Koenigs–Knorr Reactions. Part II.[1] A Mechanistic Study of Mercury(II) Cyanide-promoted Reactions of 2,3,4,6-Tetra-*O*-methyl-α-D-glucopyranosyl Bromide with Cyclohexanol in Benzene–Nitromethane

By **Jerry E. Wallace** and **Leland R. Schroeder,*** The Institute of Paper Chemistry, Appleton, Wisconsin 54911, U.S.A.

The kinetics and products of mercury(II) cyanide-promoted reactions of 2,3,4,6-tetra-*O*-methyl-α-D-glucopyranosyl bromide with cyclohexanol in benzene–nitromethane (1 : 1 v/v) at 2—20 °C were investigated by polarimetry and quantitative g.l.c. The reactions exhibited a first-order kinetic dependence on the glucosyl bromide and mercury(II) cyanide concentrations, but the rates were independent of the cyclohexanol concentration. Under the conditions employed, cyclohexyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside was the main product (*ca.* 60—80%), but in all reactions the α-glucoside was also formed. The stereoselectivity of the reactions for β-glucoside formation increased when the alcohol concentration was increased and decreased when the reaction temperature was increased. The initial reaction is believed to involve rate-determining, mercury(II) cyanide-assisted heterolysis of the carbon–bromine bond to form the glucopyranosyl carbocation. The stereochemical course of the reaction is dependent on the rate of dissociation of the carbocation and the attendant anion relative to the rate of reaction of the alcohol with the carbocation. Reasons for the observed autocatalysis in the reaction are discussed.

THE steric course of Koenigs–Knorr reactions involving 1,2-*cis*-glucopyranosyl halides having a ' non-participating ' C-2 substituent, such as 2,3,4,6-tetra-*O*-methyl α-D-glucopyranosyl bromide (TMGB), has been found to be extremely variable, ranging from predominant inversion to predominant retention of configuration at C-1.[2-4] Previously, the steric course of the reaction of TMGB with cyclohexanol was shown to be dependent on both the alcohol concentration and the promoter–solvent system employed.[1] The purpose of this investigation was to determine the mechanism of a reaction of TMGB in the presence of one of the common promoters.

Mechanistic studies of Koenigs–Knorr reactions have been limited primarily to studies of alcoholyses not involving promoters or acid acceptors,[5-7] with some notable exceptions.[8] This is probably due to the fact that the heterogeneous nature of reactions employing insoluble promoters makes it difficult to obtain reliable kinetic data. We report here the results of a study of reactions of TMGB with cyclohexanol in the presence of mercury(II) cyanide in benzene–nitromethane (1 : 1 v/v).[9] The solubility of mercury(II) cyanide in the reaction solvent permitted the use of both kinetic measurements and product analyses in the study.

RESULTS

Initial rates for the mercury(II) cyanide-promoted reactions of TMGB with cyclohexanol were calculated from the initial linear portion of plots of the glucosyl bromide concentration *versus* time. The concentration of TMGB as a function of time was determined from polarimetric data and equation (i),[10] where $[TMGB]_0 =$ initial TMGB concentration, $\alpha_t =$ optical rotation of the reaction system at time t, $\alpha_0 = \alpha_t$ at time zero (determined by extrapolation), and $\alpha_\infty = \alpha_t$ at long reaction time (equilibrium rotation). Equation (i) is valid only if the ratio of anomers in the glucosidic products is time-independent. Anomeric glucopyranoside analyses as a function of time for reactions employing various ratios of reactant concentrations and reaction temperatures, reported for selected reactions in Table 1, demonstrated that this requirement was fulfilled by the reactions of TMGB.

$$[TMGB] = [TMGB]_0(\alpha_t - \alpha_\infty)(\alpha_0 - \alpha_\infty)^{-1} \quad \text{(i)}$$

A graphical determination of the initial rate for a reaction of TMGB is shown in Figure 1. The deviation from linearity is believed to have been due to the catalysing effect of species formed by the reaction. The initial reaction rate, $(d[TMGB]/dt)_{t=0}$, was determined (method of least squares) from the initial linear portion of the curve.

The order of the reaction with respect to each reactant

[1] Part I, J. E. Wallace and L. R. Schroeder, *J.C.S. Perkin I*, 1976, 1938.
[2] A. J. Rhind-Tutt and C. A. Vernon, *J. Chem. Soc.*, 1960, 4637.
[3] H. M. Flowers, *Carbohydrate Res.*, 1971, **18**, 211.
[4] T. Ishikawa and H. G. Fletcher, jun., *J. Org. Chem.*, 1969, **34**, 563.
[5] L. Hough and A. C Richardson, in ' Rodd's Chemistry of Carbon Compounds,' ed. S Coffey, 2nd edn., Elsevier, Amsterdam, 1967, vol. I, Part F, p. 320.
[6] B. Capon, *Chem. Rev.*, 1969, **69**, 407.
[7] W. G. Overend, in ' The Carbohydrates,' ed. W. Pigman and D. Horton, 2nd edn., Academic Press, New York, 1972, vol. 1A, p. 279.
[8] G. Wulff and G. Röhle, *Chem. Ber.*, 1972, **105**, 1122.
[9] H. M. Flowers, *Methods Carbohydrate Chem.*, 1972, **6**, 474.
[10] J. E. Wallace, Doctoral Dissertation, The Institute of Paper Chemistry, Appleton, Wisconsin, June 1975.

was calculated from initial reaction rates for series of reactions at 10 °C, in which the concentration of only one reactant was varied at a time. Plots of

TABLE 1

Anomeric glucopyranoside analyses

Variable	ROH : TMGB : $Hg(CN)_2$ Molar ratio [a]	Temp. (°C)	% Reaction [b]	n_α [c]
Cyclohexanol	7.5 : 1 : 1	10	12	0.28
			33	0.27
			100	0.29
	15 : 1 : 1	10	13	0.24
			29	0.23
			100	0.23
	22.5 : 1 : 1	10	100	0.18
TMGB	15 : 0.5 : 1 [d]	10	7	0.25
			17	0.23
			100	0.24
	15 : 1 : 1	10	100	0.23
$Hg(CN)_2$	15 : 1 : 0.5	10	5	0.26
			14	0.24
			100	0.24
	15 : 1 : 1	10	100	0.23
	15 : 1 : 1.5	10	100	0.23
	15 : 1 : 2	10	100	0.21
Temperature	15 : 1 : 1	2	100	0.17
	15 : 1 : 1	5	100	0.18
	15 : 1 : 1	10	100	0.23
	15 : 1 : 1	15	100	0.23
	15 : 1 : 1	20	17	0.24
			26	0.25
			100	0.26

[a] [TMGB] *ca.* 6×10^{-3}M. [b] Determined from polarimetric data. [c] Mole fraction of α-anomer in the glucosidic products; analyses of standards indicated that n_α could be determined within ±2 mole%. [d] [TMGB] *ca.* 3×10^{-3}M.

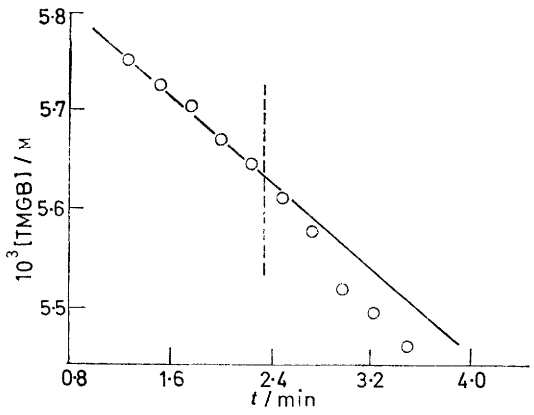


FIGURE 1 Initial reaction rate determination: 10 °C; [TMGB] 5.86×10^{-3}M; $[Hg(CN)_2]$ 5.98×10^{-3}M; initial slope = $(d[TMGB]/dt)_{t=0} = -1.75 \times 10^{-6}$ mol l^{-1} s^{-1}

log $(d[TMGB]/dt)_{t=0}$ *versus* log $[TMGB]_{t=0}$, log $[Hg(CN)_2]_{t=0}$, and log $[ROH]_{t=0}$ are shown in Figure 2. Experimentally, the order of reaction with respect to both TMGB and mercury(II) cyanide was *ca.* 1.00. The reaction rate was independent of the cyclohexanol (ROH) concentration. Therefore, the initial rate of the reaction is described by equation (ii).

$$(d[TMGB]/dt)_{t=0} = -k[TMGB][Hg(CN)_2] \quad \text{(ii)}$$

The initial rate constants, k, required for calculation of the thermodynamic functions of activation, were determined from the initial rates of reaction and equation (ii). Initial rate constants for various temperatures, and the enthalpy ($\Delta H^\ddagger$) and entropy ($\Delta S^\ddagger$) of activation

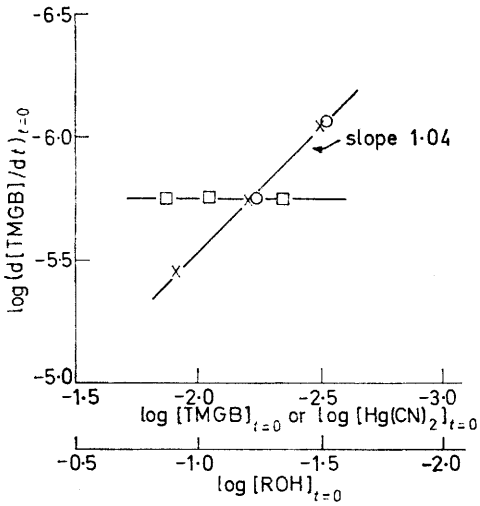


FIGURE 2 Reaction order determinations at 10 °C; (○) TMGB; (×) $Hg(CN)_2$; (□) cyclohexanol (ROH)

for mercury(II) cyanide-promoted reactions of TMGB are given in Table 2.

TABLE 2

Initial rate constants and thermodynamic functions of activation

Temp. (°C)	10^2k/ mol^{-1} s^{-1} [a]	$\Delta H^\ddagger$/ kcal mol^{-1}	$\Delta S^\ddagger$/ cal mol^{-1} K^{-1} [b]
20	8.72	10.0	−29.1
15	6.06		
10	4.67		
5	3.45		
2	2.36		

[a] Average of duplicate determinations. [b] Calculated for 20 °C.

The effects of variations in the cyclohexanol, TMGB, and mercury(II) cyanide concentrations and in the reaction temperature on the anomeric composition of the glucosidic products is shown in Table 1. Increasing the alcohol concentration or decreasing the reaction temperature resulted in an increase in the selectivity of the reaction for formation of the β-glucoside. Variation of the mercury(II) cyanide and TMGB concentrations had no apparent effect on the stereoselectivity of the reaction.

DISCUSSION

The fact that the reaction of TMGB exhibits first-order kinetic dependence on both [TMGB] and $[Hg(CN)_2]$, but is independent of [ROH] indicates that the reaction occurs by a mechanism in which heterolysis of the carbon–bromine bond is assisted by the mercury(II) cyanide in the rate-determining step. Analogous enhancement of reactions of glycosyl halides by mercury(II) halides has been demonstrated previously.[11] The rate-limiting step is then followed by a much faster reaction of the resultant glucopyranosyl carbocation with cyclohexanol to form glucosides.

[11] G. L. Mattok and G. O. Phillips, *J. Chem. Soc.*, 1956, 1836.

The mechanism by which the mercury(II) cyanide assists in heterolysis of the carbon–bromine bond of TMGB is unknown. It may complex reversibly with the glucosyl bromide (RBr). In a unimolecular, rate-determining step the carbocation ion (R^+) would be formed from the complex as depicted in equation (iii). Alternatively, the mercury(II) cyanide may assist in bond cleavage through its reaction with the glucosyl bromide in a bimolecular rate-limiting step as depicted in equation (iv). The existence of ions of the type HgX_3^-, as proposed in equations (iii) and (iv), is well established.[11,12]

$$RBr + Hg(CN)_2 \rightleftharpoons RBr,Hg(CN)_2 \overset{\text{slow}}{\rightleftharpoons} R^+ + BrHg(CN)_2^- \quad \text{(iii)}$$

$$RBr + Hg(CN)_2 \overset{\text{slow}}{\rightleftharpoons} [R^{\delta+} \cdots Br^{\delta-} \cdots Hg(CN)_2]^{\ddagger} \rightleftharpoons R^+ + BrHg(CN)_2^- \quad \text{(iv)}$$

The fact that mercury(II) cyanide assists in rate-determining heterolysis of the carbon–bromine bond is also reflected in both the enthalpy and entropy of activation for reaction of TMGB (Table 2). Such assistance would decrease the energy required for bond cleavage and this is reflected in the relatively low value for $\Delta H^{\ddagger}$ (10 kcal mol^{-1}). The loss of freedom associated with mercury(II) cyanide being co-ordinated with TMGB in the transition state of the rate-determining step of the reaction is reflected in both the sign and magnitude of $\Delta S^{\ddagger}$ (−29 cal mol^{-1} K^{-1}). Similar enthalpy and entropy of activation values have been reported for mercury(II) chloride-catalysed methanolysis of tetra-*O*-acetyl-α-D-glucopyranosyl chloride.[11]

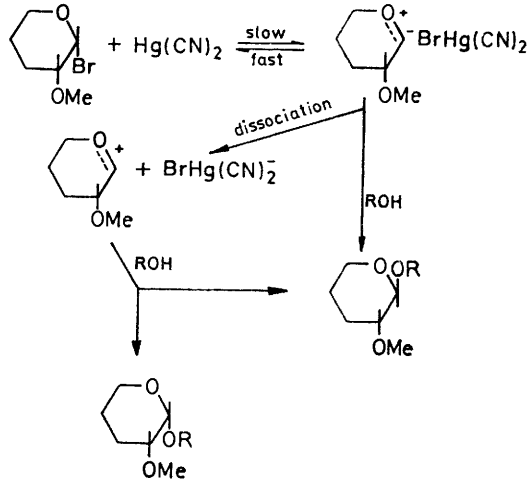
The observed influence of the alcohol concentration on the configuration of the glucosidic products (Table 1) indicates that the carbocation ion resulting from heterolysis of the carbon–bromine bond is partially shielded by the departing anion, or that these ions exist for a time as an ion pair. Reaction of the alcohol with the shielded carbocation would result in the β-glucoside. However, when dissociation of the ions is complete, the alcohol can react at either the α- or the β-side of the carbocation, resulting in both α- and β-glucosides. As the alcohol concentration is increased, the availability of the alcohol to react with the carbocation increases. Thus, the rate of reaction of the alcohol with the shielded carbocation ion or ion pair increases relative to the rate of dissociation of the ions. Therefore, an increase in the alcohol concentration leads to an increase in the proportion of β-glucoside formed (Table 1).

As mentioned, formation of the α-glucoside is believed to be due to reaction of the alcohol with the free or unshielded carbocation. Alternatively, halide exchange (α-ion pair $\overset{Br^-}{\rightleftharpoons}$ β-ion pair)[2,4,13] could potentially account for the observed partial retention of configuration at C-1. However, the latter explanation is inconsistent with the fact that the ratio of anomeric glucosides was time-independent (Table 1).[14]

[12] F. A. Cotton and G. Wilkinson, 'Advanced Inorganic Chemistry,' 3rd edn., Interscience, New York, 1972, p. 519.
[13] T. J. Lucas and C. Schuerch, *Carbohydrate Res.*, 1975, **39**, 39.

The dependence of the glucosidic product configuration on the reaction temperature (Table 1) indicates that an increase in the reaction temperature results in an increase in the relative importance of glucoside formation *via* the free or unshielded carbocation. An increase in the reaction temperature must increase the rate of dissociation of the ions to a greater degree than the rate of reaction of the alcohol with the shielded carbocation, and thereby increase the relative amount of α-glucoside formed.

The reaction Scheme shown represents what is believed to be the initial mechanism for glucoside formation. The rate-determining step, heterolysis of the carbon–bromine bond assisted by mercury(II) cyanide, results in formation of a shielded carbocation, probably



SCHEME (pyranoid 3-, 4-, and 5-substituents not shown)

an ion pair. If the alcohol reacts with the cation before the latter dissociates from its attendant anion only the β-glucoside is formed; after dissociation either the α- or the β-glucoside can be formed. The rate of dissociation of the ions relative to the rate of reaction of the alcohol with the carbocation determines the stereochemical course of the reaction.

On the basis of the observed autocatalysis for the reaction of TMGB (Figure 1),[10] species must be formed which, in addition to mercury(II) cyanide, assist in the heterolysis of the carbon–bromine bond. Species potentially capable of functioning as promoters are HgBrCN, $HgBr_2$, HCN, HBr, and H^+, which could presumably be formed by the reactions indicated in equations (v)—(x).

$$RBr + Hg(CN)_2 \rightleftharpoons R^+ + Hg(CN)_2Br^- \quad \text{(v)}$$

$$R^+ + R'OH \longrightarrow ROR' + H^+ \quad \text{(vi)}$$

$$Hg(CN)_2Br^- + H^+ \rightleftharpoons HgBrCN + HCN \quad \text{(vii)}$$

$$Hg(CN)_2Br^- + H^+ \rightleftharpoons Hg(CN)_2 + HBr \quad \text{(viii)}$$

$$RBr + HgBrCN \rightleftharpoons R^+ + HgBr_2CN^- \quad \text{(ix)}$$

$$HgBr_2CN^- + H^+ \rightleftharpoons HgBr_2 + HCN \quad \text{(x)}$$

[14] L. R. Schroeder, J. W. Green, and D. C. Johnson, *J. Chem. Soc.* (*B*), 1966, 447.

A comparison of the half-lives ($t_{1/2}$) of mercury(II) cyanide- and mercury(II) bromide-promoted reactions of TMGB is given in Table 3. The latter reaction had a

TABLE 3

Half-lives for mercury(II) cyanide- and mercury(II) bromide-facilitated reactions of 2,3,4,6-tetra-*O*-methyl-α-D-glucopyranosyl bromide with cyclohexanol (10 °C) [a]

10^3[TMGB]/ M	10^2[Cyclohexanol]/ M	10^3[$Hg(CN)_2$]/ M	10^3[$HgBr_2$]/ M	$t_{1/2}$[b]/ min
5.862	9.024	5.984		9.5
2.948	4.508		2.993	1.4

[a] Benzene–nitromethane (1 : 1 v/v) solvent. [b] Time necessary for one-half of the glucosyl bromide to react. The half-life of each reaction is a function of the concentrations of reactants, particularly the mercury(II) cyanide or bromide.

much lower $t_{1/2}$ (1.4 min) than the former (9.5 min), even though [$HgBr_2$] was approximately one-half of [$Hg(CN)_2$]. Thus, mercury(II) bromide is a more effective promoter for the reaction of TMGB under these conditions than the cyanide. It would be expected that the capability of mercury(II) bromide cyanide to facilitate the reaction of TMGB would be between those of the dibromide and the dicyanide. Previous studies have shown that hydrogen bromide is also an effective catalyst for reactions of glycosyl bromides.[11,14] Presumably hydrogen cyanide and other protic acids would act similarly to hydrogen bromide.

Equation (ii), the initial rate equation for the TMGB reaction, must therefore be expanded to include the effect of all species capable of facilitating the reaction, to arrive at the general rate expression (xi), where

$$\mathrm{d[TMGB]}/\mathrm{d}t = -[\mathrm{TMGB}]\sum_{1}^{i} k_i[\mathrm{A}_i] \qquad \text{(xi)}$$

[A_i] = concentration of catalyst i and k_i = second-order rate constant corresponding to A_i.

EXPERIMENTAL

M.p.s, elemental analyses, and ^{1}H n.m.r. spectra were determined as described previously.[1] T.l.c. was performed on silica gel G, with methanolic sulphuric acid (5 : 1 w/w) spray for component detection. The g.l.c. instrument was described previously.[1] Analyses were performed on a column (3 ft × 0.125 in o.d., stainless steel) of 30% Carbowax 20M on 60—80 mesh Chromosorb W (N_2 at 60 ml min^{-1}; column temp. 160 °C for 51 min then 160 ⟶ 220 °C at 20° min^{-1}; injector temp. 205 °C; detector temp. 265 °C). Polarimetric analyses were performed with a Perkin-Elmer 141 MC polarimeter. The constant temperature system used for kinetic studies has been described previously.[14,15] The cell used (1 dm length; 5 ml capacity) was of glass, with a glass jacket for circulating water around it.

Cyclohexanol,[14] ethanol,[16] and methanol [16] were purified according to published procedures. Mercury(II) cyanide (25 g) was dissolved in hot absolute ethanol (200 ml), and a portion of the alcohol was distilled off to dry the solution azeotropically. The mercury(II) cyanide which crystallized upon refrigeration was dried *in vacuo* at 100 °C for 24 h and stored in a vacuum desiccator (P_2O_5). Benzenethiol was dried ($CaCl_2$) and fractionally distilled (40 cm Vigreux column) with exclusion of moisture. Benzene was subjected to a preliminary drying ($CaCl_2$), refluxed with lithium aluminium hydride, and fractionally distilled (40 cm Vigreux column) from lithium aluminium hydride with the exclusion of moisture. Nitromethane was successively percolated through Drierite, fractionally distilled (40 cm Vigreux column), percolated through Drierite, and fractionally distilled with exclusion of moisture.

2,3,4,6-Tetra-*O*-methyl-α-D-glucopyranosyl bromide, n-butyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside, cyclohexyl 2,3,4,6-tetra-*O*-methyl-α-D-glucopyranoside, and cyclohexyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside were prepared as described previously.[1]

2,3,4,6-*Tetra*-O-*methyl*-1-O-*propanoyl*-D-*glucopyranose*.—2,3,4,6-Tetra-*O*-methyl-D-glucopyranose [17] (2.0 g) was treated with propanoic anhydride–pyridine (12 ml; 1 : 2 v/v) for 12 h. The solution was stirred with ice–water for 0.5 h and extracted with chloroform (3 × 20 ml). The extracts were washed (N-H_2SO_4, sat. $NaHCO_3$, and H_2O), dried ($CaCl_2$), and concentrated *in vacuo* to a syrup which was fractionally distilled at 0.05 mmHg through a 10 cm Vigreux column. The *distillate* had $[\alpha]_D$ +74° (*c* 1.0 in $CHCl_3$) (Found: C, 53.5; H, 8.4. $C_{13}H_{24}O_7$ requires C, 53.4; H, 8.4%).

Phenyl 2,3,4,6-*Tetra*-O-*methyl*-1-*thio*-β-D-*glucopyranoside*.—2,3,4,6-Tetra-*O*-methyl-α-D-glucopyranosyl bromide (4.9 g) in chloroform (100 ml) was treated with benzenethiol (37.0 g) in methanolic M-sodium methoxide (170 ml). The reaction, which was monitored by t.l.c. (benzene–ethyl acetate, 1 : 1 v/v), was complete within 1 min. The mixture was diluted with water (100 ml) and extracted with chloroform (3 × 100 ml). The extracts were washed with aqueous 10% sodium carbonate (3 × 150 ml) and water (150 ml), dried ($CaCl_2$), and concentrated *in vacuo* to a syrup (4.7 g, 87%). Crystallization of the product from petroleum (b.p. 60—110 °C) yielded the *phenyl glucoside*, m.p. 70.5—72 °C, $[\alpha]_D$ −35.9° (*c* 1.0 in $CHCl_3$), δ($CDCl_3$) 4.50 (1 H, d, $J_{1,2}$ 9.2 Hz, H-1) and 7.1—7.7 (5 H, m, Ph) (Found: C, 58.8; H, 7.3; S, 9.9. $C_{16}H_{24}O_5S$ requires C, 58.5; H, 7.3; S, 9.8%).

Reaction Initiation and Polarimetric Analysis.—Anhydrous conditions were imperative throughout the procedures because of the sensitivity of the glucosyl bromide to hydrolysis. All glassware was dried at 180 °C for 24 h and stored in a vacuum desiccator (P_2O_5). Solvent transfers and weighing of compounds were conducted in a dry atmosphere.

Mercury(II) cyanide was weighed into a 50 ml volumetric flask. Anhydrous nitromethane (35 ml) was pipetted in, and the cyanide was dissolved by heating under reflux. Subsequently, nitromethane (10 ml) was distilled out to dry the system azeotropically. The flask was allowed to cool and weighed to determine the amount of nitromethane remaining. Cyclohexanol was then weighed in.

Anhydrous benzene (35 ml) was pipetted into a second 50 ml volumetric flask. Benzene (10 ml) was distilled out to dry the system azeotropically. The flask was allowed to cool and weighed to determine the amount of benzene. 2,3,4,6-Tetra-*O*-methyl-α-D-glucopyranosyl bromide was then weighed in.

The two flasks were allowed to equilibrate thermally in a bath at the desired temperature for 30 min. A bent (45°)

[15] L. R. Schroeder, Doctoral Dissertation, The Institute of Paper Chemistry, Appleton, Wisconsin, June 1965.

[16] H. Lund and J. Bjerrum, *Ber.*, 1931, **64**, 210.

[17] D. P. Hultman, L. R. Schroeder, and F. C. Haigh, *J.C.S. Perkin II*, 1972, 1063.

connecting tube was placed between the flasks and the contents were mixed. Time zero was taken to be the point at which mixing was begun. A sampling chamber [17] was attached to the flask containing the reaction solution to reduce the possibility of contamination by water during sampling, and the flask was returned to the constant temperature bath.

A sample of the reaction solution was immediately transferred to a polarimeter cell at the desired reaction temperature. Readings were begun *ca.* 1 min from initiation.

Quantitative G.l.c. Analysis.—The reactant and carbohydrate products of the TMGB reactions were identified and measured quantitatively by g.l.c. Prior to g.l.c. analysis, samples of the reaction mixtures were subjected to a series of chemical reactions in which unchanged TMGB was converted into phenyl 2,3,4,6-tetra-*O*-methyl-1-thio-β-D-glucopyranoside, and 2,3,4,6-tetra-*O*-methyl-D-glucopyranose (the product of any hydrolysis of TMGB which might have occurred) was converted into 2,3,4,6-tetra-*O*-methyl-1-*O*-propanoyl-D-glucopyranose.

Samples (5 ml) taken to determine the ratio of anomeric glucosides as a function of time, were pipetted into a solution (0.66 ml) of benzenethiol in methanolic 0.5M-sodium methoxide (1 : 10 v/v). The desired amount of a standard solution (*ca.* 0.05M) of internal standard, n-butyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside, in chloroform was added to the samples which were then concentrated *in vacuo* to an oil. The oil was treated with propanoic anhydride–pyridine (*ca.* 2 ml; 1 : 2 v/v) at room temperature with occasional swirling for 24 h. Water (15 ml) was added and, after 15 min, the mixture was extracted with chloroform (3 × 15 ml). The extracts were washed with 2N-hydrochloric acid in saturated brine (10 ml), N-sodium hydroxide in 10% brine (10 ml), and water (10 ml). After each washing the aqueous phase was back-extracted with a comparable volume of chloroform. The chloroform solutions were then combined and concentrated *in vacuo* to an oil. In cases where residual propanoic acid was noted, it was removed as its aqueous azeotrope by adding several ml of water and reconcentrating. The oil was dissolved in chloroform (*ca.* 0.5 ml) and analysed by g.l.c.

The response factors required for quantitative g.l.c. were determined by subjecting synthetic mixtures to the analysis procedure.

The g.l.c. retention times (min) were: n-butyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside 12.3, 2,3,4,6-tetra-*O*-methyl-1-*O*-propanoyl-D-glucopyranose anomers 23.0 and 28.4), cyclohexyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside 38.4, cyclohexyl 2,3,4,6-tetra-*O*-methyl-α-D-glucopyranoside 42.8, and phenyl 2,3,4,6-tetra-*O*-methyl-1-thio-β-D-glucopyranoside 68.7.

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