when treated with ammonia, and that treatment with dilute acid resulted in the liberation of hydrogen cyanide. After three weeks of standing in a refrigerator at 5°, VII deposited crystals which upon purification proved to be bis-(3-bromo-2-tetrahydropyranyl) ether. It should be noted that this compound had been previously obtained as a hydrolysis product of I by Paul.[3] Further attempts to prepare 3-bromo-2-tetrahydropyranyl isothiocyanate by the action of phosphorus pentasulfide on II were to no avail. When an intimate mixture of II and phosphorus pentasulfide was heated gently, a vigorous exothermic reaction set in at 60° which resulted in the formation of intractable tars.

The reaction of 2,3-dibromotetrahydropyran and *o*-bromoaniline gave N-(3-bromo-2-tetrahydropyranyl)-*o*-bromoaniline (VIII), in good yield.

Acknowledgment.—The authors are indebted to the Atomic Energy Commission for financial assistance under contract AT(29-1)-787, Program B, and to Mrs. Patricia Ramey for the microanalytical data.

Experimental

3-Bromo-2-tetrahydropyranyl Isocyanate (II).—In a one-l. three-necked flask provided with a condenser, calcium chloride tube and Hershberg stirrer, were placed 170 g. (0.69 mole) of 2,3-dibromotetrahydropyran[2] and 300 ml. of dry, thiophene-free benzene. To this, in small portions, 103 g. (0.69 mole) of silver cyanate was added over a period of two hours, after which the silver bromide was removed by filtration through a Celite pad. Removal of the solvent *in vacuo* left a dark brown residue. Vacuum distillation of the latter yielded 121 g. (85% yield) of 3-bromo-2-tetrahydropyranyl isocyanate boiling at 100–102° at 2 mm.

Anal. Calcd. for $C_6H_8BrNO_2$: N, 6.80. Found: N, 6.70.

(3-Bromo-2-tetrahydropyranyl)-urea (III).—To 4.12 g. (0.020 mole) of II was added to 50 ml. of concentrated ammonium hydroxide solution. The mixture was stirred at room temperature for ten minutes, whereupon large crystals precipitated. Filtration of the product followed by recrystallization from ethyl alcohol yielded 4.26 g. of III, melting at 147–148°, yield 95%.

Anal. Calcd. for $C_6H_{11}BrN_2O_2$: N, 12.10. Found: N, 11.99.

1,3-Bis-(3-bromo-2-tetrahydropyranyl)-urea (IV).—In a 50-ml. erlenmeyer flask was placed 4.12 g. (0.020 mole) of II. To this was added 25 ml. of water, and the mixture was boiled until the carbon dioxide evolution had ceased. This required approximately ten minutes. Filtration of the solid yielded 3.74 g. of product, m.p. 149–150° dec., yield 97%.

Anal. Calcd. for $C_{11}H_{18}Br_2N_2O_3$: N, 7.26. Found: N, 7.30.

3-Bromo-2-tetrahydropyranyl Carbamate (V).—A mixture of 5.0 g, (0.0242 mole) of II and 20 ml. of 99.95% ethyl alcohol was refluxed for five minutes with careful exclusion of moisture. Refrigeration of the homogeneous solution for 48 hours failed to form crystals. The excess solvent was removed *in vacuo*, and 5 ml. of water was added to the residual sirup. Scratching induced crystallization of V. Recrystallization from ethanol gave 5.1 g. of V, m.p. 98–99°, yield 84%.

Anal. Calcd. for $C_8H_{14}BrNO_3$: N, 5.69. Found: N, 5.52.

Ethyl (3-Bromo-2-tetrahydropyranyl)-1-hydantoate (VI).—To 4.12 g. (0.020 mole) of II was added, with efficient cooling, 2.06 g. (0.020 mole) of freshly prepared ethyl glycinate. A solid formed immediately, which after recrystallization from acetone melted at 128–130°. The yield was 5.2 g., or 84%.

Anal. Calcd. for $C_{10}H_{17}BrN_2O_4$: N, 9.06. Found: N, 8.70.

Attempted Preparation of 3-Bromotetrahydropyranyl Isothiocyanate.—A mixture of 108 g. (0.445 mole) of 2,3-dibromotetrahydropyran and 300 ml. of dry, thiophene-free benzene was placed in a one-l. three-necked flask, provided with a condenser and calcium chloride tube and a Hershberg stirrer. To this was added in very small portions over a two-hour period 74 g. (0.445 mole) of dry silver thiocyanate. Upon completion of the addition the mixture was gently refluxed for two more hours, after which the precipitated silver bromide was removed by filtration. Vacuum distillation of the solvent left a residue, which distilled off at 107–110° (2 mm.) and had a strong odor, typical of a thiocyanate. The yield was 56 g. or 47% of theoretical. In view of the fact that the compound decomposed rapidly at room temperature, it was not submitted for analysis. Storage in the absence of light at 5° resulted in the deposition of crystals which, when recrystallized from ethyl alcohol, melted at 108–109° and possessed the correct analysis for di-(3-bromotetrahydro-2-pyranyl) ether. Paul reports a m.p. of 110° for this compound.[3]

Anal. Calcd. for $C_{10}H_{16}Br_2O_3$: C, 34.91; H, 4.69; Br, 46.45. Found: C, 34.88; H, 4.91; Br, 46.66.

N-(3-Bromo-2-tetrahydropyranyl)-*o*-bromoaniline (VIII).—A mixture of 71 g. (0.29 mole) of 2,3-dibromotetrahydropyran in 250 ml. of dry benzene was cooled to 5° in an ice-bath. To this was added slowly 100 g. (0.58 mole) of *o*-bromoaniline. Upon completion of the addition the mixture was gently warmed, and a vigorous reaction set in which had to be controlled by external cooling. After 20 minutes the precipitated *o*-bromoaniline hydrobromide was removed by filtration and the filtrate was stripped of solvent *in vacuo*. The solid residue weighed 78 g. and melted at 89–92°. An analytical sample, recrystallized three times from ethyl alcohol, melted at 93–95°. The yield of crude material was 79%.

Anal. Calcd. for $C_{11}H_{13}Br_2NO$: N, 4.18. Found: N, 3.96.

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[3] R. Paul, *Bull. soc. chim. France*, [5] **1**, 1397 (1934).

3-Bromotropolone Hydrobromide, a Product Obtained from the Bromination of 1,2-Cycloheptanedione[1]

BY L. GOLDMAN AND R. P. WILLIAMS

RECEIVED JUNE 21, 1954

The synthesis of 3-bromotropolone (III), involving the bromination–dehydrobromination of 1,2-cycloheptanedione (I), has been described by Cook, *et al.*,[2] and by Nozoe, *et al.*[3] The reaction of I in acetic acid with two moles of bromine at 0°[2] followed by heating on a steam-bath resulted in the formation of a dense crystalline solid, melting point not given, which it was said did not possess tropolone-like properties, and which was inadequately characterized as 3,7-dibromo-3-cyclohepten-1,2-dione (IV).[4] When warmed with aqueous methanol, 3-bromotropolone (III) was obtained, or when boiled in 6 *N* sodium hydroxide the corresponding sodium salt was obtained.

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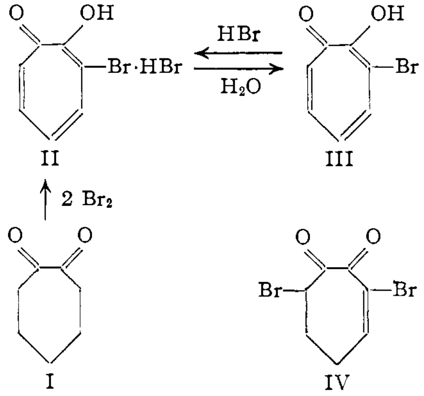
[1] Presented before the Division of Organic Chemistry, 126th National Meeting of the American Chemical Society, New York, N. Y., September 12–17, 1954.

[2] J. W. Cook, A. R. Gibb, R. A. Raphael and A. R. Somerville, *Chemistry and Industry*, 427 (1950); *J. Chem. Soc.*, 503 (1951).

[3] T. Nozoe, S. Seto, Y. Kitahara, M. Kunori and Y. Nakayama, *Proc. Japan Acad.*, **26**, 38 (1950).

[4] The only characterization of this product by Cook, *et al.*,[2] was a bromine analysis which was 3.0% lower than that required by $C_7H_6Br_2O_2$. It was pointed out that the product could be crystallized rapidly from acetic acid, but an accurate analysis could not be obtained owing to its instability.

Bromination of I (with two moles of bromine) at 12–15°[3] followed by heating at 60–80° produced a sparingly soluble compound, m.p. 173–174°, whose structure was not given, and which on being treated with water or alcohol gave III.



This reaction was reinvestigated and it was found that when 1,2-cycloheptandione was allowed to react in glacial acetic acid with two moles of bromine at temperatures ranging from 0–25° a compound separated from the reaction mixture in yields ranging from 17–38% and melting (with decomposition) variously from 95–165° to 171–172°. The purest samples melted near 172° dec. and analyzed well for $C_7H_6Br_2O_2$. This compound is undoubtedly identical with the compound of Cook, *et al.*, formulated as IV, and that of Nozoe, *et al.*, m.p. 173–174°. The ultraviolet absorption spectra of the bromination product are very similar to those of 3-bromotropolone when measured in chloroform. When measured in ethanol the spectra are identical, which is to be expected since the bromination product is converted by ethanol to 3-bromotropolone. The infrared spectra (Nujol mull) show no carbonyl band in the 5.8–5.9 μ region, present in the spectra of cycloheptanone and 1,2-cycloheptanedione. While not identical with the infrared spectra of 3-bromotropolone, this compound exhibits bands at 6.29, 6.56, 6.90, 7.59 and 7.98 μ, which bands are ascribable to the tropolone nucleus.[5]

3-Bromotropolone was treated with anhydrous hydrogen bromide to yield 3-bromotropolone hydrobromide (II), m.p. 172° dec., not depressed by admixture with the sparingly soluble product obtained from the bromination of 1,2-cycloheptanedione; the ultraviolet and infrared spectra of both products were identical in every way. That tropolones are capable of forming crystalline salts with halogen acids has been noted previously.[6]

The finding that bromination of 1,2-cycloheptanedione (I) under the aforementioned conditions leads to the formation of 3-bromotropolone hydrobromide (II) and not 3,7-dibromo-3-cyclohepten-1,2-dione (IV) is not surprising when one considers the high resonance energy calculated for tropolone, the latest value[7] being 33–36 kcal./mole (compare with the value of 36 kcal./mole for benzene). Thus, since the hydrobromide II possesses a much higher resonance energy with consequent greater stability due to its aromatic tropolonoid system than does the dibromo compound IV, it is evident that were IV formed as an intermediate, tropolonization[8] would occur by the elimination of hydrogen bromide, a double bond shift, and enolization to produce II.

3-Bromotropolone hydrobromide was readily converted to 3-bromotropolone by treating with water, sodium bicarbonate or refluxing glacial acetic acid.

Experimental[9]

3-Bromotropolone Hydrobromide (II). A. Bromination of 1,2-Cycloheptanedione with Two Moles of Bromine.—To a stirred solution of 12.6 g. (0.1 mole) of freshly distilled 1,2-cycloheptanedione[10] in 15 ml. of glacial acetic acid at 25°, protected from moisture, a solution of 32.0 g. (10.3 ml., 0.2 mole) of bromine in 30 ml. of glacial acetic acid was added during one-half hour to give a deep red-brown solution. After being allowed to stand overnight the mixture, containing some crystals, was heated for 20 minutes on a steam-bath causing a copious evolution of hydrogen bromide. After chilling and filtering, the resulting tan crystals of II were washed with a little cold acetic acid, air-dried and then dried briefly on a steam-bath; yield 7.9 g. (28%), m.p. 171–172° dec.

Anal.[11] Calcd. for $C_7H_6Br_2O_2$: C, 29.8; H, 2.1; Br, 56.7. Found: C, 30.0; H, 2.4; Br, 56.5.

The ultraviolet absorption spectra in chloroform show principal maxima at 257.5, 327.5, 363.5 and 380.5 mμ, ϵ 42,900, 9,750, 9,190 and 8,860, respectively. The infrared spectra in Nujol mull in the 6–8 μ region show bands at 6.28, 6.43, 6.57, 6.77, 7.08, 7.37, 7.55, 7.60, 7.98 and 8.08 μ.

When I was brominated as above, but the reaction mixture was allowed to stand for 3–4 days at room temperature, hydrogen bromide was continuously evolved and II crystallized from solution in the same yield as above.

The reaction of 2 moles of bromine with 1 mole of I at 0–6° (according to the procedure of Cook, *et al.*[2]) gave tan crystals, m.p. 165° dec., of crude II.

Anal.[11] Found: C, 31.7; H, 2.7; Br, 53.2.

B. Reaction of 3-Bromotropolone with Hydrogen Bromide.—A solution of 1.00 g. (0.005 mole) of 3-bromotropolone in 25 ml. of anhydrous ether was chilled by means of an ice-bath and treated with excess anhydrous hydrogen bromide. The mixture was filtered to remove pale yellow crystals which were washed with ether and dried briefly on a steam-bath. The yield of II, m.p. 172° dec., was 1.26 g. (90%). A mixed melting point with a sample of the sparingly soluble product obtained from the bromination of I showed no depression.

Anal.[11] Found: C, 29.5; H, 2.4; Br, 56.8.

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(5) *Cf.* (a) G. P. Scott and D. S. Tarbell, This Journal, **72**, 240 (1950); (b) D. S. Tarbell, G. P. Scott and A. D. Kemp, *ibid.*, **72**, 379 (1950); (c) J. R. Bartels-Keith and A. W. Johnson, *Chemistry and Industry*, 677 (1950); (d) J. R. Bartels-Keith, A. W. Johnson and W. P. Taylor, *J. Chem. Soc.*, 2352 (1951); (e) G. Aulin-Erdtman and H. Theorell, *Acta Chem. Scand.*, **4**, 1490 (1950); (f) A. W. Johnson, N. Sheppard and A. R. Todd, *J. Chem. Soc.*, 1139 (1951); (g) R. D. Haworth and J. D. Hobson, *ibid.*, 561 (1951); (h) H. P. Koch, *ibid.*, 512 (1951).

(6) *Cf.* (a) W. v. E. Doering and L. H. Knox, This Journal, **73**, 828 (1951), treated tropolone with hydrogen chloride to obtain tropolone hydrochloride; (b) J. W. Cook, A. R. M. Gibb and R. A. Raphael, *J. Chem. Soc.*, 2244 (1951), brominated tropolone to yield a complex which when sublimed gave tropolone hydrobromide, tropolone, mono- and dibromotropolones; brominated 3-bromotropolone to yield 3,7-dibromotropolone hydrobromide and 3,7-dibromotropolone; treated 3,7-dibromotropolone with hydrogen bromide to give 3,7-dibromotropolone hydrobromide; (c) J. D. Knight and D. J. Cram, This Journal, **73**, 4136 (1951); brominated–dehydrobrominated 2-hydrocycloheptanone to obtain a solid which was termed a hydrogen bromide adduct of tropolone and which when heated in cyclohexane gave hydrogen bromide and tropolone.

(7) W. N. Hubbard, C. Katz, G. B. Guthrie, Jr., and G. Waddington, This Journal, **74**, 4456 (1952).

(8) Nozoe, *et al.*, ref. 3, use the term "tropolize."

(9) All melting points are uncorrected.

(10) R. W. Vander Haar, R. C. Voter and C. V. Banks, *J. Org. Chem.*, **14**, 836 (1949).

(11) Microanalyses by L. M. Brancone and associates of these laboratories.

The ultraviolet absorption spectra in chloroform show principal maxima at 257.5, 327.5, 363.5 and 380.5 mμ, ϵ 47,800, 9,600, 9,510 and 9,710, respectively. The infrared spectra in Nujol mull in the 6–8 μ region show bands at 6.28, 6.42, 6.55, 6.75, 7.06, 7.32, 7.52, 7.57, 7.97 and 8.05 μ.

3-Bromotropolone (III).—3-Bromotropolone hydrobromide (11.00 g.) from bromination of I, was stirred with 100 ml. of water and 200 ml. of ether until all the solid was dissolved. The layers were separated and the aqueous layer was washed with 50 ml. of ether. The combined ether solutions were dried over magnesium sulfate. Evaporation *in vacuo* to dryness gave 7.90 g. (100%) of pale yellow crystals of III, m.p. 101–104.5°.

A sample of II, from bromination of I, was dissolved in boiling aqueous sodium bicarbonate (using Norite) and the filtered solution chilled and filtered to remove yellow plates of sodium 3-bromotropolone.[2] This was dissolved in the minimum amount of hot water and the solution acidified to *p*H 2. Chilling and filtering gave pale yellow crystals of III, m.p. 105–105.5°; Cook, *et al.*,[2] give m.p. 103–106°; Nozoe, *et al.*,[12] give m.p. 107–108°.

Anal.[11] Calcd. for $C_7H_5BrO_2$: C, 41.8; H, 2.5; Br, 39.8. Found: C, 41.5; H, 2.7; Br, 39.9.

The ultraviolet absorption spectra in chloroform show principal maxima at 257.5, 328.5, 264 and 381.5 mμ, ϵ 37,800, 7,450, 7,000 and 7,250, respectively. The infrared spectra in Nujol mull in the 6–8 μ region show bands at 6.24, 6.28, 6.48, 6.78, 7.09, 7.35, 7.67 and 8.07 μ.

3-Bromotropolone hydrobromide (7.46 g.), from bromination of I, was refluxed in glacial acetic acid until evolution of hydrogen bromide ceased. The solution was evaporated to dryness *in vacuo* and the residue was recrystallized from cyclohexane to give 3.30 g. of pale yellow crystals of III, m.p. 102–106.5°. Recrystallization from aqueous acetic acid, using Norite, gave pale yellow crystals of III, m.p. 103.5–105.5°.

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[12] T. Nozoe, Y. Kitahara, K. Yamane and A. Yoshikoshi, *Proc. Japan Acad.*, **27**, 18 (1951), find m.p. 107–108°, not 111° as reported in ref. 3.

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Paper Chromatography of the Anilides of Saccharinic Acids

BY JOHN W. GREEN

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Aldonic acids, as gluconic acid and the keto derivatives, have been separated on paper chromatograms by Norris and Campbell,[1] by Dyfverman, Lindberg and Wood,[2] and by Dyfverman.[3] The compounds were separated either as the free acids, or were first converted to the phenyl hydrazides. The various spots on the chromatogram were then detected by spraying the dried sheet with ammoniacal silver nitrate or with resorcinol in alcoholic hydrochloric acid. A new technique is now suggested, whereby the aldonic or saccharinic acids are first converted to the anilides, and then detected on the chromatogram by the quenching effect of the aromatic grouping on the ultraviolet fluorescence of the dye Rhodamine B. This dye has been suggested by Meigh[4] for the detection of aromatic nitro compounds on the paper chromatogram.

Paper chromatography of the crude saccharinic anilides obtained from D-glucose (or D-mannose) and D-galactose gives three very pronounced spots of R_f 0.60, 0.86 and 0.92, approximately, and a very faint spot of R_f 0.75. The crude saccharinic anilides of the two pentoses, D-xylose and L-arabinose, give three distinct spots of R_f 0.75, 0.86 and 0.92, approximately. Fractionation of mixtures on a cellulose column[5] gave two crystalline fractions—a C_6-saccharinic anilide of R_f 0.60 (obtained from D-glucose originally) and a C_5-saccharinic anilide of R_f 0.75 (obtained from L-arabinose originally). The identity of these compounds is being investigated.

This method shows promise of being a valuable tool for analyzing mixtures of saccharinic acids formed by the action of alkali on reducing sugars and polysaccharides (*i.e.*, alkaline pulping processes). It is being studied further and details will be published shortly.

Experimental

Preparation of Aldonic Anilides.—A solution of 0.1 g. of aldonic acid or lactone in 0.5 cc. of water is treated with 10 cc. of absolute ethanol, 0.2 cc. of aniline and 0.1 cc. of glacial acetic acid, and the solution concentrated to dryness on the steam-bath in 30–60 minutes. Solution of the residue, in the case of gluconic 1,5-lactone, in 15 cc. of 60% ethanol and visual comparison on a paper chromatogram with "known" spots of pure gluconic anilide showed almost complete conversion to the anilide. The rotation of the 60% ethanol solution checked within 5% of the value calculated for complete conversion. Use of ethanol and aniline alone, without the acetic acid, gave slightly lower yields. Gluconic 1,4-lactone gave slightly lower yields than did the 1,5-lactone.

Preparation of Saccharinic Anilides.—The given sugar is heated in 8 N NaOH for 8 hours on the steam-bath,[6] the alkaline solution diluted to 10 volumes and passed through a column of Amberlite IR-120 cation-exchange resin to remove the Na^+ ions, and the effluent concentrated *in vacuo* at 45°. The resulting sirup, containing crude saccharinic acids, is converted to the anilides as above, and then dissolved in 95% ethanol for spotting on the chromatographic paper.

Paper Chromatography of the Anilides.—A 7 by 24 inch sheet of Whatman No. 1 paper is spotted with 4 microliters of 1% aldonic anilide in 60% ethanol or 1 microliter of 5% crude saccharinic anilides in 95% ethanol. The mobile solvent used is a 9:1:2 v./v. mixture of acetone–water–benzene containing 4 mg. of Rhodamine B dye per 100 cc. The solvent is allowed to run the full length of the sheet (21 inches from the starting line), the paper is air-dried and then viewed under an ultraviolet light source.[7] The anilides show up as dark spots on a light yellow background. (The dye moves almost the full distance of solvent travel, so that substances with R_f values up to 0.97 can be detected. Tests with gluconic and other aldonic anilides show that 0.01 mg. can be easily detected.)

The aldonic anilides[8] were separated into C_6 and C_5 groupings, but there was little separation between stereoisomers. The R_f values also increased slightly with increasing length of solvent advance. Thus, for a solvent advance of 21 inches, the R_f values, measured at the center of each spot, were: D-galactonic anilide, 0.61; D-gluconic anilide, 0.63; D-mannonic anilide, 0.64; L-arabonic anilide, 0.70; D-xylonic anilide, 0.71; L-rhamnonic anilide, 0.82.[9]

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[1] Flora C. Norris and J. R. Campbell, *Can. J. Research*, **27c**, 253 (1949).

[2] A. Dyfverman, B. Lindberg and D. Wood, *Acta Chem. Scand.*, **5**, 253 (1951).

[3] A. Dyfverman, *ibid.*, **7**, 280 (1953).

[4] D. F. Meigh, *Nature*, **169**, 706 (1952).

[5] L. Hough, J. K. N. Jones and W. H. Wadman, *J. Chem. Soc.*, 2511 (1949).

[6] J. U. Nef, *Ann.*, **376**, 1 (1910).

[7] Mineralite Model SL 2537, obtained from the Ultra-Violet Products Co., 145 Pasadena Avenue, South Pasadena, California.

[8] E. Fischer and F. Passmore, *Ber.*, **22**, 2728 (1889); E. Kohn, *Monatsh. Chem.*, **16**, 333 (1895); Th. Van Marle, *Rec. trav. chim.*, **39**, 549 (1920).

[9] *d*-Gluconic and *d*-galactonic phenylhydrazides were also run on paper with the above solvent. The R_f values were similar to those for the anilides, so no better separation was achieved. The 60% ethanol solutions of the phenyl hydrazides tend to color on standing, but the anilide solutions showed no color after 1 month.