Tosylmethylamines as "Nonstabilized" α-Aminocarbanion Synthon Equivalents: Advantages and Limitations

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Tosylmethylamines (**1**) are advantageous synthon equivalents for "nonstabilized" α-aminocarbanions of aromatic amines. Clean reactions and high yields are observed provided one-step procedures are utilized: the intermediate "nonstabilized" α-aminocarbanions are of low stability. Reactions formally involving dianions from bis(tosylmethyl)-substituted amines have also been achieved.

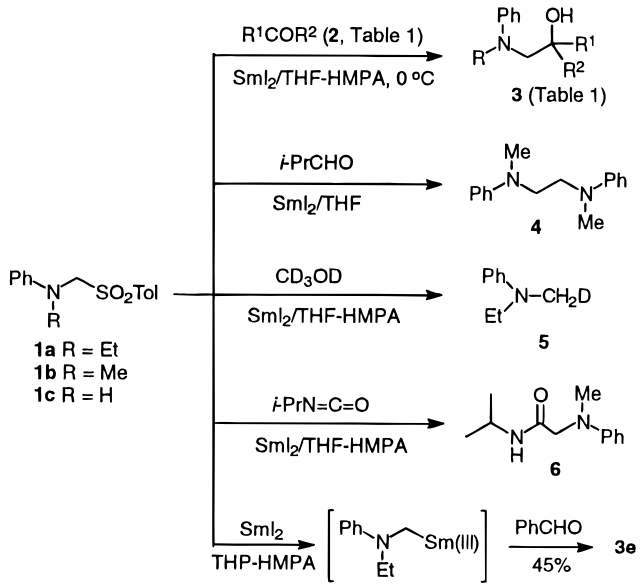
Introduction

"Stabilized" α-aminocarbanions are of great interest as synthetic intermediates and have been extensively studied over the last two decades. In contrast, the utility of "nonstabilized" α-aminocarbanions in synthetic organic chemistry is far less exploited because of the lack of appropriate methods for their generation, as recently discussed.[1] We recently reported a novel method to synthesize α-aminocarbanions as reactive intermediates from *N*-(α-aminoalkyl)benzotriazoles invoking a C−N bond scission.[1] The method provides easy access to a variety of substituted α-aminocarbanions from readily available starting materials. However, limited selectivity between the two C−N bonds present in *N*-(α-aminoalkyl)benzotriazoles sometimes leads to amine byproducts. The possibility of utilizing tosylmethylamines as the "nonstabilized" α-aminocarbanion synthon equivalents was therefore investigated, in the hope that the C−S bond would be specifically cleaved rather than the C−N bond.[2,3] We now report that this procedure, in many cases, gives good results and complements the benzotriazole methodology.

Results and Discussion

Transformations of Tosylmethylamines into α-Aminocarbanions. Transformations of tosylmethylamines into the corresponding α-aminocarbanions were achieved by treatment of tosylmethylamines with 2 equiv of samarium diiodide in the presence of an electrophile. For example, *N*-ethyl-*N*-(tosylmethyl)aniline (**1a**) reacted with 3-pentanone to afford 3-[(*N*-ethyl-*N*-phenylamino)-methyl]-3-pentanol (**3a**) in 70% yield, with no *N*-ethylaniline, which would form from the C−N bond scission, being detected in the reaction mixture (Scheme 1). Addition of HMPA (5% v/v of THF) to the reaction mixture improved the product yields to 91% for the above

Scheme 1



reaction. Use of isobutyraldehyde as the electrophile gave only the amine dimer, *N*,*N*′-dimethyl-*N*,*N*′-diphenyl-1,2-ethylenediamine[4] (**4**, 98%) when no HMPA was used; however, the addition of 5% of HMPA resulted in a 62% yield of the desired product **3d** and as little as 17% of dimer **4**. These results suggest a carbanion intermediate rather than a radical. If the reaction involves a radical intermediate, product **3d** should have formed in the isobutyraldehyde reaction without HMPA. Some further examples are shown in Scheme 1 and Table 1.

N-(Tosylmethyl)aniline (**1c**), with a proton on nitrogen, reacts with diethyl ketone and with methyl propyl ketone under the same conditions to afford the β-hydroxyamines **3f** and **3g** in 85% and 80% isolated yields, respectively (Table 1). When **1a** was treated with SmI_2 in the presence of CD_3OD, deuterium was incorporated at the α-position of the amine to give *N*-ethyl-*N*-(monodeuteriomethyl)aniline (D-/H-**5** = 4.5/1). Isocyanates can also be used as electrophiles; thus, isopropyl isocyanate reacted with *N*-methyl-*N*-(tosylmethyl)aniline (**1b**) to produce the glycine derivative **6** in 78% yield (Scheme 1).

By using these one-step reaction conditions, only a moderate yield (46%) was obtained for **1a** with aromatic benzaldehyde, therefore a two-step protocol[5] was tried. *N*-Ethyl-*N*-(tosylmethyl)aniline (**1a**) was first treated

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(1) Katritzky, A. R.; Qi, M.; Feng, D.; Nichols, D. A. *J. Org. Chem.* **1997**, *62*, 4121.

(2) Transformations have been reported of phenyl and allyl sulfones, and of geminal bis-phenyl sulfones into the corresponding carbanions, see: Alonso, E.; Guijarro, D.; Yus, M. *Tetrahedron* **1995**, *51*, 2699. Clayden, J.; Julia, M. *J. Chem. Soc., Chem. Commun.* **1994**, 2261. Chandrasekhar, S.; Yu, J.; Falck, J. R.; Mioskowski, C. *Tetrahedron Lett.* **1994**, *35*, 5441.

(3) After the present paper was written, Nájera and Yus groups reported transformation of α-aminomethyl sulfone into the α-nitrogenated organolithium compounds by using large excess of lithium and catalytic amount of naphthalene in moderate yields (25−54%, six examples), see Alonso, D. A.; Alonso, E.; Nájera, C.; Ramón, D. J.; Yus, M. *Tetrahedron* **1997**, *53*, 4835.

(4) Giezendanner, H.; Hesse, M.; Schmid, H. *Org. Mass Spectrom.* **1970**, *4*, 405.

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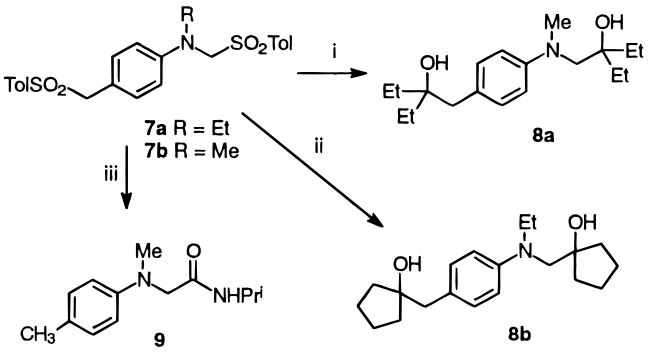
Table 1. Preparation of β-Hydroxyamines 3 by Reactions of Tosylmethylamines with Carbonyl Compounds[a]

compd	R	R^1	R^2	isolated yield (%)
3a	Et	Et	Et	91
3b	Me	Et	Et	98
3c	Me	$-(CH_2)_4-$		88
3d	Me	*i*-Pr	H	62[b]
3e	Et	Ph	H	46
3f	H	Et	Et	85
3g	H	Me	*n*-Pr	80
3h	Et	cyclohexyl	H	41

[a] All reactions were performed using the general procedure (see Experimental Section). [b] Some amine dimer was obtained, see text.

Scheme 2[a]



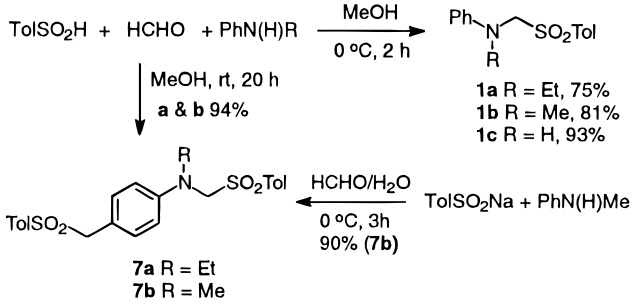
[a] (i) SmI_2 (4 equiv)/THF−HMPA, 3-pentanone, 54%; (ii) SmI_2 (4 equiv)/THF−HMPA, cyclopentanone, 33%; (iii) SmI_2 (4 equiv)/THF−HMPA, *i*-PrNCO, 65%.

with SmI_2 in tetrahydropyran (THP) and HMPA[6] at room temperature for 5 min (the purple color of SmI_2/THF−HMPA disappeared during this time) to form the organosamarium intermediate,[7] and benzaldehyde was then added to the reaction mixture to give, after the usual workup, 45% of the β-hydroxyamine **3e** (Scheme 1).

Reactions of *p*-(Tosylmethyl)-*N*-alkyl-*N*-(tosylmethyl)anilines (7). Both of the C−S bonds in the *p*-(tosylmethyl)-*N*-alkyl-*N*-(tosylmethyl)anilines (**7a**,**b**) can be reacted to produce a dianion equivalent in a one-pot procedure. Thus, treatment of *p*-(tosylmethyl)-*N*-methyl-*N*-(tosylmethyl)aniline (**7b**) with 3-pentanone and 4 equiv of samarium diiodide in THF−HMPA gives 54% yield of amino diol **8a** *via* what is formally a dicarbanion species (Scheme 2). Similarly, amino diol **8b** was obtained from the reaction of *p*-(tosylmethyl)-*N*-ethyl-*N*-(tosylmethyl)-aniline (**7a**) with cyclopentanone. When isopropyl isocyanate was used as the electrophile, only one amide group was introduced into the α-position of the amine to give **9** in 65% isolated yield.

Synthesis of Tosylmethylamines. The first reported preparations of tosylmethylamines from amines, formaldehyde, and sulfinic acids[8,cf.9] or their sodium salts[8] stem from the pre-NMR era. Our results conflict somewhat with the early reports.[8] According to ^1H and ^{13}C NMR, the reaction of sodium *p*-tolylsulfinate, formaldehyde and *N*-ethylaniline gives a mixture of *N*-ethyl-*N*-(tosylmethyl)aniline (**1a**, major) and *p*-(tosylmethyl)-*N*-ethyl-*N*-(tosylmethyl)aniline (**7a**); analogous reaction of sodium *p*-tolylsulfinate, formaldehyde, and *N*-methylaniline forms only *p*-(tosylmethyl)-*N*-methyl-*N*-(tosylmethyl)aniline (**7b**) (Scheme 3). When *p*-tolylsulfinic acid was used instead of its sodium salt, pure *N*-ethyl-*N*-(tosylmethyl)aniline (**1a**), *N*-methyl-*N*-(tosylmethyl)-aniline (**1b**)[9] or *N*-(tosylmethyl)aniline (**1c**) were each obtained from *N*-ethylaniline, *N*-methylaniline, and aniline, respectively, in high yields after 2 h at 0 °C. However, if reaction mixtures of *p*-tolylsulfinic acid, formaldehyde, and *N*-ethyl- or *N*-methylanilines were stirred for a longer time (20 h) at room temperature, pure *p*-(tosylmethyl)-*N*-ethyl- and -*N*-methyl-*N*-(tosylmethyl)aniline (**7a**,**b**), respectively, were formed in high yields, regardless of the molar ratio of *p*-tolylsulfinic acid to formaldehyde to aniline used. All synthesized tosylmethylamines have been fully characterized by ^1H, ^{13}C NMR, and microanalysis.

Scheme 3



However, there are two major limitations to the methodology presently reported. First, the procedure is limited to aromatic amines. To the best of our knowledge, there is no report on the synthesis of any α-tosyl substituted secondary aliphatic amine,[10,11] and our own attempts at reactions of *p*-tolylsulfinic acid and formaldehyde with pyrrolidine were unsuccessful. Secondly, aldehydes, other than formaldehyde, cannot be used in the condensation reaction as shown in Scheme 3,[8] so α-substituted aminocarbanions are not available using the present route. Hence, the present methodology is limited to the preparation of anions of type $ArN(R)CH_2^-$. To summarize, we have developed a new and convenient protocol for the preparation of such "nonstabilized" α-aminocarbanions, which in turn can be trapped by various electrophiles for the synthesis of poly-functionalized molecules. The present method complements the previously described benzotriazole approach:[1] for the class of α-aminocarbanions $ArN(R)CH_2^-$, the present

(5) (a) Curran, D. P.; Totleben, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 6050. (b) Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943.

(6) (a) Murakami, M.; Hayashi, M.; Ito, Y. *J. Org. Chem.* **1992**, *57*, 793. (b) Murakami, M.; Hayashi, M.; Ito, Y. *Appl. Organometal. Chem.* **1995**, *9*, 385. (c) Booth, S. E.; Benneche, T.; Undheim, K. *Tetrahedron* **1995**, *51*, 3665.

(7) SmI_2-promoted reactions have frequently been proposed to proceed by way of unstable organosamarium (III) intermediates, see ref 5. Walborsky, H. M.; Topolski, M. *J. Org. Chem.* **1992**, *57*, 370. Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1991**, *56*, 4112.

(8) Bäder, E.; Hermann, H. D. *Chem. Ber.* **1955**, *88*, 41.

(9) Beifuss, U.; Kunz, O.; Ledderhose, S.; Taraschewski, M.; Tonko, C. *Synlett* **1996**, 34.

(10) Indirect synthesis of α-tosylamines have been reported by oxidization of α-thioamines using H_2O_2, see: Kulikovskaya, E. A.; Kuznetsova, T. G.; Gvitsaev, E. I.; Slizhov, Y. E.; Dozmorov, S. V. *Tr. Tomsk. Gos. Univ.* **1973**, *249*, 31; *Chem. Abstr.* **1975**, *82*, 97618m.

(11) In this connection, we found some mistakes in CAS Online. A CAS Online substructure search for α-sulfonylamines [substructure: $G^1SO_2C(G^2)_2N(CH_2G^2)_2$, G^1 = C, G^2 = C, H, N, O, S, P, Si, Cl, Br, F, I, B] resulted in a few reports[12] which contained the expected compounds. However, inspection of these original reports demonstrated that they did not report any derivatives of type SO_2−C−N; instead, compounds of type SO_2−N (without any methylene moiety between the N and S) were described.

(12) (a) Toshuki, M. *Jpn. Kokai Tokkyo Koho JP* 05,323,541 [93,323,541]; *Chem. Abstr.* **1994**, *121*, 241576q. (b) De, A. U.; Pal, D. *J. Pharm. Sci.* **1977**, *66*, 232.

procedure gives cleaner reactions, higher yields, and a novel route to dianions. On the other hand, the limited availability of the starting α-aminoalkyl sulfones, means that the benzotriazole approach possesses wider synthetic utility.

Experimental Section

General Comments. Melting points were measured on a hot-stage microscope and are uncorrected. ^{1}H and ^{13}C NMR data were collected on a 300 MHz NMR spectrometer (300 and 75 MHz, respectively), with TMS as internal reference in $CDCl_3$. All mass spectra were determined on a HP5890 Series II Capillary GC operating in split mode with helium carrier gas and fitted with a mass selective detector (MSD). The column used was a HP5 capillary column 30 m × 0.25 mm, with 0.25 μm film thickness of 5% phenylmethylsilicone gum. The temperature program used the initial temperature of 50 °C for 1 min and then ramped at 10 °C min^{-1} to 250 °C. Column chromatography was carried out using 230−400 mesh silica.

General Procedure for One-Step Tosylmethylamines Reactions. A solution of the appropriate tosylmethylamines (2 mmol) and electrophiles (2 mmol) in THF (10 mL) was added dropwise to the SmI_2 (4.5 mmol) solution in THF−HMPA (20:1) at 0 °C under argon or nitrogen. The reaction was kept stirring until the deep purple color disappeared (generally 2−4 h) and then quenched with saturated aqueous $NaHCO_3$ solution (40 mL) at the same temperature. The reaction mixture was separated, and the aqueous phase was extracted with diethyl ether (2 × 40 mL). The combined organic extracts were washed with saturated aqueous NaCl, dried, and evaporated to give the crude product which was purified by flash column chromatography on silica gel (eluent: hexanes−ethyl acetate−0.5% triethylamine) to afford the pure product.

1-[(*N*-Phenyl-*N*-ethylamino)methyl]-3-pentanol (3a): colorless oil; ^{1}H NMR δ 0.92 (t, 6H, J = 7.5 Hz), 1.11 (t, 3H, J = 7.2 Hz), 1.55 (q, 4H, J = 7.5 Hz), 1.83 (s, 1H), 3.26 (s, 2H), 3.43 (q, 2H, J = 7.2 Hz), 6.71 (t, 1H, J = 7.2 Hz), 6.89 (d, 2H, J = 8.1 Hz), 7.21 (t, 2H, J = 7.5 Hz); ^{13}C NMR δ 7.9, 10.6, 29.2, 46.6, 58.2, 75.9, 113.9, 116.9, 129.0, 149.6. Anal. Calcd for $C_{12}H_{23}NO$: C, 75.97; H, 10.47; N, 6.33. Found: C, 75.87; H, 10.75; N, 6.54.

1-[(*N*-Phenyl-*N*-methylamino)methyl]-3-pentanol (3b):[1] colorless oil; ^{1}H NMR δ 0.93 (t, 6H, J = 7.4 Hz), 1.55 (q, 4H, J = 7.5 Hz), 1.92 (br s, 1H), 2.96 (s, 3H), 3.28 (s, 2H), 6.73 (t, 1H, J = 7.4 Hz), 6.89 (d, 2H, J = 8.0 Hz), 7.22 (t, 2H, J = 7.5 Hz); ^{13}C NMR δ 11.5, 46.2, 59.3, 71.4, 113.7, 117.3, 125.9, 127.7, 128.4, 129.3, 142.0, 148.2.

1-[(*N*-Phenyl-*N*-methylamino)methyl]-1-cyclopentanol (3c): colorless oil; ^{1}H NMR δ 1.53−1.74 (m, 6H), 1.75−1.95 (m, 2H), 2.11 (br s, 1H), 2.94 (s, 3H), 3.37 (s, 2H), 6.72 (t, 1H, J = 7.2 Hz), 6.85 (d, 2H, J = 8.5 Hz), 7.20 (t, 2H, J = 7.5 Hz); ^{13}C NMR δ 23.4, 38.3, 40.1, 62.2, 83.2, 112.9, 117.0, 128.9, 151.0. Anal. Calcd for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82. Found: C, 76.08; H, 9.68; N, 6.77.

1-[(*N*-Phenyl-*N*-methylamino)]-3-methyl-2-butanol (3d):[1] colorless oil; ^{1}H NMR δ 1.01 (d, 3H, J = 6.9 Hz), 1.05 (d, 3H, J = 6.8 Hz), 1.70−1.83 (m, 1H), 2.32 (br s, 1H), 2.95 (s, 3H), 3.17−3.37 (m, 2H), 3.65−3.74 (m, 1H), 6.79 (t, 1H, J = 7.4 Hz), 6.84 (d, 2H, J = 8.2 Hz), 7.26 (t, 2H, J = 7.4 Hz); ^{13}C NMR δ 17.7, 18.7, 31.9, 39.2, 58.4, 73.5, 113.7, 117.6, 129.1, 150.7.

1-Phenyl-2-(*N*-phenyl-*N*-ethylamino)ethanol (3e): colorless oil; ^{1}H NMR δ 1.09 (t, 3H, J = 7.1 Hz), 2.71 (br s, 1H), 3.46 (q, 2H, J = 7.1 Hz), 3.36−3.51 (m, 2H), 4.92 (dd, 1H, J = 4.4, 8.5 Hz), 6.76 (t, 1H, J = 7.4 Hz), 6.84 (d, 2H, J = 8.2 Hz), 7.20−6.45 (m, 7H); ^{13}C NMR δ 11.5, 46.2, 59.3, 71.4, 113.7, 117.3, 125.9, 127.7, 128.4, 129.3, 142.0, 148.2. Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.64; H, 7.70; N, 6.08.

3-[(Phenylamino)methyl]-3-pentanol (3f): colorless oil; ^{1}H NMR δ 0.89 (t, 6H, J = 7.4 Hz), 1.55 (q, 4H, J = 7.5 Hz), 1.87 (br s, 1H), 3.05 (s, 2H), 3.89 (br s, 1H), 6.64 (d, 2H, J = 7.8 Hz), 6.70 (t, 1H, J = 7.3 Hz), 7.16 (t, 2H, J = 8.3 Hz); ^{13}C NMR δ 7.7, 29.1, 50.8, 74.5, 113.1, 117.4, 129.1, 148.8. Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.84; H, 10.16; N, 7.27.

2-[(Phenylamino)methyl]-2-pentanol (3g): colorless oil; ^{1}H NMR δ 0.93 (t, 3H, J = 7.2 Hz), 1.21 (s, 3H), 1.30−1.56 (m, 4H), 1.94 (br s, 1H), 3.03 and 3.06 (AB, 2H, J_{AB} = 12.6 Hz), 3.93 (br s, 1H), 6.64 (d, 2H, J = 7.5 Hz), 6.70 (t, 1H, J = 7.5 Hz), 7.16 (t, 2H, J = 7.7 Hz); ^{13}C NMR δ 14.6, 17.1, 24.9, 42.6, 53.5, 72.6, 113.1, 117.5, 129.2, 148.7. Anal. Calcd for $C_{12}H_{19}NO$: C, 74.54; H, 9.91; N, 7.25. Found: C, 74.84; H, 10.30; N, 7.28.

1-Cyclohexyl-2-(*N*-phenyl-*N*-ethylamino)ethanol (3h): colorless oil; ^{1}H NMR δ 1.12 (t, 3H, J = 7.1 Hz), 1.15−1.36 (m, 5H), 1.37−1.52 (m, 1H), 1.64−1.84 (m, 4H), 1.85−1.98 (m, 1H), 2.33 (br s, 1H), 3.12 (dd, 1H, J = 10.2, 14.7 Hz), 3.25−3.55 (m, 3H), 3.58−3.68 (m, 1H), 6.74 (t, 1H, J = 7.2 Hz), 6.80 (d, 2H, J = 7.8 Hz), 7.23 (t, 2H, J = 7.2 Hz); ^{13}C NMR δ 11.5, 26.0, 26.2, 26.5, 28.2, 29.0, 41.8, 46.2, 55.3, 72.5, 113.9, 117.2, 129.1, 148.7. Anal. Calcd for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.91; H, 10.40; N, 5.83.

***N*-Ethyl-*N*-(monodeuteriomethyl)aniline (5, 82% D):** colorless oil; ^{1}H NMR δ 1.11 (t, 3H, J = 7.2 Hz), 2.87 (t, 2H, J = 1.5 Hz, D-**5**) [2.89 (s, 3H), H-**5**], 3.39 (q, 2H, J = 7.2 Hz), 6.63−6.76 (m, 3H), 7.23 (t, 2H, J = 8.4 Hz); ^{13}C NMR δ 11.2, 36.9 (t, J_{CD} = 20.5 Hz, D-**5**) [38.2, H-**5**], 46.8, 112.4, 116.0, 129.1, 149.2.

***N*-Isopropyl-(*N*-methyl-*N*-phenylamino)acetamide (6):**[1] white solid, mp 91−93 °C (lit.[1] 92−94 °C); ^{1}H NMR δ 1.12 (d, 6H, J = 6.6 Hz), 2.99 (s, 3H), 3.81 (s, 2H), 4.08−4.22 (m, 1H), 6.44 (br s, 1H), 6.73 (d, 2H, J = 8.2 Hz), 6.84 (t, 1H, J = 7.4 Hz), 7.28 (t, 2H, J = 7.7 Hz); ^{13}C NMR δ 22.5, 39.6, 41.0, 58.9, 113.1, 118.5, 129.2, 149.3, 169.3.

General Procedure for the Dianion Reactions. General procedure for one-step tosylmethylamine reactions were followed, except that 4 equiv of SmI_2 was used instead of 2 equiv.

***N*-Methyl-*N*-(2-hydroxy-2-ethylbutyl)-4-(2-hydroxy-2-ethylbutyl)aniline (8a):** colorless oil; ^{1}H NMR δ 0.91 (t, 6H, J = 7.5 Hz), 0.94 (t, 6H, J = 7.2 Hz), 1.24 (br s, 1H), 1.44 (q, 4H, J = 7.5 Hz), 1.57 (q, 4H, J = 7.5 Hz), 1.82 (br s, 1H), 2.63 (s, 2H), 2.97 (s, 3H), 3.27 (s, 2H), 6.84 (d, 2H, J = 8.7 Hz), 7.06 (d, 2H, J = 8.4 Hz); ^{13}C NMR δ 7.9, 8.0, 29.2, 30.2, 41.1, 43.6, 61.4, 74.5, 76.0, 112.8, 125.6, 131.1, 150.2. Anal. Calcd for $C_{19}H_{33}NO_2$: C, 74.22; H, 10.82; N, 4.56. Found: C, 74.02; H, 11.05; N, 4.65.

***N*-Ethyl-*N*-[(1-hydroxycyclopentyl)methyl]-4-[(1-hydroxycyclopentyl)methyl]aniline (8b):** colorless oil; ^{1}H NMR δ 1.13 (t, 3H, J = 7.2 Hz), 1.43 (br s, 1H), 1.49−1.98 (m, 16H), 2.13 (br s, 1H), 2.77 (s, 2H), 3.37 (s, 2H), 3.43 (q, 2H, J = 6.9 Hz), 6.83 (d, 2H, J = 8.7 Hz), 7.08 (d, 2H, J = 8.4 Hz); ^{13}C NMR δ 11.0, 23.5, 38.6, 39.2, 46.0, 46.2, 59.8, 82.2, 82.9, 114.0, 126.7, 130.7, 148.1. Anal. Calcd for $C_{20}H_{31}NO_2$: C, 75.67; H, 9.84; N, 4.41. Found: C, 75.25; H, 10.30; N, 4.36.

***N*-Isopropyl-[*N*-(4-methylphenyl)-*N*-methylamino]-acetamide (9):** mp 83−85 °C; ^{1}H NMR δ 1.12 (d, 6H, J = 6.3 Hz), 2.27 (s, 3H), 2.95 (s, 3H), 3.76 (s, 2H), 4.06−4.21 (m, 1H), 6.47 (br s, 1H), 6.65 (d, 2H, J = 9.0 Hz), 7.08 (d, 2H, J = 8.1 Hz); ^{13}C NMR δ 20.2, 22.7, 39.9, 41.0, 59.5, 113.5, 128.1, 129.8, 147.5, 169.6. Anal. Calcd for $C_{13}H_{20}N_2O$: C, 70.87; H, 9.15; N, 12.72. Found: C, 70.69; H, 9.49; N, 12.68.

Two-Step Reaction Procedure. A solution of *N*-(tosylmethyl)-*N*-ethylaniline (**1a**) (0.73 g, 2.5 mmol) in dry THP (10 mL) was added to a stirred SmI_2/THP−HMPA solution[6b] (4.5 mmol) at room temperature under argon for approximately 5 min. Benzaldehyde (0.32 g, 2 mmol) was then added and after 1.5 h, the reaction was quenched with water. After the usual workup, 1-phenyl-2-[(*N*-phenyl-*N*-ethylamino)methyl]ethanol (**3e**) was isolated in 45% yield.

General Procedure for Preparing Tosylmethylamines (1). Aqueous formaldehyde (37%, 1.70 g, 21 mmol) and a solution of the substituted aniline (20 mmol) in methanol (20 mL) were added, in turn, to a solution of *p*-toluenesulfinic acid (20 mmol) in methanol (20 mL) at 0 °C and stirred for 2 h. The precipitate was filtered with suction and dried under vacuum to give the product **1**.

***N*-(Tosylmethyl)-*N*-ethylaniline (1a):**[8] 4.34 g, 75% yield; mp 101−103 °C (lit.[8] 105 °C); ^{1}H NMR δ 1.15 (t, 3H, J = 7.1 Hz), 2.42 (s, 3H), 3.44 (q, 2H, J = 7.2 Hz), 4.74 (s, 2H), 6.69 (d, 2H, J = 8.5 Hz), 6.76 (t, 1H, J = 7.4 Hz), 7.14 (t, 2H, J = 7.6 Hz), 7.28 (d, 2H, J = 8.0 Hz), 7.77 (d, 2H, J = 8.2 Hz); ^{13}C NMR δ 11.5, 21.5, 45.4, 74.5, 113.7, 118.7, 128.7, 128.9, 129.7, 135.7, 144.8, 145.6. Anal. Calcd for $C_{16}H_{19}NO_2S$: C, 66.41; H, 6.62; N, 4.84. Found: C, 66.01; H, 6.70; N, 4.42.

***N*-(Tosylmethyl)-*N*-methylaniline (1b):**[8] microcrystals, mp 95−97 °C [lit.[8] 113 °C]; ^{1}H NMR δ 2.36 (s, 3H), 2.94 (s, 3H), 4.70 (s, 2H), 6.62 (d, 2H, J = 8.2 Hz), 6.72 (t, 1H, J = 7.4 Hz), 7.09 (t, 2H, J = 7.6 Hz), 7.21 (d, 2H, J = 8.2 Hz), 7.70 (d, 2H, J = 8.2 Hz); ^{13}C NMR δ 21.4, 39.1, 76.0, 113.0, 118.7, 128.7, 128.8, 129.7, 135.7, 144.8, 146.7. Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.43; H, 6.22; N, 5.09. Found: C, 65.77; H, 6.51; N, 5.10.

***N*-(Tosylmethyl)aniline (1c):**[8] mp 135−137 °C [lit.[8] 137 °C]; ^{1}H NMR δ 2.38 (s, 3H), 4.60 (s, 3H), 6.53 (d, 2H, J = 8.0 Hz), 6.72 (t, 1H, J = 7.4 Hz), 7.06 (t, 2H, J = 7.5 Hz), 7.24 (d, 2H, J = 8.0 Hz), 7.73 (d, 2H, J = 8.2 Hz); ^{13}C NMR δ 21.5, 67.4, 113.4, 119.4, 128.9, 129.1, 129.7, 135.0, 144.4, 144.9. Anal. Calcd for $C_{14}H_{15}NO_2S$: C, 64.34; H, 5.79; N, 5.36. Found: C, 64.48; H, 6.02; N, 5.35.

General Procedure for the Synthesis of *p*-(Tosylmethyl)-*N*-alkyl-*N*-(tosylmethyl)aniline (7). Aqueous formaldehyde (37%, 1.70 g, 21 mmol) and a solution of the *N*-ethylaniline or *N*-methylaniline (10 mmol) in methanol (20 mL) were added, in turn, to a solution of *p*-toluenesulfinic acid (10 mmol) in methanol (20 mL) at 0 °C. The reaction mixture was stirred at room temperature for about 20 h. The precipitate was filtered with suction and dried under vacuum to give the product.

***p*-(Tosylmethyl)-*N*-ethyl-*N*-(tosylmethyl)aniline (7a):** 4.3 g, 94% yield; microcrystals, mp 143−145 °C (lit.[8] 146−147 °C); ^{1}H NMR δ 1.12 (t, 3H, J = 7.1 Hz), 2.43 (s, 6H), 3.40 (q, 2H, J = 7.1 Hz), 4.16 (s, 2H), 4.70 (s, 2H), 6.58 (d, 2H, J = 8.5 Hz), 6.87 (d, 2H, J = 8.6 Hz), 7.26 (d, 2H, J = 8.2 Hz), 7.31 (d, 2H, J = 8.2 Hz), 7.52 (d, 2H, J = 8.1 Hz), 7.75 (d, 2H, J = 8.0 Hz); ^{13}C NMR δ 11.4, 21.6, 45.5, 62.0, 73.9, 113.2, 117.6, 128.4, 128.7, 129.4, 129.9, 131.5, 135.2, 135.4, 144.4, 145.2, 145.9. Anal. Calcd for $C_{24}H_{27}NO_4S_2$: C, 62.99; H, 5.95; N, 3.06. Found: C, 63.28; H, 6.14; N, 3.11.

***p*-(Tosylmethyl)-*N*-methyl-*N*-(tosylmethyl)aniline (7b):** microcrystals, mp 165−168 °C (lit.[8] 164−166 °C); ^{1}H NMR δ 2.41 (s, 3H), 2.43 (s, 3H), 2.95 (s, 3H), 4.15 (s, 2H), 4.72 (s, 2H), 6.55 (d, 2H, J = 8.7 Hz), 6.86 (d, 2H, J = 8.7 Hz), 7.27 (t, 4H, J = 8.4 Hz), 7.50 (d, 2H, J = 8.1 Hz), 7.75 (d, 2H, J = 8.1 Hz); ^{13}C NMR δ 21.6, 39.3, 62.0, 75.6, 112.8, 117.9, 128.5, 128.7, 129.4, 129.9, 131.5, 135.3, 135.4, 144.5, 145.3, 147.0. Anal. Calcd for $C_{23}H_{25}NO_4S_2$: C, 62.28; H, 5.68; N, 3.16. Found: C, 62.55; H, 5.43; N, 3.21.

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