spite of the low temperature. A four-membered ring intermediate is conceivable.

The reaction using **1b** was reexamined. There was no spectral evidence for the formation of **3b**; the exclusive product was the expected **2b**.

Experimental Section

Melting points are uncorrected. Ir (KBr) spectra were recorded on a Perkin-Elmer Infracord spectrometer; nmr spectra on a Perkin-Elmer Hitachi R-20 instrument ($CDCl_3$ solvent, TMS standard). Microanalyses are by Galbraith Laboratories, Knoxville, Tenn.

1-Methoxy- and 3-Methoxy-3-phenyloxindoles.—In a flask equipped with a magnetic stirrer, a dropping funnel, and drying tubes were placed 7.25 g (0.0265 mol) of α,α-diphenylchloroacetyl chloride (Aldrich) and 75 ml of dry ether. The funnel was charged with a solution of 4.7 g (0.1 mol) of methoxyamine[3] in 25 ml of ether. The mixture was kept near −20° with a Dry Ice–acetone bath while the amine was added slowly with stirring. The slurry was allowed to warm to room temperature and was stirred for an additional 4 hr. Water (100 ml) was added and the layers were separated. The ether layer was washed with 2 × 50 ml of water, dried (K_2CO_3), and evaporated to leave a pale yellow oil. When left at room temperature, this deposited transparent cubes during a period of 5 weeks. These were removed manually and triturated with a 1:1 benzene–hexane mixture at room temperature. There was obtained 0.95 g (15%) of **2a**, mp 93–95°. Its ir spectrum showed no N–H stretching, while its nmr spectrum exhibited a three-proton singlet at 4.01 ppm ($NOCH_3$) and a one-proton singlet at 4.54 ppm ($Ar_2CHC{:}O$).

Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.30; H, 5.51; N, 5.70.

The oil left after the removal of **2a** was crystallized from aqueous methanol to give 4.0 g (63%) of **3a**, mp 168–169°. Its spectra showed N–H stretching at 3200 cm^{-1} and no proton resonance near 4.5 ppm. It was identical, by ir and nmr spectral comparisons and by mixture melting point, with an authentic sample of **3a**.[2] When the total crude reaction product was crystallized directly from aqueous methanol the less soluble **3a** was isolated first.

Except for the N–H region, the ir spectra of **2a** and **3a** differ significantly only below 1200 cm^{-1}. **2a** exhibited bands at 1065, 759, and 748 cm^{-1} not shown by **3a**, whereas **3a** showed bands at 1118, 1095, 773, 753, and 706 cm^{-1}.

When **1b** was used, the crude reaction product showed no evidence in its ir or nmr spectra that any **3b** was present, and only **2b**[1] was isolated.

Attempted Isomerizations of 2a and 3a.—A mixture of 0.24 g of **2a**, 0.08 g of methoxyamine hydrochloride, and 20 ml of ether was refluxed with stirring for 6 hr and filtered. Evaporation of the filtrate gave a quantitative recovery of **2a**, identified by its melting point and ir spectrum. Similarly, **3a** was recovered unchanged. Further, **2a** and **3a** were recovered unchanged, even when seeded with the other, when each was recrystallized from aqueous methanol or from a melt.

In similar experiments, **2b** did not isomerize to **3b**.

Registry No.—**2a**, 34638-56-7; **3a**, 34638-57-8.

(3) T. C. Bissot, R. W. Parry, and D. H. Campbell, *J. Amer. Chem. Soc.*, **79**, 796 (1957).

Reductive Cleavage of Sulfonamides with Sodium Bis(2-methoxyethoxy)aluminum Hydride

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We wish to report that the new versatile reducing agent sodium bis(2-methoxyethoxy)aluminum hydride (SMAH),[1] in contrast to lithium aluminum hydride ($LiAlH_4$),[2] is a useful reagent for the regeneration of primary and secondary aliphatic and aromatic amines from the corresponding sulfonamides. This reaction provides an additional approach that complements those methods reported[2,4] for carrying out this transformation. The usual procedure consists of refluxing a mixture of the sulfonamide and excess SMAH (mole ratio 1:4) in an aromatic hydrocarbon or, if desired, in an ethereal solvent such as glyme, until sulfonamide is consumed. Addition of water or alkali quenches the reaction, and the amine may be isolated by standard procedures. Typical results are recorded in Table I.[5,6]

TABLE I

CLEAVAGE OF SULFONAMIDES WITH $NaAlH_2(OCH_2CH_2OCH_3)_2$

Series	Sulfonamides (1)	Product (2)	Solvent	Yield,[a] %
a	*N*-Tosylpiperidine	Piperidine	Benzene	75[b]
b	*N*-Tosyldeoxyephedrine	Deoxyephedrine	Benzene	64[b]
			Glyme	77[b]
c	*N*-Mesyldeoxyephedrine	Deoxyephedrine	Benzene	67[b]
d	(*S*)-*N*-Tosylamphetamine	(*S*)-Amphetamine	Toluene	27[b]
e	*cis*- and *trans*-1,5-Bis(tosyl)-3,7-dihydroxyoctahydro-1,5-diazocine[c]	*cis*-3,7-Dihydroxyoctahydro-1,5-diazocine[c]	Benzene	33[d]
f	*N*-Tosyl-2-(*N*-methylaminomethyl)-2-phenyl-1,3-dioxolane	2-(*N*-Methylaminomethyl)-2-phenyl-1,3-dioxolane	Toluene	56[e]
g	1-Tosylaziridine	*N*-Tosylethylamine	Benzene	100
h	2g	Ethylamine	Toluene	57[b]
i	3-Methoxymethoxy-3-phenyl-1-tosylazetidine[f]	3-Methoxymethoxy-3-phenylazetidine[f]	Benzene	69[g]
j	*N*-Mesylaniline	Aniline	Toluene	63[h]

[a] No special effort was made to optimize yields. [b] Isolated as picrate and compared by ir, melting point (and $[\alpha]_D$ where applicable) with an authentic sample. [c] No attempt was made to purify the trans product.[5] [d] Isolated as the ditosylate. [e] Yield as distilled free amine. [f] Reference 6. [g] Isolated as the hemioxalate. [h] Isolated as hydrochloride and compared as in *b*.

With the exception of (*S*)-*N*-tosylamphetamine (**1e**), it can be seen from Table I that both toluenesulfonamides and methanesulfonamides are cleaved by this reagent in acceptable yield. Although reduction of tertiary sulfonamides is generally readily carried

(1) (a) V. Bazant, M. Capka, M. Cerny, V. Chvalovsky, K. Kochloefl, M. Kraus, and J. Malek, *Tetrahedron Lett.*, 3303 (1968); (b) M. Cerny and J. Malek, *ibid.*, 1739 (1969); (c) M. Cerny, J. Malek, M. Capka, and V. Chvalovsky, *Collect. Czech. Chem. Commun.*, **34**, 1025 (1969); (d) M. Capka, V. Chvalovsky, K. Kochloefl, and M. Kraus, *ibid.*, **34**, 118 (1969).

(2) S. Searles and S. Nukina, *Chem. Rev.*, **59**, 1077 (1959); *cf.* p 1094. Primary sulfonamides have not been cleaved with $LiAlH_4$. Secondary sulfonamides (generally aniline derivatives) have been cleaved by using unusually vigorous conditions for this reagent, *e.g.*, reduction of *N*-ethyl-*p*-toluenesulfonanilide at 120° in dibutyl ether.[3]

(3) D. Klamann, *Monatsh. Chem.*, **84**, 651 (1953).

(4) (a) L. Horner and H. Neumann, *Chem. Ber.*, **98**, 3462 (1965); (b) W. D. Closson, P. Wriede, and S. Bank, *J. Amer. Chem. Soc.*, **88**, 1581 (1966); (c) S. Ji, L. B. Gortler, A. Waring, A. Battisti, S. Bank, W. D. Closson, and P. Wriede, *ibid.*, **89**, 5311 (1967); (d) K. Okamura, T. Iwasaki, M. Matsuoka, and K. Matsumoto, *Chem. Ind. (London)*, 929 (1971).

(5) W. W. Paudler, A. G. Zeiler, and G. R. Gapski, *J. Org. Chem.*, **34**, 1001 (1969).

(6) E. H. Gold, *J. Amer. Chem. Soc.*, **93**, 2793 (1971).

out in refluxing benzene,[7] secondary sulfonamides first form salts and thus require higher boiling solvents such as toluene or xylene.

The low yield of (*S*)-amphetamine is due to olefin formation, probably *via* abstraction of the benzylic hydrogen by base and subsequent elimination of *p*-toluenesulfonamide. In addition to (*S*)-amphetamine, the only other identifiable product, characterized by glc, in approximately 15% yield, was allylbenzene. Although β-methylstyrene is the expected primary olefinic product, it was discovered that when β-methylstyrene was treated under the reaction conditions (see Experimental Section), it disappeared completely and only allylbenzene, in about 25% yield, could be identified. Similarly, allylbenzene treated under the reaction conditions was recovered in about 25% yield, and no β-methylstyrene was formed. Since only about one quarter of the olefin survives this treatment, the 15% yield of allylbenzene obtained from the sulfonamide reduction would be equivalent to *ca.* 60%. The isomerization of β-methylstyrene to allylbenzene is base catalyzed, since no isomerization of either olefin took place in refluxing toluene.

From Table I, it is clear that protected carbonyls (*i.e.*, ketals or acetals) survive the reduction. Of course, such groups as carbonyl and carboxyl would be concomitantly reduced, and this may be useful when the corresponding amino alcohol is the desired product.

Finally, it should be noted that while this represents a practical synthesis of substituted azetidines from the corresponding sulfonamide derivatives[6] (*e.g.*, **1i**), aziridine sulfonamides are ring cleaved by this method (*e.g.*, **1g**).

Although no attempts at isolation have been made, it is reasonable to assume that the RSO_2^- moiety is further reduced to the corresponding thiol.[8]

Experimental Section[9]

Reagents.—All solvents were reagent grade and dried over 3A molecular sieves. SMAH[10] was used as a 70% benzene solution. Glc analyses were performed with a Perkin-Elmer Model 800 gas chromatograph, with a 0.125 in. × 12 ft 8% castorwax column on 80–100 mesh HMDS Chromosorb W at 150° and at a 10 ml min^{-1} flow rate. Allylbenzene and β-methylstyrene were respectively obtained from Columbia Organic Chemicals Co. and Aldrich Chemical Co. Nmr spectra were recorded on a Varian Model A-60A spectrometer.

Tosyl Amides.—All previously reported compounds (**1a**, **1e**, **1g**, **2g**, and **1j**) were prepared *via* the respective literature procedures from the amine and sulfonyl chloride.

***N*-Tosyldeoxyephedrine (1b).**—Tosyl chloride (19.1 g, 0.10 mol), dissolved in 210 ml of ether, was added to a solution of 14.9 g (0.1 mol) of deoxyephedrine in 210 ml of dry pyridine at *ca.* 5°. The mixture was stirred for 15 min, warmed to 25°, stirred for 1 hr, poured into 1 l. of ice–water, and extracted with ether. The ether extract was washed with 10% H_2SO_4, followed by water and then saturated $NaHCO_3$, dried over Na_2SO_4, filtered, and evaporated to yield crude **1b**. Recrystallization from hexane afforded 15.1 g (50%) of analytically pure **1b**, mp 63–64°.

Anal. Calcd for $C_{17}H_{21}NO_2S$: C, 67.29; H, 6.98; N, 4.62; S, 10.57. Found: C, 67.57; H, 6.78; N, 4.33; S, 10.66.

***N*-Mesyldeoxyephedrine (1c)** was prepared in an analogous manner to **1b**, using CH_3SO_2Cl, and recrystallized from hexane, mp 49–50°.

Anal. Calcd for $C_{11}H_{17}NO_2S$: C, 58.11; H, 7.53; N, 6.16; S, 14.10. Found: C, 58.09; H, 7.55; N, 5.94; S, 14.29.

(*S*)-*N*-Tosylamphetamine (1d) was synthesized in an identical manner with **1b** and was obtained as a noncrystallizable oil. It was converted into its sodium salt (2.5 *M* NaOH), which was recrystallized from isopropyl alcohol–ether and then regenerated with 10% HCl as an analytically pure oil,[11] which crystallized after 2 years, mp 44–46°.

Anal. Calcd for $C_{16}H_{19}NO_2S$: C, 66.44; H, 6.60; N, 4.84; S, 11.08. Found: C, 66.51; H, 6.75; N, 4.76; S, 11.30.

***N*-Tosyl-2-(*N*-methylaminomethyl)-2-phenyl-1,3-dioxolane (1f).**—*N*-Tosyl-α-aminoacetophenone[12] (230 g, 0.8 mol) and 100 g (1.6 mol) of ethylene glycol were refluxed for 48 hr (Dean-Stark condenser) in 500 ml of benzene containing 1 g of *p*-toluenesulfonic acid. The benzene was removed and the ketal was obtained in 90% yield after trituration with ether (mp 132–136°). An analytical sample was recrystallized from isopropyl ether–CH_2Cl_2, mp 139–139.5°.

Anal. Calcd for $C_{17}H_{19}NO_4S$: C, 61.24; H, 5.74; N, 4.20; S, 9.62. Found: C, 61.48; H, 5.81; N, 4.18; S, 9.42.

A mixture of 60 g (0.18 mol) of the ketal and 12.3 g (0.21 mol) of $NaOCH_3$ was stirred in 350 ml of dry DMF, and 43 g (0.30 mol) of CH_3I was added. The mixture was heated on a steam bath for 1.5 hr, poured into 1 l. of ice–water, extracted with three 250-ml portions of CH_2Cl_2, washed with 150 ml of 10% NaOH followed by 150 ml of saturated NaCl solution, dried (Na_2SO_4), filtered, evaporated, and crystallized from isopropyl ether–CH_2Cl_2 to afford 53.4 g (83%) of **1f**, mp 96–105°. Several recrystallizations from isopropyl ether afforded analytically pure material, mp 104.5–106.5°.

Anal. Calcd for $C_{18}H_{21}NO_4S$: C, 62.22; H, 6.09; N, 4.03; S, 9.23. Found: C, 62.50; H, 6.06; N, 3.85; S, 9.38.

3-Methoxymethoxy-3-phenyl-1-tosylazetidine (1i).—A solution of 60.7 g (0.2 mol) of 3-phenyl-1-tosyl-3-azetidinol[6] in 100 ml of dry DMF was slowly (*ca.* 15 min) added under nitrogen to a cooled (water bath), stirred mixture of 10.9 g (0.25 mol) of NaH (55% in mineral oil) in 250 ml of dry DMF. The mixture was stirred for 1 hr at 25°, then cooled to *ca.* 10° and 16.5 g (0.21 mol) of chloromethyl methyl ether was added dropwise, maintaining the temperature at 15–20°. Stirring was continued for 15 min, after which 50 ml of saturated aqueous NaCl was added, and the mixture was poured into 1 l. of ice-cold water. The product was filtered and washed with water and hexane, and 67.2 g (97%) of crude **1i** was obtained, mp 93–96°, and recrystallized from CH_2Cl_2–isopropyl ether, mp 97–97.5°.

Anal. Calcd for $C_{18}H_{21}NO_4S$: C, 62.22; H, 6.09; N, 4.03; S, 9.23. Found: C, 62.51; H, 6.22; N, 3.99; S, 8.90.

General Reduction Method.—The reductive cleavage reactions were carried out in air (calcium chloride drying tube) in a manner analogous to the reduction of **1f** described below. The reactions were terminated as soon as no more starting sulfonamide could be detected (tlc).

2-(*N*-Methylaminomethyl)-2-phenyl-1,3-dioxolane (2f).—A mixture of 0.59 mol of SMAH (172 g, benzene removed on rotary evaporator) and 52.4 g (0.147 mol) of **1f** in 320 ml of toluene was refluxed for 22 hr. The mixture was cooled, decomposed with 200 ml of 10% NaOH, extracted with ether, washed consecutively with 10% NaOH, water, and saturated aqueous NaCl, and then extracted with 250 ml of 1.1 *M* aqueous oxalic acid. The acid extract was washed with ether, basified with 50% NaOH, extracted with ether (after removing the sodium oxalate by filtration through celite), dried (Na_2SO_4), and distilled to give 15.8 g (56%) of **2f**: bp 73–75° (0.05 mm); nmr ($CDCl_3$) τ 8.63 (s, 1, NH), 7.62 (s, 3, NCH_3), 7.12 (s, 2, CH_2N), 6.12 (AA'BB', OCH_2CH_2O), 2.64 (m, 5, C_6H_5).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.61; H, 7.80; N, 7.29.

The hydrochloride salt of **2f** was prepared by addition of 1 ml of 4 *N* ethereal HCl to 0.23 g of **2f** in 25 ml of ether, filtration, and recrystallization from methanol–EtOAc, mp 227–228° (lit.[13]

(7) The reduction of **1f** required toluene to obtain an acceptable rate, presumably for steric reasons.

(8) A powerful thiol-like odor was noted throughout the reactions and work-ups. *p*-Thiocresol has been isolated in the $LiAlH_4$ reduction of *N*-tosyl-*N*-ethylaniline.[3]

(9) Melting points were determined in a capillary tube, and are corrected.

(10) Obtained from the Hynes Chemical Co., Watertree, S. C.; trade name Vite reducing agent.

(11) **1d** was isolated as an oil *via* a different route: P. Karrer and K. Ehrhardt, *Helv. Chim. Acta*, **34**, 2202 (1951).

(12) W. Kirmse and L. Horner, *Chem. Ber.*, **89**, 1674 (1956).

(13) H. Scheffer and A. Kottler, U. S. Patent 2,830,988 (1958).

mp 155–157°),[14] mass spectrum (70 eV) *m/e* 193 ($M\cdot^+$), 149, 105.

Anal. Calcd for $C_{11}H_{16}ClNO_2$: C, 57.51; H, 7.02; N, 6.10; Cl, 15.44. Found: C, 57.74; H, 7.06; N, 6.03; Cl, 15.33.

***cis*-3,7-Dihydroxyoctahydro-1,5-diazocine (2e).**—To 22.73 g (0.05 mol) of **1e** in 300 ml of benzene, 136.5 g (0.5 mol) of SMAH was added dropwise with stirring, after which the mixture was refluxed for 20 hr. The mixture was cooled and decomposed with 300 ml of water, 200 ml of ether was added, and it was filtered through Celite. The aqueous phase was acidified with HCl and washed well with ether, after which 19 g (0.11 mol) of *p*-toluenesulfonic acid was added and the solution was evaporated to dryness. The solid residue was crystallized from 150 ml of water to yield 8.0 g (33%) of the ditosylate salt **2e**, mp 279–280° dec (lit.[5] mp 279°).

3-Methoxymethoxy-3-phenylazetidine (2i).—Excess oxalic acid was added to the ether–benzene extract, obtained after decomposition of the excess SMAH, and the resulting crude hemioxalate (69%) was recrystallized from ethanol, mp 153.5–154°.

Anal. Calcd for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.95. Found: C, 54.84; H, 5.93; N, 5.02.

Addition of tosyl chloride to the hemioxalate of **2i** in pyridine regenerated **1i**. Hydrolysis of the hemioxalate of **2i** (refluxing ethanolic HCl) afforded, after basification with NaOH, 3-phenyl-3-azetidinol, mp 157–158.5° (lit.[15] mp 160–162°).

(14) Although there is a large discrepancy in melting points, our data are fully consistent with the assigned structure of **2f**.

(15) E. Testa and L. Fontanella, *Justus Liebigs Ann. Chem.*, **671**, 106 (1964).

Reduction of (*S*)-*N*-Tosylamphetamine (1d) with SMAH.—This reduction required 72 hr in refluxing toluene (0.0218 mol of **1d** and 0.089 mol of SMAH in 50 ml of toluene). The ether–toluene extract, after decomposition of the excess SMAH, was washed with 10% NaOH and water and then extracted with 0.6 *M* HCl, leaving an organic solution A. The acidic fraction was basified with NaOH, extracted with ether, dried ($MgSO_4$), filtered, and evaporated to give a 27% yield of (*S*)-amphetamine (ir), further characterized as its picrate (mixture melting point, ir, and $[\alpha]D$).

Glc analysis of solution A revealed only one component with a retention time identical with that of allylbenzene (*ca.* 0.003 mol).

Allylbenzene and β-Methylstyrene in Refluxing Toluene.—In separate experiments, 0.0015 ml of allylbenzene and of β-methylstyrene were each refluxed for 72 hr in 5 ml of toluene. Glc analysis of each experiment showed only the original olefin.

Allylbenzene and β-Methylstyrene under Conditions of the SMAH Reduction of 1d.—In separate experiments, 0.0015 mol of allylbenzene and of β-methylstyrene were each refluxed for 72 hr in 5 ml of toluene containing 0.0015 mol of *p*-toluenesulfonamide and 0.0089 mol of SMAH. The work-up procedure was identical with that used in the reduction of **1d**. Glc analysis of both experiments revealed *ca.* 0.0004 mol (25%) of allylbenzene and no detectable β-methylstyrene.

Registry No.—**1b**, 34542-10-4; **1c**, 34542-11-5; **1d**, 34542-12-6; **1f**, 34542-13-7; **1i**, 34542-14-8; **2f**, 34542-15-9; **2f** HCl, 34542-16-0; **2i**, 34542-17-1; SMAH, 34542-18-2; ketal (mp 132–136°), 34542-19-3.