Long-Range Effects of Acyl Groups in the Solvolysis of Glycofuranosyl Halides. The Synthesis of 2,3-Di-*O*-benzyl-5-*O*-*p*-nitrobenzoyl-α-D-arabinofuranosyl Chloride and of 2-*O*-Benzyl-3,5-di-*O*-*p*-nitrobenzoyl-α-D-arabinofuranosyl Chloride

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In order to investigate the effect of acyl groups at C-3 and C-5 on the properties of glycofuranosyl halides, three pentofuranosyl chlorides with a common, nonparticipating group at C-2 were studied. The first of these halides was the previously known 2,3,5-tri-O-benzyl-α-D-arabinofuranosyl chloride (I); in the course of the present work its anomeric configuration was confirmed through its nuclear magnetic resonance spectrum. The synthesis of the second and third halides, 2,3-di-O-benzyl-5-O-p-nitrobenzoyl-α-D-arabinofuranosyl chloride (VII) and 2-O-benzyl-3,5-di-O-p-nitrobenzoyl-α-D-arabinofuranosyl chloride (XIV), is described. The rates of methanolysis of these three halides, as well as the proportions of anomeric methyl glycosides formed from each of them were determined. Replacement of the benzyl group at C-5 in I by a p-nitrobenzoyl group (as in VII) decreases the rate of methanolysis; replacement of the benzyl groups at both C-3 and C-5 by p-nitrobenzoyl groups further decreases the rate of methanolysis. Thus, it appears that acyl groups more distant than C-2 exert an influence on the reactivity of glycofuranosyl halides. The relative magnitudes of the effects observed suggest that the influence of the acyl groups is exerted through the oxygen of the furanose ring.

The behavior of fully acylated aldosyl halides depends so greatly upon the nature of the acyl group at C-2 and upon the steric relationship of this group to the halogen at C-1 that very little is known about the influence of acyl groups further removed from the halogen. Owing to the limitations which fully acylated glycosyl halides present for certain synthetic purposes, we have recently studied a variety of glycofuranosyl halides, both fully blocked with nonparticipating groups (2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl chloride (I)[1]) and fully blocked but with a single nonparticipating group at C-2 (the 2-*O*-nitro-3,5-di-*O*-*p*-nitrobenzoyl-D-arabinofuranosyl halides[2,3]). The obvious diversity of reactivities among these halides has led us now to investigate the influence of acyl groups at C-3 and C-5 on the solvolysis of three glycofuranosyl halides which have the same nonparticipating substituent at C-2. The specific substances chosen were 2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl chloride (I), 2,3-di-*O*-benzyl-5-*O*-*p*-nitrobenzoyl-α-D-arabinofuranosyl chloride (VII), and 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-α-D-arabinofuranosyl chloride (XIV). The preparation of these substrates will be discussed first.

Synthesis of Substrates

2,3,5-Tri-*O*-benzyl-D-arabinofuranosyl chloride has been made through the action of hydrogen chloride on 2,3,5-tri-*O*-benzyl-D-arabinose[4] in the presence of an insoluble desiccant[1] and also by treating 2,3,5-tri-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-D-arabinofuranose, dissolved in dichloromethane, with hydrogen chloride, the relatively insoluble *p*-nitrobenzoic acid formed being removed by filtration.[1] For reasons which can only be the subject of conjecture at this time, the proportions of the anomeric forms of the halide vary according to the preparative method used. Optical rotatory power and solvolysis studies earlier indicated[1] that the second route produces nearly pure 2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl chloride (I) while the first procedure gives a mixture containing a minor but appreciable proportion of the β-halide.[5] For the purposes of the present research, the halide was prepared by the second procedure and examined by nuclear magnetic resonance spectroscopy which showed that the sirup was essentially a single substance. A singlet at τ 3.85 was assigned to H_1 confirming the earlier assumption that the halide is indeed the α-anomer (I).[6]

The synthesis of 2,3-di-*O*-benzyl-5-*O*-*p*-nitrobenzoyl-α-D-arabinofuranosyl chloride was carried out in the following fashion. Methyl α-D-arabinofuranoside (XIIIa) was selectively tritylated to give methyl 5-*O*-trityl-α-D-arabinofuranoside (II) which, in turn, was converted to the dibenzyl ether III. Mild acid hydrolysis removed the trityl group[7] and C-5 was then *p*-nitrobenzoylated to give methyl 2,3-di-*O*-benzyl-5-*O*-*p*-nitrobenzoyl-α-D-arabinofuranoside (V). The

(1) C. P. J. Glaudemans and H. G. Fletcher, Jr., *J. Org. Chem.*, **28**, 3004 (1963).

(2) C. P. J. Glaudemans and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **87**, 2456 (1965).

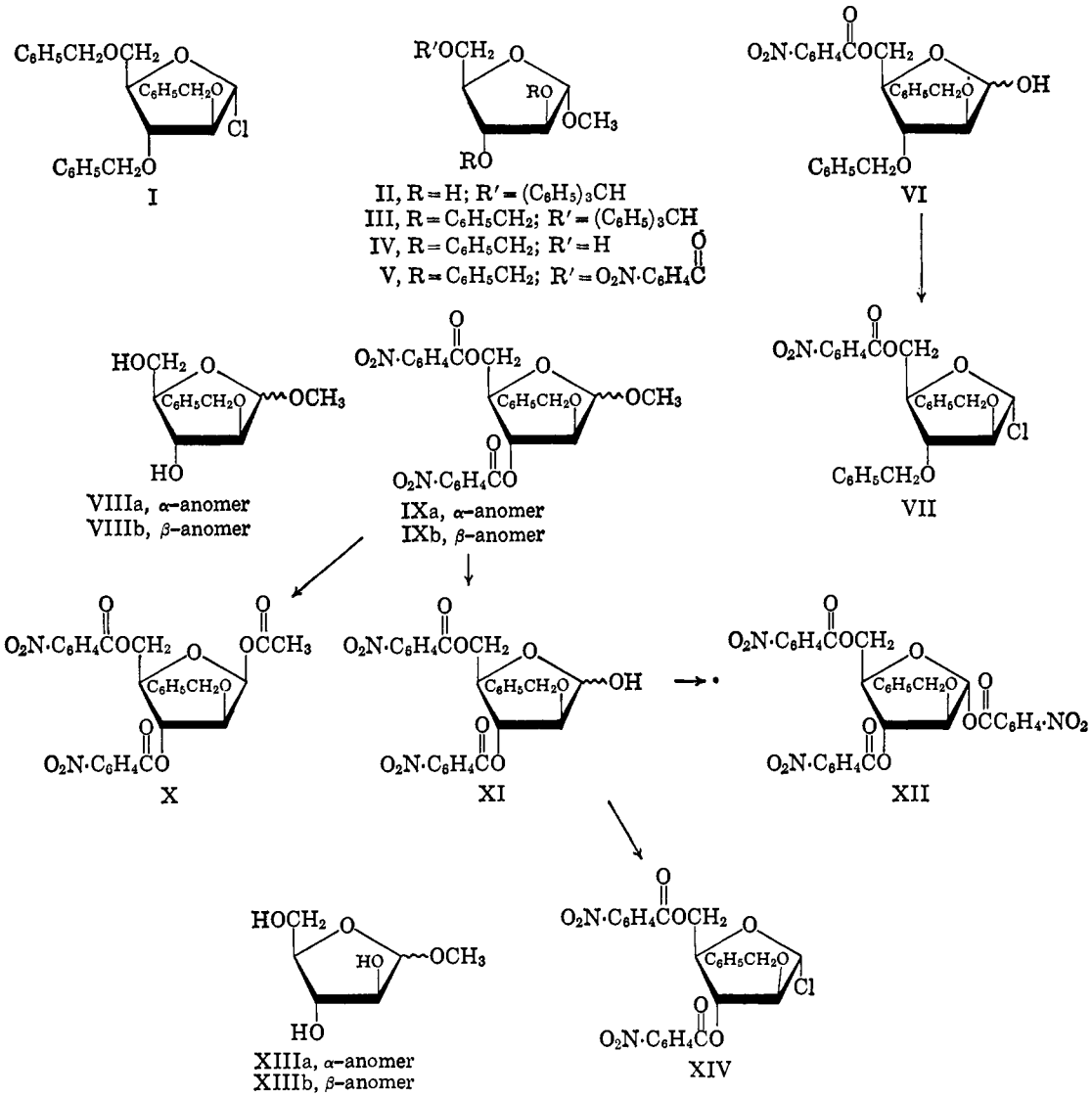
(3) C. P. J. Glaudemans and H. G. Fletcher, Jr., *J. Org. Chem.*, **29**, 3286 (1964).

(4) R. Barker and H. G. Fletcher, Jr., *ibid.*, **26**, 4605 (1961); *cf.* S. Tejima and H. G. Fletcher, Jr., *ibid.*, **28**, 2999 (1963).

(5) It is interesting to note a related example observed by P. W. Austin, F. E. Hardy, J. G. Buchanan, and J. Baddiley, *J. Chem. Soc.*, 2128 (1964). These authors found that treatment of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose with thionyl chloride gave 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl chloride which was rich in the α-anomer while hydrogen chloride in dioxane converted 1-*O*-acetyl-2,3,4,6-tetra-*O*-benzyl-D-glucopyranose to what appeared to be an equal mixture of the two anomeric chlorides.

(6) On theoretical grounds, $J_{1,2} \approx 0$ in the substituted furanoses corresponds to a projected angle for $H_{1,2}$ of 80–100°. Inspection of the n.m.r. spectra of a variety of known pentofuranose derivatives shows that H_1 normally gives a singlet in *trans* derivatives and a doublet of $J_{1,2} \approx 4.5$ c.p.s. in *cis* derivatives.

(7) To confirm the fact that ring expansion had not occurred under these conditions IV was retritylated to give III.



aglycon was removed from V and the resulting 2,3-di-*O*-benzyl-5-*O*-*p*-nitrobenzoyl-D-arabinofuranose (VI) was converted to 2,3-di-*O*-benzyl-5-*O*-*p*-nitrobenzoyl-D-arabinofuranosyl chloride through the action of hydrogen chloride in dichloromethane, magnesium sulfate being used to remove the water liberated. Like I, 2,3-di-*O*-benzyl-5-*O*-*p*-nitrobenzoyl-D-arabinofuranosyl chloride was amorphous; a sharp singlet at τ 3.77 showed the halide to be the α-anomer (VII).

In order to prepare the third halide, 2-*O*-benzyl-D-arabinose[8] was converted to a mixture of the anomeric methyl 2-*O*-benzyl-D-arabinofuranosides (VIIIa and VIIIb) from which the β-anomer (VIIIb) was isolated in crystalline form and acylated to give methyl 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-β-D-arabinofuranoside (IXb). An attempt was made to prepare the desired halide directly from IXb through the action of hydrogen chloride in glacial acetic acid. This did not prove satisfactory although condensation of the amorphous product with silver acetate afforded in low yield a levorotatory, crystalline acetate, presumably 1-*O*-acetyl-2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-β-D-arabinofuranose (X), suggesting that some halide had been formed.

(8) J. C. P. Schwartz and M. MacDougall, *J. Chem. Soc.*, 3065 (1956).

Hydrolysis of IXb (as well as of the amorphous anomer IXa) readily gave crystalline 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-D-arabinofuranose (XI); with hydrogen chloride in dichloromethane solution and magnesium sulfate, XI afforded a crystalline chloride. The dextrorotation of this substance and a singlet at τ 3.67 indicated it to be the α-anomer XIV.

Solvolysis Studies

The methanolysis of the three arabinofuranosyl halides (I, VII, and XIV) was carried out in dichloromethane solution with approximately 100-fold molar excess of methanol. The progress of the solvolysis was

Table I. Solvolysis of α-D-Arabinofuranosyl Chlorides

Substrate	ln k, min.$^{-1}$	$t_{1/2}$, min.	XIIIa/XIIIb
I	8.8×10^{-2}	7.9	8/92
VII	11×10^{-3}	63	10/90
XIV	8.3×10^{-4}	840	2/98

followed polarimetrically at 20° and the data thus obtained were used to calculate the pseudo-first-order rate constants (Table I). In order to ascertain the

steric outcome of the solvolyses, recourse was had to gas–liquid partition chromatography (g.l.p.c.). The mixture of anomeric methyl 2,3,5-tri-*O*-benzyl-D-arabinofuranosides from the methanolysis of I was suitable for direct chromatographic analysis. Successive alkaline saponification and hydrogenolysis converted the methanolysis product from VII to a mixture of the anomeric methyl D-arabinofuranosides (XIIIa and XIIIb); analysis of this mixture as its trimethylsilyl ether was carried out as described earlier.[2] The mixture obtained from the solvolysis of XIV was saponified and then trimethylsilylated, the proportions of the two anomeric methyl 2-*O*-benzyl-3,5-di-*O*-(trimethylsilyl)-D-arabinofuranosides being determined by g.l.p.c. The proportions of anomeric glycosides formed in each of the three solvolyses are shown in Table I.

Discussion

As may be seen from Table I, the fully benzylated glycosyl halide (I) is the most reactive. Replacement of a benzyl group at C-5 by a *p*-nitrobenzoyl group (as in VII) decreases the rate of solvolysis by a factor of 8; replacement of the benzyl groups at C-3 and C-5 by *p*-nitrobenzoyl groups decreases the rate by a factor of 106. It thus seems that electronegative masking groups at positions other than C-2 in acylated glycofuranosyl halides exercise a stabilizing influence on the carbon–halogen bond, a fact which may prove to have considerable utility in synthetic work. While the present study did not include an attempt to prepare and study the as yet unknown 2,5-di-*O*-benzyl-3-*O*-*p*-nitrobenzoyl-α-D-arabinofuranosyl chloride, the relationships among the solvolysis rates found suggest that the stabilizing influence on the *p*-nitrobenzoyl group is effective at both C-3 and C-5; *i.e.*, the rate of solvolysis of XIV is slower than that of VII. Since acyl groups at C-3 and C-5 are separated from C-1 by the same number and type of atoms only *via* the ring oxygen, we propose that the stabilization of the C-1–halogen bond is largely accomplished by transmission of the electron-withdrawing capacity of the acyl groups through the ring oxygen.

Let us now turn to a consideration of mechanistic and stereochemical aspects of these solvolyses. In an earlier investigation[2] we showed that the solvolysis of D-arabinofuranosyl halides having an *O*-nitro group at C-2 involves an SN1 mechanism and that, irrespective of the anomeric configuration of the halide, the β-glycoside predominated in the products. Inspection of Table I clearly shows that the three halides here investigated behave in a similar manner, giving in each case mixtures in which the α-glycoside is but a minor component. The data on anomeric proportions also throw some light upon the matter of participation by acyl groups at C-3 and C-5 in pentofuranosyl halides. Had the *p*-nitrobenzoyl group at C-5 in VII participated in the solvolysis, the proportion of α-glycoside formed would have been increased over that found with I; in fact, the anomeric proportions from I and VII are virtually identical. This is in accord with our previous finding[2] that the C-5 acyl group does not participate in methanolysis of this type.

The *p*-nitrobenzoyl group at C-3 in XIV is, of course, *cis* to the chloride and cannot, therefore, provide direct anchimeric assistance in the displacement. However, after loss of the chlorine by an SN1 mechanism, the carbonium ion formed at C-1 might, conceivably, be attacked by the acyl group at C-3. Ultimately, the steric effect of such participation would result in the formation of a β-glycoside. In fact, the proportion of β-glycoside formed from XIV is somewhat greater than that formed from the other two halides. However, it remains to be seen whether this comparatively slight difference is of real significance.[9] In any event, it should be recalled that the electron-attracting ability of the *p*-nitrophenyl group makes the *p*-nitrobenzoyl group comparatively inefficient as a participator in displacements.[2]

Experimental Section[10]

2,3,5-Tri-O-benzyl-α-D-arabinofuranosyl Chloride (I). This halide was prepared from an anomeric mixture of the 2,3,5-tri-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-D-arabinofuranoses as described in an earlier paper.[1] The clear, colorless sirup had $[\alpha]^{20}D$ +90.4° (*c* 1.1, CH_2Cl_2); the signal for H_1 in its n.m.r. spectrum appeared as a singlet at τ 3.85 indicating the α-configuration. A signal of small amplitude at τ 3.15 was also noted; *p*-nitrobenzoic acid gives a signal at this location and, owing to its mode of preparation, the halide is almost certainly contaminated with a trace of this substance.

Methyl 5-O-Triphenylmethyl-α-D-arabinofuranoside (II). Crystalline methyl α-D-arabinofuranoside (4.99 g.), prepared from its tribenzoate[11] was dissolved in dry pyridine (100 ml.) and the solution was treated with trityl chloride (12.8 g., 1.5 molar equiv.). The reaction mixture was kept at room temperature for 4 days and then poured on ice and left at 0° overnight. The crude product thus precipitated was extracted with dichloromethane, the extract then being washed with water and dried over sodium sulfate. Concentration *in vacuo* gave a sirup from which toluene was distilled in order to remove residual pyridine. The residue was dissolved in ethyl acetate–cyclohexane (1:2 v./v.) and adsorbed on a column (6 × 15 cm.) of silica gel and eluted, initially, with the same solvent mixture. The first two components to emerge from the column were triphenylcarbinol and a trityl derivative (presumably a methyl di-*O*-trityl-α-D-arabinofuranoside) which was not further investigated. Elution with ethyl acetate then removed a third component which was chromatographically pure (t.l.c., ethyl acetate–cyclohexane, 1:2) which crystallized spontaneously on removal of the solvent: 9.4 g. 76%. Recrystallization from ethyl acetate–cyclohexane (1:4 v./v.) at −5° gave pure methyl 5-*O*-triphenylmethyl-α-D-arabinofuranoside, 8.4 g., m.p. 112–113°, $[\alpha]^{20}D$ +62.4° (*c* 1.56, ethyl acetate).

(9) We know of only one reaction of a pentofuranosyl halide which seems to indicate the participation of an acyl group at C-3. See ref. 2, footnote 16.

(10) Melting points are corrected. Thin layer chromatography was conducted on standard microscope slides, using silica gel G (E. Merck A.-G., Darmstadt), the components being detected by heating at 100° after spraying with 10% sulfuric acid. Unless otherwise specified, column chromatography was carried out using silica gel, 0.05–0.20 mm. (E. Merck A.-G., Darmstadt). Nuclear magnetic resonance spectra were obtained in $CDCl_3$ using a Varian A-60 spectrometer. Rate constants were determined by polarimetry, *k* being equal to $1/t \ln (\alpha_0 - \alpha_\infty)/(\alpha_t - \alpha_\infty)$.

(11) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **80**, 2007 (1958); R. S. Wright and H. G. Khorana, *ibid.*, **80**, 1994 (1958).

Anal. Calcd. for $C_{25}H_{26}O_5$ (406.47): C, 73.87; H, 6.45. Found: C, 73.90; H, 6.62.

Methyl 2,3-Di-O-benzyl-5-O-triphenylmethyl-α-D-arabinofuranoside (III). The trityl ether II (8.3 g.) was dissolved in dry dioxane (100 ml.), powdered potassium hydroxide[12] (40 g.) was added, and the suspension was boiled under reflux while benzyl chloride (50 ml.) was gradually added over the course of 75 min. Boiling was continued for 3.5 hr. and the solution was then cooled, diluted with water, and extracted with dichloromethane. The combined extracts were washed with water, dried over sodium sulfate, and concentrated *in vacuo*, finally at 110° (bath; 1 mm.) to remove benzyl alcohol. The crude product thus obtained was fully substituted as shown by its infrared absorption spectrum; on trituration with methanol, it crystallized fully. The product was dissolved in hot ethyl acetate (10 ml.), hot methanol (75 ml.) was added, and the solution was allowed to cool slowly to 0° to yield pure III, 8.65 g. (72%), m.p. 80–81°, $[\alpha]^{20}D$ +43° (*c* 2.1, CH_2Cl_2).

Anal. Calcd. for $C_{39}H_{38}O_5$ (586.73): C, 79.83; H, 6.53. Found: C, 79.72; H, 6.53.

Methyl 2,3-Di-O-benzyl-α-D-arabinofuranoside (IV). The fully substituted derivative III (8.0 g.) was dissolved in dioxane (50 ml.), and the solution, diluted with a mixture of water (10 ml.) and glacial acetic acid (40 ml.), was heated on a steam bath for 5.5 hr. It was then cooled and poured into ice–water containing sodium acetate. The crude product was extracted with dichloromethane, the extracts were dried with sodium sulfate, and the solution was concentrated to a sirup. The latter was dissolved in ethyl acetate–cyclohexane (1:3) and added to a column (5 × 20 cm.) of silica gel. Elution with ethyl acetate–cyclohexane (1:3 v./v.) removed triphenylcarbinol; subsequent elution with ethyl acetate gave the desired product as a sirup (4.13 g., 88%). Of this sirup, 100 mg. was retritylated in conventional fashion to yield 90 mg. (53%) of III; after recrystallization from ethyl acetate–methanol, the pure material (70 mg.) melted at 80–81° either alone or on admixture with III prepared as described earlier.

Methyl 2,3-Di-O-benzyl-5-O-p-nitrobenzoyl-α-D-arabinofuranoside (V). The remainder of IV (4.0 g.) was dissolved in dry pyridine (50 ml.) and the solution was cooled in an ice bath. *p*-Nitrobenzoyl chloride (2.60 g., recrystallized from carbon tetrachloride) was added slowly and the reaction mixture was stirred at room temperature overnight. Purified in conventional fashion, the ester (5.73 g., 100%) was obtained as a sirup which was chromatographically homogeneous (t.l.c., ethyl acetate–cyclohexane, 1:3, v./v.), $[\alpha]^{20}D$ +63.6° (*c* 1.6, CH_2Cl_2). Its infrared absorption spectrum showed a sharp peak at 1720 cm.$^{-1}$ (>C=O), but no absorption for hydroxyl.

Anal. Calcd. for $C_{27}H_{27}NO_8$ (493.52): C, 65.71; H, 5.51; N, 2.84. Found: C, 65.93; H, 5.28; N, 2.93.

2,3-Di-O-benzyl-5-O-p-nitrobenzoyl-D-arabinofuranose (VI). The glycoside V (800 mg.) was heated on the steam bath with a mixture of glacial acetic acid (16 ml.) and 6 *N* hydrochloric acid (2.4 ml.) for 1 hr. and the dark solution was then poured on ice. The crude product was extracted with dichloromethane, and the combined extracts were washed with aqueous sodium bicarbonate, dried over sodium sulfate, and concentrated *in vacuo* to a sirup. Thin layer chromatography revealed (ethyl acetate–cyclohexane, 1:3, v./v.) the presence of at least nine components. The sirup was adsorbed on a column (4 × 40 cm.) of silica gel and eluted with ethyl acetate–cyclohexane (1:3, v./v.), 15-ml. fractions being collected. Fractions 40 to 55, containing a single component, were pooled and concentrated to a sirup (320 mg.) which crystallized when triturated with ether. Recrystallization from ether–cyclohexane yielded 175 mg. (23%) of pure 2,3-di-*O*-benzyl-5-*O*-*p*-nitrobenzoyl-D-arabinofuranose, m.p. 92–93°, $[\alpha]^{20}D$ +30° (*c* 1.2, CH_2Cl_2). The infrared absorption of the substance contained a sharp hydroxyl peak and the n.m.r. spectrum showed a doublet of intensity 1 (J = *ca.* 7 c.p.s.) centered around τ 4.5.

Anal. Calcd. for $C_{26}H_{25}NO_8$ (479.50): C, 65.13; H, 5.26; N, 2.92. Found: C, 65.19; H, 5.34; N, 2.93.

2,3-Di-O-benzyl-5-O-p-nitrobenzoyl-α-D-arabinofuranosyl Chloride (VII). Crystalline VI (50 mg.) was dissolved in *ca.* 8.6 ml. of dichloromethane which had previously been saturated with hydrogen chloride at room temperature and anhydrous magnesium sulfate (2 g.) was added. The rotation of the supernatant solution was observed in a 1-dm. polarimeter tube: $\alpha^{20}D$ +0.203 (17 min.) → +0.309° (301 min., no further change after 20 hr.). After filtration, the solution was concentrated *in vacuo* to a sirup from which a fresh portion of dichloromethane was evaporated. After drying *in vacuo* over sodium hydroxide for several hours, the halide was obtained as a stiff sirup. Attempts to crystallize the substance were without success, $[\alpha]^{20}D$ +74.9° (*c* 1.3, CH_2Cl_2). The infrared absorption spectrum of the halide showed no hydroxyl peak and, likewise, the n.m.r. spectrum lacked the doublet at τ 4.5 characteristic of VI. A sharp singlet at τ 3.77 showed the substance to be the α-anomer VII. A singlet at τ 1.8 with an intensity of one could not be allocated with certainty.

Methyl 2-O-Benzyl-β-D-arabinofuranoside (VIIIb). 2-*O*-Benzyl-D-arabinose[8] (7.5 g.) was dissolved in 200 ml. of methanol containing 1 ml. of sulfuric acid and the solution was left at room temperature. After 24 hr., thin layer chromatography, using ethyl acetate, showed that only a small amount of starting material was present. The solution was kept at +5° overnight, neutralized with Amberlite IR-45, and concentrated to a sirup (7.3 g.). In order to remove starting material and any methyl 2-*O*-benzyl-D-arabinopyranoside, the crude product was dissolved in 150 ml. of water containing 3.8 g. of sodium metaperiodate. After 1 hr., the solution was neutralized with sodium bicarbonate and then diluted with 250 ml. of ethanol, the precipitate formed being removed by filtration. Concentration of the filtrate gave a sirup which was extracted with hot ethyl acetate; concentration of the extract afforded a sirup (6.6 g.) which crystallized in part. A portion (1.13 g.) of the crude product was washed with ether and then recrystallized from ether–ethyl acetate to yield 400 mg. of methyl 2-*O*-benzyl-β-D-arabinofuranoside as flat needles, m.p. 102–104°, $[\alpha]^{20}D$ −90° (ethanol). The addition of more ether to the mother liquor gave a

(12) Hooker Chemical Corp., Niagara Falls, N. Y.

second crop (425 mg., m.p. 101–103°, $[\alpha]^{20}D$ −90° in ethanol), making the total yield equivalent to 60%. On recrystallization from the same solvent mixture, the pure product had m.p. 103–105° and $[\alpha]^{20}D$ −89° in alcohol (*c* 1.6).

Anal. Calcd. for $C_{13}H_{18}O_5$ (254.28): C, 61.40; H, 7.14. Found: C, 61.66; H, 7.22.

Methyl 2-O-Benzyl-3,5-di-O-p-nitrobenzoyl-β-D-arabinofuranoside (IXb). Methyl 2-*O*-benzyl-β-D-arabinofuranoside (200 mg.) was *p*-nitrobenzoylated in conventional fashion to yield, from ethyl acetate–ethanol, 280 mg. (64%) of methyl 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-β-D-arabinofuranoside, m.p. 147–148°, $[\alpha]^{20}D$ −65° (*c* 1.9, CH_2Cl_2).

The ester was also obtained by *p*-nitrobenzoylation of the anomeric mixture of methyl 2-*O*-benzyl-D-arabinofuranosides, prepared as described earlier, yield 30%.

Anal. Calcd. for $C_{27}H_{24}N_2O_{11}$ (552.51): C, 58.70; H, 4.38; N, 5.07. Found: C, 58.75; H, 4.22; N, 5.23.

N.m.r. showed a doublet ($J_{1,2} \approx 4$ c.p.s.) centered at τ 5.17.

1-O-Acetyl-2-O-benzyl-3,5-di-O-p-nitrobenzoyl-β-D-arabinofuranose (X). Methyl 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-β-D-arabinofuranoside (0.5 g.) was dissolved in 10 ml. of glacial acetic acid and the solution was saturated with hydrogen chloride. The optical rotation of the solution was observed in a 2-dm. tube, $\alpha^{20}D$ −1.594° (27 min.) → +4.978° (322 min.). Dichloromethane was then added and the solution was successively washed with ice–water and cold, aqueous sodium bicarbonate solution. Moisture was removed with sodium sulfate, the solution was concentrated to a sirup (489 mg.), and the latter was dissolved in 10 ml. of dry benzene. Silver acetate (1.0 g.) was added and the solution stirred in the dark for 2 days. Filtration and evaporation of the solution yielded a sirup which crystallized from dichloromethane–ether–pentane, 118 mg. (22%). Recrystallized twice from the same solvent mixture, the pure product showed m.p. 125–126° and $[\alpha]^{20}D$ −50° (*c* 0.3, CH_2Cl_2).

Anal. Calcd. for $C_{28}H_{24}N_2O_{12}$ (580.52): C, 57.93; H, 4.17; N, 4.83. Found: C, 57.79; H, 4.00; N, 5.11.

2-O-Benzyl-3,5-di-O-p-nitrobenzoyl-D-arabinofuranose (XI). Methyl 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-β-D-arabinofuranoside (500 mg.) was dissolved in 10 ml. of glacial acetic acid and the solution, diluted with 1.5 ml. of 6 *N* hydrochloric acid, was heated on a steam bath for 1.5 hr. It was then poured into ice–water and the mixture was allowed to stand for 5 hr. The precipitated sirup was extracted with dichloromethane, and the solution, after washing with aqueous sodium bicarbonate, was dried with sodium sulfate and filtered through Darco X. Concentration yielded a sirup which was dissolved in 2.1 ml. of 2:5 dichloromethane–ether. The crystals thus obtained (245 mg., 50%) were recrystallized from dichloromethane–ether–pentane to constant rotation, 130 mg., m.p. 125–130°, $[\alpha]^{20}D$ +14° (10 min.) → +19° (23 hr., constant) (*c* 1.0, dioxane–water, 9:1). The infrared spectrum of the substance showed a well-defined hydroxyl band.

Anal. Calcd. for $C_{26}H_{22}N_2O_{11}$ (538.48): C, 58.00; H, 4.12; N, 5.20. Found: C, 58.18; H, 4.05; N, 5.02.

The mother liquor from the crystallization of methyl 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-β-D-arabinoside presumably contained the α-anomer of that substance; after concentration to a sirup, it was hydrolyzed as described above, 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-β-D-arabinofuranose being obtained in 38% yield.

2-O-Benzyl-1,3,5-tri-O-p-nitrobenzoyl-α-D-arabinofuranose (XII). A solution of 1.20 g. of 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-β-D-arabinofuranose in 5 ml. of dichloromethane was treated with a solution of 0.5 g. of *p*-nitrobenzoyl chloride in a mixture of 3 ml. of dichloromethane and 1 ml. of pyridine and kept at room temperature for 1 day. Worked up in the usual manner, the product crystallized from dichloromethane–ether (1:2), 1.495 g. (98%). Recrystallization from 15 ml. of dichloromethane–ether (1:1) afforded 837 mg. of compact crystals, m.p. 149–152°, which were adsorbed on a column (1.6 × 18 cm.) of silicic acid (Mallinckrodt, 100 mesh) and eluted with dichloromethane–ether (1:1). Recrystallization of the first fraction to be eluted yielded pure 2-*O*-benzyl-1,3,5-tri-*O*-*p*-nitrobenzoyl-α-D-arabinofuranose, 680 mg., m.p. 151–152°, $[\alpha]^{20}D$ +54° (*c* 0.86, CH_2Cl_2). The n.m.r. showed a singlet at τ 3.24, assigned to H_1.

Anal. Calcd. for $C_{33}H_{25}N_3O_{14}$ (687.58): C, 57.64; H, 3.66; N, 6.11. Found: C, 57.99; H, 3.60; N, 5.84.

The addition of cyclohexane to the mother liquor from the first crystallization of the α-anomer above gave 525 mg. of fine needles, m.p. 138–180°. Chromatography of this substance on silicic acid afforded material of m.p. 139–151° and $[\alpha]^{20}D$ +24.8° (*c* 1, CH_2Cl_2). However, although the material then yielded analytical values corresponding closely to an *O*-benzyl-tri-*O*-*p*-nitrobenzoylpentose, thin-layer chromatography showed the substance to contain two components; it probably represented an anomeric mixture.

2-O-Benzyl-3,5-di-O-p-nitrobenzoyl-α-D-arabinofuranosyl Chloride (XIV). 2-*O*-Benzyl-3,5-di-*O*-*p*-nitrobenzoyl-D-arabinofuranose (500 mg.) was dissolved in 35 ml. of dichloromethane saturated with hydrogen chloride, and 5 g. of magnesium sulfate was added to the solution. After 1.5 hr. at room temperature, the reaction mixture was filtered and concentrated to a sirup which was then dissolved in a mixture of dichloromethane and ether. The crystals (320 mg., 62%) which formed had $[\alpha]^{20}D$ +71° (*c* 2.04, CH_2Cl_2); recrystallization failed to change this value. The melting point of the halide (75–85°) remained indefinite and the n.m.r. spectrum of the substance showed it to contain ether although a singlet at τ 3.67 indicated that it was the α-anomer.

After being powdered and dried at 50° *in vacuo*, the halide had m.p. 113–115° (sintering at 55°, followed by recrystallization) and $[\alpha]^{20}D$ +73.1° (*c* 2.1, CH_2Cl_2).

Anal. Calcd. for $C_{26}H_{21}ClN_2O_{10}$ (556.93): C, 56.07; H, 3.80; Cl, 6.37; N, 5.03. Found: C, 55.99; H, 4.06; Cl, 6.06; N, 5.17.

Methanolysis of 2,3,5-Tri-O-benzyl-α-D-arabinofuranosyl Chloride (I). 2,3,5-Tri-*O*-benzyl-α-D-arabinofuranosyl chloride (56.3 mg., 0.128 mmole) was dissolved in dichloromethane to a volume of 5.00 ml. and the solution was drained into a 2-dm., all-glass polarimeter tube. Methanol (0.50 ml., 12.35 mmoles) was added and the optical rotation of the solution was observed at 20°. After 91 min., the observed rotation

had become constant (−0.905°) and did not change thereafter during the succeeding 19 hr. The first-order rate constant, calculated from the observed data, was ln 8.8 × 10^{-2} min.$^{-1}$. At the completion of the reaction the solution was washed with aqueous sodium bicarbonate, and dried over sodium sulfate. A sample of the solution was applied directly to a column (0.25 in. × 6 ft.) of 1% SE 30 on Gaschrom P (Silanized)[13] at 250° (flame-ionization detector). The two anomeric methyl 2,3,5-tri-*O*-benzyl-D-arabinofuranosides were well resolved and, from the area under the peaks, the mixture was estimated to consist of 92% of the β-anomer and 8% of the α-anomer.

Methanolysis of 2,3-Di-O-benzyl-5-O-p-nitrobenzoyl-α-D-arabinofuranosyl Chloride (VII). The halide VII (62.2 mg., 0.125 mmole) was dissolved in dichloromethane to a volume of 5.0 ml. and the solution was then diluted with methanol (0.50 ml.). The progress of the resulting solvolysis was followed polarimetrically at 20°. The first-order rate constant, calculated from the observed data, was ln 11 × 10^{-3} min.$^{-1}$. When mutarotation had ceased, 1 ml. of 1 *N* sodium methoxide was added and the solution left for 6 days. The solution was then filtered and concentrated to a sirup which was dissolved in 80% aqueous methanol (v./v.) and deionized with Amberlite MB-1. Filtration and concentration yielded a product contaminated with methyl *p*-nitrobenzoate. In order to remove this, the mixture was dissolved in dioxane and the resulting solution, diluted with 2 ml. of 1 *N* sodium hydroxide, heated on a steam bath for 2 hr. After concentration and evaporation, the mixture was dissolved in 80% aqueous methanol and the solution deionized with Amberlite MB-1. Filtration and concentration then gave a mixture of the anomeric methyl 2,3-di-*O*-benzyl-D-arabinofuranosides. The benzyl groups were removed by hydrogenolysis over freshly prepared and well-washed palladium black suspended in methanol. After filtration and concentration the sirupy mixture was dried *in vacuo* for 2 days. Conversion to the trimethylsilyl derivatives was carried out as described by Sweeley, *et al.*,[14] and vapor phase chromatography was performed on a column (0.25 in × 5 ft.) of 3% SE 52 on Gaschrom A.[13] The mixture was found to consist of 10% of the α-anomer and 90% of the β-anomer. Both authentic methyl α- and β-arabinopyranoside separate completely from authentic methyl β-D-arabinofuranoside when run as their tri-*O*-trimethylsilyl derivatives under these conditions.

Methanolysis of 2-O-Benzyl-3,5-di-O-p-nitrobenzoyl-α-D-arabinofuranosyl Chloride (XIV). 2-*O*-Benzyl-3,5-di-*O*-*p*-nitrobenzoyl-α-D-arabinofuranosyl chloride (70.8 mg., 0.127 mmole) was methanolyzed as described for VII above, the rotation becoming constant at a value of −2.365° after 99 hr., k = ln 8.3 × 10^{-4} min.$^{-1}$. Sodium methoxide in methanol (1 *N*, 2 ml.) was added to the solution and, after 24 hr., the solution was concentrated. Water was added, the methyl *p*-nitrobenzoate was removed by filtration, and the filtrate was deionized with Amberlite MB-1. Concentration of the solution gave a crystalline residue which was dried *in vacuo* and converted to its trimethylsilyl ether. Vapor phase chromatography, using a column (0.25 in. × 6 ft.) of 3% SE 52 on Gaschrom A[13] and programming the temperature from 50 to 230°, revealed two peaks which were identified through the use of authentic samples of the bis-*O*-trimethylsilyl ethers of the two anomeric methyl 2-*O*-benzyl-D-arabinofuranosides. The peak areas of the signals indicated that the mixture contained 2% of the α-anomer and 98% of the β-anomer.

Acknowledgment. We are indebted to Dr. J. D. Stevens for his interpretation of the n.m.r. spectrum of IXb and to the Section on Analytical Services and Instrumentation for spectra and elemental analyses.

(13) Applied Science Laboratories, Inc., State College, Pa.

(14) C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).

Communications to the Editor

A Paramagnetic Octahedral Rhodium(III) Complex

Sir:

Although paramagnetic octahedral complexes of rhodium(III) have been neither known nor anticipated,[1] we wish to report the synthesis and certain properties of a complex that apparently involves retention of the 3+ oxidation state and (distorted) octahedral symmetry.

During study of the deprotonation of diamagnetic tris(ethylenediamine)rhodium(III) iodide[2] by reaction with potassium amide in liquid ammonia at −33.5° by methods described earlier,[3] stepwise deprotonation of $[Rh(en)_3]I_3$ led to the isolation and characterization of *diamagnetic* $[Rh(en\text{-}H)(en)_2]I_2$, $[Rh(en\text{-}H)_2(en)]I$, and $[Rh(en\text{-}H)_3]$, where (en-H) denotes an ethylenediamine (en) ligand from which one proton has been removed. Efforts to effect further deprotonation at −33.5° resulted in incomplete reaction; however, completion of the next deprotonation step was achieved by the use of excess potassium amide at 25°, as follows.

A solution and suspension of 1.0489 g. of $[Rh(en)_3]I_3$

(1) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1962, p. 840.

(2) G. W. Watt and J. K. Crum, forthcoming publication.

(3) G. W. Watt, L. E. Sharif, and E. P. Helvenston, *Inorg. Chem.*, **1**, 6 (1962).