monohydrate and methanol in a molar ratio (epoxide/acid/methanol) of 1:0.1:6 in anhydrous CH_2Cl_2 (10 mL) at 25 °C. The resulting mixture was stirred for 24 h at the same temperature and then treated with solid $NaHCO_3$ and saturated aqueous $NaHCO_3$. Evaporation of the washed (water) organic solvent gave a residue (0.095 g) which was analyzed by GLC (see Table I). GLC analysis of the crude product obtained by the same reaction of **4** and **5**, but stopping after different reaction times, showed the same product composition within experimental error.

Reactions of the Epoxides 4 and 5 with Trichloroacetic Acid in Several Solvents. The reactions were carried out in anhydrous benzene, cyclohexane, CCl_4, $CHCl_3$, and CH_2Cl_2 in the following way. A solution of **4** or **5** (0.10 g, 0.44 mmol) in the solvent (10 mL) at 25 °C was treated with a 1 M solution of trichloroacetic acid in the same solvent (0.48 mL), stirred for 3 h at the same temperature, washed with saturated aqueous $NaHCO_3$ and water, and evaporated to dryness. The residue obtained, consisting of mixtures of monotrichloroacetates, was hydrolyzed in the following way. The crude product was dissolved in freshly distilled THF (8 mL), treated with 1 M KOH in ethanol (2.5 mL), and then left 5 h at room temperature. Dilution with water, extraction with ether, and evaporation of the washed (water) and dried ether extracts yielded a mixture of **8** and **9** which was analyzed by GLC (see Table II). Reaction of **4** and **5** in each solvent carried out under the same conditions, but stopping after a longer reaction time of contact with the acid, yielded the same product composition within the experimental error. Experiments showed that the diols **8** and **9** are stable under the saponification conditions and that the method of saponification used does not alter the stereoselectivity of the reactions.

Acknowledgment. This work was supported in part by a grant from Consiglio Nazionale delle Ricerche (Roma).

Registry No. *cis*-**4**, 92695-13-1; (±)-*trans*-**5**, 92695-14-2; **6**, 1142-21-8; **7**, 1142-22-9; **8**, 63035-52-9; (±)-**9**, 92695-21-1; (±)-**10**, 92695-15-3; (±)-**11**, 92695-16-4; (±)-**12**, 92695-22-2; (±)-**19**, 92695-17-5; (±)-**20**, 92695-18-6; (±)-**21**, 92695-19-7; (±)-**22**, 92695-20-0; **24**, 63035-65-4; $PhCH_2CHO$, 122-78-1; $Ph(CH_2)_2P^+Ph_3 \cdot Br^-$, 53213-26-6; (*E*,*E*)-PhCH=CHCH=CHPh, 538-81-8.

Behavior of Benzyl Sulfoxides toward Acid Chlorides. Useful Departures from the Pummerer Reaction[1]

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The present study extends the reaction of certain electrophilic reagents with electron-rich sulfides and sulfoxides beyond previously known limits. Thus, treatment of methoxy- and, more particularly, aminobenzyl sulfoxides **2** with acyl or hydrogen chlorides gives rise in high yields to the corresponding benzyl chlorides, a departure from the normally expected Pummerer reaction. It is demonstrated that ideal substrates for this reaction are *o*-[(methylthio)methyl]anilines **1** derived from the well-known rearrangement of aromatic sulfilimines. Further, certain of the *o*-ammoniobenzyl chloride salts **4** so produced provide a basis for a novel and superior desulfurization of **1** to the corresponding *o*-methylaniline without resorting to Raney nickel.

The Pummerer reaction as generally defined[2] is the rearrangement of a sulfoxide (or sulfide at equivalent oxidation state) under acid conditions to form an α-substituted sulfide, the overall result being reduction of the sulfoxide group and oxidation of the adjacent carbon atom. Halomethyl sulfides or, via hydrolysis, aldehydes are the final products. The reaction is initiated by electrophilic attack at the sulfoxide moiety followed by expulsion of an α proton. Nucleophilic attachment at the α carbon with reduction at sulfur, results in an α-substituted sulfide.

Simple oxidative substitution of sulfides by halogen also produces α-halo sulfides.[3-5] Similarly, reactions of sulfoxides with sulfuryl chloride,[6,7] molecular chlorine,[8] and *N*-halosuccinimide[9] generally result in halogenation α to the sulfoxide.

Nevertheless, certain types of sulfides and sulfoxides have also been shown under halogenation conditions to give fission of the carbon–sulfur bond, producing an alkyl halide. References describing these studies explain such cleavage as due to a stabilizing carbonium ion intermediate. Thus, sulfides containing phthalimidomethyl,[10] benzyl-,[4b,11,12] *sec*-alkyl,[13] and *tert*-alkyl[4b] groups give the respective alkyl halide upon halogenation. In like manner, sulfoxides containing phthalimidomethyl[14] and benzyl or *tert*-butyl[15] moieties produce the respective alkyl halide along with sulfinic acid derivatives as cleavage products upon halogenation.

Less is known about such cleavage when nonoxidizing, acidic reagents are combined with sulfoxides capable of producing stabilized carbonium ion intermediates. It could be postulated, for instance, that halogen acids or acyl

(1) Presented at the 187th National Meeting of the American Chemical Society, St. Louis, MO, April 8–13, 1984, ORGN 218.
(2) Russell, G. A.; Mikol, G. J. In "Mechanisms of Molecular Migrations"; Thyagarajan, B. S., Ed.; Wiley: New York, 1968; Vol. 1, Chapter 4, pp 157–207.
(3) (a) Bordwell, F. G.; Pitt, B. M. *J. Am. Chem. Soc.* **1952**, *77*, 3594. (b) Truce, W. E.; Birum, G. H.; McBee, E. T. *J. Am. Chem. Soc.* **1952**, *74*, 3594.
(4) Tuleen, D. L.; Stephens, T. B. (a) *Chem. Ind. (London)* **1966**, 1555; (b) *J. Org. Chem.* **1969**, *34*, 31.
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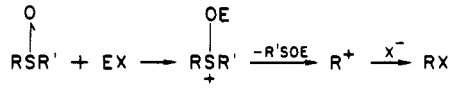
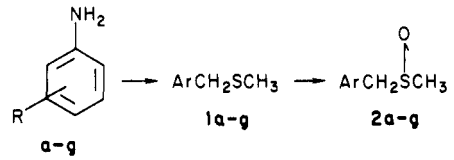
halides with such substrates could give rise to a carbonium ion by cleavage of the protonated or acylated sulfoxide, with consequent generation of alkyl halide (eq 1). In fact,



(1)

during research designed to study mechanistic pathways for sulfoxide mutarotation, Kwart[16] found ready formation of benzyl chloride and/or benzyl acetate as well as the Pummerer product benzaldehyde upon reaction of HCl with benzyl aryl sulfoxides in acetic acid/acetic anhydride or dioxane solutions. From another study,[17] cleavage rather than a Pummerer reaction was found upon expulsion of methanesulfenic acid (CH_3SOH) from acid-promoted cyclization of (methylsulfinyl)methyl dialkyldithiocarbamates.

We have therefore examined sulfoxides where the Pummerer intermediate, prior to α-proton elimination, might be induced to carbon–sulfur bond cleavage through the intermediacy of a stabilized carbonium ion. For such a study, nuclearly substituted benzyl methyl sulfoxides seemed appropriate. These materials have been subjected to previous, systematic Pummerer reaction studies where the conversion of certain electron-rich sulfoxides to aldehydes have inexplicably not been observed.[18] A particularly electron-rich type of benzyl sulfoxide is available from simple oxidation of the *o*-[(methylthio)methyl]-anilines, in turn easily derived from recently developed sulfilimine chemistry[19-22] (eq 2).



(2)

a-g

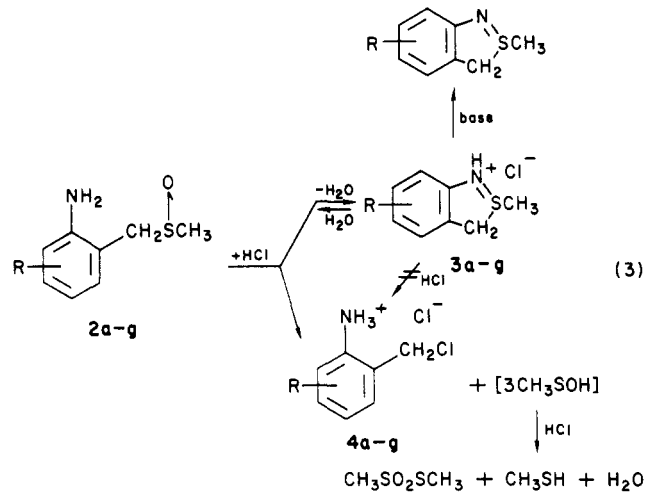
a, R = H; b, R = 2-Et; c, R = 2-Me; d, R = 2-CH_3O; e, R = 2-CO_2CH_3; f, R = 2-MeO, 3-Cl; g, R = 2-CF_3

(see Experimental Section for sulfilimine and oxidation procedures)

In order to provide uniform conditions and minimize counterions, reactions of the selected sulfoxides with HCl were carried out in inert solvents such as carbon tetrachloride, toluene, and best, 1,2-dichloroethane. With neutral substrates the mixture was washed with water, and product isolation was accomplished by solvent separation and removal. Benzyl methyl sulfoxide gave benzaldehyde as the Pummerer product, while the more electron-rich anisyl substrate gave a nearly quantitative yield of the cleavage product *p*-anisyl chloride.

The *o*-aminobenzyl sulfoxides, when treated with a stream of HCl, formed salts which were ultimately insoluble in the reaction solvent (eq 3). These materials could be filtered off and identified by spectral and micro analyses and further identified by suitable derivatization. In this manner, high yields of *o*-ammonium benzyl chloride salts could be isolated, a feat only heretofore accomplished from the requisite *o*-aminobenzyl alcohols.[23]

During the course of reaction, water is generated. Although it appears that a number of minor sulfur impurities arise during the reaction, a main destination of the sulfenic acid cleavage product is methyl methanethiolsulfonate. This thio ester could arise from disproportionation of methanesulfenic acid with simultaneous formation of methyl mercaptan (eq 3), perhaps through the intermediacy of methanesulfenyl chloride, the latter type having been shown to form on treatment of sulfenic acid with HCl.[24]



(3)

Close inspection of this reaction reveals that prior to product formation, a cyclic sulfilimine salt **3** is formed by loss of water. These salts are known materials, quite analogous to the acyclic variety alluded to earlier, and usually formed by an oxidative ring closure of an *o*-aminobenzyl methyl sulfide.[25] As with other sulfilimines, the presence of electron-withdrawing substituents renders them more stable, with the free base isolable in the case of **3g**.

It is important that the cyclic sulfilimine salt, although a precursor, does not appear to be a true intermediate in the cleavage reaction. Reaction of isolated and anhydrous cyclic sulfilimine salt **3g** with dry, gaseous HCl in a reaction solvent, or quickly azeotroping water during HCl treatment of **2g**, fail to give the benzyl chloride **4g**, giving instead **3g**. Conversely, addition of water to **3**, in the presence of HCl, or *slow* removal of water during sulfoxide treatment causes **3** to revert to **2**, which, in turn, irreversibly forms **4**.

These latter observations have led to an alternative and more direct conversion of certain sulfides to **4**. Treatment of the sulfide **1g** with an equivalent of chlorine or sulfuryl chloride was found to give good yields of **3g** (eq 4).[26] Without isolation, water is added and the mixture with HCl gives the product **4g** in high yield.

The superiority of the present synthesis as revealed here is demonstrated by comparison with the previously reported preparation of **4g**. This involves from *o*-aminobenzotrifluoride five separate steps via 7-(trifluoromethyl)isatin formation (two steps),[27] thence to 3-(trifluoromethyl)anthranilic acid.[28] The last reagent is converted

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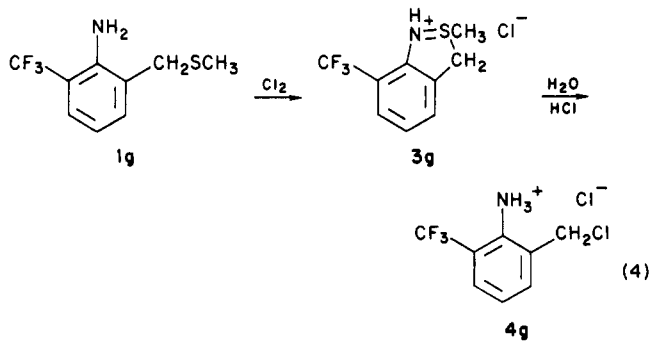
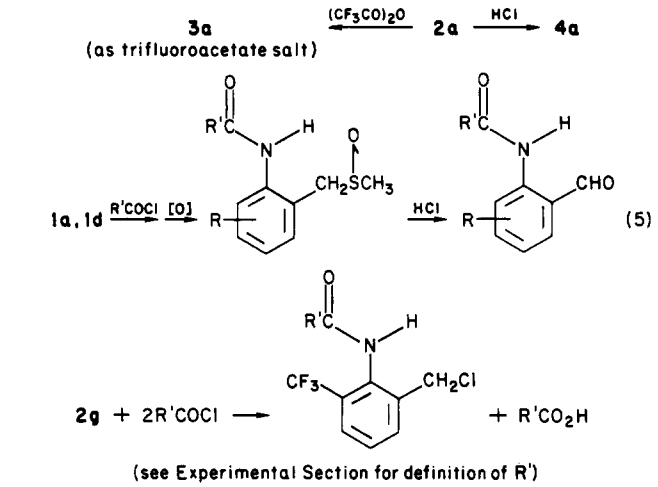
(25) Claus, P. K.; Hofbaner, P.; Rieder, W. *Tetrahedron Lett.* **1974**, 3319.
(26) This treatment with chlorinating agents is not necessarily a general reaction because *o*-aminobenzyl sulfides not bearing electron-withdrawing substituents can be sensitive to nuclear chlorination.
(27) U.S. Patent 3 882 236.



by $LiAlH_4$ reduction to the benzyl alcohol, from which **4g** is derived by treatment with either HCl or thionyl chloride.[23b]

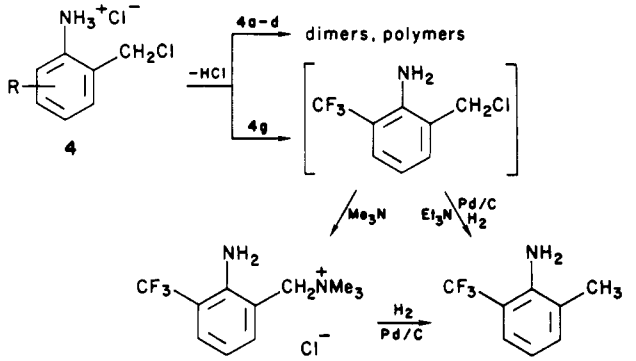
Substitution of other electrophiles in place of HCl, such as acid chlorides or anhydrides, likewise either gives **4** by the cleavage reaction or alternatively causes only dehydration, giving **3**. These results are summarized in eq 5.



It is interesting to note that treatment of an anilide under these reaction conditions leads to normal Pummerer product; on the other hand, contact of the *o*-aminobenzyl methyl sulfoxide (**2g**) with excess acid chloride gives the amido benzyl chloride. Presumably in the latter instance the cleavage reaction occurs first, followed by N-acetylation. This observation is consistent with the decreased carbonium ion stabilization available from an amide vs. an amine moiety. In the former, normal Pummerer occurs, obviating the benzyl cation, while the latter function is stabilized by an adjacent amino group, leading to the cleavage reaction.

Early investigators of the sulfilimine rearrangement[19,20] demonstrated that this reaction could be utilized to prepare *o*-toluidines by the simple expedient of desulfurizing **1** with Raney nickel. Unfortunately, the usual large excess of this expensive and hazardous reagent was necessary for this purpose, precluding its use in practical, scaleup operations. Consequently it was thought desirable to investigate the potential for catalytic hydrogenation of the cleavage-derived products **4**. It is well-known that alkyl, aryl, and particularly benzyl halides are easily cleaved by hydrogen,[29] preferably in the presence of base using Pd catalyst. Moreover, salts **4** by virtue of filtration could be freed of catalyst-poisoning sulfur byproducts prior to such treatment.

When **4** was neutralized either by aqueous base or tertiary amines before or during hydrogenation, the fast and overwhelming reaction was polymerization of the resulting *o*-aminobenzyl chlorides (eq 6). Only materials containing



inert deactivating substituents such as **4g** responded favorably. Thus, intermediate 2-(chloromethyl)-6-(trifluoromethyl)aniline could be identified by ^1H NMR and GLC upon neutralization in an inert solvent by aqueous base. This compound could then be hydrogenated in the presence of triethylamine in suitable solvents with Pd/C, but yields seldom were over 65%. Apparently formation of 6-(trifluoromethyl)-*o*-toluidine produced a more nucleophilic amino group, facilitating its reaction with the starting *o*-aminobenzyl chloride.

Surprisingly, in contrast to triethylamine, trimethylamine was observed to react spontaneously with **4g**, giving the quaternary salt as shown in eq 6. This material proved to be a stable, nonhygroscopic, filtrable solid that, dissolved either in water or alcohol, easily hydrogenated in near quantitative yield to give essentially pure product. Thus combining eq 4 with eq 6 to give a one-pot production of quaternary salt, followed by simple, low pressure hydrogenation provides a convenient desulfurization of **1g** to the *o*-toluidine.

Experimental Section

General Methods. Melting points were determined on a Laboratory Devices Mel-temp apparatus and are uncorrected. NMR spectra were obtained on Varian T-60 and JEOLCO FX-100 spectrometers. Results are reported on the δ scale, parts per million (ppm) downfield from tetramethylsilane internal standard. Mass spectra were obtained on a Varian CH-7 mass spectrometer. Microanalyses were performed by Atlantic Microlab Inc.

General Procedure for the Synthesis of 2-[(Methylthio)methyl]anilines: 3-Chloro-2-methoxy-6-[(methylthio)methyl]aniline (1f). To a rapidly stirred solution of 3-chloro-2-methoxyaniline (24.5 g, 155.5 mmol) and dimethyl sulfide (13.52 g, 217.6 mmol) in CH_2Cl_2 (400 mL) was slowly added *N*-chlorosuccinimide (29.06 g, 217.6 mmol). Reaction temperature was 15 °C. After 10 min of stirring, triethylamine (22.02 g, 217.6 mmol) was added and the mixture heated at reflux for 12 h. The solution was extracted with 10% NaOH (2 × 200 mL) and dried ($MgSO_4$), and the solvent was removed to give a red-brown liquid. Distillation (Kugelrohr, $bp_{0.03}$ 128 °C) gave 23.38 g (107.4 mmol, 69.1% yield) of the sulfide as a light yellow liquid: ^1H NMR ($CDCl_3$) δ 1.98 (s, 3, SCH_3), 3.67 (s, 2, SCH_2), 3.84 (s, 3, OCH_3), 4.37 (br s, 2, NH_2), 6.12 (s, 2, Ar H); mass spectrum (EI 100 eV), *m/e* 217 (M^+·), 170 (M^+· − CH_3S).

Anal. Calcd for $C_9H_{12}ClNOS$: C, 49.64; H, 5.57; N, 6.43. Found: C, 49.62; H, 5.49; N, 6.50.

Sulfides **1a–e,g** were prepared in an analogous manner. Physical and spectral data are as follows.

2-[(Methylthio)methyl]aniline (1a). 73% yield as a yellow liquid, $bp_{0.2}$ 90 °C (Kugelrohr); ^1H NMR ($CDCl_3$) δ 1.92 (s, 3, SCH_3), 3.63 (s, 2, SCH_2), 4.02 (br s, 2, NH_2), 6.67 (m, 2), 7.00 (m, 2); mass spectrum (high-resolution EI), calcd for $C_8H_{11}NS$ 153.0621, found 153.0618.

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2-Ethyl-6-[(methylthio)methyl]aniline (1b): as a light yellow oil, bp 120 °C (1.2 mm) n^{22}_D 1.5884; ^{1}H NMR ($CDCl_3$) δ 1.20 (t, 3, CH_2CH_3), 1.95 (s, 3, SCH_3), 2.45 (quartet, 2, CH_2CH_3), 3.61 ($ArCH_2SCH_3$), 4.0 (br, 2, NH_2), 6.75 (multiplets, 3, Ar H).

Anal. Calcd for $C_{20}H_{15}NS$: C, 66.25; H, 8.34; N, 7.73. Found: C, 66.37; H, 8.35; N, 7.72.

2-Methyl-6-[(methylthio)methyl]aniline (1c): 75.0% yield (91% purity by GLC) as an amber liquid; $bp_{0.1}$ 110 °C (Kugelrohr); ^{1}H NMR ($CDCl_3$) δ 1.92 (s, 3, SCH_3), 2.12 (s, 3, $ArCH_3$), 3.62 (s, 2, CH_2S), 3.62 (br s, 2, NH_2), 6.42–7.12 (m, 3); mass spectrum (EI 100 eV), *m/e* 167 ($M^{+\cdot}$), 120 ($M^{+\cdot} - CH_3S$).

Anal. Calcd for $C_9H_{13}NS$: C, 64.61; H, 7.85; N, 8.37. Found: C, 64.52; H, 8.40; N, 7.71.

2-Methoxy-6-[(methylthio)methyl]aniline (1d): 60% yield, distilled, bp 115–120 °C (0.1 mm) n^{22}_D 1.5975; ^{1}H NMR ($CDCl_3$) δ 2.0 (s, 3, CH_3S), 3.7 (s, 2, CH_2S), 3.8 (s, 3, CH_3O), 4.3 (s, 2, NH_2), 6.7 (d, Ar H).

Anal. Calcd for $C_9H_{13}NOS$: C, 58.98; H, 7.15; N, 7.64. Found: C, 59.02; H, 7.19; N, 8.02.

2-Carbomethoxy-6-[(methylthio)methyl]aniline (1e): 60% yield (60% pure by GLC) as a mixture with methyl anthranilate. This material was used without further purification: ^{1}H NMR ($CDCl_3$) δ 1.92 (s, SCH_3), 3.62 (s, CH_2S), 3.82 (s, OCH_3).

2-[(Methylthio)methyl]-6-(trifluoromethyl)aniline (1g): 70% yield (98% assay) from *o*-aminobenzotrifluoride, bp 72–78 °C (0.8 mm), n^{25}_D 1.5312; ^{1}H NMR ($CDCl_3$) δ 2.0 (s, 3, CH_3S), 3.7 (s, 2, CH_2S), 4.4–4.8 (br s, 2, NH_2), 6.5–7.5 (m, 3, Ar H).

Anal. Calcd for $C_9H_{10}F_3NS$: C, 48.86; H, 4.56; N, 6.33. Found: C, 48.92; H, 4.49; N, 6.23.

General Procedure for the Synthesis of 2-[(Methylsulfinyl)methyl]anilines: 6-Ethyl-2-[(methylsulfinyl)methyl]aniline (2b) (Method A). To a stirred, cold (0 °C) CH_2Cl_2 (400 mL) solution of 6-ethyl-2-[(methylthio)methyl]aniline (**1b**; 28.0 g, 0.154 mol) was slowly added 40% peracetic acid (28.65 g, 0.154 mol). After 10 min of stirring, the solution was extracted with saturated $NaHCO_3$ solution (2 × 250 mL) and dried ($MgSO_4$), and the volume was reduced to ca. 100 mL. Ether and then pentane were added to induce crystallization. Filtration gave 24.21 g (0.123 mol, 79.7%) of the sulfoxide as a white solid: mp 78–80 °C; ^{1}H NMR ($CDCl_3$) δ 1.21 (t, 3, *J* = 7 Hz, CH_2CH_3), 2.46 (s, 3, SCH_3), 2.52 (q, 2, *J* = 7 Hz, CH_2CH_3), 3.97 (AB quartet, 2, SCH_2), 4.43 (br s, 2, NH_2), 6.50–7.20 (m, 3, Ar H); mass spectrum (EI 100 eV), *m/e* 197 ($M^{+\cdot}$), 134 ($M^{+\cdot} - CH_3SO$).

Anal. Calcd for $C_{20}H_{15}NOS$: C, 60.87; H, 7.68; N, 7.10. Found: C, 60.59; H, 7.62; N, 6.98.

Method B was identical with method A except *m*-chloroperbenzoic acid was used as oxidant.

Sulfoxides **2a,c–g** were prepared in an analogous manner. Physical and spectral data are as follows.

2-[(Methylsulfinyl)methyl]aniline (2a): 79.3% yield (CH_2Cl_2/pentane) as a white solid (method B); mp 91–92 °C; ^{1}H NMR ($CDCl_3$) δ 2.48 (s, 3, SCH_3), 4.00 (AB quartet, 2, SCH_2), 4.47 (br s, 2, NH_2), 6.52–7.35 (m, 3, Ar H); mass spectrum (FD), *m/e* 169 ($M^{+\cdot}$).

Anal. Calcd for $C_8H_{11}NOS$: C, 56.76; H, 6.56; N, 8.28. Found: C, 56.79; H, 6.60; N, 8.31.

2-Methyl-6-[(methylsulfinyl)methyl]aniline (2c): 75.3% yield (CH_2Cl_2/Et_2O) as a white solid (method B); mp 79–80 °C; ^{1}H NMR ($CDCl_3$) δ 2.20 (s, 3, $ArCH_3$), 2.53 (s, 3, SCH_3), 4.05 (AB quartet, 2, SCH_2), 4.43 (br s, 2, NH_2), 6.57–7.27 (m, 3, Ar H); mass spectrum (EI, 100 eV), *m/e* 183 ($M^{+\cdot}$), 120 ($M^{+\cdot} - CH_3SO$).

Anal. Calcd for $C_9H_{13}NOS$: C, 58.97; H, 7.16; N, 7.64. Found: C, 58.88; H, 7.19; N, 7.62.

2-Methoxy-6-[(methylsulfinyl)methyl]aniline (2d). The sulfoxide **2d** obtained pure from crude amber oil by HPLC through silica with chloroform containing 2.5% (v/v) ethanol, followed by recrystallization from methylcyclohexane/ethyl acetate solution: mp 71–72 °C; ^{1}H NMR ($CDCl_3$) δ 2.50 (s, 3, CH_3SO), 3.80 (s, 2, CH_3O), 3.98 (AB quartet, *J* = ca. 12 Hz, 2, CH_2SO), 4.3–4.7 (br s, 2, NH_2), 6.54–6.86 (multiplets, 3, Ar H).

Anal. Calcd for $C_9H_{13}NO_2S$: C, 54.25; H, 6.58; N, 7.03. Found: C, 53.48; H, 6.56; N, 6.87.

2-Carbomethoxy-6-[(methylsulfinyl)methyl]aniline (2e): 81.6% yield (CH_2Cl_2/Et_2O) as a white solid (method B); mp 134–6 °C; ^{1}H NMR ($CDCl_3$) δ 2.52 (s, 3, $SOCH_3$), 3.83 (s, 3, OCH_3), 3.97 (AB quartet, 2, $SOCH_2$), 6.53 (t over br s, 3, NH_2 and Ar H para to NH_2, *J* = 7 Hz), 7.05 (d, 1, Ar H ortho to CO_2CH_3); mass spectrum (EI 100 eV), *m/e* 227 ($M^{+\cdot}$), 164 ($M^{+\cdot} - CH_3SO$).

Anal. Calcd for $C_{10}H_{13}NO_3S$: C, 52.84; H, 5.78; N, 6.16. Found: C, 52.68; H, 5.78; N, 6.00.

3-Chloro-2-methoxy-6-[(methylsulfinyl)methyl]aniline (2f): 72.8% yield (CH_2Cl_2/Et_2O) as a tan solid (method B); mp 140–1 °C; ^{1}H NMR ($CDCl_3$) δ 2.52 (s, 3, SCH_3), 3.83 (s, 3, OCH_3), 3.97 (AB quartet, 2, SCH_2); mass spectrum (EI, 100 eV), *m/e* 233 ($M^{+\cdot}$), 170 ($M^{+\cdot} - CH_3SO$).

Anal. Calcd for $C_9H_{12}ClNO_2S$: C, 46.25; H, 5.19; N, 5.99. Found: C, 46.05; H, 5.20; N, 5.83.

2-[(Methylsulfinyl)methyl]-6-(trifluoromethyl)aniline (2g): 86.9% yield (Et_2O/pentane) as a white solid (method A); ^{1}H NMR ($CDCl_3$) δ 2.53 (s, 3, SCH_3), 4.01 (AB quartet, 2, CH_2S), 5.10 (br s, 2, NH_2), 6.72 (t, 1, Ar H para to NH_2, *J* = 8 Hz), 7.15 (d, 1, Ar H ortho to CH_2, *J* = 8 Hz), 7.42 (d, 1, Ar H ortho to CF_3, *J* = 8 Hz); mass spectrum (EI, 100 eV), *m/e* 237 ($M^{+\cdot}$), 174 ($M^{+\cdot} - CH_3SO$).

Anal. Calcd for $C_9H_{10}F_3NOS$: C, 45.56; H, 4.26; N, 5.90. Found: C, 45.71; H, 4.22; N, 5.81.

General Procedure for the Synthesis of 2-(Chloromethyl)anilinium Chlorides: 6-Ethyl-2-(chloromethyl)anilinium Chloride (4b). Into a stirred, warm (ca. 50 °C) 1,2-dichloroethane (10 mL) solution of **2b** (1.0 g, 5.07 mmol) was bubbled anhydrous hydrogen chloride. The solution became cloudy and then clear. After 5 min a white precipitate formed and the HCl sparge was stopped. After cooling, pentane (5 mL) was added and the solid collected to give 0.90 g (4.37 mmol, 86.1% yield) of **4b**: mp 128 °C broad dec; ^{1}H NMR ($CDCl_3$, TFA) δ 1.28 (t, 3, *J* = 7 Hz, CH_2CH_3), 2.78 (q, 2, *J* = 7 Hz, CH_2CH_3), 4.75 (s, 2, CH_2Cl), 7.22 (s, 3, Ar H); mass spectrum (EI, 100 eV), *m/e* 169 ($M^{+\cdot} - HCl$), 134 ($M^{+\cdot} - HCl_2$).

Anal. Calcd for $C_9H_{13}Cl_2N$: C, 52.44; H, 6.37; N, 6.80. Found: C, 52.18; H, 6.43; N, 6.77.

Benzyl chlorides **4a,c–g** were prepared in an analogous manner from **2a,c–g**. Physical and spectral data are as follows.

2-(Chloromethyl)anilinium chloride (4a): 92.3% yield as a light pink solid; ^{1}H NMR ($CDCl_3/Me_2SO$-d_6) δ 4.97 (s, 2, CH_2Cl), 7.20–7.85 (m, 4, Ar H), 9.48 (br s, 3, NH_3); mass spectrum (EI 100 eV), *m/e* 141 ($M^{+\cdot} - HCl$), 106 ($M^{+\cdot} - HCl_2$).

Anal. Calcd for $C_7H_9Cl_2N$: C, 47.21; H, 5.10; N, 7.87. Found: C, 47.22; H, 5.16; N, 7.75.

2-(Chloromethyl)-6-methylanilinium chloride (4c): 87.4% yield as a white solid; mp 190–205 °C dec; ^{1}H NMR ($CDCl_3/Me_2SO$-d_6) δ 2.60 (s, 3, CH_3), 5.05 (s, 2, CH_2Cl), 7.23 (s, 3, Ar H), 9.92 (br s, 3, NH_3); mass spectrum (EI 100 eV), *m/e* 155 ($M^{+\cdot} - HCl$), 120 ($M^{+\cdot} - HCl_2$).

Anal. Calcd for $C_8H_{11}Cl_2N$: C, 50.02; H, 5.78; N, 7.29. Found: C, 49.83; H, 5.59; N, 6.93.

2-(Chloromethyl)-6-methoxyanilinium chloride (4d): 83.3% yield as a tan solid; mp, broad dec above 100 °C; ^{1}H NMR ($CDCl_3$/TFA) δ 3.93 (s, 3, OCH_3), 4.78 (s, 2, CH_2Cl), 6.90–7.53 (m, 3, Ar H); mass spectrum (EI 100 eV), *m/e* 171 ($M^{+\cdot} - HCl$), 136 ($M^{+\cdot} - HCl_2$).

Anal. Calcd for $C_8H_{11}Cl_2NO$: C, 46.17; H, 5.34; N, 6.73. Found: C, 46.16; H, 5.33; N, 6.78.

2-(Chloromethyl)-6-carbomethoxyanilinium chloride (4e): 95.5% yield as a white solid; mp 130–225 °C dec; ^{1}H NMR ($CDCl_3$/TFA) δ 3.95 (s, 3, OCH_3), 4.80 (s, 2, CH_2Cl), 7.43 (m, 2), 8.00 (dd, 1, *J* = 2 Hz, *J* = 7 Hz, Ar H ortho to CO_2CH_3); mass spectrum (EI 100 eV), *m/e* 199 ($M^{+\cdot} - HCl$), 164 ($M^{+\cdot} - HCl_2$).

Anal. Calcd for $C_9H_{11}Cl_2NO_2$: C, 45.78; H, 4.70; N, 5.93. Found: C, 45.64; H, 4.62; N, 5.88.

3-Chloro-6-(chloromethyl)-2-methoxyanilinium chloride (4f): 94.4% yield as a white solid; mp 165–230 °C dec; ^{1}H NMR (TFA) δ 3.70 (s, 3, OCH_3), 4.33 (s, 2, CH_2Cl), 6.73 (d, 1, *J* = 9 Hz), 7.08 (d, 1, *J* = 9 Hz); mass spectrum (EI 100 eV), *m/e* 205 ($M^{+\cdot} - HCl$), 170 ($M^{+\cdot} - HCl_2$).

Anal. Calcd for $C_8H_{10}Cl_3NO$: C, 39.61; H, 4.16; N, 5.78. Found: C, 39.02; H, 4.09; N, 5.56.

2-(Chloromethyl)-6-(trifluoromethyl)anilinium Chloride (4g). (A) 90.0% yield from **2g** as a white solid, mp 70–77 °C dec; ^{1}H NMR ($CDCl_3$ with deuterated Me_2SO) δ 4.66 (s, 2, CH_2Cl), 6.6–6.9 (t, 1, Ar H), 7.2–7.6 (multiplets, 2, Ar H), 8.15 (but variable) (s, 3, NH_3^+).

Anal. Calcd for $C_8H_8Cl_2F_3N$: N, 5.69. Found: N, 5.98.

(B) In a suitably equipped 5-L four-necked flask was placed 221 g (1 mol) of 2-[(methylthio)methyl]-6-(trifluoromethyl)aniline (**1g**) with 2 l of 1,2-dichloroethane. With suitable cooling by an external water/ice bath, 76.0 g (1.07 mol) of chlorine was introduced subsurface over a period of 1 h, maintaining the temperature below 20 °C. After addition, the reaction mixture was heated to 60–65 °C and treated with gaseous HCl for 10 min, followed by addition of 25 mL (1.39 mol) of water. Gaseous HCl treatment was then continued for an additional 15 min. At the end of this time, when the reaction mixture became clear, 600 mL of solvent and water were distilled off in 20 min. Hydrogen chloride was then re-introduced while cooling the reaction to 5 °C. During this time a slurry of precipitate was formed. After holding at 5 °C for 45 min [total HCl usage was 90 g (2.47 mol)], the mixture was filtered by suction and washed on the filter with 150 mL of cold ethylene dichloride. Air-drying for ca one-half hour gave 228 g of **4g**, (92% yield), identical with material produced in A.

Reaction of Benzyl Methyl Sulfoxide with Anhydrous HCl. A stirred CCl_4 (15 mL) solution of benzyl methyl sulfoxide (1.5 g, 9.7 mmol) was heated to reflux. Anhydrous HCl was passed through the solution. After 5 min the HCl was stopped and the reaction was cooled. NMR and GLC assay indicated two products: benzaldehyde (60%) and benzyl methyl sulfide (40%). The structures were confirmed by GLC–MS analysis.

Reaction of 4-Methoxybenzyl Methyl Sulfoxide with Anhydrous HCl. A stirred CCl_4 (10 mL) solution of 4-methoxybenzyl methyl sulfoxide (1.0 g) was heated to reflux. Anhydrous HCl was passed through the solution for 15 min. The solvent was removed to give a slightly pink liquid. This was shown by GLC–MS and comparison (NMR and GLC) with authentic material to be 4-methoxybenzyl chloride (100% yield, 90% conversion).

2′-[(Methylthio)methyl]acetanilide. To a cold (0 °C) methylene chloride (250 mL) solution of 2-[(methylthio)-methyl]aniline (**1a**, 13.2 g, 86.13 mmol) and triethylamine (12.00 mL) was added (5 min) acetyl chloride (6.76 g, 86.13 mmol). After 15 min of stirring, the solution was extracted with water (1 × 150 mL) and 2% HCl (1 × 150 mL). Drying ($MgSO_4$) and solvent removal gave a yellow solid. Recrystallization from CH_2Cl_2/hexane/Et_2O gave 16.63 g (85.15 mmol, 98.9% yield) of product as a white solid: mp 96–97 °C; ^1H NMR ($CDCl_3$) δ 1.97 (s, 3, SCH_3), 2.19 (s, 3, $COCH_3$), 3.68 (s, 2, CH_2S), 7.17 (m, 3), 7.84 (d, 1, J = 7 Hz), 8.22 (br s, 1, NH); mass spectrum (EI 100 eV), m/e 195 ($M^{+\cdot}$), 152 ($M^{+\cdot} - CH_3CO$), 148 ($M^{+\cdot} - CH_3S$).

Anal. Calcd for $C_{10}H_{13}NOS$: C, 61.49; H, 6.72; N, 7.17. Found: C, 61.55; H, 6.88; N, 7.11.

2′-[(Methylsulfinyl)methyl]acetanilide. To a stirred cold (0 °C) methylene chloride (150 mL) solution of 2′-[(methylthio)methyl]acetanilide (10.0 g, 51.2 mmol) was slowly added *m*-chloroperoxybenzoic acid (10.40 g, 85% assay). After 30 min of stirring, the solution was extracted with $NaHCO_3$ (2 × 100 mL) and dried ($MgSO_4$), and the solvent was removed to give a pink solid. Washing with ether gave 9.91 g (46.9 mmol, 91.6% yield) of product: mp 134–138 °C; ^1H NMR ($CDCl_3$) δ 2.11 (s, 3, $COCH_3$), 2.42 (s, 3, SCH_3), 3.63 (d, 1, J = 14 Hz), 4.62 (d, 1, J = 14 Hz), 7.28 (m, 3), 7.84 (d, 1, J = 7 Hz); mass spectrum (high resolution EI) calcd for $C_{10}H_{13}NO_2S$ 211.0676, found 211.0663.

Reaction of 2′-[(Methylsulfinyl)methyl]acetanilide with Anhydrous HCl. A stirred 1,2-dichloroethane (15 mL) solution of substrate (1.0 g) was heated to ca. 55 °C. Anhydrous HCl was passed through the solution for 24 min. The solvent was removed to give a mixture (NMR and GLC assay) of starting material (11%), 2-[(methylthio)methyl]acetanilide (40%), and 2-acetamidobenzaldehyde[30] (49%). Structures were confirmed by GLC–MS and comparison with authentic materials.

2-Chloro-2′-formyl-6′-methoxyacetanilide. 2-[(Methylthio)methyl]-6-methoxyaniline (**1d**, 5.1 g, 27.8 mmol) was dissolved in 100 mL of CH_2Cl_2 and then mixed in a suitable reaction vessel with 100 mL of 5% NaOH. At 5 °C, 3.4 g (30 mmol) of chloroacetyl chloride was added with stirring. After addition, and allowing the mixture to warm to room temperature, the layers were separated and the organic portion was washed with water followed by dilute HCl. After drying and vacuum treatment, 7.2 g of solid (acceptable NMR) 2-chloro-2′-[(methylthio)methyl]-6′-methoxyacetanilide was isolated. This material, without further purification, was dissolved in 100 mL of CH_2Cl_2, 5.5 g of *m*-chloroperbenzoic acid was added, and the mixture was allowed to stir at room temperature overnight. The organic solution was separated, washed with saturated sodium bicarbonate solution, and then vacuum treated to remove solvent, giving 6.3 g of the corresponding sulfoxide: ^1H NMR ($CDCl_3$) δ 2.50 (s, 3, $S(O)CH_3$), 3.87 (s, 3, OCH_3), 3.95 (AB quartet, J = ca. 14 Hz, $S(O)CH_2Ar$), 6.7–7.35 (multiplets, 3, Ar H), 8.45 (br s, 1, NH). The sulfoxide (2.5 g) was dissolved in toluene, heated to reflux, and treated with gaseous HCl at this temperature. Upon cooling, a solid formed which was purified by exposure first to a porous clay plate and then elution with chloroform through a silica gel HPLC column to give crystals of the title product: mp 135–138 °C; ^1H NMR ($CDCl_3$) δ 3.95 (s, 3, CH_3O), 4.25 (s, 2, $ClCH_2$), 7.1–7.6 (multiplets, 3, Ar H), 8.83 (br s, 1, NH), 10.0 (s, 1, CHO).

Anal. Calcd for $C_{10}H_{10}ClNO_3$: C, 52.76; H, 4.43; N, 6.15. Found: C, 52.23; H, 4.45; N, 6.03.

2′-(Chloromethyl)-6′-(trifluoromethyl)acetanilide. Acetyl chloride (7.8 g, 0.10 mol) was heated at reflux in ca. 100 mL of toluene with 12 g (0.05 mol) of 2-[(methylsulfinyl)methyl]-6-(trifluoromethyl)aniline (**2g**). After evaporation of solvent, HPLC with 15% ethyl acetate:85% cyclohexane, fractions 38–53 gave 3.2 g of product with fraction 42 recrystallized from methylcyclohexane/ethyl acetate, mp 137–140 °C, to give an analytical sample: ^1H NMR ($CDCl_3$) δ 2.25 (3, CH_3CO), 4.60 (s, 2, $ArCH_2Cl$), 7.15 (br, 1, NH), 7.2–7.9 (multiplets, 3, Ar H).

Anal. Calcd for $C_{10}H_9ClF_3NO$: C, 47.73; H, 3.61; N, 5.57. Found: C, 47.55; H, 3.57; N, 5.48.

Preparations and Treatment of 2,3-Dihydro-2-methyl-7-(trifluoromethyl)-2,1-benzisothiazole-2-S^{IV} Hydrochloride (3g). (A) 2-[(Methylsulfinyl)methyl]-6-(trifluoromethyl)aniline (**2g**, 2.4 g, 0.01 mol) was dissolved in toluene and dry, gaseous HCl was sparged into the solution between 25 and 40 °C. The precipitated white solid was filtered off, washed with more toluene, and then briefly (2 h) air-dried to remove traces of solvent. Although unnecessary, the cyclic sulfilimine salt **3g** can be recrystallized from acetonitrile, mp 172 °C dec.

(B) Sulfide **1g**, (4.8 g, 0.02 mol) was dissolved in 100 mL of carbon tetrachloride, and with stirring at room temperature, 2.7 g sulfuryl chloride was added dropwise. The solution became milky and then precipitated a yellowish solid. The solution was permitted to stand and most of the clear organic solution decanted while triturating the residual solid with ether, to give **3g** (identical with A). **3g**: ^1H NMR (deuterated Me_2SO) δ 1.9 (multiplet, C_2HD_5SO), 2.40 (s, 3, $>N^+{=}S(CH_3)-$), 4.65 (AB quartet, J = 18 Hz, 2, $ArCH_2S$), 6.6–7.4 (multiplets, 3, Ar H).

Anal. Calcd for $C_9H_9ClF_3NS$: C, 42.28; H, 3.55; N, 5.48. Found: C, 42.15; H, 3.49; N, 5.46.

(C) **Preparation of Neutral Cyclic Sulfilimine of 3g.** To a stirred, cold (0 °C) methylene chloride (400 mL) solution of 2-[(methylthio)methyl]-6-(trifluoromethyl)aniline (25.40 g, 114.8 mmol) was added *N*-chlorosuccinimide (NCS, 16.10 g, 120.5 mmol) as a solid. The rate of addition was such that the reaction temperature was ≤20 °C. After 10 min of stirring, triethylamine (16.80 mL, 120.5 mmol) was added. After 5 min of stirring, the solution was extracted with 10% NaOH (1 × 150 mL) and 1% NaOH (2 × 100 mL). The solution was dried ($MgSO_4$) and the solvent removed to give a yellow oil. This became a tacky solid on standing, 23.5 g (105.6 mmol, 91.98% yield): ^1H NMR ($CDCl_3$) δ 2.28 (s, 3, SCH_3), 4.30 (AB quartet, 2, SCH_AH_B), 6.60 (t, 1, J_{HH} = J_{HH} = 8 Hz, H para to N), 7.37 (m, 2, H meta to N).

Anal. Calcd for $C_9H_8F_3NS$: C, 49.30; H, 3.69; N, 6.39. Found: C, 49.18; H, 3.72; N, 6.48.

(D) **Treatment of 3g with Base.** **3g** when treated with 10% NaOH in the presence of methylene chloride gave the neutral cyclic sulfilimine in near quantitative yield after solvent removal, identical with compound isolated in C above.

(E) **Pyrolysis.** **3g** when heated in toluene with dry, gaseous HCl sparge remained essentially unchanged. In other experiments, addition of stoichiometric or greater amounts of water resulted in isolation of **4g** rather than **3g** after treatment with gaseous HCl.

Derivatives of *o*-(Chloromethyl)anilinium Chlorides 4. (A) Raney Nickel Reduction. The salt **4g** was mixed in ethanol with 20 g of fresh Raney nickel and stirred for 1 h at room

(30) Witkop, B.; Graser, G. *Liebigs Ann. Chem.* **1944**, *556*, 103.

temperature; GLC indicated no remaining neutralized substrate. After careful filtration, the ethanol was partially evaporated on a rotary vacuum apparatus, the residue taken up in methylene chloride and washed several times with water, and the organic solution dried over magnesium sulfate. After filtration and vacuum removal of solvent the residue was distilled bulb-to-bulb to give 2.1 g (60% yield) of distillate identical in spectral and GLC properties with authentic 2-methyl-6-(trifluoromethyl)aniline: bp 65 °C (5.3 mm), n^{21}_D 1.4822; ^{1}H NMR ($CDCl_3$) δ 2.1 (s, 3, $ArCH_3$), 4.05 (br, 2, NH_2), multiplets centered at 6.6 and 7.2 (3, Ar H).

Anal. Calcd for $C_8H_8F_3N$: C, 54.86; H, 4.60; N, 8.00. Found: C, 55.25; H, 4.65; N, 8.02.

(B) Reaction of 4g with Ethanol. In 150 mL of a 1.73 N sodium ethoxide (in ethanol) solution was added 25 g (0.1 mol) of solid salt **4g** portionwise. Instant reaction occurred with precipitation of sodium chloride. The material was stirred at room temperature $1^1/_2$ h and then permitted to stand overnight. Mild cooling was necessary to maintain the temperature under 30 °C during salt addition. After filtration of solid through a coarse sintered glass filter, the filtrate was vacuum treated to remove most of the alcohol. The residue was treated with 300 mL of water and then washed twice with ether. The ether extracts were dried over magnesium sulfate, filtered, and vacuum treated to remove solvent to give 19.2 g crude aniline. This oil (18.7 g) was distilled by bulb-to-bulb distillation, with 15.2 g collected from an oven temperature of 120–135 °C (0.05–0.15 mm) (69% yield) of 2-(ethoxymethyl)-6-(trifluoromethyl)aniline: ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7 Hz, 3, CH_3CH_2), 3.50 (quartet, J = 7 Hz, 2, CH_3CH_2O), 4.50 (s, 2, $ArCH_2O$), (br, 2, NH_2), 6.65 (t, 1, Ar H), 7.1–7.75 (multiplets, 2, Ar H).

Anal. Calcd for $C_{20}H_{12}F_3NO$: N, 6.39. Found: N, 6.70.

(C) Preparation of 2-Methyl-6-(trifluoromethyl)aniline by Catalytic Hydrogenation from 4g. **4g** (ca. 228 g from 1 mol of **1g**, method B) was stirred with 800 mL of ethyl acetate and 1 L of aqueous 10% sodium carbonate solution. After layer separation the aqueous layer was washed with 200 mL of ethyl acetate, and the latter was combined with the organic phase in a 2-L pressure bottle containing 1 mol of triethylamine and 14.8 g of 5% Pd/C (containing 50% by wt water). This material was then hydrogenated over 2 h at 25–50 °C at 50 psi in a Parr shaker. The contents were filtered through clay and washed with 1 L water, with the latter washed with 200 mL of ethyl acetate. The combined organic layers were stripped of solvent on a rotary evaporator and the residue distilled at 20 mm to give, bp 65–70 °C, 96.5 g of 2-methyl-6-(trifluoromethyl)aniline (55% yield from **1g**).

(D) Preparation of 2-Methyl-6-(trifluoromethyl)aniline by Hydrogenation of Quaternary Salt. The procedure for preparing **4g**, part B, was carried out to the point where 600 mL of solvent and water were distilled off rapidly. The clear, slightly yellow solution was then cooled to 40 °C, and 700 mL of ethylene dichloride was added followed by 90 g (1.5 equiv) of trimethylamine dissolved in methanol to a volume of ca. 130 mL. A mild exotherm occurred; the mixture was stirred for 20–30 min to insure complete reaction of amine. The solution was then heated to boiling and excess trimethylamine and methanol were removed by distillation. Precipitation of quaternary salt proceeded at 70–72 °C, preferably by seeding. Distillation was continued until a head temperature of 82 °C was reached. The mixture was then cooled to below 10 °C, filtered, and the salt-cake washed on the filter with fresh 1,2-dichloroethane. Yield of [2-amino-3-(trifluoromethyl)benzyl]trimethylammonium chloride after air-drying was 87% from **1g**: mp 220–221 °C; ^{1}H NMR (Me_2SO-d_6) δ 3.20 (s, 9, CH_3), 5.0 (s, 2, CH_2), 6.2 (s (br), 2, NH_2), 6.8 (t, J = 7 Hz, 1, Ar H), 7.6 (d, J = 7 Hz, 2, Ar H).

Anal. Calcd for $C_{11}H_{16}ClF_3N_2$: C, 49.17; H, 6.00; N, 10.42; Cl, 13.29. Found: C, 49.13; H, 6.01; N, 10.37; Cl, 13.31.

The quaternary salt was dissolved in water to a concentration of 3 M and then shaken over ca. 10 g of 5% Pd/C (containing 50% weight water) under 60 psi of H_2 at 50 °C in a Parr shaker. After hydrogen uptake was complete in 2–3 h, the mixture was filtered and the two-phase filtrate separated by using ca. 200 mL of methylene chloride. The lower, organic layer was dried over $MgSO_4$, filtered, and solvent distilled through a 10-in. Vigreux column. The residue was 2-methyl-6-(trifluoromethyl)aniline obtained in 99% assay and 97% yield from quaternary salt.

Registry No. **1a**, 34774-84-0; **1b**, 92643-44-2; **1c**, 34774-86-2; **1d**, 62926-90-3; **1e**, 92643-45-3; **1f**, 92643-46-4; **1g**, 88301-96-6; **2a**, 92643-47-5; **2b**, 92643-48-6; **2c**, 92643-49-7; **2d**, 92643-50-0; **2e**, 92643-51-1; **2f**, 92643-52-2; **2g**, 88301-75-1; **3g**, 92643-53-3; **4a**, 88301-81-9; **4b**, 88301-76-2; **4c**, 88301-77-3; **4d**, 88301-78-4; **4e**, 88301-79-5; **4f**, 88301-80-8; **4g**, 88301-74-0; a, 62-53-3; b, 578-54-1; c, 95-53-4; d, 90-04-0; e, 134-20-3; f, 51114-68-2; g, 88-17-5; Me_2S, 75-18-3; HCl, 7647-01-0; $PhCH_2S(O)Me$, 824-86-2; PhCHO, 100-52-7; $PhCH_2SMe$, 766-92-7; MeO-p-$C_6H_4S(O)Me$, 3517-99-5; MeO-p-$C_6H_4CH_2Cl$, 824-94-2; $MeSCH_2$-o-$C_6H_4NHC(O)CH_3$, 65134-90-9; $MeS(O)CH_2$-o-$C_6H_4NHC(O)CH_3$, 92643-54-4; AcNH-o-C_6H_4CHO, 13493-47-5; $ClCH_2C(O)Cl$, 79-04-9; AcCl, 75-36-5; 2-chloro-2′-[(methylthio)methyl]-6′-methoxyacetanilide, 92643-55-5; 2-chloro-2′-[(methylsulfinyl)methyl]-6′-methoxyacetanilide, 92643-56-6; 2-chloro-2′-formyl-6′-methoxyacetanilide, 92643-57-7; 2′-(chloromethyl)-6′-(trifluoromethyl)acentanilide, 88301-82-0; 2-methyl-6-(trifluoromethyl)aniline, 88301-98-8; 2-(ethoxymethyl)-6-(trifluoromethyl)aniline, 92643-58-8; [2-amino-3-(trifluoromethyl)benzyl]trimethylammonium chloride, 88301-97-7.

Notes

Divinorin A, a Psychotropic Terpenoid, and Divinorin B from the Hallucinogenic Mexican Mint *Salvia divinorum*

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While nonalkaloidal constituents have been implicated as being at least partially responsible for the biological activity of several hallucinogenic plants,[2] little has been reported on the structures of such possible hallucinogens. The Mexican labiate *Salvia divinorum* (Epling and Jativa-M.) is used in divinatory rites by the Mazatec Indians of Oaxaca, Mexico. An infusion prepared from the crushed fresh leaves of this plant (known locally as *ska Maria Pastora*) is used to induce "visions" and its psychotropic effects have been verified by a number of researchers.[3]

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