Mutarotation of Glucose Derivatives in Solutions of Surfactants in Organic Solvents: Co-operativity and Bimodal Catalytic Behaviour

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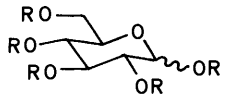
The mutarotation of glucose, 2,3,4,6-tetra-*O*-methylglucose, 3-*O*-hexyl-, 3-*O*-dodecyl-, 4,6-*O*-butylidene, 4,6-*O*-hexylidene, and 4,6-*O*-decylidene-glucose has been studied kinetically in aqueous solution and in the following surfactant–solvent systems: AOT–heptane, AOT–$CHCl_3$, CPC–$CHCl_3$, CTAC–$CHCl_3$, CPS–$CHCl_3$ and $C_{16}E_6$–tetradecane. Below a low critical surfactant concentration, mutarotation is undetectably slow, but above it the rate increases, usually in a sigmoidal fashion reaching a maximum value at concentrations above *ca.* 40 mmol l^{-1}. Maximum rates are usually less than those observed in water except for AOT-containing systems which often, but not always, give higher rates. The dependence of rate on surfactant concentration does not in general fit the pseudophase model of micellar catalysis, but can be treated using Piszkiewicz's co-operativity model. This indicates in a number of cases bimodal catalytic behaviour, a non-co-operative mode at concentrations just above the critical level, and a co-operative mode giving more efficient catalysis at higher concentrations. For AOT–heptane the bimodal pattern is reversed and evidence is presented that the co-operative effects observed at low surfactant concentrations probably represent catalysis in premicellar aggregates. N.m.r. spectroscopic studies (δ, T_1) of the protons of water solubilised in the surfactant–solvent systems are reported but do not show helpful correlations with catalytic efficiency in the systems studied. A better guide to catalytic efficiency is provided by solvatochromic measurements using *N*-hexadecylpyridinium iodides incorporated into the catalytic aggregates to report on the polarity in the interior. A possible extension to this approach is discussed.

Solutions of surfactants in organic solvents have attracted considerable interest in recent years.[1] The surfactants are known to form aggregates in which their polar head-groups form a core surrounded by a non-polar region, consisting of the surfactant hydrocarbon tails in contact with the bulk solvent, and these are usually referred to as reverse micelles. Such systems have the ability to solubilise polar molecules such as water in apolar solvents. They also have the ability to catalyse organic reactions and such catalysis has been claimed to model that of certain enzyme systems.

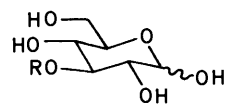
Our interest is in the catalytic functions of reverse micelles in their own right, since such catalysis may be involved, or may be induced, in a number of practical situations in which surfactants, apolar phases, and water are present. The work described here was undertaken to obtain some basic appreciation of the factors involved in systems known to form reverse micelles which lead to changes in reaction rate. Although it was our ultimate intention to examine hydrolytic reactions, we began by investigating mutarotation (*i.e.* equilibration of α- and β-anomers) of glucose derivatives for the following reasons. (*i*) Catalysis of mutarotation has been intensively investigated in homogeneous solution.[2] (*ii*) The reaction is known to take place in reverse-micellar systems containing solubilised water.[3] (*iii*) It can easily be followed even at low sugar concentrations by measurement of optical rotation. (*iv*) Manipulation of the sugar structure should permit controllable variations in the interaction of such substrates with the surfactant aggregates.

Studies of mutarotation in homogeneous aqueous solution have shown that there is usually a region around pH 7 where acid–base catalysis makes little contribution to the reaction rate. For example, for glucose (Gl) and 2,3,4,6-tetra-*O*-methylglucose (TMG), the rates of mutarotation are almost invariant over the pH range 2—7.5.[4] Moreover, in this region, ionic strength effects on the reaction rate are negligible,[5] an important property since we wish to compare the effects of anionic, cationic, zwitterionic, and non-ionic surfactants. Uncatalysed (*i.e.* water-catalysed) mutarotation is believed[6] to take place within a rather highly structured complex of the sugar molecule and two (or more) water molecules. Consequently, since water solubilised in reverse-micellar systems is thought to be ordered differently from bulk water, the rate of mutarotation should be a sensitive probe of organisation within the micellar core.

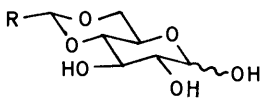
In the present paper we survey the effects of a range of reverse micellar systems on the kinetics of mutarotation of glucose and a number of glucose derivatives, TMG, 3-*O*-alkyl- and 4,6-



Gl R = H
TMG R = Me



3OHG R = n-C_6H_{13}
3ODG R = n-$C_{12}H_{25}$



4,6BG R = n-C_3H_7
4,6HG R = n-C_5H_{11}
4,6DG R = n-C_9H_{19}

Table 1. Mutarotation of glucose and some derivatives[a] in reverse micellar systems at 30 °C

Surfactant[b]	Solvent	R	$10^4 k^m_{obs}/s^{-1}$ Gl	TMG	3OHG	3ODG	4,6BG	4,6HG	4,6DG
AOT	n-C_7H_{16}	10	4.3	5.0[f]	3.9	3.0	29.0	32.9	17.9
AOT	$CHCl_3$	5	18.5	*c*	2.0	n.d.	13.6	9.5	10.4
CPC	$CHCl_3$	10	3.8	*c*	2.0	1.6	1.3	1.4[g]	1.1
CTAC	$CHCl_3$	10	n.d.	*c*	n.d.	n.d.	n.d.	1.4	n.d.
CPS	$CHCl_3$	10	3.7	0.05	n.d.	1.2	n.d.	n.d.	n.d.
$C_{16}E_6$	n-$C_{14}H_{30}$	10	n.d.	8.9[e]	*d*	4.2[e]	n.d.	8.1[e]	5.7[e]
None	H_2O		4.1	3.6	5.6	*d*	19.3	18.5	*d*

[a] Concentration 7.5 mmol l^{-1} except for TMG (5 mmol l^{-1}). [b] Concentration 0.1 mol l^{-1}. [c] No mutarotation detected. [d] Substrate will not dissolve. [e] Temperature 45 °C. [f] $R = 2$; $k^m_{obs} = 2.5 \times 10^{-4}$ s^{-1}; $R = 10$; $k^m_{obs} = 5.0 \times 10^{-4}$ s^{-1}; $R = 20$; $k^m_{obs} = 5.0 \times 10^{-4}$ s^{-1}. [g] $R = 2$; $k^m_{obs} = 0.05 \times 10^{-4}$ s^{-1}; $R = 20$; $k^m_{obs} = 1.4 \times 10^{-4}$ s^{-1}; n.d. Not determined.

Table 2. Observed rate coefficients for mutarotation of glucose derivatives[a] in water and aqueous dioxane at 30 °C

% Dioxane (v/v) in water	$10^4 k_{obs}/s^{-1}$[a] TMG	3OHG	3ODG	4,6BG	4,6HG	4,6DG
0	3.6	5.6	*b*	19.3	18.5	*b*
10	2.2	3.4	*b*		8.3	*b*
30	1.1	2.3	*b*		4.2	*b*
50			1.1			2.2
70	0.4	0.6	0.5	1.1	0.9	1.0

[a] Concentration 7.5 mmol l^{-1} except TMG (5 mmol l^{-1}). [b] Substrate not soluble in this mixture.

alkylidene-glucoses, shown above with their abbreviations. Surfactant solutions in organic solvents are notoriously fickle in their behaviour towards added substances. Water may be solubilised up to quite high levels before the onset of turbidity leading to phase separation. In closely related systems the maximum value of R (defined as $[H_2O]$/surfactant]) may be as high as 50 [sodium bis-2-ethylhexyl sulphosuccinate (AOT) in iso-octane or benzene [7,8]] or as low as 5 [AOT in hexadecane [7]]. The stability of the reverse micelles may be affected adversely or otherwise by further added substances, such as inorganic salts or organic substances, in a manner that is not easy to predict. Consequently it did not prove possible to investigate the mutarotation of particular sugars in all reverse-micellar systems and under identical conditions. Nevertheless certain patterns emerge as will be described. We concern ourselves, in this paper, with consideration of the composition of the aggregates responsible for catalysis of mutarotation and some of the factors controlling their formation. The relationship between the magnitude of the catalytic effect and some more intimate aspects of aggregage structure are also discussed.

Results

Reverse Micellar Systems.—The surfactants used were the anionic AOT, the cationics *N*-hexadecylpyridinium chloride (CPC) and hexadecyltrimethylammonium chloride (CTAC), the zwitterionic sulphobetaine n-$C_{16}H_{33}\overset{+}{N}Me_2(CH_2)_3SO_3^-$ (CPS) and the non-ionic n-$C_{16}H_{33}(OCH_2CH_2)_6OH$ ($C_{16}E_6$). All were used as anhydrous materials except for CPC which was purified and handled as the monohydrate. All except CPS form reverse-micellar solutions in chloroform in the absence of added water; aggregation numbers are reported to be small (*e.g.*, CTAC 4,[9] AOT 5 [10]). CPS is normally insoluble in chloroform unless water is added, and water in general increases aggregation numbers and the size and shape of aggregates, phenomena best documented for AOT in hydrocarbon solvents. In the present work, most experiments with AOT were conducted in heptane. The non-ionic $C_{16}E_6$ was used only in tetradecane or heptane. In these solvents sonicated solutions (R = 0—20) became turbid when allowed to stand at room temperature but were stable at 45 °C; all experiments were conducted at this higher temperature.

For the kinetic experiments, sugar substrates were usually 7.5 mmol l^{-1} (5 mmol l^{-1} for TMG), this concentration permitting reliable and reproducible rotation changes to be measured. Surfactant, solvent, and R-value were chosen so as to permit visually clear reaction solutions to be quickly and easily achieved.

Kinetics: Preliminary Survey.—With all the sugar substrates mutarotation was undetectably slow in the water-saturated organic solvents. Above a certain low surfactant concentration, which we shall regard as the operational critical micelle concentration (c.m.c.), mutarotation occurred, the rate increasing with increasing surfactant concentration at fixed R up to a maximum value k^m_{obs}. Typical values of c.m.c. were in the range 0.1—0.5 mmol l^{-1} and maximum rates were usually reached when the surfactant concentration was *ca.* 40 mol l^{-1}. Table 1 summarises values of k^m_{obs} for all the systems examined usually at a surfactant concentration of 0.1 mol l^{-1} and 30 °C. Also included are values of the rate coefficients for the spontaneous (water-catalysed) mutarotation of the substrates in neutral aqueous solution at 30 °C.

The results display a complex pattern from which we draw attention to the following points. (*i*) In most of the surfactant–solvent–water systems studied, k^m_{obs} is less than the value achievable in homogeneous aqueous solution [$k^m_{obs}(H_2O)$], but values of $k^m_{obs}/k_{obs}(H_2O)$ vary widely with the substrate and surfactant/solvent. (*ii*) For some, but not all, glucose derivatives in AOT-containing media, k^m_{obs} is substantially greater than $k_{obs}(H_2O)$, the largest rate factor approaching 2. (*iii*) Values of k^m_{obs} are lowered at low R.

The variability of $k^m_{obs}/k_{obs}(H_2O)$ can be expected to arise from a combination of factors. These will probably include the location and tightness of binding of the substrate molecules in the surfactant–water aggregate, the activity of water in the vicinity of the substrate, and the polarity of this microenvironment. As a guide to the magnitude of the kinetic effects of the last two factors, the rates of mutarotation of some of the substances in water–dioxane mixtures were measured (Table 2). All show a marked deceleration as the proportion of dioxane is increased. The solvent mixtures give wide variations in polarity and water activity which might be expected to cover the variations within the aggregates present in the surfactant solutions. Such factors

Table 3. Mutarotation of 3OHG in CPC–$CHCl_3$–H_2O (R = 10) at 30 °C

[CPC]/mmol l^{-1}	0.5	1.5	3.0	4.0	5.0	6.0	8.0	10	15	20	25
$10^4 k_{obs}/s^{-1}$	v. slow	0.10	0.43	0.83	1.30	1.50	1.74	1.85	2.0	2.01	2.06

Table 4. Mutarotation of 4,6HG in CPC–$CHCl_3$–H_2O (R = 10) at 30 °C

[CPC]/mmol l^{-1}	1.0	1.5	3.0	5.0	6.0	7.0	8.0	10	15	20	25	50
$10^4 k_{obs}/s^{-1}$	0	0.05	0.10	0.26	0.35	0.53	0.71	1.15	1.35	1.41	1.45	1.45
	(0)[a]	(0)	(0.10)	(0.40)	(0.60)			(1.4)	(2.4)	(3.7)	(4.1)	(5.6)

[a] Figures in parentheses refer to 40 °C.

Table 5. Mutarotation of 3ODG in CPS–$CHCl_3$–H_2O (R = 10) at 30 °C

[CPC]/mmol l^{-1}	0.25	0.5	1.0	2.0	3.2	5.0	6.2	7.0	7.5	8.5	9.0	10	11	12.5	25
$10^4 k_{obs}/s^{-1}$	0	0.013	0.045	0.11	0.19	0.30	0.45	0.59	0.77	0.90	0.93	0.96	0.99	1.01	1.02

Table 6. Mutarotation of TMG in AOT–heptane–H_2O (R = 20) at 30 °C

[AOT]/mmol l^{-1}	0.1	0.3	0.4	0.5	0.6	0.75	0.8	0.9	1.0	1.2	1.4	1.6
$10^4 k_{obs}/s^{-1}$	v. slow	0.70	0.87	1.10	1.28	1.40	1.49	1.55	1.60	1.63	1.65	1.66

[AOT]/mmol l^{-1}	2.5	3.0	5.0	6.2	10	12.5	20	25	40	50	60	100
$10^4 k_{obs}/s^{-1}$	1.68	1.68	2.30	2.75	3.4	3.8	4.1	4.3	4.7	4.75	5.0	5.1

can, however, only explain values of k^m_{obs} less than $k_{obs}(H_2O)$; the faster rates found in the AOT-containing solvents suggest that a more detailed consideration of the role of water at the molecular level is necessary in all systems.

The Effect of Surfactant Concentration.—In order to throw more light on the formation of the catalytically important aggregates, some of the systems in Table 1 have been examined in greater detail with respect to the effect of the surfactant concentration at fixed R. The results are compiled in Tables 3—6, and these show quantitative differences in behaviour within the general pattern described above.

(*a*) CPC–$CHCl_3$–H_2O (R = 10). Using 3OHG as the substrate, the pattern of behaviour is the simplest. Mutarotation is detectable only above [CPC] = 0.5 mmol l^{-1} whereafter the rate increases in a sigmoidal fashion to a maximum of [CPC] = *ca.* 50 mmol l^{-1}. When 4,6HG is the substrate the behaviour is rather similar but the initial rate rise immediately above the c.m.c. is less steep.

(*b*) CPS–$CHCl_3$–H_2O (R = 10). The substrate examined here was 3ODG and the c.m.c. (*ca.* 0.3 mmol l^{-1}) was less clearly defined than in the CPC solutions. Above the c.m.c. the rate of mutarotation increased steeply before reaching a maximum around 20 mmol l^{-1}.

(*c*) AOT–Heptane–H_2O (R = 20). The system with TMG as the substrate showed the most complex behaviour. The mutarotation rate rose in a clean sigmoidal fashion above the clearly defined c.m.c. (0.1 mmol l^{-1}), reaching a plateau in the concentration range 1—4 mmol l^{-1}). Thereafter the rate increased again in a sigmoidal curve to a rate maximum some three times the plateau value at *ca.* 50 mmol l^{-1} AOT. This bimodal behaviour gives a particularly clear indication of the existence of two distinct types of catalytically significant complex.

The operational c.m.c. values for CPC–$CHCl_3$ are to be compared with values of 0.17 mmol l^{-1} for CPC–benzene[11] and 0.45 mmol l^{-1} for dodecylpyridinium chloride–$CHCl_3$,[12] both determined by a tetracyanoquinodimethane (TCNQ)-solubilisation technique at 25 °C. For AOT, reported c.m.c.s[1e] are 0.49 mmol l^{-1} in iso-octane (by light scattering), 1.3 mmol l^{-1} in cyclohexane, 2—3 mmol l^{-1} in benzene (by a variety of techniques), and 0.16—0.6 mmol l^{-1} in CCl_4 (by vapour pressure osmometry and TCNQ solubilisation). Significantly, for CPC, the present c.m.c. value is concordant with those from another technique, whereas for AOT, admittedly in other solvents, the reported values span the range from the present operational value to the first plateau concentration.

N.m.r. Spectroscopic Studies of Surfactant Solutions.—In order to throw more light on the interaction of the various components of the aggregates present, solutions of surfactants in organic solvents were examined by n.m.r. spectroscopy. Attention was focused particularly on the protons of solubilised water over a range of R, but in the case of CPC–$CDCl_3$ this variation in water content led to chemical shift changes of nuclei in the surfactant itself (Table 7). These were most marked for 2-H and 6-H of the pyridinium ring and the methylene protons of the hexadecyl chain closest to the pyridinium nitrogen (C-1′). Longitudinal relaxation times (T_1) of the water protons as a function of R are also included in Table 7 where they are compared with reported values for AOT–H_2O–heptane;[13] the variation is much smaller in the cationic surfactant system than for AOT. The chemical shift of the OH protons in $C_{16}E_6$–heptane–H_2O, CTAC–$CDCl_3$–H_2O, and CPS–$CDCl_3$–H_2O together with peak widths at half height ($\nu_{\frac{1}{2}}$) again as a function of R are in Table 8. All the systems show a downfield shift of the water proton signal as R increases the value of δ_{H_2O} approaching that of bulk water (*ca.* 4.9 p.p.m.). The largest variation in chemical shift was observed with CTAC–$CDCl_3$. The results for $C_{16}E_6$–heptane are of course complicated by exchange phenomena which are presumably responsible for the dramatic variation in $\nu_{\frac{1}{2}}$.

A few experiments were also undertaken to probe the core of the aggregates in AOT–heptane solutions containing water at R = 5 and 20 in the presence of a substrate molecule, TMG. [Experiments in which *p*-nitrophenyl picolinate (PNPP) was added are also included.] The probe here was the sodium ion, the n.m.r. linewidth of which reflects, *inter alia*, the symmetry of its immediate environment, namely its solvation by water molecules.[13,14] The results are in Table 9 and it can be seen that,

Table 7. Effect of solubilised water on n.m.r. spectroscopic parameters of CPC (0.2 mmol l^{-1}) in $CHCl_3$

(*a*) Longitudinal relaxation of water protons

	$(T)^{-1}/s^{-1}$	
R	CPC–$CHCl_3$	AOT–heptane[a]
1	1.78	12.5
2	1.89	12.5
3	1.89	8.7
5	1.35	4.7_3
10	1.00	1.8_0
15		1.0_7
20		0.9_0

(*b*) ^1H Chemical shifts/p.p.m.

	δ_{H_2O}	$\delta_{o\text{-}H}$ [b,c]	$\delta_{C\text{-}1}$ [b,d]
1.0	3.3	9.54	4.97
2.4		9.32	4.91
3.8		9.22	4.86
5.2		9.15	4.83
6.6		9.13	4.81
8.0		9.10	4.79
10.7	4.3	9.08	4.77
13.5		9.07	4.77
16.2	4.5	9.06	4.77

[a] Interpolated from the data of ref. (13) for comparison. [b] $\nu_{\frac{1}{2}}$ *ca.* 4 Hz throughout. [c] $\delta_{o\text{-}H}(CD_3OD)$ 9.05 p.p.m. [d] $\delta_{C\text{-}1}(CD_3OD)$ = 4.67 p.p.m.

Table 8. Linewidths and chemical shifts in the ^1H n.m.r. spectra of water solubilised in surfactant–organic solvent systems

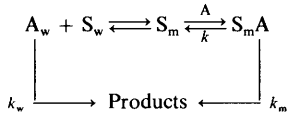
System	Concn/ mol l^{-1}	*T*/°C	*R*	δ_{OH}	$\nu_{\frac{1}{2}}$/Hz
$C_{16}E_6$–heptane	0.2	45	0	2.58	
			1	2.69	37
			2	2.78	24
			3	3.83	6
			5	3.99	5
			10	4.10	2
			20	4.21	2
CTAC–$CHCl_3$	0.2	30	0.25	2.43	7.4
			5	3.87	3.3
			10	4.25	4
			15	4.36	5
			20	4.45	5
CPS–$CHCl_3$	0.05	30	1.1	3.03	8.7
			2.2	3.22	7.3
			4.4	3.54	5.3
			8.9	3.93	10.6

over the AOT concentration range 10—100 mmol l^{-1}, $\nu_{\frac{1}{2}}$ is almost invariant but values at $R = 5$ are 3- to 4-fold higher than at $R = 20$, indicating lower symmetry in the smaller water pools. At the lowest AOT concentration examined, $\nu_{\frac{1}{2}}$ shows signs of increasing, suggesting that the aggregates at lower concentration provide a less symmetrical (or more viscous)[15] environment for the sodium ions and this may reflect a change in structure. TMG (5 mmol l^{-1}) has a negligible effect on $\nu_{\frac{1}{2}}$ at $R = 20$ and only a small one at $R = 5$. However, PNPP, even at the 0.2 mmol l^{-1} level, has a pronounced effect and this is in opposite directions at low and high AOT concentrations.

Solvatochromic Measurements.—The polarity of the surfactant aggregate–solubilised water interface was investigated by the introduction of hexadecylpyridinium iodides into the surfactant solutions. The energies of the charge-transfer transition in such salts can be used as an index of polarity as originally developed by Kosower[17] for homogeneous solutions using *N*-ethyl-4-methoxycarbonylpyridinium iodide, but problems associated with the location of such probes in the more complex environment of micellar systems have been documented.[18] The presence of the hexadecyl chain in the probes used here was expected to lead to co-micellisation so that the pyridinium iodide moiety would lie in the core of the aggregate. The probe concentrations were always less than 1% of the surfactant concentrations so as to minimise the effect of the probe on the aggregates. *N*-Hexadecylpyridinium iodide alone in organic solvents, unlike the chloride, is incapable of solubilising water. Table 10 gives the results which are compared with values obtained in dioxane–water mixtures. It can be seen that all the surfactant systems examined show polarities equivalent to dioxane and water mixtures containing 20—100% dioxane.

Discussion

Kinetic Effects of Aggregation: Co-operativity.—It is now customary to discuss catalytic effects in aqueous micellar systems in terms of the pseudophase model in which the reactant(s) A are distributed between aqueous and micellar pseudophases and have characteristic rate coefficients for reaction in these two environments (Scheme 1; S represents the surfactant and the subscripts m and w signify micelle and water).



Scheme 1.

This scheme leads to expression (1) for the dependence of the observed rate co-efficient of a reaction, first order in A only, ($k_{obs} = -d\ln[A]/dt$) on the total concentration $[S]_t$ of surfactant in the system. [More complex expressions are necessary if the rate is dependent on the concentration of a second reagent molecule, but are unnecessary here.] The form of (1) is that of Michaelis–Menten kinetics, and by rewriting the expression in reciprocal form, by analogy with the Lineweaver–Burk treatment, the characteristic parameters of binding (K/N), where N is the micellar aggregation number, and reactivity in the two pseudophases can be obtained.

$$k_{obs} = \frac{k_w + k_m K([S]_t - \text{c.m.c.})/N}{1 + K([S]_t - \text{c.m.c.})/N} \quad (1)$$

An analagous treatment may be applied to the present system with k_w replaced by k_o, the rate constant for the reaction of A in the bulk organic solvent and k_m refers to reaction in the water-containing aggregate. The corresponding expression in reciprocal form is (2). Using the operational c.m.c. values derived from the kinetic experiments, equation (2) has been tested

$$(k_{obs} - k_o)^{-1} = (k_m - k_o)^{-1}\,[1 + N/K([S]_t - \text{c.m.c.})] \quad (2)$$

against the results in Tables 3—6. With the exception of the data for AOT–heptane–H_2O ($R = 20$) with TMG as substrate at AOT concentrations greater than 4 mmol l^{-1}, the results do not fit equation (2) over any substantial range of surfactant concentration. Pronounced upward curvature is observed, and the failure is confirmed by using Eadie–Hofstee plots. Clearly there is a failure of one or more of the assumptions upon which the pseudophase model is based. These assumptions are (*i*) the c.m.c. gives the concentration of monomeric surfactant present, the remainder being in the form of micelles that are

Table 9. Effects of concentration and additives on linewidths of the ^{23}Na n.m.r. signal[a] from solutions of AOT in heptane at 30 °C[b]

		[AOT]/mol l^{-1}			
		0.1	0.05	0.01	0.005
Additive	R	$10^{-2}\nu_{\frac{1}{2}}$/Hz			
None	5	6.0 ± 0.2	4.6 ± 0.2	6.7 ± 0.2	14.2 ± 2.5
TMG (5 mmol l^{-1})	5	5.3 ± 0.2		5.5 ± 0.2	5.7 ± 0.2
PNPP (0.2 mmol l^{-1})	5	3.2 ± 0.2	3.5 ± 0.5	4.0 ± 0.5	22.5 ± 3.3
None	20	1.7 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	2.0 ± 0.5
TMG (5 mmol l^{-1})	20	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	2.5 ± 0.5

[a] At 66.165 MHz. [b] Measurements by Dr. D. Attwood.[16]

Table 10. Charge-transfer transition energies (kcal mol^{-1}) for hexadecylpyridinium iodides in solution at 30 °C

(*a*) Surfactant solutions (0.1 mol l^{-1})

R	AOT–heptane	CPC–$CHCl_3$[c]	CPS–$CHCl_3$	$C_{16}E_6$–heptane[d]
0	78.2,[a] 78.5[b]			78.1[a]
1	78.7[a]	77.9[b]	78.6[a]	
2	78.9[a]		78.7[a]	78.5[a]
3	79.2[a]		78.8[a]	
5	79.3[a]		78.9[a]	
10	79.6,[a] 80.0[b]	78.6[b]	78.9[a]	78.8[a]
20	80.2[a]			

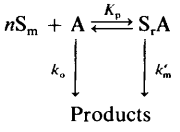
(*b*) Homogeneous solutions

% Dioxane in water (v/v)			
100	70	50	20
78.1	78.8	79.4	80.2[e]

[a] CPI (1 mmol l^{-1}). [b] CPI (0.11 mmol l^{-1}). [c] [CPC] = 0.025 mol l^{-1}. [d] At 45 °C. [e] By extrapolation.

monodisperse; (*ii*) binding of reactants (and products) does not significantly alter the equilibrium between monomeric and aggregated surfactant. The shortcomings of equation (1) in aqueous micellar systems close to the c.m.c. have been recognised, but are usually ignored.[19]

The results in Table 1, showing that the efficiency of catalysis of mutarotation by a given surfactant–solvent system can vary markedly from one glucose substrate to another, suggest that the nature of the catalytic aggregates is substrate dependent. The co-operativity model of Piszkiewicz[20] thus appears to be a more realistic way of viewing the present systems. In this model, the substrate is seen as critically influencing the formation of the aggregates in which catalysis takes place. Scheme 2 is a modified version of Piszkiewicz's original formulation which emphasises the fact that the surfactant is aggregated (S_m) even in the absence of reactant. Reaction occurs in aggregates that are different both in aggregation number and because of the presence of the reactant, and these aggregates are formed by the interaction of one or more S_m with each A. If $[S]_t \gg [S]$ and $[S_rA] \ll [S_m]$,



Scheme 2.

then $[S_m] = [S]_t/N$, where N is the aggregation number in the absence of A, and the expression for k_{obs} ($= -d\ln[A]/dt$) is equation (3), which can be tested in the logarithmic form (4). The exponent n is usually referred to as the index of co-operativity, values of $n > 1$ signifying the co-operative binding of A and S to form the reactive aggregates. When $n = 1$, expression (3) has a form identical to equation (1) as is required if the binding of A does not affect the equilibrium between S and S_m.

$$k_{obs} = \frac{k_o + k'_m K_p N^{-n}[S]_t^n}{1 + K_p N^{-n}[S]_t^n} \quad (3)$$

$$\log \frac{k_{obs} - k_o}{k'_m - k_{obs}} = \log(K_p N^{-n}) + n \log[S]_t \quad (4)$$

The present results have been fitted to equation (4) using $k_o = 0$ and taking k'_m as the limiting value of k_{obs} at high $[S]_t$. The resulting correlations are shown in the Figure. It should be borne in mind that in the case of mutarotation, for the sample expression to apply, K_p has to be the same for the binding of both anomers in the reactive complex and that all rate coefficients refer to the sum of rate constants for $\alpha \longrightarrow \beta$ and $\beta \longrightarrow \alpha$. For the mutarotation of 3OHG in CPC–$CHCl_3$–H_2O ($R = 10$) simple Piskiewicz behaviour is observed with $n = 2.71$ ($r = 0.995$) and $\log(K_p N^{-n}) = 6.36$. However, mutarotation of 4,6HG in the same medium shows apparent bimodal behaviour with two linear correlations according to equation (4), one at low CPC concentration having $n = 1.05$, $\log(K_p N^{-n}) = 1.53$, the other at concentrations above 5 mmol l^{-1} with $n = 3.87$ ($r = 0.995$) $\log(K_p N^{-n}) = 8.16$. Rather similar behaviour is observed with 3ODG in CPS–$CHCl_3$–H_2O ($R = 10$) n being 1.17 ($r = 0.995$), $\log(K_p N^{-n}) = 2.25$ up to *ca.* 5 mmol l^{-1} and thereafter rising abruptly to $n = 6.82$ ($r = 0.995$), $\log(K_p N^{-n}) = 14.9$. Bimodal behaviour is most pronounced with TMG in AOT–heptane–H_2O ($R = 20$); in this case the two sigmoidal rate increases with surfactant concentration have been treated separately using the values of k_{obs} in the two plateau regions as k'_m for the low- and high-concentration ranges. In this case the n values are 3.00 [$r = 0.991$; $\log(K_p N^{-n}) = 10.2$] for the low-concentration range (up to 3 mmol l^{-1}) and 1.21 [$r = 0.997$; $\log(K_p N^{-n}) = 2.73$] at higher concentrations, the reverse of the pattern found in the other bimodal systems. It seems necessary to put forward different interpretations of the two types of bimodal behaviour found with CPC–$CDCl_3$ and CPS–$CDCl_3$ on the one hand and AOT–heptane on the other. It should be noted that the discontinuities in the Piszkiewicz plots all occur at surfactant concentrations of the same order of magnitude as the substrate concentration.

For $CDCl_3$ solutions of CPC and CPS, an apparently non-co-operative interaction occurs at low surfactant concentration for 4,6HG and 3ODG but not for 3OHG. At these low concentrations the aggregation behaviour of the surfactant is not well understood even in the absence of the complications resulting from the presence of the substrate, but the pseudophase assumption of monodisperse aggregates at all

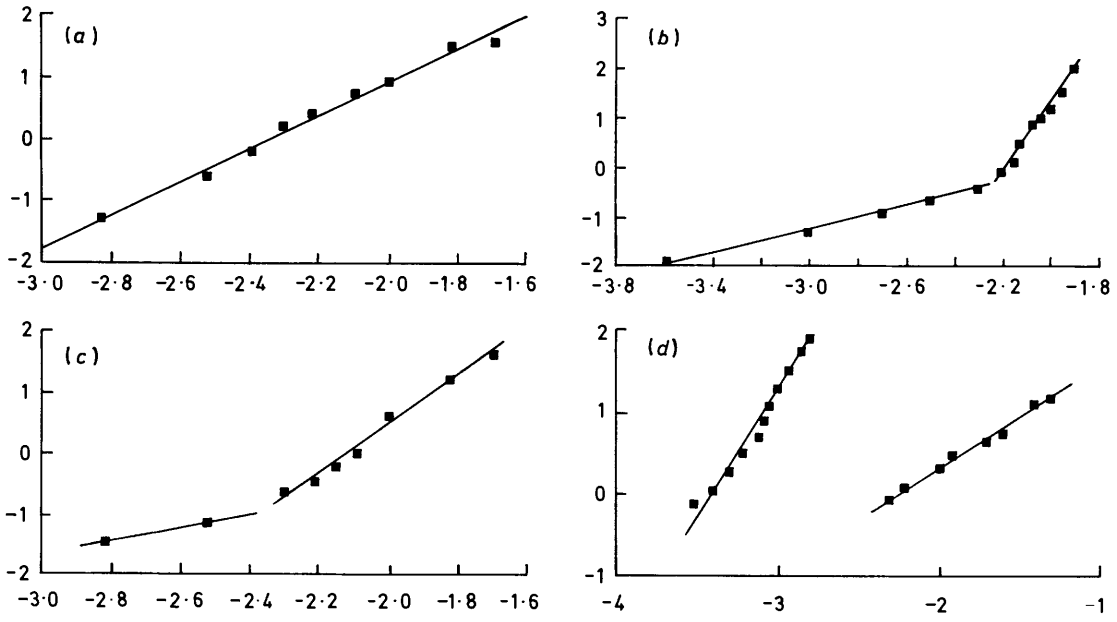


Figure. Piszkiewicz plots according to equation (4). In each case the ordinate is log $\{(k_{obs} - k_o)/(k'_m - k_{obs})$ and the abscissa log $[S]_t$. (*a*) Mutarotation of 3OHG in CPC–$CHCl_3$–H_2O ($R = 10$) with $k'_m = 2.06 \times 10^{-4}$ s^{-1}, $k_o = 0$; (*b*) 4,6HG in CPC–$CHCl_3$–H_2O ($R = 10$), $k'_m = 1.45 \times 10^{-4}$ s^{-1}, $k_o = 0$; (*c*) 3ODG in CPS–$CHCl_3$–H_2O ($R = 10$), $k'_m = 1.02 \times 10^{-4}$ s^{-1}, $k_o = 0$; (*d*) TMG in AOT–heptane–H_2O ($R = 20$), $k'_m = 1.68 \times 10^{-4}$ s^{-1} (low-concentration range), 5.1×10^{-4} s^{-1} (high-concentration range) $k_o = 0$.

surfactant concentrations above the c.m.c. is probably invalid. The simplest interpretation of the observed non-co-operative behaviour is, then, that mutarotation occurs in a complex of approximately 1:1 stoicheiometry of substrate and surfactant plus associated water molecules. Once the surfactant concentration is in excess over that of the substrate, larger aggregates are formed, the composition of which is now substrate-dependent. Co-micellisation of the substrate molecules, particularly 3ODG, may be expected, but the reason why this substrate shows non-co-operative behaviour at low concentration when 3OHG behaves co-operatively over the concentration range is hard to understand.

For AOT in hydrocarbon solvents, more detailed information is available concerning aggregation both as a function of [AOT] and of R. The high-concentration range studied here which shows non-co-operative behaviour corresponds roughly to a range over which it is known from proton-correlation spectroscopy that AOT aggregates have a constant Stokes radius. The assumption of monodisperse aggregates would thus seem to be a good one; at $R = ca.$ 20, N_{AOT} is reported to be *ca.* 300 with some 6 000 water molecules per aggregate.[21] In consequence it is not perhaps surprising that the aggregates can accommodate one (or several) TMG molecules without serious disturbance to such a large entity. At low concentrations, say below 10 mmol l^{-1}, aggregates are known to be smaller and here binding of substrate molecules might be expected to be a co-operative phenomenon. Clearly the disruption of aggregates by the substrate must stop short of the complete disruption and subsequent formation of the sort of complex postulated for the CPC and CPS systems. On the other hand it must be recognised that the concentration range is in that grey area where it cannot be unambiguously determined whether a c.m.c. has been reached, since different physical measurements give conflicting answers. We may indeed be dealing with pre-micellar aggregates which have been much discussed in this field.[21] On the other hand, a multiple, equilibrium model of aggregation in these systems can be used and the behaviour of AOT in benzene has been described in terms of two aggregates (a hexamer and tetradecamer) the formation of which begins around 10^{-4} mol l^{-1} AOT.[22] Qualitatively there is a clear parallel with the present results.

While recognising that our inferences can only be tentative because of the restricted number of data available to us, it appears to us that the index of co-operativity is a sensitive measure of the substrate's interaction with the surfactant. This suggests that a complete understanding of the origins of the catalysis requires an intimate knowledge at the molecular component level of the interactions within the aggregates present, especially, in the case of mutarotation, with regard to the average location and orientation of the substrate in relation to the water molecules solvating the surfactant head-group. We attempt to support this view below.

The Microenvironment at the Reaction Site.—Co-operativity of binding of the substrate, surfactant, and water molecules provides a framework for the understanding of the effect of surfactant concentration on catalytic efficiency in different systems. The interactions giving rise to the co-operative binding may also be responsible for the rate differences between the various surfactant–solvent systems towards a given substrate in the fully bound state, as exemplified in Table 1. The general pattern is that AOT-containing systems lead to the most effective catalysis, often more effective than in water; cationic surfactant–$CHCl_3$ systems are the least effective and the non-ionic and zwitterionic surfactants show behaviour that is highly substrate dependent. Such results require detailed knowledge of the microenvironment of the bound substrate. It has to be recognised that the aggregates in these systems are dynamic entitities and the probes that we have used give only an average measure of the environment of the probe molecule.

The water molecule in the core of the aggregates provided one such probe. The proton chemical shift downfield from $SiMe_4$ increases as the amount of solubilised water increases in all surfactant–organic solvent systems. Comparison of the present results (Tables 7 and 8) with those for AOT–heptane reported by Wong *et al.*[13] indicates that, for the system used for mutarotation, δ_{OH} most nearly approaches that in bulk water in AOT–heptane–H_2O ($R = 20$) (4.7 p.p.m.), is smaller for the

cationics in $CHCl_3$ with $R = 10$, and is least for CPS–$CHCl_3$–H_2O ($R = 10$). Clearly δ_{H_2O} provides no simple guide to the likely kinetic effect. Similarly T_1 values fail to discriminate between a system showing efficient catalysis and one much less effective. Thus the T_1 values for the AOT–heptane system reproduced in Table 7 indicate considerable motional restriction at low R, but at $R = 20$ the solvation needs of the sodium and sulphonate ions are satisfied and the 'free' water dominates the relaxation situation. Comparison of the results with those in CPC–$CHCl_3$ show that here T_1 varies relatively little as R increases, values being comparable to the more aqueous AOT solutions over the whole range of R. Indeed T_1, in CPC–$CHCl_3$–H_2O ($R = 10$) is very close to that interpolated for AOT–heptane–H_2O ($R = 20$). It would seem that, over the whole range of R studied, water molecules are more loosely bound in CPC–$CHCCl_3$ around the pyridinium nitrogen and Cl^-; the linewidths observed in this system and CTAC–$CHCl_3$ bear this out.[23] Thus both the most effective catalytic systems and the least effective contain essentially 'free' water, *i.e.* water–water interactions are more important than interaction between water molecules and the surfactant head-groups, a situation that Eicke[1e] at least would regard as characteristic of microemulsions rather than reverse micelles.

The use of hexadecylpyridinium iodides CMPI and CPI to probe the polarity of the aggregate cores does give a crude parallel with the efficiency of catalysis of mutarotation. The observed Z-values of the surfactant systems studied correspond approximately to values observed for dioxane–water mixtures ranging from *ca.* 100% for $C_{16}E_6$ or AOT–heptane with no added water to 20% dioxane for AOT–heptane–H_2O ($R = 20$). For the surfactant solutions used in the mutarotation studies, the Z-values span most of this range and vary in a sequence which roughly and qualitatively matches the observed rates for, say, 4,6HG. That this correspondence, albeit imperfect, is so good is surprising; CMPI and CPI measure the average polarity of the environment of pyridinium iodide moieties in the core of the co-micelle and this may not correspond exactly to the average location of the substrate molecules used. Moreover, a change in the balance between the hydrophilic and hydrophobic properties of the substrate such as a change from 4,6BG to 4,6DG could be expected to lead to a shift in the average location of the substrate to a less aqueous environment. The usefulness of polarity probes thus depends on the degree to which they are able to match the binding of substrates in the aggregate.

A more fruitful way forward may be to try to use the substrate as its own polarity probe, and we offer some additional results here for 4,6HG in CPC–$CHCl_3$–H_2O ($R = 10$). We have observed that in the ^{13}C n.m.r. spectrum of 4,6HG in dioxane–D_2O mixtures, the chemical shift of C-1* in the α-anomer relative to dioxane is invariant over the range 10—70% dioxane. By contrast the signal for C-1 of the β-anomer shifts downfield by 0.4 p.p.m., and that for C-7 in both anomers shifts upfield by 0.6 p.p.m. Over this range of solvent mixtures the shifts of C-7 and C-1β relative to C-1α, which are highly reproducible, are linear functions of the percentage dioxane in D_2O. In CPC–$CDCl_3$–D_2O ($R = 10$), the only surfactant system in which comparable measurements could be conveniently made, the shift of C-7 and C-1β relative to C-1α fell within the range observed in dioxane–D_2O, that for C-7 corresponding to 29.5% dioxane and that for C-1β to 70% dioxane. Taken at face value, the present results seem to suggest that the rather rigid 4,6HG molecule binds to the CPC–D_2O aggregate in $CDCl_3$ with an average location and orientation that places the site of reaction in a rather non-polar environment and the hexylidene moiety in a more aqueous region. Such an orientation could be a factor contributing to retardation of reaction compared with homogeneous aqueous solution and other surfactant systems. We recognise that ^{13}C chemical shifts are determined by a complex combination of factors, but we believe this sort of approach merits further investigation. The results also call attention to the fact that in micellar situations, substrate molecules can span a range of microenvironments and this must be reflected in their behaviour.

* Assignments were made by comparison with methyl 4,6-*O*-hexylidene-α-D-glucoside with assistance from the reported ^{13}C spectrum of methyl 4,6-benzylidene-α-D-glucopyranoside[24] and knowledge of the proportions of α- and β-anomers in the sample of 4,6HG from the ^1H n.m.r. spectrum.

Conclusions

The aggregates formed by surfactant and water in organic solvents are complex entities, the size and nature of which are very sensitive to the conditions including the total surfactant concentration. The concept of a critical micelle concentration, representing a maximum concentration of monomeric surfactant above which monodisperse aggregates form, the situation for aqueous solutions of surfactants, is by no means as clearly established.

The results described here on the mutarotation of glucose derivatives in diverse surfactant–solvent systems are, we recognise, not comprehensive, but they do permit us to make some tentative generalisations. (*i*) There is a surfactant concentration (at fixed R) which can be pinpointed within quite narrow limits, below which mutarotation is undetectably slow and above which reaction occurs. This critical concentration is close to c.m.c. values assigned on the basis of quite different physical measurements. (*ii*) Catalysis of mutarotation varies in efficiency depending not only on the surfactant and solvent but also on the substrate and can show bimodal behaviour. A non-co-operative interaction of substrate and surfactant plus associated water molecules leads to catalysis at concentration just above the critical concentration. At higher surfactant concentrations, co-operative binding of substrate, surfactant aggregates, and water enhances the catalytic effect which reaches a maximum at *ca.* 50 mmol l^{-1} with rates usually lower than are found for the substrate in homogeneous aqueous solution. (*iii*) AOT-containing systems can lead to mutarotation rates higher than in water. Bimodal catalysis is found but this involves co-operative binding at low concentrations and non-co-operative binding above *ca.* 4 mmol l^{-1} AOT in heptane. Here the catalysis in the low concentration range is attributed to premicellar aggregates, while that in more concentrated solutions involves aggregates that, from the work of others, seem to approach the monodisperse ideal and can be treated using the pseudophase model. (*iv*) Catalytic efficiency in mutarotation shows rough parallels with solvatochromic measures of polarity obtained using the probes CMPI and CPI that can form co-micelles with a variety of surfactants. However, a fuller understanding of the catalysis will probably require a more detailed knowledge of the microenvironment of the substrate molecule within the catalytic aggregate and the molecular interactions involved.

Experimental

Apparatus.—N.m.r. spectroscopy. Routine ^1H n.m.r. spectra were recorded at 220 MHz with a Perkin–Elmer R34 CW spectrometer, and ^{13}C spectra at 25.2 MHz using a Varian XL-100 spectrometer, reference: $SiMe_4$. Proton T_1 measurements were made on the latter machine by the 180°–τ–90° pulse sequence method using the intensity expression $A = A_{lim}[1 - 2\exp(-\tau/T_1)]$ where A_{lim} is the limiting peak intensity when the interval τ was large (*ca.* 20 s). ^{23}Na N.m.r. spectra were recorded at 66.2 MHz on a Bruker WM 250 spectrometer.

Optical rotation. A Thorn-NPL automatic digital polarimeter (type 234) was used throughout, operating at 589 nm. The optical cell was of 20 mm path-length and was fitted with a jacket through which thermostatted water circulated. Rotations were recorded directly from the electronic control unit using a Servoscribe 15 chart recorder.

Procedures.—Preparation of solutions. Solutions were made up from carefully dried surfactants and solvents. Solutions of AOT or $C_{16}E_6$ in heptane can be kept for long periods. Chloroform solutions of CPC and CTAC were made up from freshly purified solvents and were used within a day or so. The sulphobetaine CPS shows unusual behaviour; it will dissolve in chloroform only if water is added.

Required R values were obtained by adding the correct volume of water to prepared solutions of the surfactant (suspensions in the case of CPS). All solutions were then sonicated for 5 min before further use. Weighed amounts of substrates or other additives were then introduced and the mixture was subjected to a further period of sonication to facilitate solubilisation.

For optical rotation measurements, solutions were filtered immediately prior to introduction into the cell.

Kinetic Measurements.—Rates of mutarotation were measured polarimetrically on solutions of the glucose substrates (7.5 mmol l^{-1}) in the surfactant solutions prepared as shown above. The change in optical rotation (r_t) with time t followed a first-order kinetic law accurately over several half-lives. Values of the observed first-order rate coefficient k_{obs} ($=k_{\alpha\beta} + k_{\beta\alpha}$, the sum of the forward and reverse rate constants for interconversion of the anomers) were obtained either by a least-squares analysis of sets of values of $\ln(r_t - r_\infty)$ and t or, in cases where difficulties were experienced in determining r_∞, by the Guggenheim method, again with linear regression.

Within runs correlations were excellent, but it proved more difficult to achieve reproducibility from one surfactant solution to another than with homogeneous solutions. Nevertheless reproducibility was always to within better than 10%.

Materials.—Solvents. Water was doubly distilled in an all-glass apparatus. Heptane was distilled through a 10-inch, helix-packed column, rejecting the first and last 10% of the distillate. Tetradecane was a commercial sample and was used without further purification. Chloroform (A.R. grade) was passed through an alumina (Fluka 507C) column immediately prior to use. Dioxane was distilled from sodium under an atmosphere of argon, it was stored frozen.

Surfactants. AOT was purified by the method of Menger and Saito.[25] Commercial CPC·H_2O was recrystallised twice from ethyl acetate–ethanol (95:5) and had m.p. 80—82 °C (lit.,[26] 77—83 °C). *N*-Hexadecylpyridinium iodide (CPI) was prepared from CPC and KI; recrystallised from aqueous KI, it had m.p. 100—102 °C (lit.,[25] 101 °C).

N-*Hexadecyl-4-methoxycarbonylpyridinium iodide* (CMPI). This was prepared by a modification of the procedure of Grob and Renk[27] for the *N*-ethyl salt. A solution of 4-methoxycarbonylpyridine (2 g) and n-hexadecyl iodide (6 g) in dry acetone (4 ml) was allowed to stand at room temperature for 48 h and then refluxed for 30 min. After having been concentrated under reduced pressure, the residue was diluted with light petroleum (b.p. 40—60 °C) and filtered. Recrystallisation from ethyl acetate gave the pure salt as yellow cubes; m.p. 75—85 °C (Found: C, 56.35; H, 8.3; N, 2.75. $C_{23}H_{40}INO_2$ requires C, 56.44; H, 8.18; N, 2.86%).

Pure samples of CTAC and CPS were kindly supplied by Mr. R. Clarke (URPSL) and were used without further purification.

The non-ionic $C_{16}E_6$ was prepared *via* $C_{16}E_3$ as follows. Sodium was added under a nitrogen atmosphere to an excess of triethylene glycol at 70—100 °C, and, when it had all reacted, redistilled hexadecyl bromide was added dropwise with stirring. The reaction mixture was partitioned between saturated aqueous ammonium hydrogencarbonate and butanol, and the butanol layer was washed repeatedly with brine and evaporated. The residual $C_{16}E_3$ was distilled (190—194 °C °C/0.5 mmHg) and recrystallised from light petroleum (b.p. 40—60 °C), m.p. 19—22 °C. After having been converted into the methanesulphonate using methanesulphonyl chloride in ether in the presence of triethylamine (45% molar excess), the first stage was repeated using $C_{16}E_3$-dimethanesulphonate in place of hexadecyl bromide. The crude $C_{16}E_6$ was recrystallised three times from light petroleum (b.p. 40—60 °C) as needles, m.p., 37—38 °C (lit.,[28] 30.3 °C).

Glucose Derivatives.—Commercial (+)-D-glucose was used without purification; m.p. 156—158 °C, $[\alpha]_D^{30}$ +130° ⟶ +54° (*c* 0.135 in H_2O), α-anomer *ca.* 95% by ^1H n.m.r. spectroscopy.

2,3,4,6-Tetra-*O*-methyl-D-glucose (TMG) was prepared and purified by the method of West and Holden,[29] m.p., 89—93 °C (lit., 90—93 °C), $[\alpha]_D^{30}$ +114 ⟶ 90° (*c* 0.177 in H_2O), α-anomer 75% (^1H n.m.r. spectroscopy).

4,6-*O*-Butylidene-D-glucose (4,6BG) was prepared by the method of Bonner *et al.*,[30] m.p. 158—162 °C (lit., 150—157 °C), $[\alpha]_D^{30}$ + 56° ⟶ 4° (*c* 0.76 in H_2O), α-anomer 77% (^1H n.m.r. spectroscopy).

4,6-O-*Hexylidene-D-glucose* (4,6HG). This has not been previously described and was prepared by a modification of the method of Bonner *et al.* for 4,6BG. Freshly distilled hexanal (12.5 g), concentrated hydrochloric acid (0.3 ml), and glucose (11.3 g) were shaken together for 12 h. The mixture was then taken up in toluene and extracted with water. The aqueous layer was extracted repeatedly with ethyl acetate and the extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure to give 4,6HG (4.1 g). This was recrystallised from ethyl acetate, m.p. 135—142 °C (Found: C, 54.75; H, 8.6. $C_{12}H_{22}O_6$ requires C, 54.95; H, 8.40%); $[\alpha]_D^{30}$ +75 ⟶ 20° (*c* 0.207 in H_2O), α-anomer 75%; n.m.r. spectrum of the anomeric protons in CD_3OD: 4.52 (0.25 H, d, $J_{1,2}$ 7.5 Hz, 1-H β-anomer), 5.10 (0.75 H, d, $J_{1,2}$ 4 Hz, 1-H α-anomer).

4,6-O-*Decylidene-D-glucose* (4,6DG). Also not previously described, this was prepared by a method similar to that of Evans *et al.*,[31] from decanal dimethyl acetal and glucose using toluene-*p*-sulphonic acid in dimethylformamide. Recrystallisation of the product from ethyl acetate gave a solid, m.p. 132—136 °C (Found: C, 60.5; H, 9.6. $C_{10}H_{30}O_6$ requires C, 60.38; H, 9.43%); $[\alpha]_D^{30}$ +42 ⟶ 3° (*c* 0.240 in 50% dioxane–H_2O), α-anomer 70%; n.m.r. spectrum of the anomeric protons in (CD_3OD): δ 4.50 (0.30 H, d, $J_{1,2}$ 7.5 Hz, 1-H β-anomer), 5.05 (0.70 H, d, $J_{1,2}$ 4 Hz, 1 H α-anomer).

3-O-*Alkyl-D-glucoses.* These were all prepared following the basic approach of Blazeji and Kosik.[32] 1,2,5,6-Di-*O*-isopropylidene-α-D-glucofuranose, prepared by Bell's procedure,[33] was treated with sodium hydride in DMF and then the appropriate alkyl bromide at room temperature. After having been poured into water, the mixture was extracted with light petroleum (b.p. 40—60 °C), the solvent was evaporated off, and the residue, without purification, was hydrolysed by refluxing it with 0.2M-sulphuric acid. The 3-*O*-alkylglucoses were precipitated during the course of the hydrolysis and were extracted from the neutralised mixture using light petroleum (b.p. 40—60 °C) and butan-1-ol. Recrystallised from ethyl acetate, 3-O-*dodecyl-D-glucose* was obtained as colourless plates, m.p. 102—110 °C (Found: C, 62.2; H, 10.3. $C_{18}H_{30}O_6$ requires C, 62.06; H, 10.34%); $[\alpha]_D^{30}$ +17° ⟶ 39° (*c* 0.26 in 50% dioxane–H_2O), β-anomer 81%; n.m.r. spectrum of the anomeric protons in

CD_3OD: δ, 4.45 (0.81 H, d, $J_{1,2}$ 7.5 Hz, 1-H β-anomer), 5.17 (0.19 H, d, $J_{1,2}$ 4 Hz, 1-H α-anomer).

3-O-*Hexyl*-D-*glucose*. This was obtained analogously, m.p. 128—132 °C (Found: C, 53.8; H, 9.1. $C_{12}H_{24}O_6$ requires C, 54.48; H, 9.15%); $[\alpha]_D^{30}$ + 15 ⟶ 44° (*c* 0.198 in H_2O), β-anomer 73%; n.m.r. spectrum of the anomeric protons in CD_3OD: δ 4.66 (0.73 H, d, $J_{1,2}$ 7.5 Hz, 1-H β-anomer), 5.19 (0.27 H, d, $J_{1,2}$ 4 Hz, 1-H α-anomer).

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