Aryl Carbamate Derivatives of D-Glucosan $<1,5>\beta<1,6>$ and of 1,2-Isopropylidene-D-glucose

BY IVAN A. WOLFF AND CARL E. RIST

In connection with other studies on the reactions of carbohydrates with aromatic isocyanates, levoglucosan tricarbanilate and tri-N-α-naphthylcarbamate, and 1,2-isopropylidene-D-glucose tricarbanilate and tri-N-α-naphthylcarbamate have been prepared.

The completely substituted derivatives were easy to prepare in good yield and were quite insoluble in water. They were best purified either by precipitation with water from their acetone or dioxane solutions or by digestion with organic solvents in which they were insoluble. All these derivatives could be crystallized from either glacial acetic or propionic acid solutions. However, the materials crystallized slowly, and the products, although analytically pure, had lower and less sharp melting points than those purified as described. Data on the products are collected in Table I.

TABLE I

Compound →			Levoglucosan tricarbanilate	1,2-Isopropylidene-D-glucose tricarbanilate	Levoglucosan tri-N-α-naphthylcarbamate	1,2-Isopropylidene-D-glucose tri-N-α-naphthylcarbamate
M. p., °C.			234–235	258–259	270–271.5	238.5–240
$[\alpha]^{25}$D in pyridine	Deg.		−44.9	−6.1	−25.3	−77.7
	c =		1.791	0.961	1.060	0.762
Formula			$C_{27}H_{25}O_8N_3$	$C_{30}H_{31}O_9N_3$	$C_{39}H_{31}O_8N_3$	$C_{42}H_{37}O_9N_3$
Analyses, %	Carbon	Calcd.	62.4	62.4	70.0	69.3
		Found	62.3	62.5	69.9	69.1
	Hydrogen	Calcd.	4.8	5.4	4.6	5.1
		Found	4.8	5.4	4.9	5.0
	Nitrogen	Calcd.	8.1	7.3	6.3	5.8
		Found	8.0	7.2	6.4	5.6

The stability of the aryl carbamate grouping toward mild acid and alkaline reagents[1] suggests the possible use of the esters here reported in the preparation of selectively substituted glucose derivatives of known structure.

Experimental

Levoglucosan Tricarbanilate.—A mixture of levoglucosan (1.62 g., 10 millimoles) and dry pyridine (15 ml.) was treated with phenyl isocyanate (4 g., 33.6 millimoles) and allowed to stand at room temperature for three days. Ten ml. of methanol was added, the mixture was warmed for ten minutes on a steam-bath, and then poured into approximately 150 ml. of water. The resulting white precipitate was dissolved in hot acetone. On cooling, 1.8 g. of amorphous solid separated. One further precipitation of this material from acetone gave an analytically pure product. Evaporation of the first mother liquors gave two additional crops, weighing 2.9 g., or a total of 90% of the theoretical amount.

1,2-Isopropylidene-D-glucose-tricarbanilate.—A mixture of 1,2-isopropylidene-D-glucose (2.20 g., 10 millimoles), dry pyridine (25 ml.) and phenyl isocyanate (5.4 g., 45.3 millimoles) was allowed to stand overnight. Ten ml. of methanol was added. After the mixture had stood for several hours a voluminous precipitate formed. The mixture was poured into approximately 150 ml. of methanol and filtered, giving 5.05 g. (87.5% of theory) of product which melted sharply at 258–259°. Solution in dioxane and reprecipitation with water gave a product of unchanged melting point, which was analytically pure.

Levoglucosan Tri-N-α-naphthylcarbamate.—Traces of water were removed from 3.24 g. (20 millimoles) of levoglucosan by azeotropic distillation, using pyridine. The mixture (containing 100 ml. of pyridine at this point) was cooled to 100°, and 15 g. (88.8 millimoles) of α-naphthyl isocyanate was added. Reaction was carried out at 100° with stirring for three and one-half hours, after which the oil-bath was removed and 10 ml. of methanol was added to the hot mixture. After standing overnight the mixture was filtered, the filtrate was evaporated to dryness *in vacuo*, and this solid was then digested with 200 ml. of boiling acetone and filtered. The residue weighed 12.1 g., representing a 90% yield of crude levoglucosan tri-N-α-naphthylcarbamate. An analytically pure sample was prepared by solution of the crude material in dioxane, reprecipitation with water, and extraction of the reprecipitated material with hot acetone.

1,2-Isopropylidene-D-glucose Tri-N-α-naphthylcarbamate.—Reaction was carried out as above, using 4.4 g. (20 millimoles) of 1,2-isopropylidene-D-glucose, 100 ml. of pyridine, and 15 g. (88.8 millimoles) of α-naphthyl isocyanate. The cooled reaction mixture was poured into 500 ml. of absolute ethanol and the clear solution was then added to 1 liter of water. The crude product which precipitated weighed 14.9 g. This material was dissolved in boiling acetone (700 ml.) and reprecipitated with 2 volumes of water, giving 13.4 g. of 1,2-isopropylidene-D-glucose tri-N-α-naphthylcarbamate, melting at 226–233°. An analytically pure sample was obtained by twice redissolving the crude product in dioxane and reprecipitating with water, followed by extraction of the reprecipitated material with boiling ethanol.

Acknowledgment.—The authors are grateful to C. H. Van Etten and M. Wiele for carrying out the carbon, hydrogen and nitrogen analyses reported.

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RECEIVED JULY 19, 1948

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[1] Hearon, Hiatt and Fordyce, THIS JOURNAL, 66, 995 (1944).

Willgerodt–Kindler Reaction with a Pyrrole

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The preparation of pyrroles containing acetic acid substituents is of interest because of the structure proposed for uroporphyrin.[1] Previous studies have not applied the Willgerodt reaction for the preparation of pyrrole acetic acids.[2,3,4,5] We have used the Willgerodt reaction as described by Schwenk[6] with 2,4-dimethyl-3-acetyl-5-carbethoxypyrrole. It was possible to obtain the thiomorpholide, but not to hydrolyze it to the substituted acetic acid. Vigorous alkaline hydrolysis gave only an amorphous neutral material, perhaps a polymer of 2,3,4-trimethylpyrrole. The thiomorpholide was reduced by Raney nickel to the expected amine.

Experimental

Thiomorpholide from Acetylpyrrole.—To 10.5 g. of 2,4-dimethyl-3-acetyl-5-carbethoxypyrrole was added 4 g. of sulfur and 25 g. of morpholine. The mixture was refluxed for two hours. It was cooled, diluted with water, and extracted with chloroform. The chloroform solution was washed with water, 10% hydrochloric acid, and again with water, dried and distilled to small volume. There crystallized a first crop of 6.2 g. m. p. 171–172°. This was extracted with carbon disulfide to remove sulfur and recrystallized from chloroform–carbon tetrachloride and then from acetone, m. p. 176–177° (178–179° cor.).

Anal. Calcd. for $C_{15}H_{22}N_2O_3S$: C, 58.0; H, 7.15; S, 10.75; N, 9.0. Found: C, 58.3; H, 7.14; S, 10.4; N, 8.7.

The nitrogen and sulfur analyses exclude the possibility that the 5-carbethoxy group underwent aminolysis as occurred with the keto-acids of Schwenk.[6]

A sample of the compound heated on the steam-bath for thirty minutes in 50 cc. of ethanol and 30 cc. of 0.1 *N* sodium hydroxide gave a mixture from which only the starting material was obtained pure. No crystalline product could be obtained when the substance was hydrolyzed by the methods of Schwenk[6] or Newman.[7]

2,4-Dimethyl-5-carbethoxy-3-morpholinoethylpyrrole.—To 500 mg. of the above thiomorpholide was added 150 cc. of boiling absolute ethanol and 50 cc. of a suspension of Raney nickel[8] W-7, containing 7.5 g. of catalyst. The mixture was allowed to stand with occasional shaking for one day. It was filtered and evaporated *in vacuo*. The product was crystallized from ether–pentane, giving 340 mg., m. p. 110–111.5°.

Anal. Calcd. for $C_{15}H_{24}N_2O_3$: C, 64.3; H, 8.63. Found: C, 64.2, 64.3; H, 8.48, 8.60.

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[1] Fischer and Orth, "Die Chemie des Pyrrols," Vol. II, Leipzig, 1937, p. 504.

[2] Ref. 1, Vol. I, p. 260.

[3] Fischer and Müller, *Z. physiol. Chem.*, **246**, 31 (1937).

[4] Fischer and Elhardt, *ibid.*, **257**, 61 (1939).

[5] Fischer, Neumann and Hirschbeck, *ibid.*, **279**, 1 (1943).

[6] Schwenk and Papa, *J. Org. Chem.*, **11**, 798 (1946).

[7] Newman, *ibid.*, **9**, 521 (1944).

[8] Adkins and Billica, THIS JOURNAL, **70**, 695 (1948).

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RECEIVED JULY 7, 1948

NEW COMPOUNDS

N,N-Dicyclohexyl Phthalamide

A solution of 9.9 g. (0.1 mole) of cyclohexylamine in 22.2 g. (0.1 mole) of diethyl phthalate was allowed to stand in a glass-stoppered bottle at room temperature. Crystals were noted at the end of four months. These continued to form slowly. They were filtered off after seven months and washed with dry ether; yield, 0.8936 g., calcd., 16.4 g., 5.4%; the colorless, silky needles did not melt under 300°.

Anal. Calcd. for $C_{20}H_{28}O_2N_2$: N, 8.53. Found: N, 8.4, 8.41.

The substance is soluble in methanol, ethanol, propanol, dioxane, benzene, toluene, chloroform, carbon tetrachloride, formic acid, acetone, methyl ethyl ketone; insoluble in water, heptane, ether, ethyl acetate.

Cyclohexylamine and diethyl phthalate were recovered from the filtrate by distillation under reduced pressure. There was no evidence of the formation of ethyl N-cyclohexylphthalamate.

N-Cyclohexyl phthalimide is known.[1]

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[1] R. W. Wegler and W. Frank, *Ber.*, **70B**, 1279 (1937); Gustave Vanags, *Acta Univ. Latviensis Kim. Facultat.*, Ser. 4, No. 8, 405 (1939); E. H. Gregler and S. I. Gertler, *J. Econ. Entomol.*, **39**, 549 (1946).

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RECEIVED AUGUST 5, 1948

Trimethylcyclotrisiloxane

In an account of the siloxanes derived from methyldichlorosilane[1] the failure to find the cyclic trimer $(CH_3SiHO)_3$, trimethylcyclotrisiloxane, was noted. Since the relative amount of the corresponding derivative of dimethyldichlorosilane is much larger in the thermally rearranged hydrolyzate than in the untreated hydrolyzate,[2] a search for trimethylcyclotrisiloxane in the products obtained by pyrolysis of the hydrolyzate of methyldichlorosilane was indicated. The desired compound was prepared by this method. It is more sensitive toward acid catalyzed rearrangement than is the tetramer, so much so that a molecular weight determination was not attempted. Its molecular weight can be deduced by comparison of its boiling point with those of related compounds.

Procedure.—Thermal rearrangement, by the method of Patnode and Wilcock,[2] of the liquid hydrolysis product,[1] 1216 g., of methyldichlorosilane at 300 to 350° in a stream of nitrogen yielded 1182 g. of distillate. A rough fractionation of this distillate yielded, initially, a fraction of 60 g. boiling below 133°, of which about 40 ml. boiled between 90 and 96°. This fraction, which contained a trace of aqueous acid, was diluted with an equal volume of ether, dried for a few hours over potassium carbonate, and stored in the refrigerator for four days. Upon fractionation none of the trimer was recovered; the first siloxane to distil was the tetramer. The once-cracked oil stock from which the crude trimer had been distilled was again subjected to thermal rearrangement, this time yielding 34 ml. of crude trimer. Fractional distillation yielded, besides some low boiling material, four fractions:

Frac.	B. p., °C.	Vol. cc.	n^{20}_D	d^{20}_4	R^{20}_D
1	92.2–92.6	3.7	1.3745	0.9055	0.2525
2	92.6–93.0	11.7	1.3753	.9242	.2479
3	93.0–93.8	11.6	1.3768	.9528	.2413
4	93.8–93.9	7.3	1.3770	.9677	.2377

Of these, the density and refractive index of fraction (4) were determined immediately after its collection. The constants for the first three fractions are those taken the next day. Their refractive indices were found to have increased slightly overnight. The best specimen was fraction (4) of which the specific refraction is in best agreement with the calculated[3] value of 0.2378. The lower density of

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[1] Sauer, Scheiber and Brewer, THIS JOURNAL, **68**, 962 (1946).

[2] Patnode and Wilcock, *ibid.*, **68**, 358 (1946).

[3] Calculated from the constants of Sauer, THIS JOURNAL, **68**, 954 (1946).