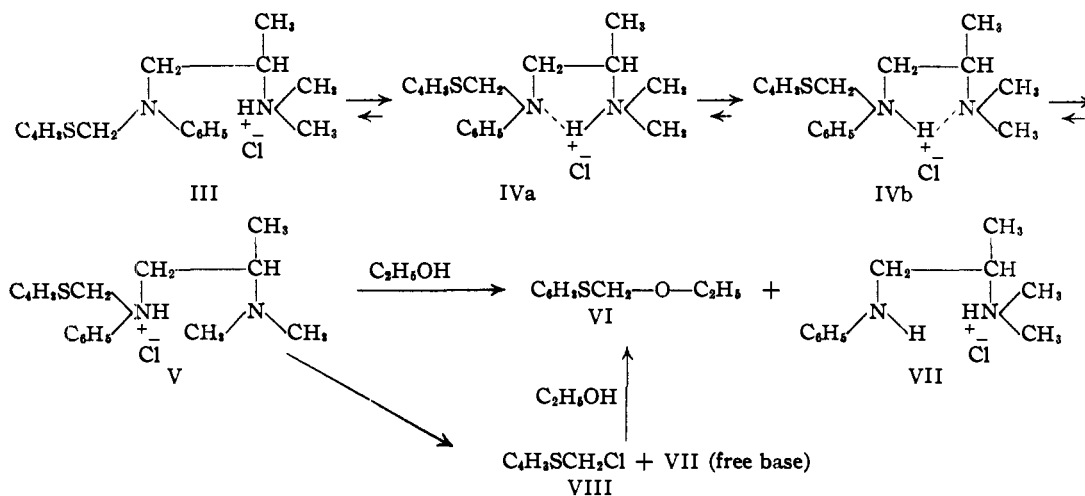


neutralization mixture left a sirup which possessed an unexpected, strong sweet odor. Fractionation of the sirup yielded 2-thenyl ethyl ether (VI), N^2, N^2 -dimethyl- N^1 -phenyl-1,2-propanediamine (VII) and recovered tertiary amine.

We feel that this decomposition can be accounted for by the formulation¹⁰



The monohydrochloride (III)¹¹ which is obtained upon neutralization of amine 3 can be in equilibrium, because of intramolecular hydrogen bonding with the quasi-five-membered ring systems (IVa and IVb) which may open to yield (V). Since the electronegativity of the N^1 -atom in amine 3 is small, due to the phenyl substituent, the localization of the proton at this point will further decrease the charge to such a low value that the strongly electropositive 2-thenyl radical will only be weakly bound. (V) will therefore be able to enter into metathetical reactions of the type $A^+B^- + C^+D^- \rightarrow AD + BC$ in much the same manner as esters of toluene sulfonic acids and some of the quaternary ammonium halides. In our case (III) was formed in the presence of ethanol (which was used as a solvent) with which its isomer (V) may have reacted to form 2-thenyl ethyl ether (VI) and N^2, N^2 -dimethyl- N^1 -phenyl-1,2-propanediamine hydrochloride (VII). The formation of these stable products would then shift the equilibrium of all the intermediate forms to the right. Another route to (VI) and (VII) may involve a decomposition of (V) to 2-thenyl chloride (VIII) and the free base of (VII). Subsequent reaction of (VIII) with ethanol would produce the ether (VI) and cause a shift of the equilibrium to the right as before.

Since all of our straight chain diamine monohy-

(10) This formulation can be applied equally well to the possible decomposition of the isomeric N^1, N^1 -dimethyl- N^2 -phenyl- N^2 -(2-thenyl)-1,2-propanediamine.

(11) Since the K_b of dialkylamines is in general of the order of magnitude of 10^{-4} to 10^{-5} while that of N -alkylanilines is 10^{-10} it is reasonable to assume that the dimethylamino is more basic than the N -(2-thenyl)-anilino group and will be involved in the primary neutralization of the diamine

drochlorides are stable compounds it would seem that the instability of the hydrochlorides of amines 3 and 7 can be related to their C-methyl branch. It is conceivable that this substituent crowds the dimethylamino hydrochloride group at least close enough to the N -thenylanilino group for intramolecular hydrogen bonding, rearrange-

ment and subsequent decomposition to occur. The degree of stability of all of these hydrochlorides therefore probably depends directly upon the internitrogen distance in the "horseshoe shaped" rotational configuration. This distance and the stability appear to be at a minimum in the branched chain diamines (III).

The stability of the picrate and bisuccinate salts of bases 3 and 7 may be due to the greater bulk of their anions which are unable to approach closely enough the nitrogen bearing the large phenyl and 2-thenyl groups to form an intermediate corresponding to (V). This would have the effect of keeping the electrical center of the molecule in the neighborhood of the nitrogen bearing the two methyl radicals and result in a stable configuration.

Experimental¹²

2-Thenyl chloride,¹³ γ -dimethylaminopropyl chloride^{14, 15} and hydrochlorides of β -dimethylaminoethyl chloride,¹⁶ β -piperidinoethyl chloride¹⁷ and β -dimethylaminopropyl chloride^{16, 18} were obtained by methods described in the literature.

Procedure 1: N^2, N^2 -Dimethyl- N^1 -phenyl-1,2-propanediamine.—A mixture of 37.2 g. (0.40 mole) of aniline, 31.6 g. (0.20 mole) of β -dimethylaminopropyl chloride hydrochloride, 55.2 g. (0.40 mole) of anhydrous potassium carbonate and 100 cc. of dry toluene was stirred and refluxed for seven hours, cooled, water added and the organic

(12) Microanalyses by Mr. L. Dorfman and Miss B. Baumgarten of this institute.

(13) Blicke and Leonard, *THIS JOURNAL*, **68**, 1936 (1946).

(14) Marxer, *Helv. Chim. Acta*, **24**, 209E (1941).

(15) Prepared by Dr. G. C. van Wessem.

(16) Slotta and Behnish, *Ber.*, **68**, 754 (1935).

(17) Blicke and Kaplan, *THIS JOURNAL*, **65**, 1967 (1943); Dunlop, *J. Chem. Soc.*, **101**, 2002 (1912).

(18) Office of The Publication Board, Department of Commerce Report P. B. 981, p. 96-A.

TABLE I
HYDROCHLORIDES OF TERTIARY AMINES $C_4H_9SCH_2$ $\left. \begin{array}{l} \\ \\ \end{array} \right\} NR_2B \cdot HCl$

Compound 1 was recrystallized from alcohol, compound 3 from a mixture of ethyl methyl ketone and ether, compound 7 from ethyl methyl ketone. All of the others were recrystallized from a mixture of absolute ethanol and ether.

R ₁	R ₂ B	Proce- dure	Bases			Formula	M. p., °C.	Hydrochlorides Analyses, %			
			B. p. °C.	Mm.	Yield, %			Nitrogen		Chlorine	
							Calcd.	Found	Calcd.	Found	
1 C ₆ H ₅	CH ₂ CH ₂ N(CH ₃) ₂	5	183-185	7	69.8	C ₁₂ H ₁₄ SN ₂ Cl	186-187	9.44	9.44	11.95	11.90
2 C ₆ H ₅	CH ₂ CH ₂ NC ₄ H ₉	6	215-218	5	58.0	C ₁₀ H ₁₆ SN ₂ Cl	187-188	8.32	8.11	10.52	10.75
3 C ₆ H ₅	CH ₂ CH(CH ₃)N(CH ₃) ₂	5, 6	164-171	3	44.7, 77.0	C ₁₀ H ₁₆ O ₂ SN ₂	99-100 ^a	7.14	7.15		
4 C ₆ H ₅	CH ₂ CH ₂ CH ₂ N(CH ₃) ₂	6	158-161	3	78.6	C ₁₂ H ₁₈ SN ₂ Cl	138-139	9.01	9.13	11.40	11.47
5 2-C ₆ H ₄ N	CH ₂ CH ₂ N(CH ₃) ₂	5	166-168	2	64.8	C ₁₂ H ₁₆ SN ₂ Cl	162-163	14.11	14.05	11.90	11.87
6 2-C ₆ H ₄ N	CH ₂ CH ₂ NC ₄ H ₉	5	189-194	1	67.5	C ₁₇ H ₁₉ SN ₂ Cl	135-136	12.44	12.71	10.49	10.49
7 2-C ₆ H ₄ N	CH ₂ CH(CH ₃)N(CH ₃) ₂	5	162-169 ^b	1.5	53.2	C ₁₀ H ₁₆ O ₂ SN ₂	101-102 ^{a, b}	10.68	10.90		
8 2-C ₆ H ₄ N	CH ₂ CH ₂ CH ₂ N(CH ₃) ₂	6	171-174	4	33.1	C ₁₂ H ₁₈ SN ₂ Cl	122-124	13.43	13.28	11.33	11.54

^a Bisuccinate. ^b Prepared by Dr. C. P. Hutterr.

layer separated. The aqueous phase was extracted with ether, the combined organic layers washed with water and dried. Solvents were removed and the residual oil fractionated. The amine was obtained as a yellow oil, b. p. 97-102° (3 mm.), n_D^{20} 1.5300; yield 26.1 g. (73.3%). It was characterized by conversion to a monopicate, m. p. 158-159° after recrystallization from ethanol.

Anal. Calcd. for C₁₇H₂₁N₃O₇: C, 50.12; H, 5.20; N, 17.20. Found: C, 49.83; H, 5.44; N, 16.91.

Procedure 2: N²,N²-Dimethyl-N¹-(2-pyridyl)-1,2-propanediamine.—A suspension of 14.16 g. (0.36 mole) of sodamide, 28.2 g. (0.30 mole) of 2-aminopyridine and 250 cc. of dry toluene was stirred and refluxed for two hours. Heating was stopped and a solution of 40.1 g. (0.33 mole) of β -dimethylaminopropyl chloride in 40 cc. of dry toluene added dropwise with stirring. The mixture was refluxed for five hours, cooled, water added, the organic layer separated, washed with water and dried. Fractionation gave 46.4 g. (86.5%) of the secondary amine, b. p. 128-131° (5 mm.), n_D^{20} 1.4969. The dipicrate melted at 210°.

Anal. Calcd. for C₂₂H₂₃N₃O₄: C, 41.44; H, 3.61; N, 19.78. Found: C, 40.92; H, 3.79; N, 19.78.

Procedure 3: N-(2-Thenyl)-aniline.—Aniline, 93.0 g. (1.0 mole) was dissolved in 150 cc. of dry benzene, 24.5 g. (0.25 mole) of anhydrous potassium carbonate added to the solution, the mixture heated to boiling and a solution of 33.0 g. (0.25 mole) of 2-thenyl chloride in 50 cc. of dry benzene added dropwise with constant stirring. The mixture was stirred and refluxed for four hours, cooled and worked up as in procedure 1. Fractionation at 12 mm. gave 34.0 g. (72.3%) of a product which boiled at 174-177°, solidified to a tan solid, m. p. 37-39°, and yielded a hydrochloride melting from 170-171°.

Anal. Calcd. for C₁₁H₁₂NSCl: N, 6.21; Cl, 15.71. Found: N, 6.32; Cl, 15.93.

Procedure 4: 2-(2-Thenylamino)-pyridine.—Freshly distilled 2-thiophenealdehyde,¹⁹ 45.9 g. (0.41 mole) was added to a solution of 37.6 g. (0.40 mole) of 2-aminopyridine in 75 cc. of 95% formic acid. The mixture was refluxed for seventeen hours, diluted with water and neutralized from sodium hydroxide. The precipitate was washed with water and dried, m. p. 73-76°; yield 40.7 g., (53.5%). A sample recrystallized from a toluene-petroleum ether (b. p. 90-110°) mixture, melted at 78-80°.

Anal. Calcd. for C₁₀H₁₀SN₂: C, 63.12; H, 5.30; N, 14.73. Found: C, 63.02; H, 5.16; N, 14.57.

Procedure 5: N,N-Dimethyl-N'-phenyl-N'-(2-thenyl)-ethylenediamine Hydrochloride.—A solution of 32.4 g. (0.198 mole) of N,N-dimethyl-N'-phenylethylenediamine²⁰ in 50 cc. of dry toluene was added to a suspension

of 8.5 g. (0.217 mole) of sodamide in 100 cc. of dry toluene. The mixture was stirred and heated at 100° for three hours, heating discontinued and a solution of 28.8 g. (0.217 mole) of 2-thenyl chloride in 30 cc. of dry toluene added dropwise. After refluxing for two hours, the mixture was cooled and worked up in the usual way. Distillation *in vacuo* yielded 36.17 g. (69.8%) of a dark yellow oil, b. p. 183-185° (7 mm.), n_D^{20} 1.5902. Hydrochloride formation was generally effected by solution of the amine in ether and treatment of the resulting solution with a slight excess of ethanolic hydrochloric acid with cooling. In a number of instances the salt precipitated at once in crystalline form, in others it oiled out or remained in solution. In these cases it was necessary to remove the solvents *in vacuo* and crystallize the residual sirups. This amine was dissolved in 85 cc. of absolute alcohol and treated with 74.5 cc. (1% excess) of 1.885 N alcoholic hydrochloric acid. The monohydrochloride was filtered off, washed with alcohol and ether and dried; yield 35.6 g., m. p. 185-186°. Recrystallized from ethanol the salt melted at 186-187°.

Anal. Calcd. for C₁₅H₂₁SN₂Cl: C, 60.69; H, 7.13; Cl, 11.95. Found: C, 60.49; H, 7.11; N, 9.44; Cl, 11.90.

N²,N²-Dimethyl-N¹-(2-pyridyl)-N¹-(2-thenyl)-1,2-propanediamine Bisuccinate.—A stirred suspension of 8.5 g. (0.22 mole) of sodamide and 35 g. (0.20 mole) of N²,N²-dimethyl-N¹-(2-pyridyl)-1,2-propanediamine and 320 cc. of dry toluene was refluxed for two hours, heating stopped and a solution of 2-thenyl chloride in 30 cc. of toluene added dropwise. The mixture was refluxed for two hours, cooled and worked up as before to give the tertiary amine, b. p. 162-169° (1.5 mm.), n_D^{20} 1.5755, in 53.2% yield (29.3 g.). The dipicrate, recrystallized from acetone melted at 136-138°.

Anal. Calcd. for C₂₇H₂₇N₃O₄S: C, 44.20; H, 3.70; N, 17.18; S, 4.37. Found: C, 44.36; H, 3.89; N, 17.23; S, 4.68.

The bisuccinate formed in the same manner as that of the phenyl analog (see procedure 6) melted at 101-102° after recrystallization from ethyl methyl ketone.

Anal. Calcd. for C₁₉H₂₇O₄SN₂: C, 57.99; H, 6.92; N, 10.68. Found: C, 57.88; H, 6.93; N, 10.90.

Procedure 6: N²,N²-Dimethyl-N¹-phenyl-N¹-(2-thenyl)-1,2-propanediamine Bisuccinate.—A sodium salt prepared by stirring and refluxing for two hours a mixture of 29.8 g. (0.157 mole) of N-(2-thenyl)-aniline, 6.15 g. (0.157 mole) of sodamide and 240 cc. of dry benzene was treated dropwise with 19.2 g. (0.157 mole) of β -dimethylaminopropyl chloride in 45 cc. of dry benzene. The material was stirred and refluxed for eight hours and the product obtained in the usual way; b. p. 164-171° (3 mm.), n_D^{20} 1.5792; yield 34.5 g. (77.0%).

Anal. Calcd. for C₁₆H₂₃SN₂: C, 70.02; H, 8.08; N, 10.21; S, 11.68. Found: C, 70.13; H, 8.34; N, 10.09; S, 11.98.

(19) Dunn, Waugh and Dittmer. *THIS JOURNAL*, **68**, 2118 (1946).

(20) Prepared in 81.5% yield by procedure 1. We found b. p. 100-104° (6 mm.), n_D^{20} 1.5395. Hutterr, Djerassi, Becars, Mayer and Scholz (ref. 1f) reported b. p. 103-107° (0.2 mm.), n_D^{20} 1.5380.

The base gave a monoplicate which melted at 139–140° after recrystallization from benzene.

Anal. Calcd. for $C_{22}H_{28}O_7SN_2$: C, 52.47; H, 5.00; N, 13.91; S, 6.37. Found: C, 52.39; H, 5.26; N, 14.09; S, 6.43.

The bisuccinate was formed by adding 11 cc. of a saturated alcoholic solution of succinic acid to a solution of 2.328 g. of the base in 10 cc. of ether. The mixture was kept at room temperature overnight, concentrated to a sirup *in vacuo* and crystallized under ether. Recrystallized twice from an ethyl methyl ketone-ether mixture, the salt melted at 99–100°.

Anal. Calcd. for $C_{20}H_{28}O_4SN_2$: C, 61.20; H, 7.19; N, 7.14. Found: C, 61.35; H, 7.37; N, 7.15.

Attempted Hydrochloride Formation of Amine 3 and Identification of Decomposition Products.— N^2,N^2 -Dimethyl- N^1 -phenyl- N^1 -(2-thenyl)-1,2-propanediamine, 18.28 g. (0.059 mole) was dissolved in 27 cc. of dry ether, treated with 27.6 cc. of 2.15 *N* ethanolic hydrochloric acid, let stand at room temperature overnight and placed in the refrigerator. After several days the solution was evaporated and the sirupy residue found to have a strong, sweet odor. Water was added to the sirup, the solution made strongly alkaline with sodium hydroxide, the oily layer taken up in ether and the solution dried. After removal of ether the residual oil was fractionated *in vacuo*. Three definite fractions were obtained.

Fraction 1, b. p. 52° (3 mm.), n_D^{20} 1.5061, was the sweet smelling component. It was redistilled, b. p. 58.7° (5 mm.). 184–185° (760 mm.), n_D^{20} 1.5061 and analyzed.

Anal. Found: C, 58.69; H, 6.79; S, 23.00; N, 0.35.

Disregarding the nitrogen as a trace impurity the analysis indicates an empirical formula of C_7H_9SO or $C_7H_{10}SO$. The analytical and physical data agree reasonably well with that of 2-thenyl ethyl ether,²¹ $C_7H_{10}SO$,

(21) Leonard, Ph. D. Thesis, University of Michigan, 1946.

which has the following constants: b. p. 84–86° (22 mm.), 181–182° (740 mm.), n_D^{20} 1.5062, and percentage composition C, 59.12; H, 7.09; S, 22.54.

Fraction 2, b. p. 106–108° (3 mm.), n_D^{20} 1.5321, was redistilled (b. p. 111–113° (4 mm.)) with no change in refractive index and gave a monoplicate which melted at 155–156°. This data and the analysis of the base was in good agreement with that of N^2,N^2 -dimethyl- N^1 -phenyl-1,2-propanediamine (see procedure 1).

Anal. Calcd. for $C_{11}H_{15}N_2$: C, 74.11; H, 10.18; N, 15.72. Found: C, 74.33; H, 10.28; N, 15.56.

Fraction 3, b. p. 163–165° (3 mm.), n_D^{20} 1.5800. These constants showed that this fraction was recovered tertiary amine.

Acknowledgment.—The authors wish to express their appreciation to Drs. H. M. Wuest and J. A. King for their interest in this project and to Mr. I. Ehrenthal for his help in a number of the preparations.

Summary

Six new and two previously reported 2-thenyl substituted diamines, $C_6H_5SCH_2(R_1)NR_2B$, have been synthesized in which R_1 is a phenyl or 2-pyridyl radical, R_2 is a straight or branched alkylene chain of two or three carbon atoms and B is a dimethylamino or piperidino group. An interesting decomposition of one of these in the presence of hydrogen halides has been observed, the products identified and a mechanism suggested.

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The Resolution of *dl*-Arteranol

BY B. F. TULLAR

Recently the resolution of *dl*-arteranol, α -aminomethyl-3,4-dihydroxybenzyl alcohol, was announced together with a brief description of the physiological characteristics of the active *l*-isomer.¹ The present paper deals with the method of effecting this resolution.

An observation that *dl*-arteranol is almost quantitatively converted to its methyl ether by evaporating *in vacuo* a solution of the hydrochloride in methanol² suggested that ether formation might occur during resolution attempts in anhydrous alcohols. Accordingly, aqueous alcohols seemed to offer more promise as resolution solvents.

The presence of water in the resolution mixture afforded an additional advantage since only the *l*-arteranol forms a *hydrated* salt with *d*-tartaric acid. This *l*-arteranol *d*-bitartrate monohydrate possesses greater solubility in aqueous methanol

(1) Twinter, Tullar and Luduena, *Science*, **107**, 39–40 (1948).

(2) A similar reaction of epinephrine was described by Öppinger and Vetter, *Med. u. Chemie*, **4**, 343–367 (1942). see *C. A.*, **66**, 5928 (1944). Johnson, *et al.*, *THIS JOURNAL*, **69**, 2945 (1947). reported alkylation of a hydroxymethylene group under quite similar conditions.

and considerably lower water solubility than does the *non-hydrated d*-arteranol *d*-bitartrate, permitting an easy separation of the diastereomers.

The bitartrates were purified by repeated recrystallization from water (*l* isomer) and from 95% methanol (*d* isomer) and converted to the free bases by treatment with ammonium hydroxide. The hydrochlorides were prepared by dissolving the base in isopropanol with slightly more than the calculated amount of concentrated hydrochloric acid and crystallizing by cooling.

d-Arteranol was racemized by heating at 90° for two hours in dilute hydrochloric acid solution with an 83% recovery of the racemic base.

Experimental

Resolution. (a) In Aqueous Methanol.—In a solution of 155 g. of *d*-tartaric acid in 100 ml. of water 169 g. of *dl*-arteranol was dissolved by vigorous stirring. The solution was diluted slowly with methanol to one liter. Crystallization was induced by scratching and after several hours at room temperature there was a nearly solid mass of crystals which was separated and washed with a little 90% methanol. After drying *in vacuo* at