Carbohydrate Research, 41 (1975) 63–76

THE REACTION OF PHOSPHORUS PENTACHLORIDE WITH AMIDES, IN PARTICULAR 2-ACETAMIDO-2-DEOXYALDOHEXOPYRANOSES

ANTHONY M DEMPSEY AND LESLIE HOUGH

Department of Chemistry, Queen Elizabeth College (University of London), Campden Hill Road, London W8 7AH (Great Britain)

(Received August 20th, 1974, accepted for publication, October 16th, 1974)

ABSTRACT

2-Acetamido-2-deoxyaldohexopyranose polyacetates are transformed by the action of phosphorus pentachloride into 2-tetrachloroethylideneamino derivatives, the *trans*-2-acetamido-1-acetate system reacting more rapidly than the *cis* A 1-acetamido-pyranosyl polyacetate afforded the 1-tetrachloroethylideneamino derivative and 2-*O*-trichloroacetyl-β-D-glucopyranosyl chloride The latter was also observed, amongst other products, from the reaction of β-D-glucopyranosyl azide tetra-acetate with phosphorus pentachloride. Similar reactions on acetamidocyclohexane and its 2-acetoxy derivative afforded dichloroacetamido, trichloroacetamido, and tetrachloroethylideneamino derivatives Likewise, 1-acetamido-2-acetoxyethane gave the 1-dichloroacetamido derivative

INTRODUCTION

In 1921, Brigl[1] treated penta-*O*-acetyl-β-D-glucopyranose (**1**) with phosphorus pentachloride at 95° and obtained 3,4,6-tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glucopyranosyl chloride[2] (**2**) Other studies[3–9] extended this reaction to similar acetate derivatives, which also yielded the corresponding 1-chloro-2-trichloroacetyl β-D anomers

It was, therefore, envisaged that treatment of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose (**3**) with phosphorus pentachloride might yield the 2-trichloroacetamido derivative (**4**)

RESULTS AND DISCUSSION

Phosphorus pentachloride reacted with the tetra-acetate **3** to give a crystalline product in 60% yield ($C_{16}H_{19}Cl_4NO_9$) It gave no precipitate with silver nitrate solution and therefore did not contain a chlorine atom on C-1 Hydrogenation gave 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride, and treatment with 4M hydrochloric acid at 100° produced 2-amino-2-deoxy-D-glucose hydrochloride Hence the configuration of the molecule had not changed and C-1 had

retained its acetate group The i r. spectrum showed no NH-stretch at 3270, no amide II band at 1560, and no trichloroacetamido carbonyl-stretch at 1710 cm^{-1} The presence of chlorine was indicated by bands at 750 and 780 cm^{-1}, and an N=C grouping was indicated by the peak at 1675 cm^{-1} The ^{1}H-n m r spectrum (Table I) showed four acetate-methyl signals, but the acetamido-methyl signal of the starting material and the NH doublet were both absent

TABLE I

^{1}H-N M R PARAMETERS[a]

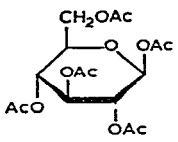
Compound	**5**	**6**	**7**	**10**	**12**	**18**
Solvent	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$
H-1	4 18d	4 28d	5 45d	3 8d	4 04d	4 70t
H-2	—	—	6 11s	—	5 62q	4 90t
H-3	4 62t	4 65q	4 70q	—	4 79q	4 98t
H-4	4 93t	4 94t	4 98t	—	4 62t	5 06t
H-5	—	6 18cm	6 31cm	—	6 15o	6 21o
H-6a	—	5 6–6 1cm	5 65–6 0cm	—	5 65q	5 72q
H-6b	—			—	5 99q	5 98q
OAc	7 95	7 94	7 96	7 92	7 96	7 95
	7 97	7 95		7 98	7 98	7 98
	8 00	7 97		8 00	8 00	8 00
	8 07	7 99			8 04	
OMe			6 56			
NH		2 77d	3 14	3 30	—	5 60
$J_{1\,2}$	8 0	8 8	8 1	—	1 5	9 0
$J_{2\,3}$	9 1	9 7	10 2	—	3 4	9 0
$J_{3\,4}$	9 1	9 7	9 7	—	9 5	7 0
$J_{4\,5}$	9 1	10 2	9 7	—	9 5	9 0
$J_{5,6a}$		5 0	5 0	—	5 0	4 2
$J_{5\,6b}$		2 0	2 5	—	2 5	2 0
$J_{6a\,6b}$	—	12 5	11 7	—	12 0	12 0
$J_{2\,N}$		11 0	8 8		—	—

[a]First-order chemical shifts (τ values) and coupling constants (Hz) at 100 MHz Key s, singlet, d, doublet, t, triplet, q, quartet, o, octet, cm, complex multiplet

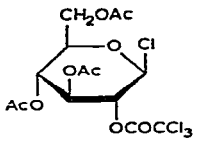
The large coupling-constants for the ring hydrogens confirmed the *β*-D-*gluco* configuration with the $^4C_1$ conformation The mass spectrum[10] indicated a molecular weight of 509 (Cl = 35) which, combined with the elemental analysis, gave a molecular formula of $C_{16}H_{19}Cl_4NO_9$ The compound was therefore 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-tetrachloroethylideneamino-*β*-D-glucopyranose (**5**) It is noteworthy that the ^{1}H-n m r. spectrum of **5** was very similar to that of 1,3,4,6-tetra-*O*-acetyl-2-anisylideneamino-2-deoxy-*β*-D-glucopyranose, which also contains a double-bonded nitrogen on C-2

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-trichloroacetamido-*β*-D-glucopyranose (**6**) was synthesised by reaction of trichloroacetyl chloride in pyridine on 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-*β*-D-glucopyranose hydrochloride This compound was

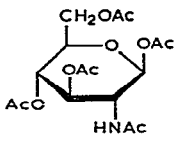
reported by Osawa[11] in 1960, and further preparations have been described by the authors[12] and by Wolfrom and Bhat[13] Proof of the structure was obtained from the ^{1}H-n m r. spectrum (Table I), which indicated the $^4C_1$ conformation Treatment of **6** with aluminium chloride gave starting material and not the required β-D chloride **4**, whereas treatment with phosphorus pentachloride gave a very complex mixture However, treatment of **6** with glacial acetic acid saturated with hydrogen bromide gave a syrupy bromide which, with methanol and active silver carbonate, afforded methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**7**), as confirmed by the ^{1}H-n m r. spectrum (Table I) G l c of the reaction mixture suggested the presence of ~4% of the α-D anomer **8**



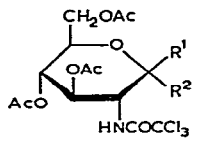
1



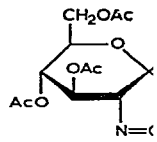
2



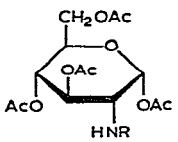
3



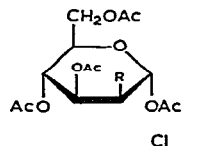
4 R^1 = Cl , R^2 = H
6 R^1 = OAc R^2 = H
7 R^1 = OMe R^2 = H
8 R^1 = H R^2 = OMe



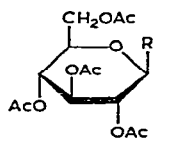
5 R^1 = OAc R^2 =
11 R^1 = H , R^2 = C



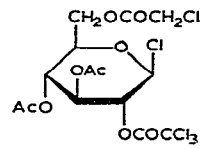
9 R = $COCH_3$
10 R = $COCCl_3$



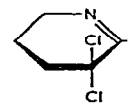
12 R = N=C(Cl)CCl_3
13 R = NHAc



14 R = N_3
16 R = NHAc
17 R = N=C(Cl)CCl_3
18 R = $NHCOCCl_3$



15



19

The reaction of hydrogen bromide in glacial acetic acid with the tetrachloroethylideneamino derivative **5** gave a syrupy product which, with methanol and active silver carbonate, yielded a mixture of the trichloroacetamido derivatives **6** and **7** Hence, the tetrachloroethylideneamino group of **5** had been hydrolysed to the trichloroacetamido group during the treatment with hydrogen bromide in acetic acid Von Braun and Haymans[14] observed the hydrolysis of the chloro-imine **19** to 3,3-dichloropiperid-2-one and finally to 5-amino-2,2-dichloropentanoic acid

The reaction of phosphorus pentachloride with 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose (**9**) gave a complex mixture containing two major products which were isolated crystalline, albeit in small yield, by column chromatography From the mass spectrum[10] of the faster moving derivative, the structure was deduced as 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-tetrachloroethylideneamino-α-D-glucopyranose (**11**). The ^{1}H-n m r. spectrum of the second derivative (Table I) showed an

NH resonance, but the methyl signal for the 2-acetamido group was absent, indicating substitution here, and the mass spectrum[10] showed it to be 1,3,4,6-tetra *O*-acetyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranose (**10**)

Repetition of the chlorination reaction on 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-mannopyranose (**13**) produced 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-tetrachloroethylideneamino-α-D-mannopyranose (**12**), as shown by the ^{1}H-n m r spectrum (Table I) which contained no NH resonance and only four acetate-methyl singlets The above reactions suggested that the tetrachloroethylideneamino derivatives (**5**, **11**, and **12**) are produced in higher yield from *trans*-2-acetamido-1-acetates of pyranoses (**3**, **13**) than from the *cis*-isomer (**9**)

Extension of the reaction of phosphorus pentachloride to 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**14**) produced a mixture of four chlorinated products which were separated by column chromatography The major product was the slowest moving compound, which was indistinguishable from 3,4,6-tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glucopyranosyl chloride (**2**) The next product was isolated in very small yield, its ^{1}H-n m r spectrum resembled that of the tetrachloro derivative **2**, but differed in that the methyl signal for the 6-acetate was absent and the centre of the resonances for H-6,6′ was shifted upfield from τ 5 85 to 6 45 This evidence suggested that further chlorination had occurred at position 6 (*e g* , **15**) The two fastest-moving compounds crystallised as a mixture Their ^{1}H-n m r spectra were similar to that of the tetrachloro derivative **2**, except that the resonances for H-6,6′ occurred as a doublet at τ 5 75 and the methyl signal for the 6-acetate group was absent Thus, the 6-acetate group seemed to have been attacked in the last three compounds, and this could be visualised by extending Lemieux's mechanism (see below) to include participation by the carbonyl group at C-6 with subsequent activation and chlorination

Reduction and acetylation of the azide **14** gave *N*-acetyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (**16**), and treatment of this derivative with phosphorus pentachloride gave a crystalline, but labile, product in 49% yield The i r. spectrum showed the absence of NH and acetamido-carbonyl groups, but contained a band at 1690 cm^{-1}, indicating an imine group Attempted purification by dissolution in dichloromethane and washing with water gave crystals of 2,3,4,6-tetra-*O*-acetyl-1-deoxy-1-trichloroacetamido-β-D-glucopyranose (**18**) The p m r. spectrum (Table I) showed a doublet at τ 5 60 assigned to NH, which, compared to that of the starting material (**16**), had moved downfield due to the influence of the chlorine atoms in the trichloroacetamido group Thus, the original product was 2,3,4,6-tetra-*O*-acetyl-*N*-tetrachloroethylidene-β-D-glucopyranosylamine (**17**) Repetition of the reaction, using a larger excess of phosphorus pentachloride, produced a complex mixture which was fractionated on a column of silica gel, giving crystalline 3,4,6-tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glucopyranosyl chloride (**2**) in 16% yield

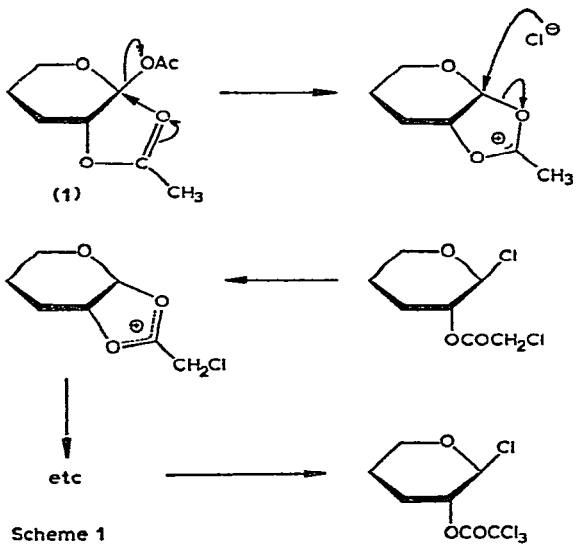
Brigl suggested[1] that the 2-*O*-trichloroacetyl-β-D-glucopyranosyl chloride (**2**) arose from the penta-acetate **1**, whereby the acetate group was eliminated from C-1, then chlorinated, and exchanged *via* an oxonium-ion intermediate However, this

mechanism did not explain the formation of the β-D chloride **2** Dauben and Vaughan[15] prepared 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl 1-[carboxy-^{14}C]-acetate, treated it with phosphorus pentachloride, and found no isotope incorporation into the product, thereby disproving this hypothesis. Hickinbottom[16] noted that there was no change in the optical rotation of solutions of the tetrachloro derivative **2** in benzene, acetonitrile, or acetone, whereas the corresponding 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl chloride mutarotated rapidly. Abramovitch[17] suggested that there were two processes involved, namely, replacement of the 1-acetoxy group followed by chlorination of the 2-acetoxyl group This mechanism was favoured due to the inductive (−I) effect of the new chlorine atom on C-1.

Lemieux *et al*[18–24] showed that the nature and stereochemistry of the substituents at C-2 are important in determining the mechanism of solvolysis and anomerisation of glycosyl halides, glycosyl acetates, and glycosides Thus, investigation into the rate of exchange of the 1-acetoxyl groups in penta-*O*-acetyl-β-D-glucopyranose and 1,3,4,6-tetra-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glucopyranose showed that the latter exhibited a 390-fold reduction in reactivity compared to the former due to the reduced participation and inductive effect Similar experiments with the α-D anomers showed only a 50-fold reduction due to different inductive effects Lemieux showed that increased steric effects due to the large trichloroacetyl group were negligible because the point of equilibrium in the hydrolysis was affected only slightly by successive introductions of chlorine substituents into the 2-acetoxyl group, and consequently the velocity constants for the forward and backward reactions were equally affected Newth and Phillips[25], however, contended that a strong, shielding effect was exerted at C-1 by a trichloroacetate group on C-2

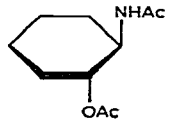
Lemieux[18] proposed the following mechanism for the formation of the tetrachloro derivative **2** Initially, AcO-2 participates in the elimination of AcO-1 to give a resonance-stabilised, cyclic 1,2-acetoxonium ion Successive ring-opening, chlorination, and participation reactions would yield the final product (see Scheme 1) However, Lemieux did not explain in detail the chlorination of the methyl group of the 2-acetate substituent, nor did he comment on the latter stages of the participation by the partially chlorinated group on C-2 The step-wise chlorination of AcO-2 would successively decrease the ability of this group to participate in reactions at C-1, but once one chlorine substituent had been introduced into the methyl group of AcO-2, the necessity to postulate further participation becomes less important Since the reaction of phosphorus pentachloride on 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose (**3**) gave **5** with AcO-1 intact, it seemed likely that no participation involving the 2-acetamido grouping was taking place Hence, a different mechanism from that with penta-*O*-acetyl-β-D-glucopyranose (**1**) must have operated However, the compounds having a *trans*-diaxial (α-D-*manno*) or *trans*-diequatorial (β-D-*gluco*) arrangement of the 1-acetoxy and 2-acetamido groups gave better yields of the tetrachloroethylideneamino derivatives than did that having an axial–equatorial arrangement (α-D-*gluco*) The absence of participation in these reactions implies that the carbonyl function of the 2-acetamido group in, for example, 2-acetamido-1,3,4,6-

tetra-*O*-acetyl-β-D-glucopyranose (3) is attacked first, giving a product containing the N=CCl–CH_3 group However, only small quantities of the tetrachloroethylideneamino derivative **5** were detected when the reaction was carried out with 1 or 2 moles of phosphorus pentachloride in carbon tetrachloride; in chloroform, 2-acetamido-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl chloride was formed. Alternatively, participation could be prevented by initial conversion of the acetamido group into the trichloroacetamido group which could then be further chlorinated to give the tetrachloroethylideneamino derivative However, treatment of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranose (**6**) with phosphorus pentachloride did not yield any of the tetrachloroethylideneamino derivative **5**.

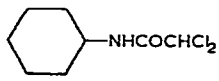


Scheme 1

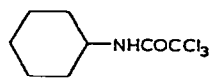
In order to investigate the mechanism of formation of the chloro-imine derivatives further, the reactions of phosphorus pentachloride on some simpler derivatives were undertaken. The reactions with acetamidocyclohexane produced three products Limited quantities of phosphorus pentachloride gave the dichloroacetamido derivative (**21**) and the trichloroacetamido derivative (**22**) in yields of 30 and 47%, respectively, but, with excess reagent, **22** (65% yield) and the tetrachloroethylidene derivative **23** were formed The products were characterised from i r. and n m r. data (Table II) Treatment of trichloroacetamidocyclohexane (**22**) with phosphorus pentachloride produced no further reaction Repetition of the reaction with 1-acetamido-2-acetoxyethane and limited quantities of phosphorus pentachloride produced crystalline 1-acetoxy-2-(dichloroacetamido)ethane (**24**) in 35% yield The structure was determined from the H^1-n m r (Table II) and mass spectra (Table III)



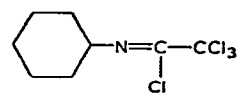
20



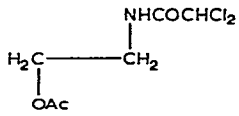
21



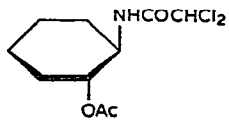
22



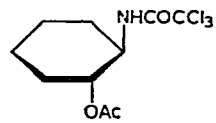
23



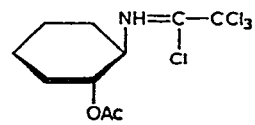
24



25



26



27

TABLE II

^{1}H-N M R PARAMETERS[a]

Compound	21	22	23	24	25	26	27
Solvent	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$	$CDCl_3$
H-1	6 35cm	6 35cm	6 40cm	6 51q	6 26cm	6 30cm	6 20cm
$CHCl_2$	4 2s	—	—	4 18s	4 30s	—	—
NH	3 7d	3 58d	—	2 90cm	3 43d	3 20d	—
CH_NO				5 88t	5 40cm	5 33cm	5 10cm
OAc				7 95s	8 02s	8 02s	8 02s

[a]First-order chemical shifts (τ values) and coupling constants at 100 MHz

TABLE III

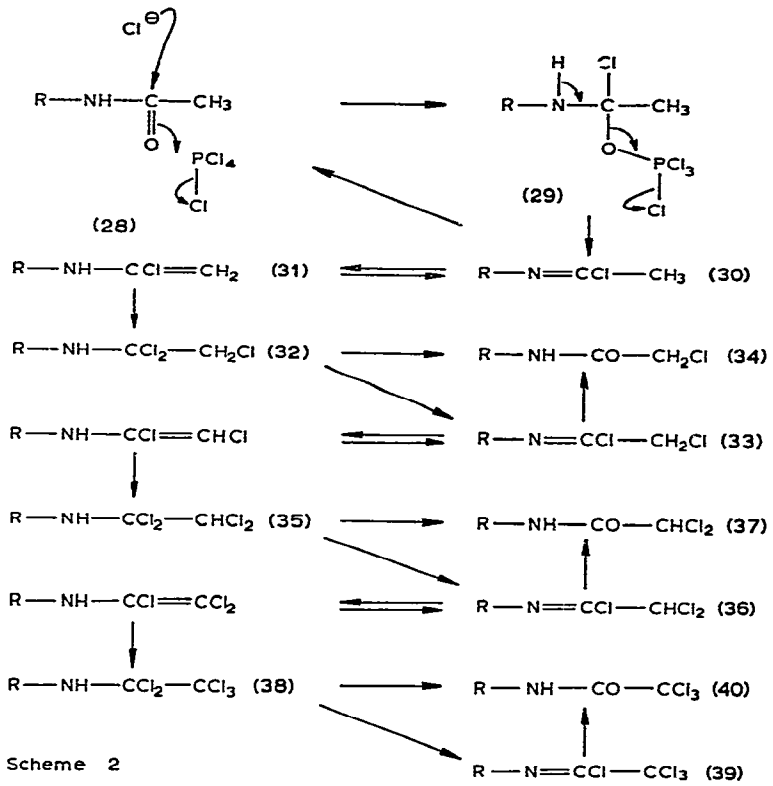
MASS SPECTRA (*m/e* VALUES) OF *N*-SUBSTITUTED DERIVATIVES OF *trans*-2-ACETOXYCYCLOHEXYLAMINE

20 *RNHAc*[a]	26 *RNHCOCCl*$_3$	27 *RN=CClCCl*$_3$	24 *R NHCOCHCl*$_2$	*Loss of*
199(M^+)				
	266	284		$Cl^\bullet$
157			171	$CH_2CO^\bullet$ from NHAc
156	258	276	172	$CH_3CO^\bullet$ from OAc
140		260	154	$CH_3COO^\bullet$
139	241	259	153	CH_3COOH
			141	
	224	242		$CH_2CO^\bullet + Cl^\bullet$
		241		$CH_3CO^\bullet + Cl^\bullet$
114				$CH_3CO^\bullet + CH_2CO$
	206	224		$CH_3COOH + Cl^\bullet$
			130	$CHCl_2^+$

[a]R = *trans*-2-Acetoxycyclohexyl, R′ = 2-acetoxyethyl.

When (±)-*trans*-1-acetamido-2-acetoxycyclohexane was treated with limited quantities of phosphorus pentachloride, (±)-*trans*-1-acetoxy-2-(dichloroacetamido)-cyclohexane (**25**) and (±)-*trans*-1-acetoxy-2-(trichloroacetamido)cyclohexane (**26**) were isolated in yields of 4 and 3%, respectively They were characterised by their ^{1}H-n m r. (Table II) and i r spectra, as in previous cases Mass-spectral data (Table III) confirmed the structure of the trichloroacetamido derivative (**26**). With larger quantities of phosphorus pentachloride, two further liquid products were isolated from the reaction mixture by fractional distillation The first, and the slower-moving on t l c , showed one acetate-methyl signal but no NH doublet in the ^{1}H-n m r spectrum (Table II), and an acetate carbonyl-stretching frequency and a peak at 1690 cm^{-1}, assigned to an –N=C– group, but no NH peaks, in the i r. spectrum On exposure to air for a few days, hydrolysis occurred, producing the trichloroacetamido derivative (**26**) On this evidence, coupled with the mass spectrum (Table III), the product was identified as (±)-*trans*-1-acetoxy-2-(tetrachloroethylideneamino)cyclo-hexane (**27**) The second compound gave a p m r spectrum (Table II) that was devoid of acetoxy-methyl signals and NH resonance The i r. spectrum confirmed the absence of the NH and carbonyl groups and showed peaks at 1690 (N=C) and 1630 cm^{-1} (C=C) On exposure to air, the strength of the peak at 1630 cm^{-1} decreased, and both the NH and trichloroacetamido-carbonyl peaks appeared, indicating the presence, originally, of a tetrachloroethylideneamino function Further structural determination was not carried out As in the case of trichloroacetamidocyclohexane, the 1-acetoxy-2-trichloroacetamido derivative **26** could not be further chlorinated with phosphorus pentachloride

The mechanism (see Kirsanov[27] and Von Braun[28]) that accounts for the above data involves attack by the carbonyl oxygen on phosphorus pentachloride (**28**) to give the intermediate **29**, followed by the elimination of phosphorus oxychloride and hydrogen chloride with the formation of the chloro-imine **30** Enolisation of **30** to the chloro-ene **31** would facilitate direct chlorination to the trichloride **32**, which could then either be hydrolysed to the monochloroacetamido derivative (**34**) or eliminate hydrogen chloride to give the dichloro-imine **33** Repetition of these reactions would produce the tetrachloride **35** and the trichloro-imine **36**, both of which could then be hydrolysed to the dichloroacetamido derivative (**37**) The final step would involve (see Scheme 2) the formation of the pentachloride **38** followed by elimination of hydrogen chloride to give the tetrachloroethylideneamino derivative (**39**) Hydrolysis of both the pentachloride **38** and the tetrachloroethylideneamino derivative (**39**) would give the trichloroethylideneamino derivative (**40**) The tetrachloroethylideneamino derivatives (*e g* , **39**) cannot enolise and were isolated, provided care was exercised to prevent hydrolysis Since all of the mono-, di-, and tri-chloro-imines (**31**, **33**, and **36**) could enolise and further chlorinate, this would explain why they were not isolated. Explanation of the failure to convert the trichloroacetamido derivative (**40**) into the tetrachloroethylideneamino derivative (**39**) must be due to the inductive effect of the trichloro group preventing the carbonyl group from attacking the phosphorus pentachloride, as in the initial formation of the intermediate **29**



Scheme 2

EXPERIMENTAL

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-tetrachloroethylideneamino-β-D-glucopyranose (5) — 2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose (5 g) and phosphorus pentachloride (11 g) were thoroughly mixed together in a dry flask Dry carbon tetrachloride (5 ml) was added and the mixture heated to 95° It became homogeneous after 30 min and was left for a further 5 h, by which time t l c (ether–light petroleum, 5 1) showed the preponderance of one fast-moving component Extraction with dry ether followed by evaporation gave crystals which were dissolved in chloroform The solution was quickly washed with cold water, dried ($MgSO_4$), and evaporated to give a syrup which crystallised from dry ether to give **5** (3 5 g, 60%), m p 164–165°, $[\alpha]_{365}$ −6° (*c* 2, chloroform) (Found· C, 37.6; H, 3 7, N, 2 7 $C_{16}H_{19}Cl_4NO_9$ calc C, 37 6; H, 3 7, N, 2 7%) The i r [1675 (N=C), 750 and 780 cm^{-1} (chlorine)], p m r (Table I), and mass[10] spectra were consistent with the assigned structure

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranose (6) — 1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride (5 g) was suspended in pyridine (150 ml), trichloroacetyl chloride (5 g) was slowly added, and the mixture was gently warmed until a yellow precipitate appeared. After standing for

1 h at room temperature, the solution was poured onto ice and water, and extracted with chloroform The extract was washed successively with dilute sulphuric acid, aqueous sodium hydrogen carbonate, and water, and dried ($MgSO_4$) Decolourisation and evaporation gave a pale-yellow syrup which crystallised from ethanol (3 5 g, 70%) Recrystallisation from ethanol gave needles of **6**, m p 167 5–168 5°, $[\alpha]_D$ +0 5° (*c* 1 0, chloroform) (Found· C, 39 5, H, 4 3, Cl, 21 7, N, 2 3 $C_{16}H_{20}Cl_3NO_{10}$ calc · C, 39 1, H, 4 1, Cl, 21 6, N, 2 8%). The i r. [3370 (NH), 1750 (OAc), 1710 ($NHCOCCl_3$), and 1535 cm^{-1} (amide II)], p m r. (Table I), and mass[10] spectra supported the structure **6** Osawa[11] reported m p 135–136° Wolfrom and Bhat[13] reported m p 159–160°, $[\alpha]_D^{22}$ +7°

*Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-*D*-glucopyranoside* (**7**) — 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranose (8 g) was dissolved in glacial acetic acid saturated with hydrogen bromide (60 ml) and left in the dark for 24 h. Cold chloroform was added and the solution was poured into cold, aqueous sodium hydrogen carbonate until no effervescence occurred After washing with water and drying ($MgSO_4$), concentration gave a syrup which showed many impurities on t l c (ether–light petroleum, 10 1) Dry methanol (50 ml) was added, and active silver carbonate (0 5) and calcium sulphate (0 5 g) were stirred in After shaking for 24 h in the dark, the solution was filtered and evaporated to a syrup which crystallised from ethanol, the product had m p 125–129° G l c showed these crystals to be a mixture of two components in the ratio of 20 1 in favour of the compound having the faster retention time T l c showed R_F values of ~0 5 and ~0 45 (ether–light petroleum, 2 1), the major component being the faster Repeated recrystallisation from ethanol–light petroleum gave **7** (4 5 g, 60%), m p 131–133°, $[\alpha]_D$ −2 3° (*c* 2, chloroform) (Found C, 38 7, H, 4 4, N, 3 0 $C_{16}H_{20}Cl_3NO_{10}$ calc C, 38 8, H, 4 3, N, 3 0%) The i r [3280 (NH), 1750 (OAc), 1695 ($NHCOCl_3$), 1550 cm^{-1} (amide II)], p m r (Table I), and mass[10] spectra supported the structure The minor component was not isolated

*Reaction of hydrogen bromide in acetic acid, followed by methanol, with 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-tetrachloroethylideneamino-β-*D*-glucopyranose* (**5**) — A solution (2 g) of **5** in glacial acetic acid saturated with hydrogen bromide (32 ml) was left in the dark overnight A further quantity of glacial acetic acid saturated with hydrogen bromide (8 ml) was then added, and the solution was again left in the dark overnight Cold chloroform (80 ml) was added and the solution was washed until acid-free with cold, saturated, aqueous sodium hydrogen carbonate, and finally with water. After drying ($MgSO_4$), evaporation gave a dark syrup which was redissolved in dry chloroform, and the solution was decolourised and evaporated A solution of the resulting, clear syrup in dry methanol (50 ml) was treated with active silver carbonate (2 g) and calcium sulphate (2 g) After filtration and decolourisation, evaporation gave a syrup which crystallised. Recrystallisation from ethanol–light petroleum gave needles (1 2 g), m p 130–153°. T l c (ether–light petroleum) showed the presence of two components (confirmed by g l c) in the ratio of 4 1. The mixture (350 mg) was chromatographed on a column of silica gel with ether–light petroleum (3 1) The faster

component, when crystallised from ethanol–light petroleum, had m p 130–132° and was indistinguishable from methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**7**) The second component was not isolated.

Treatment of the tetrachloroethylideneamino derivative **5** (100 mg) with dry methanol (20 ml) and active silver carbonate (100 mg) for 24 h in the dark at room temperature gave no reaction, and starting material was recovered in 90% yield

*Action of phosphorus pentachloride on 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose* (**9**) — Compound **9** (0 21 g) was thoroughly mixed with phosphorus pentachloride (1.1 g), and dry carbon tetrachloride (1 ml) was added The mixture was heated to 95° for 4 h T l c (ether–light petroleum, 2 1) showed a complex mixture, the fastest being the major component The mixture was extracted with ether, and the extract was washed with water, dried ($MgSO_4$), and evaporated to a syrup which was fractionated on a column of silica gel, using ether–light petroleum (2 1) The first fraction crystallised from di-isopropyl ether–ether–light petroleum, giving 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-tetrachloroethylideneamino-α-D-glucopyranose (**11**, 10 mg, 4%), m p 101–102° Another fraction crystallised from di-isopropyl ether–ether–light petroleum to give 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranose (**10**, 13 mg, 5%), m p 159–160° (Found C, 39 5, H, 4 15. $C_{16}H_{20}Cl_3NO_{10}$ calc C, 39 2, H, 4 1%)

*Action of phosphorus pentachloride on 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-mannopyranose* (**13**) — Compound **13** (640 mg) was thoroughly mixed with phosphorus pentachloride (1.7 g), and dry carbon tetrachloride was added (2 ml) The mixture was heated for 5 h at 95°, and t l c (ether–light petroleum, 2 1) then showed the presence of a major product The mixture was fractionated on silica gel with ether–light petroleum (2 1), giving 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-tetrachloroethylideneamino-α-D-mannopyranose (**12**) (225 mg, 27%), m p. 141–143°, $[\alpha]_D$ −50° (*c* 1, chloroform) (Found C, 37 6, H, 3 7, N, 2 7 $C_{16}H_{19}Cl_2NO_9$ calc C, 37 6, H, 3.7, N, 2 7%)

*Action of phosphorus pentachloride on 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide* (**14**) — Compound **14** (1 g) was thoroughly shaken with phosphorus pentachloride (5 g), and carbon tetrachloride (2 ml) was added The mixture was heated to 95° and became homogeneous after 30 min After 18 h, t l c showed four products and no starting material The solution was evaporated to a syrup that was extracted with dry ether, and the extract was filtered and chromatographed on silica gel with ether–light petroleum (1 1) The first fraction (20 mg) contained a mixture which was separated by fractional crystallisation (m p 82–86° and 122–126°), but the structures were not determined

The second fraction (50 mg) crystallised from di-isopropyl ether–light petroleum and had m p. 120–122° (Found C, 39.5, H, 4 5), but the structure could be only partially assigned The third fraction contained the major product, 3,4,6-tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glucopyranosyl chloride (**2**) (330 mg, 27%), which crystallised from di-isopropyl ether–light petroleum, with m p and mixture m p. 141–142° (Found C, 35 8, H, 3 6, Cl, 30 0 $C_{14}H_{16}Cl_4O_9$ calc · C, 35 8; H, 3 4, Cl, 30 2%)

Reaction of phosphorus pentachloride with N-*acetyl-2,3,4,6-tetra*-O-*acetyl-β-*D-*glucopyranosylamine* (**16**) — (*a*) Compound **16** (800 mg) was heated to 95° with phosphorus pentachloride (2 g) and dry carbon tetrachloride (2 drops) After 4 h, the reaction mixture was evaporated to remove most of the phosphorus-containing components, ether was added to the residue, and the resulting extract was filtered and evaporated to a syrup Crystals of 2,3,4,6-tetra-*O*-acetyl-*N*-tetrachloroethylidene-*β*-D-glucopyranosylamine (**17**, 510 mg, 49%) were obtained from ether–di-isopropyl ether–light petroleum, with m p 140–148°. The i.r spectrum [1690 cm^{-1} (N=C)] was consistent with the structure The crystals had a tendency to decompose giving off hydrogen chloride A solution of **17** in dichloromethane was washed with water and then evaporated to give another product (400 mg, 40% based on **16**) Recrystallisation from ethanol–light petroleum gave 2,3,4,6-tetra-*O*-acetyl-1-deoxy-1-trichloroacetamido-*β*-D-glucopyranose (**18**), m p 113–115° (Found C, 39 1, H, 4 35, N, 2 85, Cl, 21 3 $C_{16}H_{20}Cl_3NO_{10}$ calc C, 39 0, H, 4 1, N, 2 85, Cl, 21 6%) The ^{1}H-n m r (Table I) and i r [3300 (NH), 1710 ($NHCOCCl_3$), 1530 cm^{-1} (amide II)] spectra verified the structure **18**

(*b*) The reaction was repeated on **16** (1 g) and phosphorus pentachloride (5 g) for 6 h. T l c (ether–light petroleum, 2 1) showed the presence of three major products moving ahead of the previous two products (**17**, **18**) After concentration of the solution, extraction with ether, and evaporation of the extract, the resulting syrup was separated on silica gel, using ether–light petroleum (1 4) The third component crystallised from the eluate on slow evaporation, yielding 3,4,6-tri-*O*-acetyl-2-*O*-trichloroacetyl-*β*-D-glucopyranosyl chloride (**2**, 90 mg, 16%), m p and mixture m p 140–141°

Reaction of phosphorus pentachloride on acetamidocyclohexane — (*a*) The acetamido derivative (4 g) was thoroughly mixed with phosphorus pentachloride (25 g), when the mixture became warm and liquefied with evolution of hydrogen chloride The solution was heated to 95° for 3 h T l c (ether–light petroleum, 1 10) then showed the presence of three products The solution was evaporated at 60° on a water-bath to remove the volatile phosphorus by-products (PCl_3, $POCl_3$, etc.) The residual, viscous liquid was chromatographed on silica gel, using light petroleum Only a trace of the fastest component was obtained in the first fraction, but the second fraction gave (trichloroacetamido)cyclohexane (3 2 g, 47%), m p 97–99° (from di-isopropyl ether–light petroleum) (Found C, 39 4, H, 4 95, Cl, 43 5, N, 5 75 $C_8H_{12}Cl_3NO$ calc C, 39 2, H, 4 9, Cl, 43 5, N, 5 7%) P m r spectrum, Table II, mass spectrum, Table III, i r spectrum 3300 (NH), 1690 ($NHCOCCl_3$), 1520 cm^{-1} (amide II)

The third fraction gave crystals from di-isopropyl ether–light petroleum of (dichloroacetamido)cyclohexane **21** (1 8 g, 30%), m p 138–140° (Found· C, 45 2, H, 6 1, N, 6 3. $C_8H_{13}Cl_2NO$ calc· C, 45 7; H, 6 2, N, 6.7%) P m r spectrum, Table II, i r spectrum, 3280 (NH), 1670 ($NHCOCHCl_2$), 1540 cm^{-1} (amide II)

(*b*) The experiment was repeated using 10 g of acetamidocyclohexane, the volatile phosphorus compounds were removed by evaporation, and the remaining

liquid was fractionally distilled A colourless liquid was collected at 80°/1 5 mmHg, which corresponded (t l c) to the fastest compound in (*a*) Redistillation gave (tetrachloroethylideneamino)cyclohexane (**23**, 12 1 g, 65%) (Found C, 36 3, H, 4 5, N, 5 15 $C_8H_{11}Cl_4N$ calc C, 36 5, H, 4 2, N, 5 3%) P m r spectrum, Table II, i r spectrum, 1680 cm^{-1} (N=C)

Action of phosphorus pentachloride on 1-acetamido-2-acetoxyethane — 1-Acetamido-2-acetoxyethane (2 g) was boiled under reflux with phosphorus pentachloride (8 g) and carbon tetrachloride (5 ml) The mixture became very dark and was homogeneous after 1 h After 5 h, the solution was treated with charcoal, filtered, and concentrated to dryness After further decolourisation in ethanol, crystals of 1-acetoxy-2-(dichloroacetamido)ethane (**24**) (0 17 g, 35%), m p 79–80°, were obtained (Found C, 33 4, H, 4 3, N, 6 5 $C_6H_9Cl_2NO_3$ calc C, 33 6, H, 4 2, N, 6 55%) The i r [1685 cm^{-1} ($NHCOCHCl_2$)], p m r (Table II), and mass[10] spectra supported the structure

Action of phosphorus pentachloride on (±)-trans-1-*acetamido-2-acetoxycyclohexane* (**20**) — (*a*) The cyclohexane derivative (2 g) was thoroughly mixed with phosphorus pentachloride (20 g) and calcium carbonate (5 g), and dry carbon tetrachloride (3 ml) was added The mixture was heated to 60° for 4 h, and t l c (ether–light petroleum, 1 4) then showed the presence of three products and no starting material The mixture was evaporated to a syrup and fractionated on silica gel, using ether–light petroleum (1 4) The first fraction contained only a trace of **27** and no further characterisation was possible The second fraction crystallised from ether and light petroleum, yielding (±)-*trans*-1-acetoxy-2-(trichloroacetamido)-cyclohexane (**26**, 700 mg, 30%), m p 90–91° (Found C, 39 7, H, 4 7, N, 4 75 $C_{10}H_{14}Cl_4NO_3$ calc C, 39 7, H, 4 65, N, 4 65%) The p m r (Table II) and i r spectra [3300 (NH), 1730 (OAc), 1710 ($NHCOCCl_3$), 1540 cm^{-1} (amide II)] supported the structure The third fraction crystallised from ether and light petroleum, yielding (±)-*trans*-1-acetoxy-2-(dichloroacetamido)cyclohexane (**25**) (100 mg, 4%), m p 116–117° (Found C, 44 5, H, 5 6, N, 5 1 $C_{10}H_{15}Cl_2NO_3$ calc C, 44 7, H, 5 6, N, 5 2%) The p m r (Table II) and i r. spectra [3280 (NH), 1745 (OAc), 1675 ($NHCOCHCl_2$), 1580 cm^{-1} (amide II)] supported the structure

(*b*) (±)-*trans*-1-Acetamido-2-acetoxycyclohexane (500 mg) was thoroughly mixed with phosphorus pentachloride (5 g), and dry carbon tetrachloride (1 ml) was added The mixture was heated to 100° for 4 h Fractional distillation of the products produced a clear liquid (**27**), whose p m r (Table II), i r [1745 (OAc), 1690 cm^{-1} (N=C)], and mass spectra (Table III) supported the assignment of the structure (±)-*trans*-1-acetoxy-2-(tetrachloroethylideneamino)cyclohexane (**27**)

ACKNOWLEDGMENT

One of us (A M D) thanks the S R C for an award

REFERENCES

1 P BRIGL, *Z Physiol Chem*, 116 (1921) 1.
2 R U LEMIEUX AND J HOWARD, *Methods Carbohyd Chem*, 2 (1963) 400.
3 P BRIGL, *Z Physiol Chem*, 126 (1923) 120
4 V E. HARDEGGER AND R M MONTAVON, *Helv Chim Acta*, 30 (1947) 632
5 A M GAKHOKIDZE AND N D KUTIDZE, *Zh Obshch Khim*, 22 (1952) 139, 247
6 J. DE PASCUAL TEREZA AND F GARRIDO ESPINOSA, *Acta Salmanticensia, Ser Cienc*, 2 (1958) 53
7 J DE PASCUAL TEREZA AND F GARRIDO ESPINOSA, *An Real Soc Espan Fis Quim, Ser. B*, 52 (1956) 447.
8 S N DANILOV, O P KOZMINA, AND A N SHIRSHOVA, *J Ger Chem USSR (Eng Transl)*, 27 (1957) 1026
9 F GARRIDO AND M. L CANESSA, *Bol Soc Chilena Quim*, 13 (1963) 36
10 Unpublished data
11 T OSAWA, *Chem Pharm Bull*, 8 (1960) 597
12 C H BOLTON, A M DEMPSEY, AND L HOUGH, *Chem Commun*, (1967) 658
13 M L WOLFROM AND H B BHAT, *J Org Chem*, 32 (1967) 1821
14 J VON BRAUN AND A HEYMONS, *Ber*, 63B (1930) 502
15 W G DAUBEN AND C W VAUGHAN, *J Amer Chem Soc*, 77 (1955) 1674
16 W J HICKINBOTTOM, *J Chem Soc*, (1928) 3140, (1929) 1676
17 R A ABRAMOVITCH, *J Chem Soc*, (1951) 2996
18 R U LEMIEUX, *Can J Chem*, 29 (1951) 1079
19 R U LEMIEUX AND C BRICE, *Can J Chem*, 30 (1952) 295
20 R U LEMIEUX AND G HUBER, *Can J Chem*, 31 (1953) 1040
21 R U LEMIEUX AND C BRICE, *Can J Chem*, 33 (1955) 109
22 R U LEMIEUX AND W P SHYLUK, *Can J. Chem*, 33 (1955) 120
23 R U LEMIEUX AND G HUBER, *Can J Chem*, 33 (1955) 128
24 R U LEMIEUX, C BRICE, AND G HUBER, *Can J Chem*, 33 (1955) 134
25 F H NEWTH AND G O PHILLIPS, *J. Chem Soc*, (1953) 2904
26 C A VANDERWERF, R Y HEISLER, AND W E MCEWEN, *J Amer Chem Soc*, 76 (1954) 1231
27 A V KIRSANOV, *Bull Acad Sci USSR (Eng Transl)*, (1954) 551
28 J VON BRAUN, *Ber*, 60 (1927) 92, J VON BRAUN, F JOSTES, AND K. MUNCH, *Ann*, 453 (1927) 118