H, br), 3.4–3.7 (4 H, m); mass spectrum, m/z (M^+) calcd for $C_8H_{16}O_2$ 144.1150, obsd 144.1160.

4-*tert*-Butylcyclohexyl methyl ether (9): bp 84–85 °C (13.5 mmHg) [lit.[3a] bp 90 °C (14 mmHg)]; IR (neat) 1480, 1470, 1455, 1370, 1110 cm^{-1}; ^1H NMR (CCl_4) δ 0.84 (9 H, s), 0.9–2.2 (9 H, m), 2.8–3.1 (1 H, m), 3.19, 3.20 (total 3 H, each s); mass spectrum, m/z (M^+) calcd for $C_{11}H_{22}O$ 170.1671, obsd 170.1658.

Benzyl ethyl ether (10): bp 72–73 °C (16 mmHg) [lit.[20] bp 70 °C (15 mmHg)]; IR (neat) 1495, 1450, 1375, 1355, 1115, 1105, 730, 695 cm^{-1}; ^1H NMR (CCl_4) δ 1.21 (3 H, t, J = 7 Hz), 3.44 (2 H, q, J = 7 Hz), 4.39 (2 H, s), 7.20 (5 H, s); mass spectrum, m/z (M^+) calcd for $C_9H_{12}O$ 136.0888, obsd 136.0865.

***l*-Menthyl methyl ether (11)**: bp 85–87 °C (14 mmHg) [lit.[23] bp 83 °C (12 mmHg)]; IR (neat) 1460, 1445, 1365, 1110, 1100 cm^{-1}; ^1H NMR (CCl_4) δ 0.76 (3 H, d, J = 7 Hz), 0.88 (3 H, d, J = 7 Hz), 0.93 (3 H, d, J = 6 Hz), 0.9–1.7 (7 H, m), 1.9–2.3 (2 H, m), 2.83 (1 H, dt, J = 10, 4 Hz), 3.24 (3 H, s); mass spectrum, m/z (M^+) calcd for $C_{11}H_{22}O$ 170.1671, obsd 170.1655.

Ethyl *l*-menthyl ether (12): bp 72 °C (9 mmHg); IR (neat) 1465, 1455, 1375, 1115, 1085 cm^{-1}; ^1H NMR (CCl_4) δ 0.76 (3 H, d, J = 7 Hz), 0.88 (3 H, d, J = 7 Hz), 0.91 (3 H, d, J = 6 Hz), 1.16 (3 H, t, J = 7 Hz), 0.9–1.8 (7 H, m), 1.9–2.4 (2 H, m), 2.90 (1 H, dt, J = 10, 4 Hz), 3.21 (1 H, dq, J = 9, 7 Hz), 3.58 (1 H, dq, J = 9, 7 Hz); mass spectrum, m/z (M^+) calcd for $C_{12}H_{24}O$ 184.1827, obsd 184.1814.

(17) Under these conditions cyclohexene was hydroborated. So there is a possibility that the real reducing species is borane. However, the present method is much more effective than the use of borane itself. See ref 7.

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Facile Preparation of (2*R*,3*S*)- and (2*S*,3*R*)-3-[[(4-Bromobenzyl)oxy]methyl]oxirane-2-methanol via Asymmetric Epoxidation

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The availability of small homochiral building blocks is an important consideration in the synthesis of enantiomerically pure natural products. For a projected synthesis of an insect pheromone, we required a C_4 unit like the epoxy alcohol **1a**. This highly oxygenated homochiral building block may be prepared via a multistep synthesis (seven steps, 18% overall yield) from D-(−)-tartaric acid.[1,2] In principle, epoxy alcohols **1** and **2** should also be easily available via Sharpless asymmetric epoxidation[3,4] of

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