[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CONNECTICUT]

The Chlorination of Aliphatic Amines[1]

BY LAWRENCE H. AMUNDSEN AND LEONARD S. PITTS

A method has been developed for the direct chlorination of aliphatic amines. Using this method, N,N-dimethylpropylamine has been chlorinated yielding 2-chloro-N,N-dimethylpropylamine, 3-chloro-N,N-dimethylpropylamine, 2,2-dichloro-N,N-dimethylpropylamine, 2,3-dichloro-N,N-dimethylpropylamine and 3,3-dichloro-N,N-dimethylpropylamine. *n*-Propylamine and N,N-dimethyl-*n*-butylamine have also been chlorinated but the products of the chlorination were not isolated. The chlorination method has been used to observe the directive effect of the $-NHMe_2^+$ group in aliphatic chlorination. The results of these experiments indicate that the inductive effect of the $-NHMe_2^+$ group is greater even than that of the trifluoromethyl group.

The purpose of this investigation was to develop a direct method for the chlorination of aliphatic amines and by means of this method to observe the directive effects of the amino group in aliphatic substitution reactions. Such investigations have been undertaken with respect to other functional groups in aliphatic molecules,[2] but the lack of a direct method for chlorinating amines on remote carbon atoms (*i.e.*, on other than the alpha carbon atoms) has been lacking up to the present time.

Previous investigators, studying the reactions of free amines with various chlorinating agents have observed either nitrogen chlorination in the case of primary and secondary amines[3] or carbon-to-nitrogen bond rupture in the case of tertiary amines.[4] Although remote carbon chlorination has been suspected in some instances of amine chlorination, such compounds have never been isolated and characterized from these reaction mixtures.[4b] Jülicher[5] has described the preparation of β-chloroisopropylamine by the direct chlorination of isopropylamine. Whereas he was able to isolate a 90% yield of β-chloroisopropylamine, we obtained a solid carbonaceous product which we were unable to distil as he reported doing. His method appears to be extremely unpromising, both from the extensive decomposition observed in our repetition of his experiment and from the extensive evidence[3] for nitrogen chlorination under conditions similar to those that he used.

It seemed likely that if the presence of a free amino group and conditions favoring an ionic mechanism could be avoided in the chlorinations, considerable remote carbon chlorination would result. This appeared likely if it were possible to chlorinate the amine hydrochloride by a free radical mechanism. In the absence of a hydroxylic solvent, under conditions which favor free radical formation, the amine hydrochloride might be expected to undergo substitution in the following manner. The electron withdrawal effect of the quaternary nitrogen group should prevent the alpha hydrogen from leaving with its electron, that is, as a free radical, thus inhibiting participation by the alpha hydrogens in a free radical chlorination. Thus, such a chlorination should give principally remote carbon chlorinated products and little if any alpha chlorinated product.

Chlorination of N,N-Dimethylpropylamine Hydrochloride.—Most of our chlorinations were carried out using N,N-dimethylpropylamine, primarily because the 2- and 3-chloro derivatives of this amine are known compounds.[6] A tedious characterization of the monochlorinated reaction products was thus avoided.

Attempts to chlorinate this amine hydrochloride using benzoyl peroxide generation of chlorine free radicals were not successful. Successful chlorinations of the amine hydrochloride were observed when sealed ampules containing an equimolecular mixture of the amine hydrochloride and chlorine in chloroform were exposed to the light from a 200-watt incandescent lamp. The ampules were used because bubbling chlorine through the open solution did not permit a ready estimation of the amount of chlorine reacting. Using sealed ampules containing a known amount of chlorine it was possible to see the gradual diminution of color as chlorine was consumed. The considerable pressure in the ampule indicated that there was a higher concentration of chlorine in the chloroform than there could have been if the system had been open. Thus the use of the sealed container was advantageous on this basis also.

Initially, the utmost precautions were observed to ensure dry conditions as it was felt that the presence of moisture would bring about concurrent ionic reactions due to the generation of hypochlorous acid. It was later found that moisture has no such deleterious effect, however, and successful chlorinations eventually were carried out with water as a solvent. This result was contrary to what had been anticipated on the basis of our hypothesis that hydroxylic solvents by favoring an ionic mechanism would favor alpha chlorination. This may indicate that in the aqueous chlorination of free tertiary amines, which has commonly resulted in carbon–nitrogen bond rupture,[4] the initial attack is on the free electron pair on the nitrogen atom. This, of course, would account satisfactorily for our failure to get the anticipated preponderance of rupture in the aqueous chlorination of an amine salt. The difference in the results obtained with the salt cannot be considered to have established, however, that the initial attack in the case of the free tertiary amines is on the nitrogen atom. Other mechanisms involving the free electron pair are con-

(1) From the Ph.D. thesis of Leonard S. Pitts, June, 1950; presented at the Philadelphia Meeting of the American Chemical Society, April, 1950.

(2) Ash and Brown, *Record of Chem. Progress* (Kresge-Hooker Sci. Lib.), **9**, 81 (1948).

(3) (a) Wurtz, *Ann. chim. phys.*, [3] **30**, 454 (1850); (b) Tcherniac, *Ber.*, **9**, 146 (1876); (c) Berg, *Compt. rend.*, **114**, 1379 (1892).

(4) (a) Meisenheimer, *Ber.*, **46**, 1148 (1913); (b) Crane, Forrest, Stephenson and Waters, *J. Chem. Soc.*, 827 (1946); (c) Price, Pohland and Velzen, *J. Org. Chem.*, **12**, 308 (1947).

(5) Jülicher, British Patent 445,206, April 6, 1936.

(6) (a) Schultz and Sprague, THIS JOURNAL, **70**, 48 (1948); (b) Knorr and Roth, *Ber.*, **39**, 1425 (1906).

ceivable. For example, the attack may well be on the hydrogen attached to the alpha carbon atom as some have supposed, followed by hydrolysis of the chlorides and subsequent nitrogen–carbon bond rupture. If so, it now seems likely that it must be an electrophilic attack of chlorine aided by an electromeric effect from the free electron pair on the nitrogen atom. If there is an electrophilic attack of chlorine on hydrogen, with the hydrogen atom taking with it its pair of bonding electrons, it is conceivable that such an electromeric shift of the free electrons from the nitrogen atom might aid the attack.

Table I gives the results of a number of chlorinations using either water or chloroform as a solvent. The yields shown in Table I were estimated from volume–temperature distillation curves. In chloroform under the conditions employed the best ratio of chlorine to amine for monochlorination appears to be about 3 to 1. If the chlorine to amine ratio is increased beyond this, dichlorinated products begin to appear in significant amounts.

The percentage loss of original amine in Table I appears to be quite large, but much of this loss can be accounted for. Putting a known amount of the amine through the isolation procedure indicated that about 20% of the amine is lost during the isolation. It seems, therefore, that the loss of amine listed in Table I is not due to side reactions involving chlorination of the amine.

TABLE I

Run	Ratio of chlorine to amine	Yield of $\beta + \gamma$ chloroamine, %	Yield of unreacted amine recovered, %	Yield of dichloroamine, %	Weight of hydrazone obtained, g.	% of original amine lost
A. Chlorination of Dimethyl-*n*-propylamine Hydrochloride in Chloroform in Presence of Phosphorus Pentoxide						
1	1 to 1	12	65	0	2	23
2	2 to 1	37	34	0	6	29
3	2 to 1	33	48	0	..	19
4	3 to 1	50	29	0	6	21
5	3 to 1	52	30	Trace	5	18
6[a]	3 to 1	25	43	0	14	32
7[b]	3 to 1	27	42	0	12	31
8	4 to 1	49	15	5	..	31
9	4 to 1	49	10	6	..	35
10	5 to 1	56	7	13	5	24
B. Chlorination of Dimethyl-*n*-propylamine Hydrochloride in Chloroform in Absence of Phosphorus Pentoxide						
1[a]	2 to 1	17	56	0	10	22
2	3 to 1	45	11	8	6	37
3	3 to 1	50	4	7	4	39
4	4 to 1	47	7	23	5	23
C. Chlorination of Dimethyl-*n*-propylamine Hydrochloride in Water						
1	1 to 1	30	32	Trace	None	38
2	2 to 1	40	0	30	None	30
3	3 to 1	12	0	55	None	33

[a] The chloroform used in these runs was contaminated with phosgene. [b] Yields estimated on the basis of fractionation data.

An estimate of the extent of the alpha chlorination was obtained by converting all aldehydic products to the 2,4-dinitrophenylhydrazones. It was not possible to separate and identify the components of the mixture of hydrazones which was obtained in this manner. The maximum yield of alpha chlorinated product calculated as if the hydrazone mixture were pure hydrazone of formaldehyde, does not exceed 3% in most runs. Only in runs 6A, 7A and 1B does the amount of alpha chlorination exceed this value. In these runs, however, the solvent had stood for some time after purification and had formed considerable hydrogen chloride and phosgene. The latter compound acting as a halogen carrier might be expected to increase the amount of alpha chlorination and chlorination of the solvent.

Very probably in all runs which resulted in measureable yields of monochlorinated product, there occurred some concurrent dichlorination. However only in those runs which involved over 50% monochlorination was the dichloroamine detectable by the distillation method. Probably all three dichlorinated products, 3,3-dichloro-N,N-dimethylpropylamine, 2,2-dichloro-N,N-dimethylpropylamine and 2,3-dichloro-N,N-dimethylpropylamine are formed during the chlorination, although only two of these isomers were obtained during the distillation of the products of a regular run.

The third isomer, 2,2-dichloro-N,N-dimethylpropylamine was prepared by chlorinating the 2-chloro-N,N-dimethylpropylamine under conditions similar to those under which the other two isomers were formed during the chlorination of the original amine. It is likely, therefore, that the third isomer occurred only in small quantity and thus could not be isolated before decomposing in the still-pot.

Proof of Structure of the Dichloro Isomers.—In order to identify each of the dichloro isomers formed in the chlorination of N,N-dimethylpropylamine, each pure monochloro isomer was chlorinated to give its two possible dichlorinated products. Each chlorination gave two isomers, one of which was common to both chlorinations. Obviously, this was the 2,3-dichloro-N,N-dimethylpropylamine. The other isomer arising from the chlorination of the 2-chloro-N,N-dimethylpropylamine was the 2,2-dichloro-N,N-dimethylpropylamine, and the remaining isomer from the chlorination of 3-chloro-N,N-dimethylpropylamine was 3,3 dichloro-N,N-dimethylpropylamine. Because the picrate of 2,3-dichloro-N,N-dimethylpropylamine from the chlorination of 3-chloro-N,N-dimethylpropylamine could not be purified, this isomer was synthesized from 3-chloro-1,2-propanediol as additional proof of its structure.

Directive Effect of the Quaternary Nitrogen Group.—Recently, Ash and Brown[2] have arranged a number of functional groups with respect to their deactivating effect on carbon substitution in aliphatic chlorinations. Because of the lack of experimental data at the time of their compilation, they were unable to include either the amino group or the $-NR_3^+$ group in their scale. Through our investigation we have been able to get some idea of the position of the $-NMe_2H^+$ group with respect to the functional groups they considered.

Table II lists the ratios of beta and gamma chlorination obtained in a number of our runs. The ratio in most cases approached 2 to 3. From Hass' data[7] on the chlorination of hydrocarbons it can be predicted that if there were no directive influence of the $-NHMe_2^+$ group, the ratio of beta to gamma chlorination would be 2 to 1. Thus, our value indicates that there is considerable deactivation of the beta carbon as well as the alpha carbon in N,N-dimethylpropylamine hydrochloride. The substitution ratio of 2 to 3 indicates that the directive influence and hence the inductive effect of the $-NHMe_2^+$ group is greater than any of the twelve groups listed by Ash and Brown[2] the most strongly deactivating of which is $-CF_3$.

TABLE II

PERCENTAGES OF REMOTE MONOCHLORINATION GOING TO THE BETA AND THE GAMMA POSITIONS

Run	β-chlorination, %	γ-chlorination, %
A. Chlorination in Presence of P_2O_5		
2	38	62
3	35	65
4	36	64
5	39	61
6	31	69
7	30	70
8	37	63
9	36	64
10	38	62
B. Chlorination in Absence of P_2O_5		
1	33	67
2	42	58
3	43	57
4	40	60

The value listed in Table II may be slightly in error due to the decrease in yield of one of the monochloro isomers brought about by inter or intramolecular quaternary salt formation during the distillations, as in most cases about 5% of the crude product formed non-volatile salts. This error, however, would not be great enough to affect the position of the $-NHMe_2^+$ in Ash and Brown's scale.

Chlorination of *n*-Propylamine Hydrochloride and N,N-Dimethyl-*n*-butylamine Hydrochloride.—The chlorination of these amine hydrochlorides in chloroform was found to proceed in a manner similar to N,N-dimethylpropylamine hydrochloride. It was not possible to isolate the chlorinated products of either of these amines, however, as the chloroamines were found to polymerize almost completely when heated during the distillation. Conversion of the chlorinated products to stable derivatives for isolation was not satisfactory. An estimation of the extent of remote carbon chlorination was obtained by weighing the sodium chloride formed when the mixture of chlorinated products was refluxed in alcoholic sodium ethoxide. The yield of remote chlorination products, calculated as if it were all monochlorinated products, was 60% based upon the quantity of *n*-propylamine hydrochloride originally used, and was 66% in the case of N,N-dimethyl-*n*-butylamine.

(7) Groggins, "Unit Processes in Organic Synthesis," 3rd ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1947, p. 186.

Experimental

Preparation of Ampules.—The ampules were constructed of 30-cm. lengths of 5-cm. inside-diameter Pyrex tubing rounded at each end to a test-tube bottom. One end of the ampule had a 20-cm. length of 4-mm. inside-diameter Pyrex tubing attached, through which reagents could be introduced by means of a gas delivery tube or a fine-stemmed funnel. The ampule was sealed by drawing off a small portion of the 4-mm. tubing. The ampules were dried by heating at 200° for 12 hours, allowing them to cool under vacuum, and then admitting air through a tube of Drierite.

***n*-Propylamine.**—The product from Commercial Solvents Corporation was dried over sodium hydroxide and then over sodium.

N,N-Dimethylpropylamine.—A mixture of 117 g. (1.5 moles) of *n*-propyl chloride and 135 g. (3 moles) of liquefied dimethylamine was prepared in a Pyrex reaction tube at −75°. The reaction tube was sealed, placed in a steel bomb equipped with a heating mantle and heated over a period of 2 hours until the temperature inside the bomb had reached 120°, where it was maintained for 5 hours. The bomb was allowed to cool and the reaction mixture removed. The supernatant liquid was decanted from the solid plug of amine hydrochloride at the bottom of the reaction tube and dried over sodium hydroxide pellets. The dried amine was distilled through a four-foot helices-packed column, the fraction boiling at 64.5–65.1° was collected as product and stored over sodium; yield 84 g. (64%) $n^{20}D$ 1.3877, d^{20}_{20} 0.7081, picrate m.p. 109.2–109.9° (cor.). The reported m.p. of the picrate is 108–109°.[8]

N,N-Dimethyl-*n*-butylamine.—This compound was prepared in the same manner as N,N-dimethyl-*n*-propylamine; yield 100 g. (50%), b.p. 93–94°, $n^{20}D$ 1.3980. The reported b.p. is 95°.[9]

Purification of Chloroform.—Commercial chloroform was shaken with concentrated sulfuric acid, washed with water, dried over calcium chloride and distilled from phosphorus pentoxide.

Chlorination of N,N-Dimethylpropylamine Hydrochloride in Chloroform in the Presence of Phosphorus Pentoxide.—(Runs A1 to A10) Two hundred cubic centimeters of purified chloroform was distilled from phosphorus pentoxide into a dry ampule and 29 g. (0.33 mole) of N,N-dimethylpropylamine added. Dry hydrogen chloride was bubbled into the ampule, the ampule being cooled with an ice-bath. When no further fuming occurred when the gas delivery tube was raised above the surface of the solution, the passage of gas was stopped. The contents of the ampule were boiled to remove excess hydrogen chloride and the ampule cooled. Two grams of phosphorus pentoxide in 50 cc. of freshly distilled chloroform was added and the ampule cooled to approximately −75°. Dry chlorine was passed into the ampule until the gain in weight was 24 g. (0.33 mole of chlorine). The ampule was then sealed and the mixture placed 2 inches from a 200-watt incandescent lamp. After 2 to 3 days exposure, the chlorine was completely consumed as evidenced by the colorless reaction mixture. When more than 0.33 mole of chlorine was to be used, the ampule was cooled to −75° and the seal broken. The hydrogen chloride formed was boiled off and additional chlorine introduced at −75° after which illumination was resumed.

After the desired amount of chlorine had reacted, the ampule was opened and the hydrogen chloride driven off by boiling. The contents of the ampule were extracted with five 50-cc. portions of water. The water extracts were combined and distilled to remove 200 cc. of distillate. This distillate was diluted to 500 cc. and a 2.5-cc. portion from this was added to 10 cc. of 2,4-dinitrophenylhydrazine reagent. The precipitate which formed was allowed to stand overnight. It was then filtered, air dried and weighed.

The sirup of hydrochlorides resulting from the distillation was cooled to −75° and 100 cc. of a saturated sodium hydroxide solution added slowly. The amine layer was separated and dried at 0° over sodium hydroxide pellets. The dried amine was rectified at atmospheric pressure through a 50-cm. semimicro Vigreux column to remove unreacted N,N-dimethylpropylamine and at 49–50 mm. to remove 2-chloro-N,N-dimethylpropylamine (b.p. 44–45°) and 3-chloro-N,N-dimethylpropylamine (b.p. 54–55°). The higher boiling material of runs A8, A9 was taken off as

(8) Hanhart and Ingold, *J. Chem. Soc.*, 997 (1927).

(9) Clarke, *ibid.*, 1689 (1913).

quickly as possible at 49–50 mm. to prevent polymerization in the still-pot. After removal of the monochloroamines from the product of run 10A, the pressure was reduced to 5–7 mm. and two fractions were removed. The first fraction (yield 2.0 g.) boiling 35–36° gave a picrate which melted at 132.0–133.2° (cor.). The second fraction (yield 0.9 g.) boiling at 44° gave a picrate which melted at 104.5–105.1° (cor.).

Chlorination of N,N-Dimethylpropylamine Hydrochloride in Absence of Phosphorus Pentoxide.—(Runs B1–B3) These chlorinations were carried out following the procedure used for Runs A1–A10 except that no phosphorus pentoxide was added.

Chlorination of N,N-Dimethylpropylamine Hydrochloride in Water.—(Runs C1–C3) One-third mole of amine (29 g.) was placed in an ampule and cooled to −75°. Thirty cubic centimeters of concentrated hydrochloric acid was added slowly with alternate shaking and cooling until one liquid phase was obtained. Dry chlorine gas was then passed into the ampule at −75° until the gain in weight was 24 g. The ampule was sealed and placed two inches from a 200-watt incandescent lamp to react. Additional chlorine was added to runs C2 and C3 when the reaction mixture became colorless. After the desired amount of chlorine had reacted, the solution of hydrochlorides was removed from the ampule and diluted with 250 cc. of water. This solution was treated in a manner similar to the solution of hydrochlorides in runs A1–A10.

Chlorination of *n*-Propylamine Hydrochloride and N,N-Dimethyl-*n*-butylamine Hydrochloride.—These amines were chlorinated using a procedure similar to that in runs A1–A10 for N,N-dimethylpropylamine hydrochloride. The following proportions of reagents were used. *n*-Propylamine: 250 cc. of chloroform, 0.25 mole of amine, 0.66 mole of chlorine. N,N-Dimethyl-*n*-butylamine: 100 cc. of chloroform, 0.25 mole of amine, 0.75 mole of chlorine. The products of these reactions could not be rectified because of the ease with which they formed quaternary salts. The dried chlorinated amines were refluxed for 1 hour in a sodium ethoxide solution prepared by adding 23 g. of sodium to 300 cc. of absolute ethanol. The precipitated sodium chloride was filtered, washed with absolute ethanol, dried and weighed. The *n*-propylamine reaction yielded 8.7 g. of sodium chloride (equivalent to 60% remote monochlorination). The N,N-dimethyl-*n*-butylamine reaction yielded 9.5 g. of sodium chloride (equivalent to 66% remote monochlorination).

Proof of Structure of Dichloro-N,N-dimethylpropylamine Isomers.—A sample of 120 g. of the combined monochloroamines obtained from runs A1–A10 was carefully rectified through the 50-cm. Vigreux column at 48 mm. The following fractions were obtained: 2-chloro-N,N-dimethylpropylamine; 50.0 g. b.p. 43–43.5° (48 mm.); $n^{20}D$ 1.4250, d^{20}_{20} 0.9093; picrate, m.p. 100.5° (cor.). The reported melting point of this picrate is 101–103°.[6a] 3-Chloro-N,N-dimethylpropylamine; 28.7 g., b.p. 53–53.5° (48 mm.); $n^{20}D$ 1.4313; d^{20}_{20} 0.9287; picrate, m.p. 109.8–110.1° (cor.). The reported melting point of the picrate is 110°.[6b]

One-third of a mole of purified 2-chloro-N,N-dimethylpropylamine was chlorinated using the procedure developed for N,N-dimethylpropylamine. The dried chlorinated product from this reaction was rectified through the semi-micro Vigreux column at 48–49 mm. to remove unreacted 2-chloro-N,N-dimethylpropylamine. The pressure was reduced to 19–20 mm. and 2,2-dichloro-N,N-dimethylpropylamine was collected at 42–42.5°, $n^{20}D$ 1.4372. A picrate prepared from ethanol came down as an oil. An analysis was therefore run on the free amine. *Anal.* Calcd. for $C_5H_{11}NCl_2$: Cl, 45.44. Found: Cl, 45.45, 44.87. 2,3-Dichloro-N,N-dimethylpropylamine was collected at 66.5–67°, $n^{20}D$ 1.4586. Picrate: m.p. 106.8–107.5° (cor.). *Anal.* Calcd. for $C_{11}H_{14}O_7N_4Cl_2$: Cl, 18.41. Found: Cl, 18.60, 18.70.

One-quarter mole of 3-chloro-N,N-dimethylpropylamine was chlorinated similarly to 2-chloro-N,N-dimethylpropylamine. Rectification of the dichloroisomers at 19–20 mm. gave 3,3-dichloro-N,N-dimethylpropylamine, b.p. 55–56°, $n^{20}D$ 1.4492. Picrate: m.p. 133.2–133.5°. *Anal.* Calcd. for $C_{11}H_{14}O_7N_4Cl_2$: Cl, 18.41. Found: Cl, 18.56, 18.70. 2,3-Dichloro-N,N-dimethylpropylamine, b.p. 64–65.5°, $n^{20}D$ 1.4588. The picrate could not be purified.

Synthesis of 2,3-Dichloro-N,N-dimethylpropylamine.—A mixture of 27.6 g. (0.25 mole) of 3-chloro-1,2-propanediol and 25 g. (0.55 mole) of liquefied dimethylamine was prepared at −75° and sealed in a glass tube and placed in a steel bomb. The sealed bomb was maintained at 190° for 5 hours. The bomb was then cooled and opened. The semi-solid crystalline mass in the tube was filtered and washed with 50 cc. of chloroform. The filtrate was placed in a 500-cc. flask equipped with a dropping funnel and a reflux condenser and a solution of 120 g. of thionyl chloride in 50 cc. of chloroform was added slowly while cooling the reaction mixture in an ice-bath. After addition of the thionyl chloride solution, the unreacted thionyl chloride was distilled off with the chloroform and 50 cc. of water was added to the still-pot. The distillation was continued until the temperature of the vapors reached 100°. The sirup of hydrochlorides was then cooled and the amine freed using 75 cc. of saturated sodium hydroxide solution. The dried amine (7 g.) was distilled at 19–20 mm. and the fraction boiling at 66–68° collected, $n^{20}D$ 1.4582. A picrate crystallized from *n*-propyl alcohol melted at 104.0–104.7° (cor.). *Anal.* Calcd. for $C_{11}H_{14}O_7N_4Cl_2$: Cl, 18.41. Found: Cl, 18.04, 18.18.

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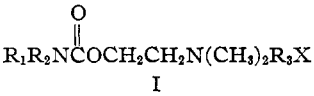
Some New Choline Type Thiols

BY JOHN WEIJLARD AND MAX TISHLER

Twenty-five new thiols of the choline type have been prepared, and several of these compounds are effective antispasmodics of low toxicity.

A class of urethan derivatives of choline type compounds, having the general formula of I, were found to be effective as antispasmodics.[1]



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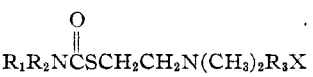

II

One compound of this class, Dibutoline, where R_1 and R_2 are *n*-butyl, R_3 is ethyl and X sulfate, has been subjected to considerable clinical study.[2] Since a major defect of Dibutoline is its low activity when administered orally, we undertook the preparation of a number of related compounds of the general formula II, containing a sulfur atom in place of an oxygen atom in the ester linkage. The new class of compounds were prepared by quater-

(1) Swan and White, *J. Pharmacol. Exper. Therapy*, **80**, 285 (1944).

(2) Featherstone and White, *ibid.*, **84**, 105 (1945); Peterson and Peterson, *ibid.*, **84**, 236 (1945), and *Gastroenterology*, **5**, 169 (1945); Cummins, Marquardt and Grossman, *ibid.*, **8**, 205 (1947); and others.