chlorination observed. That the quaternary salt from II could be isolated while that from I was not, is possibly attributable to the relative electronegativities of the cyano and ester groups in I and II; β-elimination occurring more readily with the group possessing the greater electron-withdrawing effect.

EXPERIMENTAL

The following general procedure was used in the reaction of 3-chloropropionitrile and alkyl 3-chloropropionates with amines. To a solution of the amine in absolute ethanol (200–300 ml. per mole) was added an equimolar quantity of the 3-chloropropionic acid derivative. With aliphatic amines the reaction was usually exothermic, while no temperature rise was noted with most aromatic amines. The resulting solution was refluxed from 0.5 to 90 hr., and the ethanol was distilled off under reduced pressure until solidification occurred. The residue was washed with anhydrous ether to remove unreacted starting materials and ethanol, and dried in a vacuum oven at 40–50°. The products obtained with a variety of amines are reported in Table I. Those from I were generally crystalline solids (either IV or V), while those from II ranged from waxy solids to gels. Recrystallization, where possible, was from ethanol-ether mixtures. All products (III, IV and V) were hygroscopic.

1-(2-Cyanoethyl)pyrrolidinium chloride. This material was prepared by reaction of pyrrolidine and I, from hydrogen chloride and 3-(1-pyrrolidinyl)propionitrile, and by cyanoethylation of pyrrolidine hydrochloride. A solution of 43 g. (0.4 mole) of pyrrolidine hydrochloride, 21 g. (0.4 mole) of acrylonitrile, and 80 ml. of absolute ethanol was refluxed for 72 hr., and worked up as above to give 55 g. (90%) of a slightly yellowish solid. One recrystallization from ethanol-ether gave white plates, m.p. 168–170°, of 3-(1-pyrrolidinyl)-propionitrile hydrochloride. A mixed melting point of this material and that prepared by reaction of I and pyrrolidine (Table I) was not depressed.

CENTRAL RESEARCH DEPARTMENT
MONSANTO CHEMICAL CO.
DAYTON 7, OHIO

Arylthiomethyl Quaternary Ammonium Salts from the Alkylation of Some Dialkylaminomethyl Aryl Sulfides

GERALD F. GRILLOT AND HAROLD G. THOMPSON

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Grillot *et al.*[1] have prepared in this laboratory dialkylaminomethyl aryl sulfides by the condensation of secondary amines and formaldehyde with thiophenols. It was of interest to us to determine if alkylation of these aminomethyl sulfides with an equivalent of an alkyl halide would produce quaternary ammonium salts rather than sulfonium salts. This was to be expected on the basis of reports by Kirchner, Soria, and Cavallito[2] who prepared quaternary ammonium salts of dialkylaminopropyl alkyl sulfides by allowing the latter to react with methyl and ethyl iodide and of Renshaw and Searle[3] who earlier observed that ammonium salt formation took precedence over sulfonium salt formation when the nitrogen and sulfur in an aminoalkyl alkyl sulfide were separated by from one to three carbon atoms.

Since alkylation of dimethylaminomethyl phenyl sulfide by benzyl chloride produces a salt which is identical to the benzyl phenylthiomethyl dimethylammonium chloride prepared by Barber and Green[4] by the action of *N,N*-dimethylbenzylamine on phenyl chloromethyl sulfide,[5,6] then in these aminomethyl aryl sulfides alkylation must occur preferentially on the nitrogen atom. In this latter synthesis it was found to be more satisfactory to prepare phenyl chloromethyl sulfide by the method of Bordwell and Pitt[7] than by Barber's method.[5,6]

Data concerning a group of new phenylthiomethyl trialkylammonium iodides and picrates prepared by the action of an alkyl iodide on a dialkylaminomethyl phenyl or *p*-chlorophenyl sulfide are listed in Table I.

It was expected that the quaternary ammonium iodides formed would be crystalline since crystallinity is a general characteristic of this type of salt. However there are several instances in the literature where compounds of this nature are not crystalline. For instance, Barber and Green[4] found that some of the quaternary salts prepared from *N,N*-dimethylbenzylamine were oils. Renshaw and Searle[3] found that derivatives obtained from methyl iodides were highly crystalline, while those from ethyl iodide tended to form oils. A characteristic common to these oils is the bulkiness of at least one of the substituents attached to the nitrogen. It appears possible that these large groups prevent the molecules from orienting themselves into a crystal structure.

EXPERIMENTAL

Benzyl phenylthiomethyl dimethylammonium chloride. Method A. Thioanisole was prepared by the method of Gilman and Beaber.[8] The fraction distilling at 69–71°/11 mm., obtained in a yield of 91%, was collected. The boiling point reported in the literature[8] is 58–60°/6 mm.

The method of Bordwell and Pitt[7], in which thioanisole is treated with sulfuryl chloride, was employed in the preparation of phenyl chloromethyl sulfide. The latter compound was obtained as an oil boiling at 85–87°/3 mm. in a yield of

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(8) H. Gilman and N. J. Beaber, *J. Am. Chem. Soc.*, **47**, 1449 (1925).

TABLE I

TRIALKYL ARYLTHIOMETHYLAMMONIUM IODIDES AND PICRATES

Cation	Melting Point, °C.	Iodide Analysis % Carbon Calcd.	Iodide Analysis % Carbon Found	Iodide Analysis % Hydrogen Calcd.	Iodide Analysis % Hydrogen Found	Picrate Melting Point °C.	Picrate Analysis % Carbon Calcd.	Picrate Analysis % Carbon Found	Picrate Analysis % Hydrogen Calcd.	Picrate Analysis % Hydrogen Found
Phenylthiomethyl triethylammonium	150.4–152.2[a,b]					121–122.4	50.43	50.71	5.35	5.52
Ethyl phenylthiomethyl piperidinium	oil					90.6–92	51.72	52.05	5.21	5.40
Ethyl phenylthiomethyl morpholinium	oil					102.6–104	48.92	48.79	4.75	4.88
Ethyl *p*-chlorophenylthiomethyl morpholinium	oil					133–135	45.56	45.42	4.23	4.34
Ethyl *p*-chlorophenylthiomethyl piperidinium	oil[c]					131.4–133	48.14	48.33	4.65	4.80
Phenylthiomethyl triethylammonium	152.4–154[a,d]	38.84	39.09	5.216	5.363	126–127.6	46.82	46.96	4.42	4.74
p-Chlorophenylthiomethyl triethylammonium	155–156[d,e]	40.47	40.35	5.488	5.338	103.8–105	46.86	47.40	4.76	4.94

Picrates recrystallized from ethyl alcohol. Carbon and hydrogen analysis performed by Drs. Weiler and Strauss, 164 Banbury Road, Oxford, England.

[a] Recrystallized from ethyl acetate. [b] Yield about 25%. [c] Yield about 28% based on yield of crude sample. [d] Recrystallized from ethyl acetate–chloroform mixture. [e] Yield about 20%.

47%. Bordwell and Pitt[4] reported a boiling point of 103–104°/12 mm.

Benzyl phenylthiomethyl dimethylammonium chloride was obtained by the action of *N*,*N*-dimethylbenzylamine on phenyl chloromethyl sulfide according to the procedure of Barber *et al.*[4] The crude product was obtained in a yield of 84% and melted at 164–170°. After recrystallization from a chloroform-ethyl acetate mixture, it melted at 168–171°. The melting point previously reported was 161–165°.[4] The picrate melted at 125–126°, (literature; 124–125°).

Method B. Dimethylaminomethyl phenyl sulfide was prepared by adding dropwise 20.5 ml. (0.2 mole) of thiophenol to 13 ml. (0.2 mole) of cold dimethylamine and then adding to the resulting mixture 18 g. (0.2 mole) of formalin. This reaction mixture was heated at 80° for 2 hr. and after cooling was extracted with ether. The ether extract was dried over anhydrous $MgSO_4$. After removal of the ether, a fraction boiling at 112–116°/9–11 mm. was obtained in a yield of 23.8 g. or 71%.

Benzyl phenylthiomethyl dimethylammonium chloride was then prepared by following the general method described by Wagner and Zook.[9,10]

To a solution of 8.4 g. (0.05 mole) of dimethylaminomethyl phenyl sulfide in 20 ml. of benzene was added 5.8 ml. (6.33 g.; 0.05 mole) of benzyl chloride. After standing for 17 hr. 3 g. of material separated. If the mother liquor was heated for 4 hr. at 60° an additional 2.7 g. of the product precipitated giving combined a yield of 40%. After two recrystallizations from a chloroform-ethyl acetate mixture it melted at 170.2–171° and gave no depression of the melting point when mixed with the quaternary ammonium salt prepared by Barber's method.

This chloride salt was converted to the picrate which melted at 124.8–125.4° and gave no depression of the melting point when mixed with the picrate obtained by the method of Barber.

Trialkyl phenylthiomethylammonium iodides. General method. The dialkylaminomethyl aryl sulfide, prepared by the method previously described by Grillot *et al.*,[1] was dissolved in a small volume of benzene and to this solution was added an equivalent quantity of ethyl or methyl iodide. If a crystalline precipitate did not form at once, the reaction mixture was heated at 60° until either a crystalline product or an oily residue formed. Although many of these compounds were oils that would not crystallize, all could be converted to crystalline picrates. Melting points, solvents for recrystallization, and analytical data for the crystalline iodides and picrates obtained are detailed in Table I.

CHEMISTRY DEPARTMENT
SYRACUSE UNIVERSITY
SYRACUSE, 10, N. Y.

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Synthesis of Potential Anticancer Agents. V. Convenient Synthesis of 4(5)-Amino-5(4)-carboxamido-1,2,3-triazole[1]

L. L. BENNETT, JR. AND HARRY T. BAKER

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The ribotide of 4-amino-5-imidazolecarboxamide (AIC) has been implicated for some time as an intermediate in biosynthesis of purines.[2] Since many of the agents that temporarily inhibit growth of

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(2) See, among others, (a) G. R. Greenberg, *Federation Proc.*, 13, 745 (1954). (b) M. P. Schulman and J. M. Buchanan, *J. Biol. Chem.*, 196, 513 (1954).