After 20 hr. at reflux temperature, the solution was concentrated under reduced pressure. The residue was diluted with water and was extracted with ether. The organic phase was washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo*. One recrystallization of the residue from methanol gave 25 mg. (30%) of white lustrous plates, m.p. 199–201° (plates in part characteristically rearrange to needles as the melting point is approached; melt solidifies to long needles); melting point of a mixture with a sample of naturally occurring solasodine (m.p. 199–201°) 199–201°; infrared spectrum (KBr) identical with that given by a specimen of natural solasodine: 10.3, 10.4, 11.2, 11.5 μ (azaoxaspirane bands).

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Synthetic Polysaccharides. VII. Preparation of Polyglucose Nitrate

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In order to prepare water soluble cationic derivatives of the synthetic polysaccharides for macromolecular interaction studies and for biochemical applications,[1] various reactions were recently investigated[2] for the introduction of amine groups into the synthetic polyglucose.[3] One of these reactions was the attempted reduction of polyglucose nitrate with sodamide in liquid ammonia. Unfortunately, the reduction attempt gave only highly degraded unidentified products of low molecular weight. The preparation and the properties of the nitrate ester of the synthetic polyglucose are given, however, for the following reasons:

The chemically synthesized polymer of glucose is a highly branched polysaccharide,[3] having on the average three free hydroxyls available for esterification per anhydroglucose unit. A polymer with high nitrate content has a large number of nitrate groups in a very small space, held together by the covalently linked, branched, spherical carbohydrate skeleton:[4] In this regard it was interesting to note that a polyglucose dinitrate detonated with one half of the impact force necessary for nitrocellulose of similar degree of substitution; also it ignited at lower temperature (155°). These observations indicate that the close proximity of the nitrate groups attached to different monosaccharide residues also increases the instability of the polysaccharide nitrates as does the degree of substitution or the ratio of nitrogen to carbon and oxygen.

Undoubtedly this method of nitration of polyglucose can be applied to the numerous different synthetic polysaccharides which were prepared by similar polycondensation of various other carbohydrates.[5]

EXPERIMENTAL

Concentrated nitric acid (70% reagent grade; sp. gr. 1.42) 400 ml. and 500 ml. of concentrated sulfuric acid (96% reagent grade; sp. gr. 1.84) were mixed in a round bottomed flask, 2 l. capacity, equipped with a glass stirrer and a thermometer. The mixture was then chilled (ice-salt bath) to −3° to −4° and 20 g. (0.123 anhydroglucose unit) of finely divided polyglucose (number average molecular weight $\overline{M}_n$ = 6,600, intrinsic viscosity $[\eta]$ = 0.05, sample A, Ref. 2) was added as rapidly as possible with stirring. The temperature of the reaction mixture rose to −2° for several minutes then dropped to −3° where it was maintained for 90 min. with continued stirring. The ice bath was replaced with a warm water bath and the mixture was heated gradually over a 20-min. period to 34 ± 1°, maintaining this temperature for 10 min. The mixture was then poured onto 2000 g. of crushed ice plus 300 ml. of water. After the ice had melted the white lumpy product was separated from the aqueous phase by centrifugation. In order to free the ester from acidic material the former was exhaustively washed with water, 5% sodium bicarbonate, and finally with water again until neutral to litmus, separating it from the washings each time by centrifugation. The product, after storing under water in the refrigerator (+3°) overnight, became slightly acidic again. Next, in order to preclude the possibility that acidic material was being entrapped in the slightly granular state of the ester, the latter was carefully ground to a fine powder under water with an all glass mortar. The slurry was transferred to a sheet of filter paper (Whatman #54) in a Buchner funnel and again washed with water until free of acidic material. After being dried for about a week in a vacuum (0.1 mm.) desiccator over calcium chloride (anhyd.) and sodium hydroxide pellets, the polyglucose nitrate was obtained as a fine white powder with a slight but still persistent odor of nitrogen oxides. The nitrate was quite soluble in acetone, abs. ethanol, 95% ethanol–abs. ether mixture (1:1); fairly soluble in 95% ethanol; very slightly soluble in abs. ether; and insoluble in water. On continued periods of storage in the dry state the nitrate was observed to give off increasing amounts of the yellow oxides of nitrogen when shaken or stirred, and it finally became lemon-yellow in color. It was then concluded that the persistence of the acidity in the nitrate was due to some auto-catalytic decomposition of the nitrate linkages in the ester structure, possibly initiated by presence of small amount of sulfuric acid esters[6] and not to any mechanical entrainment of nitric acid in the granular or powdered material. From then on it was decided that for periods of storage longer than two to three days the poly-

(1) *Cf.* for example P. T. Mora and B. G. Young, *Arch. Biochem. Biophys.*, **82**, 6 (1959); P. T. Mora, B. G. Young, and M. J. Shear, *Makromol. Chemie*, **38**, 212 (1960); and B. G. Young and P. T. Mora, *Virology*, **12**, 493 (1960).

(2) J. W. Wood and P. T. Mora, in preparation.

(3) P. T. Mora and J. W. Wood, *J. Am. Chem. Soc.*, **80**, 685 (1958), P. T. Mora, J. W. Wood, P. Maury, and B. G. Young, *J. Am. Chem. Soc.*, **80**, 693 (1958).

(4) P. T. Mora, *J. Polymer Sci.*, **23**, 345 (1957).

(5) P. T. Mora and J. W. Wood, *J. Am. Chem. Soc.*, **82**, 3418 (1960).

(6) R. W. Kerr in *Chemistry and Industry of Starch*, Academic Press, Inc., New York, N. Y., 2nd Ed. 1950, p. 303, mentions this possibility in the case of the instability of starch nitrates.

glucose nitrate could best be stablized by covering it with 10% sodium bicarbonate solution and storing in a refrigerator at 3° to 5°. The yield was 30.5 g. (97.9% of theor. for a di-nitrate substitution).

Anal. Calcd. for $[C_6H_8O_5(NO_2)_2]_n$: C, 28.58; H, 3.20; N, 11.11. Found: C, 26,72; H, 3.17; N, 11.15 (Dumas), 12.14 av. (Dupont Nitrometer[7]). On the basis of the nitrogen content (11.65%, average) the ester contains 2.2 nitrate groups per anhydroglucose unit.

The impact sensitivity test was run[7] according to a modified U. S. Bureau of Mines procedure. Our sample of polyglucose nitrate was detonated when placed in a combination metal cylinder and piston arrangement and a 5 kg. weight in turn was dropped from a height of 200 mm. onto the piston. A typical grade of nitrocellulose of 12.60% nitrogen usually detonates at a weight distance of 400 mm. under the same condition of testing. In the ignition test[7] small samples were placed in test tubes which were then heated in a Wood's metal bath at the rate of 5° per minute. Our sample ignited at 155° whereas the typical nitrocellulose sample ignited at 189°. The conclusion was that our sample of polyglucose nitrate is an extremely sensitive and unstable material and should be handled with due precautions.

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(7) We are indebted to Dr. W. C. Cagle and his co-workers at the U. S. Naval Propellant Laboratory, Indian Head, Md., for these analyses.

Unusual Pressor Agents: Acetylenic Carbamates

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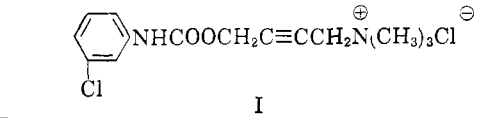
In the course of a routine examination of compounds of diverse chemical nature for cardiovascular and autonomic activity, it was found that 4-[*N*-(3-chlorophenyl)carbamoyloxy]-2-butynyltrimethylammonium chloride (I) possesses unique pharmacological properties. In the chloralose-anesthetized dog or cat this compound (also known as McN-A-343) produces an initial depressor response followed by a large pressor response at 8 μg./kg., i.v. The pressor activity was partially blocked by Dibozane [1,4-(bis-1,4-benzodioxan-2-yl methyl)piperazine] (1 mg./kg., i.v.) while hexamethonium [hexamethylenebis(trimethylammonium bromide)] (1 mg./kg., i.v.) did not inhibit and actually potentiated this action. Unexpectedly, atropine (1 mg./kg., i.v.) blocked both the pressor and depressor activity. It was concluded by Roszkowski[1] that this material (I) did not fall into the classical pressor-depressor categories of acetylcholine and related choline esters as defined by Dale many years ago.[2]

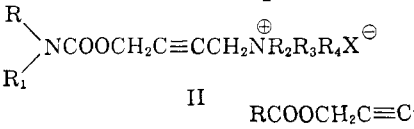
Further studies have shown that McN-A-343 is a ganglionic stimulant which acts at receptor sites or ganglionic cells distinct from those ganglionic sites which are activated by acetylcholine and which are blocked by conventional agents.[3]

Several related compounds which conform to structure II have been prepared due to the current interest in McN-A-343. These are, in general, very hygroscopic compositions which are obtained initially as gums or sirups. The trimethylammonium compounds are usually the highest melting materials in a given series and are more readily obtained in a pure state. The method of purification used for the compounds in Tables I–IV consisted of successive recrystallizations from absolute alcohol–ether mixtures. All the quaternary salts prepared were found to melt with decomposition.

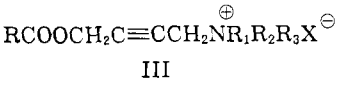
No acetylenic carbamates of this type (II) have been reported prior to this work. However, the closely related acetylenic esters (III) have been prepared and tested as ganglionic blocking agents by Biel[4,5] and as fungistatic agents by Waters.[6] The synthesis of 1-acetamido-2-butynyltrimethylammonium chloride also has been described by Marszak-Fleury.[7]



I



II



III

In addition to pharmacological studies, all compounds prepared were screened as pesticides. It is of some interest that only 4-(3-chlorophenylcarbamoyloxy)-2-butynyltributylammonium chloride possesses post-emergent herbicidal activity toward wild oats (*Avena fatua*) while being tolerant toward wheat and barley at identical rates. This activity is of the same type, but of a lesser degree, as that of the parent compound, 4-chloro-2-butynyl *N*-(3-chlorophenyl)carbamate (barban), now sold commercially as a selective wild oat herbicide.

(1) A paper entitled "McN-A-343: An Unusual Pressor Agent" was presented by A. P. Roszkowski at the Fall Meeting of the American Society for Pharmacology and Experimental Therapeutics at Seattle, Wash., 1960.

(2) H. H. Dale, *J. Pharmacol. Exptl. Therap.*, **6**, 714 (1914).

(3) A. P. Roszkowski, *J. Pharmacol. Exptl. Therap.*, **132**, 156 (1961).

(4) J. H. Biel, U. S. Patent **2,867,619** (1959).

(5) J. H. Biel, E. P. Sprengler, and H. L. Friedman, *J. Am. Chem. Soc.*, **79**, 6184 (1957).

(6) J. A. Waters and G. A. Wiese, *J. Am. Pharm. Assoc.*, **49**, 112 (1960).

(7) A. Marszak-Fleury, *Compt. rend.*, **241**, 752 (1955).