On the Mechanism of Formation of *p*-Aminobenzyl Aryl Sulfides, Selenides, or Sulfones by the Acid-Catalyzed Condensations of Aromatic Amines with Formaldehyde and Arenethiols, Selenols, or Sulfinic Acids

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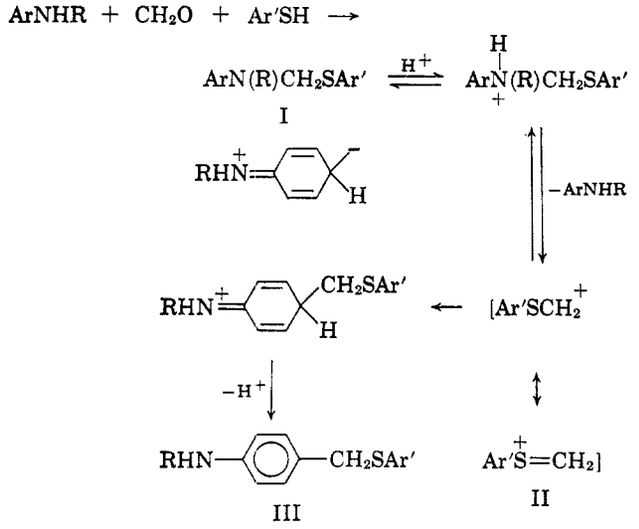
Evidence is brought against the significance of a resonance-stabilized carbonium–sulfonium ion that has been postulated in the literature to account for the formation of *p*-aminobenzyl aryl sulfides when arenethiols are condensed with formaldehyde and aromatic amines in the presence of mineral acids. A new mechanism is postulated that accounts very satisfactorily not only for the formation of these sulfides but also for the formation of the analogous selenides and sulfones that arise under identical conditions. The new mechanism postulates the formation of an N-(*p*-aminobenzyl)aniline as an intermediate when primary and secondary aromatic amines are used in the condensations and the mechanism involves the formation of *p*-aminobenzyl alcohols as intermediates when tertiary aromatic amines are used. In support of this mechanism, it is shown that a model intermediate, N-(*p'*-dimethylaminobenzyl)-N-methyl-*p*-toluidine, arises readily and in high yields under the reaction conditions for which the carbonium–sulfonium intermediacy has been postulated. Furthermore, it is shown that such a model compound, as well as *p*-dimethylaminobenzyl alcohol, when treated with thiols, selenols, or sulfinic acids in the presence of a mineral acid, forms the respective *p*-aminobenzyl aryl sulfides, selenides, or sulfone in practically quantitative conversions in a relatively short reaction time.

To account for the formation of *p*-aminobenzyl aryl sulfides (III) when some anilines are condensed with formaldehyde and thiophenols in the presence of acids, Grillot and Lau[2] postulated essentially the reaction mechanism shown in Scheme I. Accordingly, it was

SCHEME I



suggested that initially the reactions involve the formation of the "normal" Mannich bases (I), S,N-acetals. These bases, on protonation, are then postulated to cleave at the methylene C–N bonds to liberate amine molecules with the simultaneous formation of resonance-stabilized "carbonium–sulfonium" ions (II). These ions are then postulated to couple at the *para* positions with active aromatic amines, in analogy to the diazonium coupling reactions.

In the present paper we would like to present some considerations which would indicate that the above reaction scheme does not correspond to the true course of these reactions. Further, we would like to suggest an alternative general reaction mechanism which can account not only for the formation of the aminobenzyl sulfides but also for the analogous *p*-aminobenzyl selenides that are obtained from the corresponding selenols[3] and the *p*-aminobenzyl sulfones that are obtained from the sulfinic acids[4] under similar conditions.

Evidence Against the "Carbonium–Sulfonium Ion Mechanism"

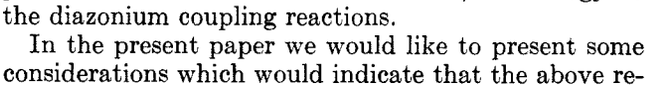
On the basis of the ready reactions of alkoxymethylamines with Grignard reagents to afford tertiary amines according to eq 1, Robinson and Robinson[5] postulated that these types of compounds—O,N-acetals—are highly polarized with the methylene C–O bonds

$$ROCH_2NR_2 + RMgX \longrightarrow RCH_2NR_2 + ROMgX \quad (1)$$

attenuated and they therefore suggest that these compounds should be represented as $RO^{\delta-}\cdots CH_2{}^{\delta+}\cdots NR_2$. Since the S,N-acetals I also react readily with Grignard reagents to afford the corresponding amines,[6] it would appear that these compounds have their methylene C–S bonds attenuated and should therefore be represented as $RS^{\delta-}\cdots CH_2{}^{\delta+}\cdots NR_2$.

Stewart and Bradley,[7] who have studied the mechanism of the acid-catalyzed hydrolysis of N-alkoxymethyl-N,N-dialkylamines, concluded that there is "no doubt that the separation of the alkoxyl group precedes rupture of the carbon–nitrogen attachment" and they explained this to be due to the formation of a resonance-stabilized carbonium–immonium ion, according to Scheme II, and from analogy it would be expected that S,N-acetals would behave similarly, *i.e.*, the methylene

SCHEME II



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(2) G. F. Grillot and P. T. S. Lau, *J. Org. Chem.*, **30**, 28 (1965).

(3) I. E. Pollak and G. F. Grillot, *ibid.*, **31**, 3514 (1966).

(4) E. Bader and H. D. Hermann, *Chem. Ber.*, **88**, 41 (1955); H. Bredereck and E. Bader, *ibid.*, **87**, 129 (1954).

(5) G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **123**, 532 (1923).

(6) I. E. Pollak, A. D. Trifunac, and G. F. Grillot, *J. Org. Chem.*, **32**, 272 (1967). I. E. Pollak and G. F. Grillot, *ibid.*, **32**, 2892 (1967). K. L. Mizuch and R. A. Lapina, *Zh. Obshch. Khim.*, **26**, 839 (1956); *Chem. Abstr.*, **50**, 14754 (1956).

(7) T. D. Stewart and W. E. Bradley, *J. Am. Chem. Soc.*, **54**, 4172 (1932).

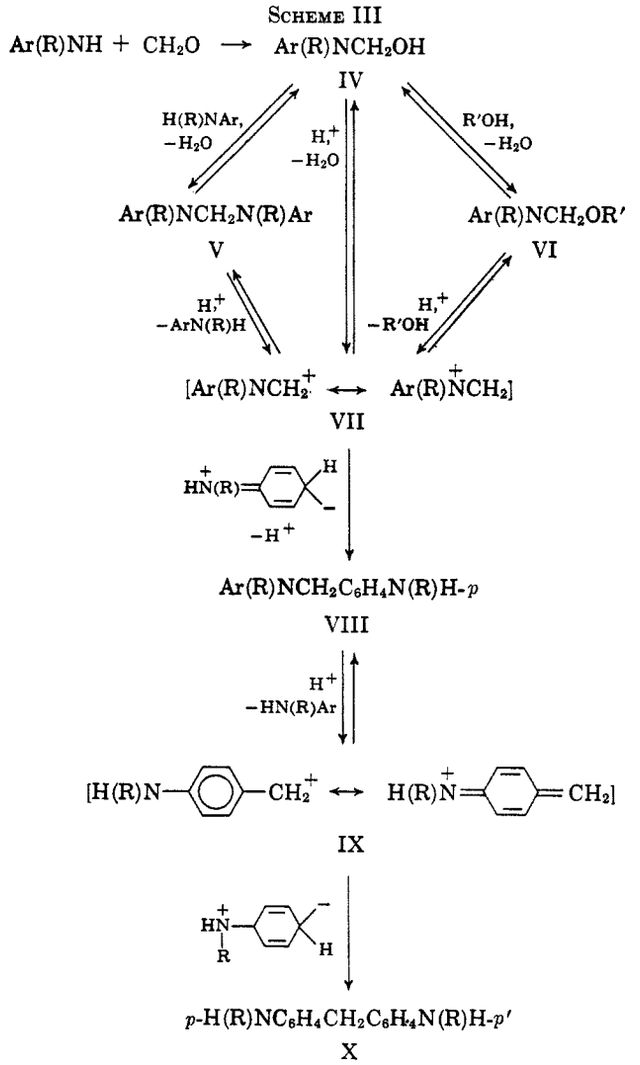
C–S bond should rupture before the C–N attachment. In fact, Schubert and Motoyama[8] have recently shown that $EtSCH(Ph)NMe_2$ hydrolyzes with the EtS^- group coming off first.

That this expected cleavage pattern is not altered when the S,N-acetals contain arylamines can be seen from our findings that, when either an alcoholic solution of N-phenylthiomethyl-N-methylaniline was refluxed with 1 equiv of hydrochloric acid in the presence of *p-t*-butylthiophenol or when N-(*p-t*-butylphenylthiomethyl)-N-methylaniline was refluxed with acid in the presence of 1 equiv of thiophenol, the products in either case were primarily a mixture of *p*-methylaminobenzyl phenyl sulfide and *p*-methylaminobenzyl *p-t*-butylphenyl sulfide. In both instances, the product distribution, determined by nmr spectroscopy, favored the *t*-butyl-substituted sulfide and, furthermore, the yield of the mixed benzyl sulfides corresponded to approximately an 80% conversion of the starting S,N-acetal. If S,N-acetals were to have cleaved at the C–N bonds, according to Scheme I, with the formation of carbonium–sulfonium ion II in the presence of a strong nucleophile like ArSH (which was present in these "crossover" experiments in onefold excess), it would have formed a bis(arylthio)methane, $ArSCH_2SAr'$.[9] Since we found that upon refluxing for 30 min an alcoholic solution of bis(phenylthio)methane together with 1 equiv of hydrochloric acid and 1 equiv of methylaniline, the starting bis(phenylthio)methane is recoverable in over 90%, the formation of *ca.* 80% of mixed aminobenzyl aryl sulfides in these "crossover" experiments could not have come from species like $ArSCH_2^+$. More significantly, these results show unequivocally that Mannich bases like $ArSCH_2N(R)Ar'$ in the presence of acids are not cleaved at all at the C–N bonds, but are cleaved at the C–S bonds.

The insignificance of species like $ArSCH_2^+$ for the formation of *p*-aminobenzyl aryl sulfides can also be seen from the fact that none of the other potential precursers of this species—$PhSCH_2OH$[10] and $PhSCH_2Cl$—yielded appreciable amounts of *p*-dimethylaminobenzyl phenyl sulfides when treated with dimethylaniline.

Further shortcomings of the "carbonium–sulfonium mechansim" become apparent when the condensations of anilines with formaldehyde and selenols or sulfinic acids are considered. In the absence of an acid catalyst, the products are the Mannich bases—N-(selenomethyl)anilines[3] and N-(sulfonylmethyl)anilines.[4] In the presence of 1 equiv of hydrochloric acid, the products are the *p*-aminobenzyl selenides[3] and sulfones[11] in yields of over 80% when N-unsubstituted or N-monosubstituted anilines are used. When dimethylaniline is used, the products are *p*-dimethylaminobenzyl selenides[3] and sulfones in yields of less than 10%. Thus the structures as well as the magnitude of the yields of the products that are obtained under identical conditions

SCHEME III



are similar with thiols, selenols, and sulfinic acids. These facts suggest that a related or the same mechanism is involved in these three cases. Even if it would be assumed that selenium could stabilize species like $ArSeCH_2^+ \leftrightarrow ArSe^+{=}CH_2$,[12] a carbonium ion of the type $ArSO_2CH_2^+$ is not going to be stabilized by a sulfur atom that already carries formal positive charges.[13]

The Presently Postulated Reaction Mechanism

The above considerations suggested that in all these acid-catalyzed reactions, the critical intermediates are not the "normal" Mannich bases—the S,N-acetals, Se,N-acetals, or the SO_2,N-acetals—but some intermediates that are formed from the reactants that are common to all these systems, *i.e.*, the aromatic amines, formaldehyde, and the acid catalyst.

The literature revealed that primary and secondary aromatic amines condense with formaldehyde to yield bis(arylamino)methanes, $ArN(R)CH_2N(R)Ar$. In the presence of acid, on the other hand, the products are bis(*p*-aminophenyl)methanes, $p\text{-}H(R)NC_6H_4CH_2C_6H_4N(R)H\text{-}p'$. Wagner,[14] in an extensive review of these acid-catalyzed amine–formaldehyde condensations, postulated the widely accepted reaction mechanism shown in Scheme III.

(8) W. M. Schubert and Y. Motoyama, *J. Am. Chem. Soc.*, **87**, 5507 (1965).

(9) H. Böhme, H. Fischer, and R. Frank, *Ann.*, **563**, 54 (1949); F. G. Bordwell, G. D. Cooper, and H. Morita, *J. Am. Chem. Soc.*, **79**, 376 (1957).

(10) P. T. S. Lau, Ph.D. Dissertation, Syracuse University, 1962.

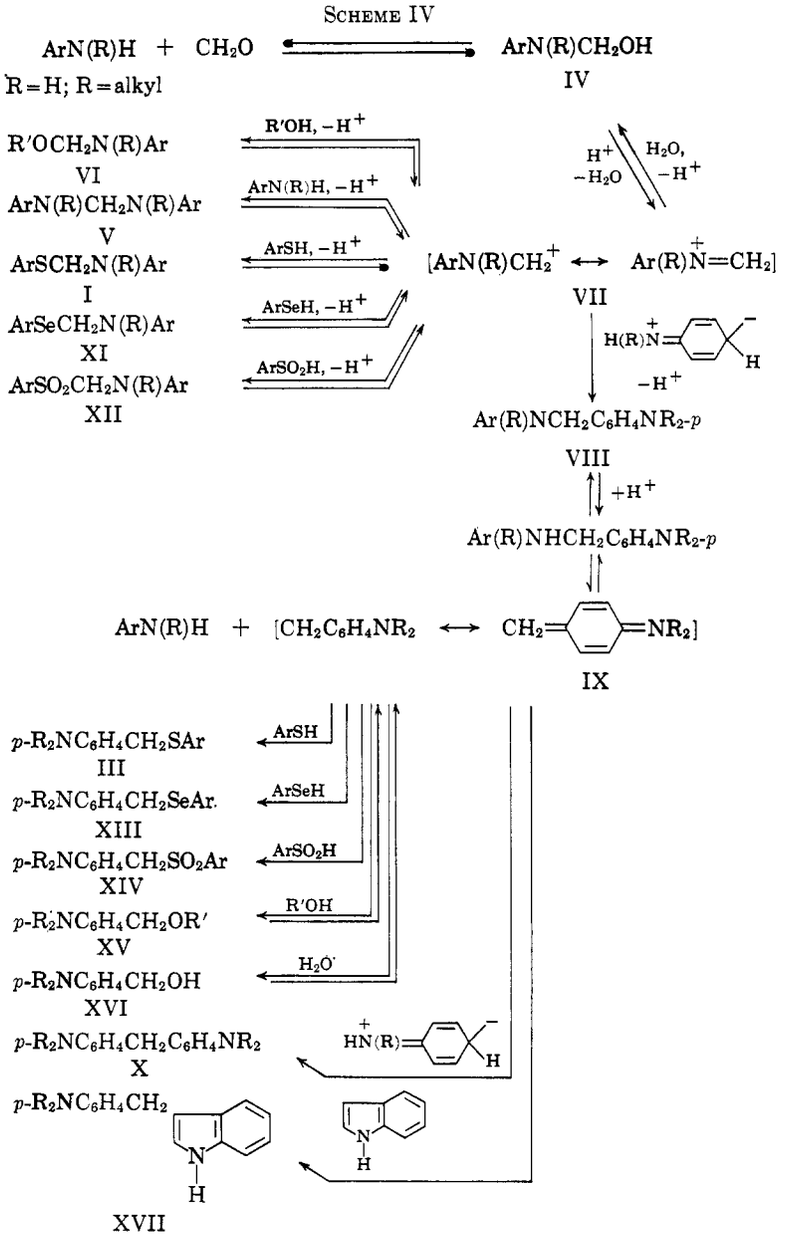
(11) These sulfones were first reported by Bader, *et al.*;[4] however, the yields and conditions for reaction of some of the compounds of interest were either not fully described somewhat for differed from those used in the reactions with thiols or selenols. The sulfinic acid reactions were therefore repeated under the reaction conditions of the thiols and selenols; see Experimental Section.

(12) J. W. Baker, G. F. Barrett, and W. T. Tweed, *J. Chem. Soc.*, 2831 (1952).

(13) C. C. Price and S. Oae, "Sulfur Bonding," The Ronald Press Co., New York, N. Y., 1962, Chapter 2, p 8.

(14) E. C. Wagner, *J. Org. Chem.*, **19**, 1862 (1954).

SCHEME IV



Essentially, this mechanism involves the reversible formation of a resonance-stabilized carbonium–immonium ion (VII) which couples in the *para* position of an aromatic amine, forming an N-(*p*-aminobenzyl)arylamine (VIII). This compound can then form a second resonance-stabilized ion, IX (*p*-aminobenzylium ion), which is a phenylog of the first carbonium–immonium ion, VII. Subsequently, the *p*-aminobenzylium ion (IX) couples with another aromatic amine molecule to produce the final product, bis(*p*-aminophenyl)menthane (X).

An adaptation and extension of Wagner's mechanism to the condensations with thiols, selenols, and sulfinic acids suggested the reaction mechansim that is shown in Scheme IV and which is presently believed to be the major of two routes that give rise to the *p*-aminobenzyl sulfides, selenides, and sulfones. Essentially, this mechanism involves the initial reaction of primary and secondary arylamines with formaldehyde to produce the N-(methanol)amine (IV). This N,O-hemiacetal or a resonance-stabilized carbonium–immonium ion (VII) reacts very rapidly and reversibly with strong nucleophiles in the medium to give rise to the Mannich bases—O,N-acetals (VI) with alcohols, S,N-acetals (I) with thiols, Se,N-acetals (XI) with selenols, N,N-acetals (V) with amines, and SO_2,N-acetals (XII) with sulfinic acids. The acetals are of variable stability and the more stable ones, like the S,N-acetals, are isolable if the reaction is interrupted early.[2] However, all these acetals, in the presence of an acid, revert to the resonance-stabilized ion VII. This carbonium–immonium ion can also couple in the *para* position of arylamines in a most likely rate-determining step to produce an N-(*p*-aminobenzyl)-N-arylamine (VIII). This compound on protonation liberates a free amine molecule and a second resonance-stabilized *p*-aminobenzylium ion (IX). Attack of nucleophiles in the medium on this second ion (IX) gives rise to the generally stable "rearranged" products—*p*-aminobenzyl sulfides (III), selenides (XIII), and sulfones, (XIV).

Evidence for the Presently Postulated Reaction Mechanism

That an N-(*p*-aminobenzyl)aniline (VIII) can form under the reaction conditions used for the formation of

the *p*-aminobenzyl sulfides (III), selenides (XIII), and sulfones, (XIV) is seen from the fact that, when an alcoholic solution of dimethylaniline, N-methyl-*p*-toluidine, formaldehyde, and hydrochloric acid was mixed together in the ratio of 1:1:1:1 and stirred at room temperature for 30 min or were refluxed for 30 min at the boiling temperature of alcohol, N-(p-dimethylaminobenzyl)-N-methyl-*p*-toluidine was produced in approximately 70% yields of theory. Similar yields of the same compound were obtained when bis-(N-methyl-*p*-toluidino)methane was mixed with dimethylaniline and hydrochloric acid in a 1:1:1 ratio in an alcoholic medium and stirred for 30 min at room temperature.

That an N-(*p*-aminobenzyl)aniline, the presently postulated type of intermediate, readily reacts in an acidic medium with a variety of nucleophiles to yield "rearranged" products is seen from Table I. In this

TABLE I

PRODUCTS OBTAINED FROM THE REACTION OF N-*p*-DIMETHYLAMINOBENZYL-N-METHYLANILINE WITH SOME NUCLEOPHILES IN THE PRESENCE OF HYDROCHLORIC ACID

Nucleophile	Product X in p-$Me_2NC_6H_4CH_2X$	Yield,[a] %
Thiophenol	Thiophenoxy	68 (95)
Selenophenol	Selenophenoxy	76 (97)
Benzenesulfinic acid	Benzenesulfonyl	(95)
Indole	3-Indolyl	64

[a] Values in parentheses are of crude products.

table are listed the results obtained when alcoholic solutions of N-*p*-dimethylaminobenzyl-N-methylaniline were mixed with thiophenol, selenophenol, benzenesulfinic acid, or indole and hydrochloric acid in a 1:1:1 ratio and the mixture was heated for 10 min. From these results it can be seen that a model of the postulated intermediate yields the so-called "rearranged" products in practically quantitative yields (at least of the crude products) and in the course of only a short reaction time. Thus there should be very little doubt that the N-*p*-aminobenzylanilines are the true intermediates in the acid-catalyzed reactions with thiols, selenols, and sulfinic acids. Such an intermediate may perhaps also be involved in the acid-catalyzed transformation with indoles, observed by Thesing *et al.*,[15] antipyrine, observed by Bodendorf and Raaf,[16] the mechanisms of which are under dispute, and in a score of similar reactions that are still to be described.

The condensations with tertiary aromatic amines obviously cannot proceed by the same mechanism that is presently suggested for primary and secondary aromatic amines because the carbonium–immonium ion (VII) necessary for the reaction cannot form. Of necessity, since the "carbonium–sulfonium" mechanism is eliminated as a significant route to the product, there remains only one other route and that is *via* a *p*-dialkylaminobenzyl alcohol that arises from the acid-catalyzed methanolization of an N,N-dialkylaniline with formaldehyde.[17] In connection with this, it was found, contrary to what has been claimed in the literature[2], that, when *p*-dimethylaminobenzyl alcohol is treated with thiophenol, selenophenol, or benzenesulfinic acid in the presence of 1 equiv of hydrochloric acid for only 10 min, the corresponding benzyl sulfides, selenides, or sulfones are produced in practically quantitative yields. These results are given in Table II. Considering the fact that the yields of the *p*-

TABLE II

PRODUCTS OBTAINED FROM THE REACTION OF *p*-DIMETHYLAMINOBENZYL ALCOHOL WITH SOME NUCLEOPHILES IN THE PRESENCE OF HYDROCHLORIC ACID

Nucleophile	Product Y in p-$Me_2NC_6H_4CH_2Y$	Yield, %
Thiophenol	Thiophenoxy	91
Selenophenol	Selenophenoxy	91
Benzenesulfinic acid	Benzenesulfonyl	93

dimethylaminobenzyl sulfides,[2] selenides,[3] and sulfones[11] obtainable from the direct condensation of dimethylaniline, formaldehyde, and thiols, selenols, or sulfinic acids are only of the order of 10%, the data shown in Table II suggest that *p*-dimethylaminobenzyl alcohol could and of necessity must be the intermediate in these acid-catalyzed reactions with dimethylaniline.

In principle the intermediacy of a *p*-aminobenzyl alcohol is also operative with primary and secondary arylamines and may very well be a minor route in the formation of these "rearranged" products. It stands to reason that the fraction of the product that can be due to this route will not exceed 10%. The route that is responsible for over 90% of the product would seem to be most likely *via* the one suggested in Scheme IV.

Experimental Section

The nmr spectra were obtained on a Varian A-60 spectrometer; TMS was used as an internal standard. The infrared spectra were obtained on a Perkin-Elmer Infracord. The elemental analyses were carried out by Drs. Weiler and Strauss, Oxford, England. Unless otherwise indicated, the chemicals were obtained from commercial sources and were used without further purification. The following three compounds were obtained by the method of Grillot and Schaffrath.[18]

N-(Phenylthiomethyl)-N-methylaniline had mp 35–37° (lit.[18] mp 36.4–38°). The nmr spectrum in CCl_4 showed singlets at 2.73 (NCH_3) and 4.82 (SCH_2N) ppm and a complex aromatic signal between 6.55 and 7.50 ppm. The areas were 3:2:10.

N-(Phenylthiomethyl)-N-methyl-*p*-toluidine was obtained as an oil, 93% of theory, after removing all materials that boiled below 70° (1–2 mm). Its infrared spectrum between salt disks showed no N–H or S–H stretching bands in the 2.9- and 3.9-μ regions.[19] It did, however, show strong bands at 12.4 (*para*-disubstituted benzene), 13.4, and 14.5 μ (monosubstituted benzene). Its nmr spectrum in $CDCl_3$ exhibited four types of protons: singlets at 2.17 (CH_3C), 2.60 (CH_3N), and 4.78 (SCH_2N) ppm and a complex signal for the aromatic protons between 6.50 and 7.45 ppm. The areas were 3:3:2:9.

Anal. Calcd for $C_{15}H_{17}NS$: C, 74.02; H, 7.05; N, 5.76. Found: C, 78.85; H, 7.25; N, 5.98.

N-(*p*-*t*-Butylphenylthiomethyl)-N-methylaniline produced crystals (from ligroin), mp 36–37° (74% of theory). Its infrared spectrum showed no N–H or S–H stretching bands, but it did contain strong bands at 12.1 (*para*-disubstituted benzene) 13.4, and 14.5 μ (monosubstituted benzene). Its nmr spectrum in CCl_4 showed four types of protons: singlets at 1.25 (*t*-butyl), 2.78 (CH_3N), and 4.79 ppm (SCH_2N) and complex multiplets between 6.5 and 7.4 ppm (aromatic protons). The areas were 9:3:2:9.

(15) J. Thesing, H. Mayer, and S. Klussendorf, *Chem. Ber.*, **87**, 901 (1954); J. Thesing and H. Mayer, *ibid.*, **87**, 1084 (1954); J. Thesing, H. Zieg, and H. Mayer, *ibid.*, **88**, 1978 (1955).

(16) K. Bodendorf and H. Raaf, *Ann.*, **592**, 26 (1955).

(17) L. H. Smith and K. W. Welch, *J. Chem. Soc.*, 730, 1136 (1934).

(18) G. F. Grillot and R. E. Schaffrath, *J. Org. Chem.*, **24**, 1035 (1959).

(19) R. M. Silverstein and G. C. Bassler, "Spectrometric Identifications of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1963, Chapter 3, p 49.

Anal. Calcd for $C_{18}H_{23}NS$: C, 75.76; H, 8.12; N, 4.91. Found: C, 75.58; H, 8.01; N, 5.09.

Bis(N-methyl-*p*-toluidino)methane.—To a cooled solution of 12.2 g (0.1 mole) of N-methyl-*p*-toluidine in 35 ml of 95% alcohol, 3.8 ml of 37% formaldehyde was added. The reaction mixture was refluxed for 2 hr, diluted with 50 ml of 10% NaOH, and extracted with ether. After drying the ether phase with NaOH pellets, all materials boiling below 71° (1–2 mm) were removed, leaving behind 9.5 g (75% of theory) of an oily residue that solidified on chilling. On recrystallization from ligroin, colorless flat needles were obtained, mp 66.5–69° (lit.[20] mp 68°). The reported yield without the alcohol solvent and much longer reaction time was only 25%.[20] Its nmr spectrum in $CDCl_3$ showed five types of hydrogens: sharp singlets at 2.25 (*p*-Me), 2.70 (N-Me), and 4.48 (NCH_2N) ppm and two sets of unsymmetrical doublets (J = 9 cps) centered at 6.68 and 6.93 ppm (aromatic protons). The areas were 3:3:1:4.

α-Chlorothioanisole was prepared by the method of Scherer and Fink;[21] colorless liquid resulted (18% of theory), bp 77–81° (1–2 mm) (lit.[22] bp 98° (12 mm). Its nmr spectrum had a sharp singlet at 4.78 ppm (SCH_2Cl) and a complex multiplet centered at 7.25 ppm (C_6H_5S). The areas were 2:5.

Bis(phenylthio)methane was prepared by the method of Taylor;[23] crystals formed (from alcohol), mp 34–35° (lit.[24] mp 35–36°.

Selenophenol was prepared by the method of Foster;[25] colorless liquid resulted (61% of theory), bp 80–85° (23–25 mm) (lit.[25] bp 84–86 (25 mm).

Benzenesulfinic acid was prepared by the method of Smiles and Bere;[26] crystals formed (63% of theory), mp 80–82° (lit.[27] mp 83–84°.

***p*-Dimethylaminobenzyl alcohol** was prepared by the method of Chaikin and Brown[28] as follows. In a 1-l. flask equipped with a stirrer were placed 4 g of $NaBH_4$, 50 ml of methanol, and 14.9 g (0.1 mole) of *p*-dimethylaminobenzaldehyde. After 20 min, when the reaction subsided, 100 ml of 10% NaOH was added and the reaction mixture was warmed for 15 min. The mixture was then transferred into a separatory funnel and the lower aqueous phase was drawn off. The organic layer was not purified any further and was used soon after preparation as a source of *p*-dimethylaminobenzyl alcohol. This was done in order to avoid possible decomposition of this highly sensitive alcohol[17] and also since the reported yield of this reaction is 96% of theory.[28]

***p*-Methylaminobenzyl phenyl sulfide** was obtained by the method of Lau and Grillot;[29] crystals formed from 95% ethanol (73% of theory), mp 98–101° (lit.[29] mp 99–101.5°). Its nmr spectrum in CCl_4 showed three types of nonaromatic protons: singlets at 2.77 (NCH_3), 3.42 (NH), and 3.96 (SCH_2Ar) ppm. In addition, there were signals between 6.2 and 7.4 ppm (aromatic protons). The areas were 3:1:2:9.

***p*-Methylaminobenzyl *p'*-*t*-butylphenyl sulfide** was obtained by the method of Lau and Grillot;[29] crystals formed from 95% EtOH (60% of theory), mp 71.5–73.5°. Its infrared spectrum showed a single N–H stretching band at 2.9 μ for a secondary amine and very strong bands at 12.1 μ for *para*-disubstituted benzene rings. Its nmr spectrum in $CDCl_3$ showed four types of nonaromatic protons: singlets at 1.25 (*t*-butyl), 2.63 (NCH_3), 3.47 (NH), and 3.99 (SCH_2N) ppm. These had areas in the ratio of 9:3:1:2. In addition, there were signals in the aromatic region between 6.2 and 7.4 ppm corresponding to eight protons. These were further resolved into two sets of doublets (J = 9 cps), centered at 6.4 (*ortho* protons of the aniline) and 7.1 (*meta* protons of the aniline, and a sharp single band centered at 7.2 ppm (thiophenoxy protons).

Anal. Calcd for $C_{18}H_{23}NS$ (285.4): C, 75.76; H, 8.12; N, 4.91. Found: C, 75.54; H, 8.20; N, 5.13.

***p*-Dimethylaminobenzyl-N-methylaniline** was already described elsewhere.[3]

***p'*-Dimethylaminobenzyl-N-methyl-*p*-toluidine.**—To the Grignard reagent obtained from 22 g (0.11 mole) of *p*-bromo-N,N-dimethylaniline and 3 g (0.12 g-atom) of magnesium turnings in 50 ml of tetrahydrofuran (THF), freshly distilled over $LiAlH_4$, was added slowly a solution of 24.3 g (0.1 mole) of N-(phenylthiomethyl)-N-methyl-*p*-toluidine (see above) in 50 ml of THF. At the end of the addition, the reaction mixture was refluxed for an additional 30 min, and hydrolyzed in 500 g of crushed ice and a saturated solution of ammonium chloride. After extraction with ether, washing the extract with 10% NaOH, and drying with KOH pellets, the volatile solvents were removed by distillation at atmospheric pressure. The residue oil was then further fractionated under a vacuum using a short Vigreux column. After a small forerun there was collected 19.4 g (77% of theory) of a light yellow oil that boiled at 180–181° (1–2 mm) and that on chilling and thawing crystallized, mp 25–28°. Its infrared spectrum between salts showed no N–H stretching bands, but it did contain, among others, strong bands at 7.4–7.5 μ (C–N stretching for tertiary aromatic amines) and only one intense band above 11.0 μ that came at 12.4 μ, indicating that all benzene rings were *para* disubstituted. Its nmr spectrum in $CDCl_3$ showed four sharp singlets at 2.17 (p-CH_3), 2.69 (–NMe_2), 2.74 (–NMe–), and 4.23 ($ArCH_2N$), an aromatic complex between 6.4 and 6.75 (*ortho* protons of anilines), and another set of aromatic protons between 6.75 and 7.15 ppm (*meta* protons of anilines). The areas were in the ratios of 3:6:3:2:4:4, respectively.

Anal. Calcd for $C_{17}H_{22}N_2$: C, 80.27; H, 8.72; N, 11.01. Found: C, 80.05; H, 8.70; N, 10.93.

Condensations of Benzenesulfinic Acid with Formaldehyde and Aromatic Amines in the Presence of Hydrochloric Acid. *p*-Methylaminobenzyl Phenyl Sulfone.—In a reaction flask equipped with a stirrer and a reflux condenser were placed, in sequence, 7.1 g (0.05 mole) of benzenesulfinic acid, 50 ml of 95% ethanol, 5.5 ml (0.05 mole) of methylaniline, 3.8 ml (0.05 mole) of 37% formaldehyde, and 4.5 ml of concentrated hydrochloric acid. The reaction mixture was refluxed for 30 min, transferred into a separatory funnel, and then made strongly basic with 10% NaOH. The crystalline solid that formed was collected by suction filtration, washed with water, and dried in an oven at 115° for 3 hr. The dried material weighed 11 g (85% of theory) and melted at 157–159°. Its infrared spectrum showed, among other bands, a sharp single absorption at 2.9 (N–H stretching of a secondary amine), strong bands at 7.70 and 7.73 (C–N stretching of a secondary aromatic amine and S–O stretching of a sulfone), strong bands at 8.63 and 8.73 (characteristic of sulfones), two bands of equal intensity and of medium strength at 11.9 and 12.2 (*para*-disubstituted benzene), and bands at 13.0, 13.9, and 14.6 μ (monosubstituted benzene). Its nmr spectrum in $CDCl_3$ showed a sharp singlet at 2.80 (NCH_3), a broad singlet at 3.60 (N–H), a sharp singlet at 4.20 ($ArCH_2SO_2$), a doublet with suggestions of secondary splittings ($J \approx 9$ cps) centered at 6.45 (*ortho* protons of a *para*-substituted aniline), a doublet with suggestion of secondary splittings (J = 9 cps) centered at 6.88 (*meta* protons of a *para*-substituted aniline), a cluster of signals between 7.2 and 7.55 (*meta* and *para* protons of the $PhSO_2$ group), and another cluster of signals between 7.55 and 7.8 ppm (*ortho* protons of $PhSO_2$ group). The areas were in the ratios of 3:1:2:2:2:3:2, respectively.

Anal. Calcd for $C_{14}H_{15}NO_2S$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.50; H, 5.65; N, 5.17.

***p*-Aminobenzyl phenyl sulfone** was obtained in the same way as the preceding compound, by the use of aniline in place of methylaniline, as a crystalline solid (97% of theory) that melted at 170–176° (lit.[30] mp 176°). Its infrared spectrum showed, among others, absorptions at 2.84, 2.92, 7.72, 8.62, 11.8, 11.95, 13.4, 13.9, and 14.6 μ. Its nmr spectrum in $CDCl_3$ showed signals at 3.65 (2 H), 4.20 (2 H), 6.55 (2 H), 6.88 (2 H), 7.25–7.58 (3 H), and 7.58–7.72 ppm (2 H).

***p*-Dimethylaminobenzyl phenyl sulfone** was obtained by the same general procedure that was employed for the two preceding compounds, except that dimethylaniline was utilized as the amine component and the refluxing time was prolonged to 1 hr. Crystalline material (8.7% of theory) melted at 145–148° (lit.[31] mp 147°. Its infrared spectrum contained bands, among others, at 7.38, 7.7, 8.6, 8.72, 12.0, 12.1, 12.8, 13.1, 13.7, and 14.45 μ. Its nmr spectrum in $CDCl_3$ showed signals at 2.88 (6 H), 4.18

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(2 H), 6.52 (2 H), 6.92 (2 H), 7.2–7.53 (3 H), and 7.53–7.7 ppm (2 H).

Acid-Catalyzed "Rearrangements" of N-Arylthiomethyl-N-methylaniline in the Presence of a Tagged Thiophenol. A. "Rearrangement" of N-Phenylthiomethyl-N-methylaniline in the Presence of *p*-*t*-Butylthiophenol.—In a 250-ml three-necked flask equipped with a magnetic stirrer, reflux condenser, thermometer, and an addition funnel were placed 22.93 g (0.1 mole) of N-phenylthiomethyl-N-methylaniline, 18.03 g (0.1 mole) of *p*-*t*-butylthiophenol, and 50 ml of 95% ethanol. The stirring was started and through the addition funnel was added 8.6 ml (0.1 mole) of concentrated hydrochloric acid at such a rate that the internal temperature of the reaction mixture stayed below 30°. At the end of the hydrochloric acid addition, the reaction mixture was heated to reflux for 30 min, cooled in an ice bath, transferred into a separatory funnel, and made strongly basic with a cold 10% solution of NaOH. The oil that separated was extracted with two 100-ml portions of ether. The alkaline aqueous phase was set aside for further work-up. The ether extracts were combined, washed with 50 ml of 10% NaOH, and dried with KOH pellets. The volatile solvents, ether and alcohol, were removed by distillation at atmospheric pressure. (When the temperature of the distilling head reached 80°, the process was stopped.) The residue was further distilled under vacuum. At 70° (25 mm), a few drops of an oil came over that was identified by its infrared spectrum as N-methylaniline. There was thus left behind 22.9 g of a residue which was dissolved in CCl_4. To an aliquot of this solution was added 1 drop of TMS (tetramethylsilane) and its nmr spectrum was taken. The spectrum showed signals at 1.27 (22), 2.63 (*ca.* 7.5), 2.78 (*ca.* 2.5), 3.37 (*ca.* 2.5) 3.93 (6), 4.80 (*ca.* 1), and aromatic signals between 6.2 and 7.3 ppm (22.5 units). By comparing these signals with the chemical shifts of *p*-H(Me)N$C_6H_4CH_2SPh$ and *p*-H(Me)NC_6H_4-$CH_2SC_6CMe_3$-*p*′ and by using the area at 1.27 ppm (for the Me_3C-group) as the basis for calculating the relative concentration of *p*-N-methylaminobenzyl-*p*′-*t*-butylphenyl sulfide and the area at 3.93 ppm (for $-SCH_2Ar$) as the basis for calculating the sum of the concentrations of *p*-N-methylaminobenzyl *p*′-*t*-butylphenyl sulfide and *p*-N-methylaminobenzyl phenyl sulfide, the molar ratios of these two compounds were determined. This method indicated that the 22.9-g residue consisted of approximately 81 mole % of the former *vs.* 19 mole % of the latter. It should be noted, however, that these values contain an estimated uncertainty of *ca.* 20%. This estimation is based on the consideration of the signal at 4.80 ppm (for SCH_2N, probably some unreacted $PhSCH_2N(Me)Ph$, but it could also be *p*-$Me_3CC_6H_4$-$SCH_2N(Me)Ph$ or $ArSCH_2N(Me)C_6H_4CH_2SAr$). Regardless of this inherent error, it is safe to conclude that in this reaction the *p*-*t*-butylthiophenol has entered the "rearranged" product to a larger extent than thiophenol.

The alkaline aqueous phase was acidified with concentrated hydrochloric acid, extracted with three 25-ml portions of ether, and the ether extract dried with anhydrous $MgSO_4$. The ether was removed by distillation at atmospheric pressure and the residue was fractionated under reduced pressure, using a short Vigreux column. At 80° (35 mm), 5.6 g (approximately 50% recovery on the basis of 0.1 mole) of a colorless liquid was collected that was identified by its odor and its infrared spectrum as thiophenol contaminated with small amounts of *p*-*t*-butylthiophenol. In the distilling flask remained behind 5.4 g (*ca.* 30% recovery) of a residue which was identified by its infrared spectrum as *p*-*t*-butylthiophenol contaminated with small amounts of thiophenol. Thus, the recovered thiols also support the conclusion that the *p*-*t*-butylthiophenol has entered the "rearranged product" to a larger extent than thiophenol.

B. "Rearrangement" of N-(*p*-*t*-Butylphenylthiomethyl)-N-methylaniline in the Presence of Thiophenol.—In a 50-ml three-neck flask equipped with a magnetic stirrer, addition funnel, reflux condenser, and a thermometer were placed 5.7 g (0.02 mole) of N-(*p*-*t*-butylphenylthiomethyl)-N-methylaniline, 2.2 g (0.002 mole) of thiophenol, and 10 ml of 95% ethanol. The stirring was started and through the funnel was added dropwise 1.7 ml (0.02 mole) of concentrated hydrochloric acid. At the end of the acid addition, the reaction mixture was heated to reflux for 30 min, cooled, transferred into a separatory funnel, made basic with 10% NaOH, and extracted with three 50-ml portions of ether. The ether extracts were combined, dried with KOH pellets, filtered, and the ether was removed by distillation at atmospheric and subsequently under reduced pressure. At 70° (25 mm), a few drops of an oil came over that was identified by its infrared spectrum as N-methylaniline. The residue weighed 3.98 g. This was dissolved in CCl_4 and on an aliquot the nmr spectrum was taken.

The nmr spectrum showed signals at 1.26 (17.5), two peaks poorly resolved at 2.64 and 2.70 (8 units total), a broad signal centered at *ca.* 3.42 (?), a singlet at 3.90 (5), and aromatic signals between 6.18 and 7.35 ppm (23.5 units total). By comparing the areas at 1.26 and 3.90 ppm (see preceding case), the 3.98 g of residue is calculated to consist essentially of 22 mole % of *p*-N-methylaminobenzyl phenyl sulfide and approximately 78 mole % of *p*-N-methylaminobenzyl *p*′-*t*-butylphenyl sulfide. Once again, as in the preceding case, these values contain 10–20% of uncertainty.

Reactions of Aromatic Amines with Potential Precursors of "Carbonium–Sulfonium" Ions. A. Reaction of N,N-Dimethylaniline with α-Chlorothioanisole.—In a 100-ml round-bottom flask equipped with a stirrer were placed 6.02 g (0.05 mole) of N,N-dimethylaniline, 25 ml of 95% ethanol, and 7.93 g (0.05 mole) of α-chlorothioanisole. The reaction mixture was heated to reflux for 2 hr, transferred to a separatory funnel, made strongly basic with 10% NaOH, and extracted with ether. The ether extract was dried with KOH pellets and the volatile solvents were removed by distillation initially at atmospheric and subsequently under reduced pressure. There was thus left 12.3 g of residue whose infrared spectrum showed only very weak absorption between 12.0 and 12.6 μ, the region where *para*-disubstituted benzenes characteristically absorb strongly. Thus, the residue contained only a small amount of the expected *p*-N,N-dimethylaminobenzyl phenyl sulfide. The entire residue was transferred into a separatory funnel, made strongly acidic with concentrated hydrochloric acid, and extracted with ether. The aqueous phase was then made strongly basic with 10% NaOH. The oil that separated, on addition of ice, solidified. The solids were collected by suction filtration, washed with water, and air dried over night. The still slightly wet material weighed 0.4 g (3.3% of theory) and melted at 75–92°. Its infrared spectrum matched the spectrum of an authentic sample of *p*-dimethylaminobenzyl phenyl sulfide.

B. Reaction of N-Methylaniline with Bis(phenylthio)methane.—In a 100-ml round-bottom flask equipped with a magnetic stirrer were placed 11.6 g (0.05 mole) of $(PhS)_2CH_2$, 50 ml of 95% ethanol, 5.4 g (0.05 mole) of N-methylaniline, and 4.5 ml (0.05 mole) of concentrated hydrochloric acid. A condenser was attached to the flask. The reaction mixture was heated to reflux for 30 min, transferred to a separatory funnel, made strongly acid with concentrated hydrochloric acid, and extracted with ether. The ether extracts were dried with anhydrous $MgSO_4$ and filtered; the ether was distilled off first at atmospheric and later under vacuum. There was thus left 10.5 g (90.5% recovery) of an oil that on seeding with a crystal of bis(phenylthio)-methane immediately crystallized. Its structure was further supported by its infrared spectrum and by not giving a mixture melting point depression with a known sample of bis(phenylthio)-methane.

From the acidic aqueous phase, on making it strongly basic, N-methylaniline was recovered. There was no indication of the formation of *p*-methylaminobenzyl phenyl sulfide.

The Formation of a "Model Intermediate", N(*p*′-Dimethylaminobenzyl)-N-methyl-*p*-toluidine, under the Acid-Catalyzed "Rearrangement" Conditions of Grillot and Lau. A. Reaction of Bis(N-methyl-*p*-toluidino)methane with N,N-Dimethylaniline in the Presence of Acid.—In a 50-ml round-bottom flask equipped with a magnetic stirrer were placed 3.08 g (0.012 mole) of bis-(N-methyl-*p*-toluidino)methane, and 25 ml of 95% ethanol. The reaction flask and its contents were kept at approximately 25° on a water bath. The stirring was started and through an addition funnel was added dropwise over a 10-min period a solution of 2.34 g (0.02 mole) of N,N-dimethylaniline and 1.72 ml (0.02 mole) of concentrated hydrochloric acid in 10 ml of 95% ethanol. At the end of the addition, the reaction mixture was stirred for an additional 30 min at room temperature, transferred to a separatory funnel, made basic with 10% NaOH (100 ml), and extracted with 50 ml of ether. The ether extract was dried with KOH pellets and the volatile solvents were removed by distillation under atmospheric pressure. The residue was then fractionated under vacuum. After removal of the material that distilled below 75° (2–3 mm), there was left 2.2 g (72% of theory, based on 0.012 mole) of an oily residue whose infrared and nmr spectra were identical with the spectra of N-(*p*-dimethylaminobenzyl)-N-methyl-*p*-toluidine prepared previously (see above).

Condensation of N,N-Dimethylaniline with Formaldehyde and N-methyl-p-toluidine in the Presence of Acid. A. At Room Temperature.—In a 200-ml round-bottom flask equipped with a magnetic stirrer were placed 12.1 g (0.1 mole) of dimethylaniline, 12.1 g (0.1 mole) of N-methyl-*p*-toluidine, 50 ml of 95% ethanol, and 7.6 ml (0.1 mole) of 37% formaldehyde. The reaction flask was placed on an ice-water bath and to the reaction mixture was added dropwise through an addition funnel, over a 10-min period, 8.6 ml of concentrated hydrochloric acid. At the end of the acid addition, the reaction mixture was stirred for an additional 30 min at room temperature, transferred into a separatory funnel, made strongly basic with 10% NaOH, and extracted with ether. The ether extract was dried with KOH pellets and the ether was removed by distillation at atmospheric pressure. The residue was then further distilled under vacuum and the material that came over below 130° (15 mm) was removed. There was thus left behind 17 g (67% of theory) of an oily residue whose infrared spectrum was identical with that of N-(*p*-dimethylaminobenzyl-N-methyl-*p*-toluidine.

B. At Reflux Temperature of Alcohol.—The preceding experiment was repeated with the sole exception that after the acid addition the reaction mixture was heated to reflux for 30 min. The residue, after removal of the material that distilled below 135° (15 mm), weighed 16 g (64% of theory) and its infrared spectrum was identical with that of N-(*p*-dimethylaminobenzyl)-N-methyl-*p*-toluidine.

Reactions of N-(p-Dimethylaminobenzyl)-N-methylaniline with Thiophenol, Selenophenol, Benzenesulfinic Acid, or Indole in the Presence of Hydrochloric Acid. A. Reaction with Thiophenol.—In a 200-ml reaction flask equipped with a magnetic stirrer were placed, in sequence, 12.0 g (0.05 mole) of p-Me_2N-$C_6H_4CH_2N(Me)Ph$, 50 ml of 95% ethanol, and 5.8 g (0.05 mole) of practical grade thiophenol. The mixture was stirred and cooled over an ice bath and through an addition funnel was added dropwise 4.5 ml (0.05 mole) of concentrated hydrochloric acid. At this point a clear solution was obtained. The reaction mixture was then heated to reflux for 10 min, transferred into a separatory funnel, made basic with 100 ml of 10% NaOH, and extracted with 200 ml of ether. The ether extract was washed with two 50-ml portions of 10% NaOH, dried with KOH pellets, and filtered into a distilling flask. The ether was removed at atmospheric pressure and the residue was fractionated under vacuum. At 65° (1–2 mm), a colorless liquid came over that weighed 3.5 g (66% recovery) and that was identified by its infrared spectrum as N-methylaniline. The residual oil in the distilling flask weighed 11.5 g (95% of theory) and solidified on cooling to room temperature. On recrystallization from alcohol and drying over P_2O_5, 8.4 g (68% of theory) of crystals were obtained that melted at 103–106° and gave no mixture melting point depression with a sample of dimethylaminobenzyl phenyl sulfide.[29] Furthermore, the infrared and nmr spectra of the sulfide obtained by these two different methods were identical.

B. Reaction with Selenophenol.—To a cooled mixture of 12.0 g (0.05 mole) of p-$Me_2NC_6H_5CH_2N(Me)Ph$, 25 ml of 95% ethanol, and 7.85 g (0.05 mole) of selenophenol was added slowly 4.5 ml (0.05 mole) of concentrated hydrochloric acid. The reaction mixture was rapidly heated to reflux for 10 min, cooled, and made strongly basic with 100 ml of 10% NaOH, upon which a crystalline solid formed. The solid was collected, washed with water, and dried over P_2O_5. The dried crude material weighed 14 g (97% of theory) and melted at 93–97°. On recrystallization from 200 ml of 95% ethanol and drying, 11 g (76% of theory) of colorless columnar crystals that melted at 99–101° were obtained. These gave no mixture melting point depression with authentic samples of *p*-dimethylaminobenzyl phenyl selenide.[3] Furthermore, the infrared and nmr spectra of the selenides prepared by these two different methods were identical.

C. Reaction with Benzenesulfinic Acid.—To a cooled mixture of 12.0 g (0.05 mole) of p-$Me_2NC_6H_4CH_2N(Me)Ph$, 50 ml of 95% ethanol, and 7.1 g (0.05 mole) of benzenesulfinic acid was added 4.5 ml (0.05 mole) of concentrated HCl. The reaction mixture was heated rapidly to reflux for 10 min and made strongly basic with 100 ml of NaOH, whereupon a crystalline solid formed. The solid was collected, washed with water, and dried in an oven at 115° for 2 hr. The dried material weighed 13 g (95% of theory) and melted at 147–150°. It gave no mixed melting point depression with a sample of N,N-dimethylaminobenzyl phenyl sulfone that was obtained previously by the direct condensation of benzenesulfinic acid with formaldehyde and dimethylaniline in the presence of hydrochloric acid (see above). Furthermore, the infrared and nmr spectra of the sulfones prepared by these two different methods were identical.

D. Reaction with Indole.—In a reaction flask were placed 5.85 g (0.05 mole) of indole, 12.0 g (0.05 mole) of N-*p*-(N′,N′-dimethylamino)benzyl-N-methylaniline, 50 ml of 95% ethanol, and 4.5 ml (0.05 mole) of concentrated hydrochloric acid. The reaction mixture was rapidly heated to reflux (the total heating time was 10 min), transferred into a separatory funnel that contained approximately 200 g of ice, and was made strongly basic with 10% NaOH. An oil separated that soon solidified. The solid was collected, washed with water, and recrystallized from cyclohexane. The weight of the air-dried recrystallized material was 8.0 g (64% of theory) and the colorless needles melted at 141–144°. One reported melting point of 3-(dimethylamino)benzylindole is 143.5–144.5°.[15]

The nmr spectrum of this material in $CDCl_3$ showed two sharp singlets at 2.85 (NMe_2) and 3.99 ($Ar'CH_2Ar$), a distorted doublet which suggests secondary splittings ($J \approx 9$ cps), centered approximately at 6.7 (*ortho* protons of the aniline and another proton, most likely the 7 proton of the indole), a cluster of signals between 6.85 and 7.3 (the *meta* protons of the aniline and the 2–6 protons of the indole), and a broad signal between 7.3 and 7.8 ppm (N–H of the indole). The areas were approximately in the ratio of 6:2:3:4:1, respectively, in full agreement with the structure of 3-(N′,N′-dimethylamino)benzylindole.

Reactions of p-Dimethylaminobenzyl Alcohol with Thiophenol, Selenophenol, and Benzenesulfinic Acid in the Presence of Hydrochloric Acid. A. Reaction with Thiophenol.—In a 200-ml reaction flask equipped with a stirrer were placed 11 g (0.1 mole) of thiophenol, 50 ml of 95% ethanol, and 9.0 ml (0.1 mole) of concentrated hydrochloric acid. The stirring was commenced and to the solution was added, all at once, freshly prepared *p*-dimethylaminobenzyl alcohol obtained from the reduction of 0.1 mole of *p*-N,N-dimethylaminobenzaldehyde with 3 g of $NaBH_4$ (see above). The reaction mixture was then heated rapidly to reflux (total heating time was 10 min), transferred into a separatory funnel containing approximately 100 g of ice, and made strongly basic with 10% NaOH. A white crystalline solid formed. This was collected, washed with water, and dried over P_2O_5. The material weighed 22 g (91% of theory) and melted at 102–104°. It gave no mixed melting point depression with a sample of *p*-dimethylaminobenzyl phenyl sulfide obtained by two other methods (see above). Furthermore, the infrared and nmr spectra of the sulfides obtained by these different methods were identical.

B. Reaction with Selenophenol.—To a stirred solution of 15.7 g (0.1 mole) of selenophenol, 50 ml of 95% ethanol, and 9.0 ml (0.1 mole) of concentrated hydrochloric acid was added *p*-dimethylaminobenzyl alcohol obtained from the reduction of 0.1 mole of *p*-dimethylaminobenzaldehyde with $NaBH_4$ (see above). The reaction mixture was then heated rapidly to reflux (total heating time was 10 min), transferred into a separatory funnel that contained *ca.* 10 g of ice, and made strongly basic with 10% NaOH. A crystalline solid separated. The solid was collected, washed with water, and dried over P_2O_5. The dried material weighed 26.5 g (91.5% of theory) and melted at 93–98°. It gave no mixture melting point depression with a sample of *p*-dimethylaminobenzyl phenyl selenide prepared previously by two different methods (see above). Furthermore, the infrared and nmr spectra of the selenides from these different preparations were identical.

C. Reaction with Benzenesulphinic Acid.—To a stirred solution of 14.2 g (0.1 mole) of benzenesulfinic acid, 50 ml of 95% ethanol, and 9.0 ml (0.1 mole) of concentrated hydrochloric acid was added *p*-dimethylaminobenzyl alcohol obtained from the reduction of 0.1 mole of *p*-dimethylaminobenzaldehyde (see above). The reaction mixture was heated rapidly to reflux (total heating time was 10 min), transferred into a separatory funnel, and made strongly basic with 10% NaOH. A crystalline solid formed. This was collected, washed with water, and dried in an oven at 115° for 2 hr. The dried material weighed 25.6 g (93% of theory) and melted at 142–145°. It gave no mixture melting point depression with *p*-dimethylaminobenzyl phenyl sulfone prepared previously by two different methods (see above). Furthermore, the infrared and nmr spectra of these sulfones prepared by different methods were all identical.

Registry No.—Formaldehyde, 50-00-0; N-(phenylthiomethyl)-N-methylaniline, 13641-16-2; N-(phenyl-

thiomethyl)-N-methyl-*p*-toluidine, 13641-17-3; N-(*p*-*t*-butylphenylthiomethyl)-N-methylaniline, 13641-18-4; bis(N-methyl-*p*-toluidino)methane, 7137-82-8; α-chlorothioanisole, 13641-20-8; *p*-methylaminobenzyl phenyl sulfide, 13641-21-9; *p*-methylaminobenzyl *p'*-*t*-butylphenyl sulfide, 13641-22-0; *p'*-dimethylaminobenzyl-N-methyl-*p*-toluidine, 10509-65-6; *p*-methylaminobenzyl phenyl sulfone, 13641-24-2; *p*-aminobenzyl phenyl sulfone, 13640-67-0; *p*-dimethylaminobenzyl phenyl sulfone, 13640-68-1.

The Reactions of β-Aminoalkyl Hydrogen Sulfates. III. The Effect of Alkyl Substituents on the Rates of Cyclization of β-Aminoalkyl Sulfate Ions[1]

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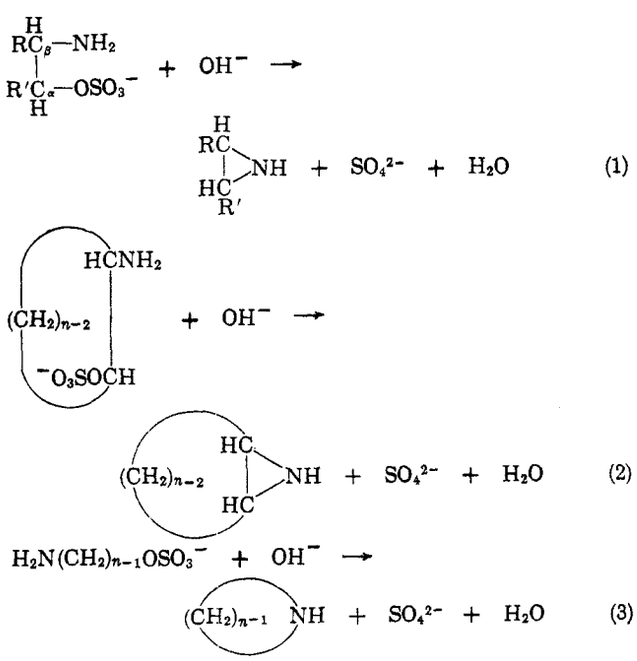
The cyclization of aminoalkyl sulfate ions to form aziridines has been studied at 75°. The rate constants and acidity constants have been determined for 20 alkyl- and aryl-substituted aminoalkyl sulfate ions. In the cyclization of β-aminoalkyl sulfate ions, alkyl substituents can be both rate enhancing and rate retarding, the over-all effect and its magnitude being dependent on the structure and position of the substituent. Rate retardation is ascribed to steric hindrance of the type found in SN2 reactions. Rate enhancement is probably partially due to stabilization of the three-membered ring by hyperconjugation. Any driving force from relief of compressive strain through ring formation is minor. Polar effects are not significant except where the substituent is aromatic, in which case it can be rate enhancing or rate retarding.

As part of our study of the reaction of β-aminoalkyl hydrogen sulfates with potassium ethyl xanthate,[3] we found it necessary to determine the rates for the cyclization of aminoalkyl sulfate ions to the corresponding aziridines (reactions 1, 2, and 3). These results



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are being reported because we believe that they disclose new information about the influence of alkyl substituents on the formation of three-membered rings. The specific rate constants for the cyclization, at 75°, of 20 aminoalkyl sulfate ions have been determined.

Experimental Section

The preparation of the aminoalkyl hydrogen sulfates and the techniques used to measure reaction rates and acidity constants (pK_a') have been reported.[3] Specific rate constants were determined graphically from log (reactant) against time plots and are the average of two to four runs.

Aziridines.—The aziridines were prepared by distilling a mixture of 0.05 mole of the aminoalkyl hydrogen sulfate and 25 ml of 50% aqueous potassium hydroxide solution and adding water periodically to the mixture until no further aziridine came over. The distillate was saturated with potassium hydroxide, and the organic layer was separated and dried over potassium hydroxide pellets. The aziridines were identified through published physical properties and their phenyl isothiocyanate addition products. Data for several new compounds[4] follows.

2-Isopropylaziridine was found to have a boiling point of 103–104° ($n^{25}D$ 1.4179).

Anal. Calcd for $C_5H_{11}N$: C, 70.55; H, 12.94; N, 16.45. Found: C, 70.38; H, 13.19; N, 16.41.

The N-phenylthiocarbamyl derivative has a melting point of 75.0–75.6°.

Anal. Calcd for $C_{12}H_{16}N_2S$: C, 65.43; H, 7.32; N, 12.72. Found: C, 65.39; H, 7.29; N, 12.40.

2-*t*-Butylaziridine has a boiling point of 111–112° ($n^{25}D$ 1.4229).

Anal. Calcd for $C_6H_{13}N$: C, 72.80; H, 13.12; N, 14.14. Found: C, 72.80; H, 13.17; N, 14.14.

The N-phenylthiocarbamyl derivative has a melting point of 86.0–86.3°.

Anal. Calcd for $C_{13}H_{18}N_2S$: C, 66.60; H, 7.69; N, 11.95. Found: C, 66.21; H, 7.79; N, 11.71.

Results

The specific rate constants for the cyclization reaction and the acidity constants of the aminoalkyl sulfate ions are summarized in Tables I, II, and III. In the concentration range studied (0.5–0.2 *M*), all cyclizations were first order with respect to aminoalkyl sulfate ion concentration and zero order with respect to sodium hydroxide concentration. Each run was followed for at least two half-lives or 72 hr, over which period none of the reactions deviated from first-order kinetics. In none of the examples studied was there

(1) (a) In part from the R. A. Bafford Ph.D. Thesis, University of Maryland, June 1960. (b) Presented at the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966, Abstracts, K077.

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(3) (a) C. S. Dewey and R. A. Bafford, *J. Org. Chem.*, **30**, 491 (1965). (b) C. S. Dewey and R. A. Bafford, *ibid.*, 495 (1965).

(4) Elemental analyses were carried out by Dr. Franz Kasler, University of Maryland, College Park, Md., and Galbraith Laboratories, Inc., Knoxville, Tenn.