that such reagents as pyridine, which carries no charge to be acted on electrostatically, but which has an electron pair available for orbital overlap, are still strongly subject to the activating effect of the α-carbonyl group in displacement reactions.

CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF DEPAUW UNIVERSITY]

Heterocyclic Compounds via 1,1,1-Trichloro-3-nitropropene and 1,1,1-Trichloro-3-aminopropanol-2[1]

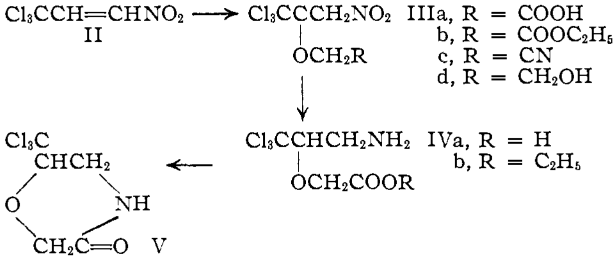
BY HOWARD BURKETT, GUNNER NELSON AND WILLIAM WRIGHT

RECEIVED MAY 3, 1958

Certain new heterocyclic compounds have been prepared from 1,1,1-trichloro-3-nitropropene and 1,1,1-trichloro-3-aminopropanol-2. Non-cyclic intermediates also are described.

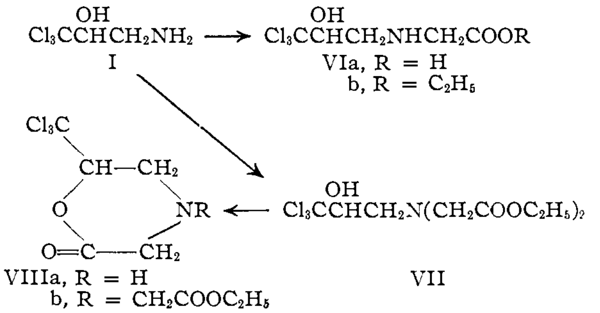
1,1,1-Trichloro-3-aminopropanol-2[2] (I) and 1,1,1-trichloro-3-nitropropene[3] (II) possess two functional groups and are potential starting materials for the synthesis of several types of heterocyclic compounds. This paper reports the results of some of these synthetic attempts.

Since alcohols added readily to the double bond in II,[4] it was expected that glycolic acid, ethyl glycolate or glycolonitrile would add in a similar manner to give IIIa, b or c, respectively, from which 6-trichloromethyl-3-morpholinone (V) might be prepared.



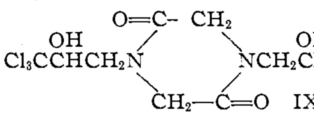
Numerous attempts with each of the glycolate compounds under neutral, basic and acidic conditions failed to yield any desired product. The synthesis of IIIa was accomplished indirectly. The reaction of II with excess ethylene glycol produced 1,1,1-trichloro-3-nitro-2-(2-hydroxyethoxy)-propane (IIId) in good yield. Oxidation of IIId with nitric acid produced the corresponding acid IIIa. Reduction of IIIa with stannous chloride and hydrochloric acid yielded 1,1,1-trichloro-3-amino-2-propoxyacetic acid (IVa), which gave V upon heating.

It had been expected that V or, more likely, the isomeric compound 6-trichloromethyl-2-morpholinone (VIIIa) could be synthesized *via* the reaction of I with ethyl bromoacetate.[5] This reaction, carried out in the presence of a tertiary amine, yielded principally ethyl 2-hydroxy-3,3,3-trichloro-1-propylaminoacetate (VIb) or diethyl (2-hydroxy-3,3,3-trichloro-1-propylimino)-diacetate (VII) depending upon the amount of ethyl bromoacetate used. Omission of the tertiary amine lowered the yield. Attempts to react the hydrochloride of I with ethyl bromoacetate (hoping to favor the formation of IVb) gave only recovered I. Important evidence for the structure of VIa, obtained from the acid hydrolysis of VIb, includes the facts that it differs from IVa in melting point, infrared spectrum and the nature of the product obtained upon heating.



Heating VII produced ethyl 6-trichloromethyl-4-morpholin-2-oneacetate (VIIIb).

Attempts to synthesize 6-trichloromethyl-2-morpholinone (VIIIa) were unsuccessful. Heating VIa or VIb at a temperature between 100 and 150° caused loss of water or alcohol, but the product did not have the expected properties for VIIIa. It was high-melting and did not form the hydrochloride salt. It was resistant to hydrolysis in dilute hydrochloric acid. It would sublime at a pressure less than 0.1 mm. but with some decomposition. Analysis and the infrared spectrum were consistent with the 2,5-piperazinedione structure, IX. Ebullioscopic measurements indicated a molecular weight about one and one-half times that required for IX but were very inaccurate due to the low solubility of the substance in the solvents.



IX

Other attempts to prepare VIIIa also failed. Refluxing the hydrochloride of VIa or b in several different solvents, including benzene and toluene,

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(1) Supported in part by Research Corporation to whom the authors are grateful. Taken in part from the Masters theses of G. N. and W. W.

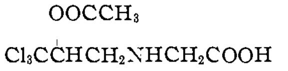
(2) (a) F. D. Chattaway and P. Witherington, *J. Chem. Soc.*, 137 1623 (1935); (b) M. Compton, H. Higgins, L. MacBeth, J. Osborn and H. Burkett, THIS JOURNAL, **71**, 3229 (1949).

(3) F. Brower and H. Burkett, *ibid.*, **75**, 1082 (1953).

(4) I. Thompson, S. Louloudes, R. Fulmer, F. Evans and H. Burkett, *ibid.*, **75**, 5006 (1953).

(5) For evidence that this kind of reaction may take place at the oxygen atom or the nitrogen atom see H. S. Mosher, M. B. Frankel and M. Gregory, *ibid.*, **75**, 5326 (1953).

yielded only the starting material; VIb was recovered unchanged after subliming through a heated (250–260°) helix-packed tube at 0.2 mm. Attempts in which samples of VIa were dissolved in concd. sulfuric acid and allowed to stand or were heated on the steam-bath were also unsuccessful. Heating either VIa or b (or the corresponding hydrochloride) with acetic anhydride or acetyl chloride gave either recovered starting material or, in one case, 2-acetoxy-3,3,3-trichloro-1-propylaminoacetic acid (X). Treating VIa hydrochloride with thionyl chloride at room temperature gave

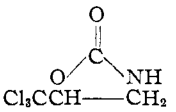


$$\overset{OOCCH_3}{Cl_3C\overset{|}{C}HCH_2NHCH_2COOH}$$

X

recovered VIa. The same reagent at the reflux temperature for fifteen hours gave a resinous, intractable material.

Reaction of I with ethylene carbonate in refluxing toluene gave 5-trichloromethyloxazolidone (XI)



XI

in low yield. The use of ethyl chlorocarbonate in refluxing benzene produced N-carbethoxy-1,1,1-trichloro-3-aminopropanol-2 in good yield.

Experimental[6]

1,1,1-Trichloro-2-(2-hydroxyethoxy)-3-nitropropane (IIId).—A mixture of 190.5 g. (1 mole) of 1,1,1-trichloro-3-nitropropene[3] and 248 g. (4 moles) of redistilled ethylene glycol was heated at 100–110° for four days. The reaction mixture was distilled through a short Vigreux column, yielding 154.9 g. (61%) of colorless liquid, b.p. 134–137° (2.5 mm.), n^{20}_D 1.4958. Other preparations gave yields up to 72%.

Anal. Calcd. for $C_5H_8O_4NCl_3$: C, 23.80; H, 3.17; N, 5.54. Found: C, 23.65; H, 3.31; N, 5.62.

1,1,1-Trichloro-3-nitro-2-propoxyacetic Acid (IIIa).—To 180 ml. of concd. nitric acid was added 50.5 g. (0.2 mole) of 1,1,1-trichloro-2-(2-hydroxyethoxy)-3-nitropropane during two hours with good stirring. The mixture was cooled to keep the temperature below 50°. After the reaction had subsided the mixture was kept at 45–50° for a few hours. Air was passed through the mixture for several minutes to remove the oxides of nitrogen. After diluting with 200 ml. of water, the mixture was extracted with 500 ml. of dichloromethane in several portions. The extract was washed with two small portions of water and dried over anhyd. magnesium sulfate. The volume of solvent was reduced to 50 ml. Chilling and filtering gave 32.2 g. of white crystals. Recrystallization from benzene–ligroin yielded 30.1 g. (57%) of product, m.p. 76–77°.

Anal. Calcd. for $C_5H_6O_5NCl_3$: C, 22.52; H, 2.25; N, 5.25. Found: C, 22.39; H, 2.34; N, 5.12.

1,1,1-Trichloro-3-amino-2-propoxyacetic Acid (IVa).—To a solution of 54 g. (0.24 mole) of stannous chloride in 37 ml. of concd. hydrochloric acid was added 10.6 g. of 1,1,1-trichloro-3-nitro-2-propoxyacetic acid in one portion. The temperature rose rapidly to 110°. After heating to 115° for a few minutes the mixture was allowed to cool to room temperature, then chilled in ice for several hours. The resulting white solid (15.1 g.) was filtered, dried and dissolved in 200 ml. of water. Saturation with hydrogen sulfide, filtration and evaporation of the filtrate under reduced pressure left 7.2 g. (65%) of white solid, m.p. 205–206° dec.

Anal. Calcd. for $C_5H_9O_3NCl_4$: C, 21.99; H, 3.30; N, 5.13. Found: C, 22.02; H, 3.39; N, 5.06.

The final solid above was dissolved in 50 ml. of water and filtered. The filtrate was adjusted to *p*H 5.0–6.0. The white needles which separated upon cooling were filtered and dried, affording 3.2 g. of product, m.p. 182–183° dec., with rapid heating 191–192° dec.

Anal. Calcd. for $C_5H_8O_3NCl_3$: C, 25.38; H, 3.38; N, 5.92. Found: C, 25.33; H, 3.52; N, 5.75.

6-Trichloromethyl-3-morpholinone (V).—In an open test-tube 1.0 g. of 1,1,1-trichloro-3-amino-2-propoxyacetic acid was heated for 15 minutes in an oil-bath at 180–185°. The material melted and bubbled. Upon crystallization from ethanol the crude product (m.p. 174–176°) yielded 0.76 g. of white crystals, m.p. 175.5–176.5°.

Anal. Calcd. for $C_5H_6O_2NCl_3$: C, 27.48; H, 2.75; N, 6.41. Found: C, 27.39; H, 2.91; N, 6.30.

A small sample of the above product was refluxed for one hour with 17% hydrochloric acid. Evaporation of the resulting solution left a white solid, m.p. 206–207° dec. The solution of this solid in a small amount of water was neutralized with sodium hydroxide, giving a white, crystalline precipitate, m.p. 184–185°.

Ethyl 2-Hydroxy-3,3,3-trichloro-1-propylaminoacetate (VIb).—To a suspension of 60 g. (0.34 mole) of 1,1,1-trichloro-3-aminopropanol-2 in 400 ml. of warm benzene was added 56 g. (0.34 mole) of ethyl bromoacetate and 40 g. (0.38 mole) of triethylamine during 10 minutes with stirring and heating. The ethyl bromoacetate was added a little more rapidly than the triethylamine. The mixture was refluxed for 40 minutes longer. The reaction mixture was filtered while still warm. Addition of ligroin to the filtrate and chilling gave 73.3 g. of crude product. Two crystallizations from ethanol afforded 44.5 g. (50%) of white crystals m.p. 101.5–102.5°.

Anal. Calcd. for $C_7H_{12}O_3NCl_3$: C, 31.76; H, 4.54; N, 5.29. Found: C, 31.56; H, 4.68; N, 5.18.

A sample of the pure product was dissolved in excess 20% hydrochloric acid. Evaporation under reduced pressure left a white, crystalline solid, m.p. 198° dec.

Anal. Calcd. for $C_7H_{13}O_3NCl_4$: C, 27.91; H, 4.32; N, 4.65. Found: C, 27.85; H, 4.49; N, 4.51.

Diethyl (2-Hydroxy-3,3,3-trichloro-1-propylamino)-diacetate (VII).—To a warm suspension of 18 g. of 1,1,1-trichloro-3-aminopropanol-2 in 250 ml. of dry benzene was added 38 g. of ethyl bromoacetate and 33 ml. of triethylamine dropwise during 0.5 hour. The ethyl bromoacetate was added more rapidly than the triethylamine. After refluxing for two hours, the mixture was filtered while warm. The benzene was evaporated on the steam-bath. The residue was crystallized from ethanol, adding water when cold, giving 17.0 g. (48%) of white, crystalline solid, m.p. 67–67.5°.

Anal. Calcd. for $C_{11}H_{18}O_5NCl_3$: C, 37.63; H, 5.14; N, 4.00. Found: C, 37.48; H, 5.30; N, 4.09.

2-Hydroxy-3,3,3-trichloro-1-propylaminoacetic Acid (VIa).—Refluxing ethyl 2-hydroxy-3,3,3-trichloro-1-propylaminoacetate with excess 10% hydrochloric acid for three hours and evaporating to dryness left a white solid. Water was added and the small amount of insoluble material was filtered. Neutralization of the filtrate to *p*H 6 gave a white precipitate, m.p. 218–220° dec. Both this precipitate and the water-insoluble material (m.p. 218–220° dec. (were immediately soluble in dil. hydrochloric acid and in dil. sodium hydroxide.

Anal. Calcd. for $C_5H_8O_3NCl_3$: C, 25.38; H, 3.38; N, 5.92. Found: C, 25.42; H, 3.45; N, 5.91.

The Ethyl 6-Trichloromethyl-4-morpholin-2-oneacetate (VIIIb).—Two grams of diethyl (2-hydroxy-3,3,3-trichloro-1-propylamino)-diacetate was heated at 154–158° under a pressure of approximately 5 mm. until the melt ceased bubbling (75 minutes). The cooled residue was extracted with boiling 90–100° ligroin, decanting from the insoluble dark oil. Chilling and filtering gave 0.50 g. of prismatic crystals, m.p. 73–75°. Two crystallizations from ethanol raised the melting point to 74.5–75.5°. The melting point of a sublimed sample was the same.

Anal. Calcd. for $C_9H_{12}O_4NCl_3$: C, 35.48; H, 3.94; N, 4.59. Found: C, 35.35; H, 4.11; N, 4.47.

An Attempt to Prepare 6-Trichloromethyl-2-morpholinone (VIIIa). 1,4-Di-(2-hydroxy-3,3,3-trichloro-1-propyl)-piperazinedione-2,5 (IX).—A 0.69-g. sample of ethyl 2-hydroxy-

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[6] Temperatures are uncorrected. Some of the analyses were by Clark Microanalytical Laboratory, Urbana, Ill. Infrared spectra were done by Mr. Roland Yunghans or by Eli Lilly and Co. to whom the authors are grateful.

3,3,3-trichloro-1-propylaminoacetate was heated at 105–110° in an open tube for 24 hours. The residue was crystallized from a large volume of ethanol, yielding a white powder, m.p. 266–267° dec. This product was insoluble in dil. hydrochloric acid and in refluxing 20% hydrochloric acid. The recovered solid from the latter decomposed at 270°. A small sample of the original product was sublimed at 0.2 mm. with some decomposition. The sublimed material decomposed at 271°.

Anal. Calcd. for $C_{10}H_{12}O_4N_2Cl_6$: C, 27.48; H, 2.75; N, 6.41. Found: C, 27.62; H, 2.69; N, 6.57.

An Attempt to Prepare 6-Trichloromethyl-2-morpholinone (VIIIa). 2-Acetoxy-3,3,3-trichloro-1-propylaminoacetic Acid (X).—The solid residue, obtained by refluxing 6.0 g. of ethyl 2-hydroxy-3,3,3-trichloro-1-propylaminoacetate with 150 ml. of 10% hydrochloric acid for three hours and evaporating to dryness under reduced pressure, was refluxed with 40 ml. of acetic acid and 10 ml. of acetyl chloride for 6 minutes. After adding 1 ml. more of acetyl chloride, the mixture was refluxed for 2 minutes longer. The residue from evaporating the reaction mixture under reduced pressure was crystallized from methanol–ether, giving a white, crystalline solid, m.p. 177–178° dec.

Anal. Calcd. for $C_7H_{11}O_4NCl_4$: C, 26.69; H, 3.49; N, 4.45. Found: C, 26.50; H, 3.63; N, 4.32.

The above solid was placed in water and sodium hydroxide was added with cooling in ice to *p*H about 7.5. The resulting solid was filtered and crystallized in succession from propanol-2, acetone and dry dioxane. The melting point of the material from each solvent was about the same, 111–119° with bubbling. If the melting point was retaken immediately it was about 116–122°. Droplets of liquid were noted on the upper part of the melting point tube. As this would indicate, this material was very hygroscopic. A heat and vacuum-dried sample gained weight rapidly in an open tube on the micro-balance. The total gain in weight after 1.5 hours and the nitrogen analysis on this sample (3.92%) indicated about five molecules of water of hydration. Another analysis (reported below) was run on a sample dried in a weighing tube under vacuum over phosphorus pentoxide, stoppering the weighing tube as quickly as possible after removing it from the drying apparatus. The material so dried was immediately soluble in dil. hydrochloric acid and in dil. sodium hydroxide and was precipitated from either solution by adjusting the *p*H to about 7.5.

Anal. Calcd. for 2-acetoxy-3,3,3-trichloro-1-propylaminoacetic acid dihydrate ($C_7H_{14}O_6NCl_3$): N, 4.44. Found: N, 4.43.

5-Trichloromethyloxazolidone (XI).—To a solution of 24 g. of 1,1,1-trichloro-3-aminopropanol-2 in 150 ml. of refluxing toluene was added 11.5 g. of ethylene carbonate. After refluxing for 15 hours and cooling, a viscous oil separated. The toluene was decanted from the oil and evaporated to 30 ml. Chilling and filtering afforded a solid which was crystallized from acetone–alcohol, giving 1.0 g. (3.7%) of white plates, m.p. 125–125.5°.

Anal. Calcd. for $C_4H_4O_2NCl_3$: C, 23.49; H, 1.96; N, 6.85. Found: C, 23.54; H, 2.20; N, 6.72.

N-Carbethoxy-1,1,1-trichloro-3-aminopropanol-2.—To a solution of 5.5 g. (0.031 mole) of 1,1,1-trichloro-3-aminopropanol-2 in 50 ml. of benzene was added an excess of ethyl chlorocarbonate. The mixture was refluxed for 50 hours, partially evaporated and chilled. Recrystallization of the resulting solid from benzene–acetone gave 6.03 g. (78.3%) of white plates, m.p. 72–73°.

Anal. Calcd. for $C_6H_{10}O_3NCl_3$: C, 28.78; H, 4.00; N, 5.59. Found: C, 28.71; H, 4.09; N, 5.49.

GREENCASTLE, IND.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF COLUMBIA UNIVERSITY]

Solvent Effects and Initiator Efficiency in the Benzoyl Peroxide–Dimethylaniline System[1]

BY CHEVES WALLING AND NORMAN INDICTOR

RECEIVED APRIL 17, 1958

The second-order reaction between benzoyl peroxide (Bz_2O_2) and dimethylaniline (DMA) has been followed in two ways: directly by measuring undecomposed peroxide, and indirectly, by observing *changing* polymerization rates while the pair was being used as polymerization initiator. The latter method was checked by using initiators of known decomposition rate and afforded a rapid reasonably precise method of obtaining initiator efficiency. Efficiencies were measured for bulk and solution polymerization from 0 to 80°. The reaction was strongly accelerated by pyridine; variation in rate with other solvents was also noted. The reaction of benzoyl peroxide with triethylamine yielded diethylvinylamine implying a new general path to enamine preparation. It is concluded that the tertiary amine–benzoyl peroxide reaction involves the initial formation of an unstable intermediate which may decompose by competing radical and non-radical forming processes.

Introduction

The second-order reaction between benzoyl peroxide and tertiary amines has been frequently studied,[2] mainly by Horner[3] and co-workers and Imoto[4] and co-workers. The products isolated[3d] from dimethylaniline (after aqueous treatment) are mainly benzoic acid, methylaniline and formaldehyde plus smaller amounts of *p*-benzoyloxydimethylaniline and *p,p′*-di-(dimethylamino)-diphenylmethane. Rate studies of the reaction have indicated that electron donor groups on the amine accelerate the reaction,[3c] as do electron acceptor groups on the peroxide.[2a,e]

The system Bz_2O_2–*t*-amine has been found to initiate polymerization[3b,4,6] with a variety of monomers. The observed relationship

$$R_p \propto [Bz_2O_2]^{1/2} \text{ to } (\text{amine})^{1/2}$$

is consistent with a bimolecular radical forming process. Meltzer and Tobolsky[5] have noted that with styrene the relation between polymerization

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[1] Taken from the dissertation of Norman Indictor submitted in partial fulfillment of the requirements of the Ph.D. degree, 1958. Support of this work by a research contract with the Office of Ordnance Research, U. S. Army, is gratefully acknowledged.

[2] For a more comprehensive review, see C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 590–594.

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[4] (a) M. Imoto and S. Choe, *J. Polymer Sci.*, **15**, 485 (1955); (b) M. Imoto, T. Otsu and K. Kimura, *ibid.*, **15**, 475 (1955); (c) M. Imoto, T. Otsu and T. Ota, *Makromol. Chem.*, **16**, 10 (1955); (d) M. Imoto, S. Choe and H. Taketsugi, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, **58**, 451 (1955); (e) M. Imoto and K. Takemoto, *J. Polymer Sci.*, **19**, 579 (1956).

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[6] K. Noma, O. Nisiura and A. Ichiba, *Chem. High Polymer Japan*, **10**, 231 (1953); J. Lal and R. Green, *J. Polymer Sci.*, **17**, 403 (1955).