solution. Preliminary X-ray photographs displayed monoclinic symmetry, and precise lattice constants of a = 38.725 (8) Å, b = 10.727 (2) Å, c = 13.231 (4) Å, and β = 67.88 (2)° were determined from a least-squares analysis of 15 diffractometer measured 2θ values. The crystal density (~1.12 g/cm^3) indicated that eight molecules of composition $C_{26}H_{36}O_5$ were in this unit cell. Systematic absences were consistent with either space group *Cc* or *C*2/*c*. The latter choice ultimately proved to be the correct one through successful refinement. This requires that **5** be a racemic mixture. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a four-circle computer-controlled diffractometer using graphite monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å) and variable speed, 1° ω scans. Of the 3434 reflections collected in this fashion, only 1538 (45%) were judged observed ($|F_o| \geq 3\sigma(F_o)$) and used in subsequent calculations.[3] A phasing model was found uneventfully using the MULTAN family of programs, and all nonhydrogen atoms were located on *E*-syntheses. Hydrogens were located on difference syntheses following partial refinement. Block diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic hydrogens have converged to a standard crystallographic residual of 0.0597 for the observed reflections. A final difference map showed no anomalous electron density. Additional crystallographic details are available and are described in the supplementary material paragraph at the end of this manuscript.

(3) All crystallographic calculations were done on a PRIME 9950 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer program for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by P. Main, S. E Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1978 and 1980; BLS78A, an anisotropic block diagonal least-squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1980; BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu and G. Van Duyne, Cornell University, 1985.

Acknowledgment. We thank Dr. John Sutherland for providing information on the *Siphonaria* species of the Eastern Tropical Pacific. This research was supported by grants from the National Science Foundation (CHE81-21471 and INT 14133), the New York Sea Grant Program and the National Institutes of Health (AI 11969 and CA 24487).

Registry No. **5**, 100082-10-8; **6**, 100046-03-5; **7**, 100046-04-6; **8**, 100046-05-7; **9**, 100046-02-4.

Supplementary Material Available: Tables of fractional coordinates, thermal parameters, interatomic distances, and interatomic angles for **5** (4 pages). Ordering information is given on any current masthead page.

Mechanism of Acid-Catalyzed Anomerization of Methyl D-Glucopyranosides

James L. Jensen,* Sho-Chein Tsuang, and Arif H. Uslan[1]

Chemistry Department, California State University, Long Beach, California 90840

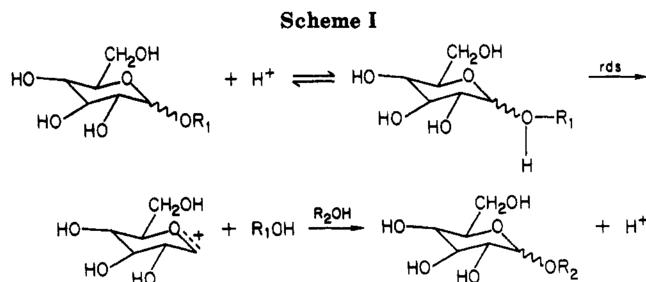
Received July 9, 1985

The anomerization of methyl D-glucopyranosides catalyzed by D_2SO_4 in Me_2SO/CD_3OD solvent was monitored by proton magnetic resonance and by changes in optical rotation. The rate of anomerization was found to be zero order in methanol, yet methanol (or a similar nucleophilic species) was required to effect anomerization. It has been shown that the solvent plays a dominant role in controlling the stereochemistry of reactions at the anomeric carbon; however, the transition-state interactions must be between solvent cage molecules and substrate and are thus solvational forces rather than a more direct nucleophilic participation inside the solvent cage. Evidence is presented supporting the notion that glucoside hydroxyls orient solvent cage molecules to assist attaining a suitable transition-state structure.

The process by which glycosides hydrolyze or exchange algyons has received much attention, and the mechanism generally cited for this process is A-1; for the glucosides, exocyclic C–O bond cleavage has always been observed.[2,3]

For example, Capon[4] has shown that acid-catalyzed anomerization of methyl D-glucopyranosides in methanol-d_4 occurs with incorporation of a solvent CD_3O moiety at the anomeric carbon. This requires in Scheme I that R_1OH (CH_3OD in the Capon experiment) not to be able to produce the anomeric product. In other words, CH_3OD either recombines with the oxycarbocation to reform the reactant anomer or becomes lost in bulk solvent. This is perhaps not a surprising result when methanol is the solvent.

Scheme I



The purpose of the present investigation is to separate the effects of methanol acting as solvent and as reagent,

(1) Present address: Faculty of Chemistry, Ege University, Bornova-Izmir, Turkey.
(2) Ferrier, R. J.; Collins, P. M. "Monosaccharide Chemistry", Penguin Books: Baltimore, MD, 1972, and references therein.
(3) (a) Moiseev, Y. V., Khalturinskii, N. A., and Zaikov, G. E. *Carbohydr. Res.* **1976**, *47*, 3. (b) Lonnberg, H.; Kankaanpera, A.; Haapakka, K. *Ibid.* **1977**, *56*, 277. (c) DeBruyne, C. K. and DeBock, A. *Ibid.* **1979**, *68*, 71. (d) O'Connor, J. V. and Barker, R. *Ibid.* **1979**, *73*, 227.
(4) Capon, B.; Thacker, D. *J. Chem. Soc. B* **1967**, 1010.

0022-3263/86/1951-0816$01.50/0 © 1986 American Chemical Society

by studying anomerization in Me_2SO/methanol mixtures. We have extended Capon's findings by demonstrating that not only does CD_3OD replace CH_3OD during anomerization when CD_3OD is the solvent, but such nucleophilic participation is required for anomerization to occur in Me_2SO/methanol mixtures. This result requires modification of the mechanism presented by Scheme I, since we have shown that the CH_3OD leaving group does not compete with the CD_3OD reagent in the anomerization process; CH_3OD only reverts to the isomer from which it came.

Experimental Section

Materials. CH_3OD, CD_3OD, D_2O, and D_2SO_4 were purchased from Aldrich Chemical Company. Me_2SO-d_6 (Merck) was reclaimed from the NMR experiments by removing the methanol in vacuo and neutralizing the acid with anhydrous Na_2CO_3, followed by vacuum distillation. The methyl α- and β-D-glucopyranosides were obtained from Sigma Chemical Company. The hydroxyl-exchanged methyl glucosides were prepared by dissolving 0.4 g of the commercial glucoside $(OH)_4$ in 2 mL of Me_2SO-d_6 and diluting with 25 mL of CH_3OD. The CH_3OD/CH_3OH mixture was removed at 3–4 torr; after 3 treatments the glucoside appeared to be 100% glucoside $(OD)_4$, according to ^1H NMR.

Kinetic Method. The kinetic solutions were contained in sealed NMR tubes. Reactions were initiated by immersing the tubes in a Haake constant-temperature water bath maintained at the appropriate temperature, usually 70 °C; the tubes were removed and quickly cooled prior to recording the ^1H NMR spectrum on a Perkin-Elmer R12B nuclear magnetic resonance spectrometer at a probe temperature of 36 °C. Because of the elevated temperatures required to produce a measurable rate of reaction under these solvent conditions, removal of the tube from the bath to record the NMR spectrum was a kinetically unobservable event (i.e., no reaction was observed during the short time periods the tube was out of the constant-temperature bath).

Rates of anomerization were obtained by following the disappearance or appearance of the α-anomer, starting from pure α- or β-D-glucopyranoside, respectively. The C_1–H proton signal of the α-anomer was integrated, by using the solvent isotopic impurity (Me_2SO-d_5) as the internal reference. These relative areas were measured at various times, t, and denoted α_t; at equilibrium the analogous quantity is α_e.

First-order plots of log $(\alpha_t - \alpha_e)$ or log $(\alpha_e - \alpha_t)$ against time were reasonably linear for 2–3 half-lives of reaction time (correlation coefficient, $r \geq 0.99$); however, at lower sulfuric acid or methanol concentrations, the first-order behaviour was not as good (e.g., at 0.92 M D_2SO_4, linearity with $r \geq 0.99$ covered two half-lives of reaction time; at 1.84 M D_2SO_4, linearity with $r > 0.99$ exceeded 3 half-lives of reaction time). For convenience, and because of the limited accuracy of the NMR method, the rate constants reported were calculated from the relationship, $k_{obsd} = 0.693/t_{1/2}$.

Rate constants were also measured polarimetrically. While satisfactory results could be obtained by withdrawing samples from a 70 °C Haake water bath and reading optical rotations, it was more convenient to construct a water-jacketed tube designed to fit into the polarimeter; this allowed 70 °C water to be circulated around the glucoside solution, and thus optical rotations could be obtained continuously. The 0.4 M methyl glucoside solutions yielded rotation changes of 5–10°; these were easily measured by using a Kerr polarimeter (Cenco). The specially designed polarimeter tubes were calibrated against 1-dm commercial tubes. Since this procedure required substantially larger amounts of solution, and since there is no advantage to measuring rotation of deuterated solutions, these measurements employed H_2SO_4, Me_2SO, CH_3OH, and the normal methyl glucosides. kinetics exhibited good first-order behaviour; typically plots of ln $(\alpha_e - \alpha_t)$ against time were linear for 3 half-lives of reaction time when the reaction was initiated using the β anomer. Plots of ln $(\alpha_t - \alpha_e)$ for reactions initiated using the α anomer often showed scatter and/or curvature after 2 half-lives because of the smaller rotational changes observed: the reading error of the polarimeter used is ± 0.2°, and the typical rotational change for the anomer was from 12.4° to 7.5°; thus the observed rotational change during the third half-life was only three times the reading error. However, the same rate constant was obtained whether the equilibrium was approached from the α or the β side.

The observed rate constant is the sum of the anomerization rates of the methyl α- and β-D-glucopyranosides; these may be calculated from the ratio of anomers present at equilibrium. The defining equations are below:

$$k_{obsd} = k_\alpha + k_\beta \quad (1)$$

$$\frac{[\beta]_e}{[\alpha]_e} = \frac{k_\alpha}{k_\beta} = K_{eq} \quad (2)$$

The value of K_{eq} was 0.64 under deuterated solvent conditions and appeared independent of D_2SO_4 and CD_3OD concentrations. the value of K_{eq} was 0.60 in normal solvent; since the polarimetric data are more precise, an apparent slight increase in K_{eq} with increasing Me_2SO could be discerned. However, the intepretative results are not affected by these trival changes in K_{eq}, and therefore, the kinetic data are discussed as k_{obsd} for the sake of simplicity. The two mean values of K_{eq}, 0.60 obtained by polarimetry in normal solvent and 0.64 obtained by NMR in deuterated solvent, are easily the same within the experimental error.

^1H NMR Analyses. All spectra were obtained on a Perkin-Elmer R12B nuclear magnetic resonance spectrometer. The spectra of the hydroxyl-exchanged methyl α- and β-D-glucopyranosides were identical with those reported;[4,5] the anomeric protons were clearly distinguishable doublets at 4.6 and 4.1 ppm, respectively. Anomerization was most easily quantitated by observing the increase/decrease of the α doublet with time. Anomerization rates were the same whether measured beginning with the α or the β anomer (within the ± 10% experimental error) and the infinity spectra were identical.

Acidity Function Experiments. The effective acidites of 0.92M H_2SO_4 in Me_2SO/CH_3OH mixtures were measured spectrophotometrically using a Beckman Model 25 recording spectrophotometer and *p*-nitroaniline (PNA) as the Hammett indicator (Aldrich Chemical Co.). The procedures followed were traditional, as reported in detail in an analogous study.[6] The choice of Hammett indicator was based on an acidity-function study in Me_2SO and ethylene glycol, carried out by Cook and Mason.[7]

Results

The objective is to measure the effect of decreasing the methanol concentration on the rate of anomerization. This is not a simple matter, since the anomerization process is acid-catalyzed and at any given acid molarity, changing the mix of CH_3OH/Me_2SO also alters the effective acidity of the solution. This "double variable" experiment can be sorted out as follows: the protonation equilibrium of the Hammett base, *p*-nitroaniline (PNA), can be used as a measure of the effective acidity; the rate of anomerization incorporates changes in the effective acidity of the solution *and* may also be affected by changes in the methanol molarity. We refer to changes in the effective acidity as changes brought about by methanol acting as a solvent in contrast to its behavior as a reagent; the latter ought to manifest itself as a first-order rate dependence.

By using the standard acidity function development,[12,13]

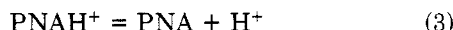
(5) Rowe, J. J. M.; Hinton, J.; Rowe, K. L. *Chem. Rev.* **1970**, *70*, 1.
(6) Jensen, J. L.; Gardner, M. P. *J. Phys. Chem.* **1973**, *77*, 1557.
(7) Cook, A. G.; Mason, G. W. *J. Inorg. Nucl. Chem.* **1966**, *28*, 2579.
(8) Sinnott, M. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 2026.
(9) Hirst, E. L.; Percival, E. In "Methods in Carbohydrate Chemistry", Whistler, R. L., Wolfram, M. L., Eds.; Academic Press, New York, 1963; Vol. 2, pp 146–7.
(10) Methyl D-glucopyranoside has a half-life of about 4 h under these conditions (not good first-order kinetics; maltoside-type products are largely formed); the extent of reaction on the pentamethyl derivative after 84.5 h did not exceed 10%, thus $t_{1/2} > 420$ h.
(11) Miljkovic, M.; Habash-Marino, M. *J. Org. Chem.* **1983**, *48*, 855.
(12) Jensen, J. L.; Uaprasert, V.; Fujii, C. R. *J. Org. Chem.* **1976**, *41*, 1675.
(13) (a) Rochester, C. H. "Acidity Functions"; Academic Press: New York, 1970. (b) Liler, M. "Reaction Mechanisms in Sulphuric Acid", Academic Press: New York, 1971.

Table I. Rate Constants for the Sulfuric Acid Catalyzed Anomerization of Methyl D-Glucopyranosides (0.4 M) in Methanol-Me_2SO Solutions at 70 °C[a]

[methanol]	[sulfuric acid]	$[PNAH^+]/[PNA]^b$	$10^4 k_{obsd}$
24.7	0.92	25	3.0
	1.5	50	5.2
12.3	0.92	0.81	0.55 (1.17)[c]
	1.5	1.74	0.78
9.8	0.92	0.51	0.42 (0.94)[c]
	1.5	0.91	0.69
7.4	0.92	0.33	0.35 (0.68)[c]
	1.5	0.63	0.55
4.9	0.92	0.23	0.30 (0.53)[c]
	1.5	0.44	0.52

[a] Means of replicate measurements, beginning with the α- and β-anomers; the average deviation is typically ±5%. $K_{eq} = 0.6$ in all cases (cf. eq 1). [b] The molarity ratio of *p*-nitroanilinium ion ($PNAH^+$) to *p*-nitroaniline (PNA) measured spectrophotometrically at λ_{max} PNA, where $PNAH^+$ is transparent; the temperature is 25 °C, which does not affect the correlation using eq 5, 9, or 10. [c] Values in parentheses were measured by NMR in Me_2SO-d_6, CD_3OD, D_2SO_4, solutions. The $[PNAD^+]/[PNA]$ ratios would differ from those listed, although the trend would be quantitatively the same. The kinetic deuterium solvent isotope effect is 2.0 ± 0.2.

the above conceptional statements can be expressed quantitatively.



$$PNAH^+ = PNA + H^+ \quad (3)$$

$$K_{PNAH^+} = \frac{[PNA][H^+]}{[PNAH^+]}\frac{\gamma_{PNA}\gamma_{H^+}}{\gamma_{PNAH^+}} \quad (4)$$

$$\log \frac{[PNAH^+]}{[PNA]} = \log [H^+]\frac{\gamma_{H^+}\gamma_{PNA}}{\gamma_{PNAH^+}} - \log K_{PNAH^+} \quad (5)$$

$$\log (\text{protonation ratio}) = \log (\text{effective acidity}) - \text{constant} \quad (6)$$

The state of the proton in these solutions is certainly not "free", just as it is not "free" in aqueous acidic media. The major acidic specie present is the methanol solvated proton. As in aqueous systems, we take the effective acidity term (eq 6) to include stoichiometric acid molarity, expressed as $[H^+]$, and activity coefficient terms. The latter, of course, may change substantially as the nature of the solvent changes. Thus, if the data in Table I are treated according to eq 5 (using $[H^+]$ = molarity of H_2SO_4), five two-point lines are defined, one for each CH_3OH/Me_2SO solution. The slopes are all about 1.4, reflecting the fact that the activity coefficient terms contribute substantially to the effective acidity; that is, the effective acidity increases significantly more than the stoichiometric molarity of acid. Further, it is expected that solutions containing less methanol (and more Me_2SO) should have a greater effective acidity because of the decreased hydrogen bond donating ability of the solvent, as is evident from the protonation ratios in Table I.

Thus the protonation ratios in Table I define the role of methanol acting as solvent, and eq 5 and 6 can be used to quantitatively measure the impact on the effective acidity of these solvent changes.

Using a similar development of the Bronsted rate law for the anomerization process and neglecting any contribution from methanol acting as reagent:

$$S + H^+ \rightarrow \text{prod} \quad (7)$$

$$k_{obsd} = k[H^+]\frac{\gamma_{H^+}\gamma_S}{\gamma_{tr^+}} \quad (8)$$

$$\log k_{obsd} = \log [H^+]\frac{\gamma_{H^+}\gamma_S}{\gamma_{tr^+}} + \log k \quad (9)$$

The substrate of eq 7 is one anomer of methyl D-glucopyranoside; the product is the other anomer. The γ_{tr^+} term in eq 8 and 9 is the activity coefficient of the positively charged transition state for anomerization. Equation 9 has a distinct parallel in eq 5 and equating the $[H^+]$ H^+ terms yields:

$$\log k_{obsd} = \log \frac{[PNAH^+]}{[PNA]} + \log \frac{\gamma_S\gamma_{PNAH^+}}{\gamma_{tr^+}\gamma_{PNA}} + \log k\, K_{PNAH^+} \quad (10)$$

Success in the traditional acidity function treatment relies on the behaviour of the activity coefficient term in eq 10: if this term is constant, then a plot of log k_{obsd} against log $[PNAH^+]/[PNA]$ will be linear and have a slope near unity. The fit to eq 10 will thus be determined by a suitable choice of Hammett base: we chose PNA because its protonation ratio is near unity in the acidity range where kinetics could be conveniently measured and because PNA is neutral and the conjugate acid cationic, as the glucoside is neutral and the transition state cationic. Obviously the match is not perfect, since there are gross solvational differences between ammonium ions ($PNAH^+$) and onium ions (tr^+) as there are between amines (PNA) and glucosides. Nonetheless, it was our expectation that the data of Table I would be adequately defined by eq 10. Such proved to be the case, as all the data fitted to eq 10 yields a slope of 0.50, an intercept of −4.2 (log 6.5×10^{-5}), and a correlation coefficient of 0.994.

Were methanol to act as a simple reagent, then eq 9 and 10 should be replaced by

$$\log k_{obsd} = \log [4^+]\frac{\gamma_{H^+}\gamma_S\gamma_{CH_3OH}}{\gamma tr^+} + \log [CH_3OH] + \log k \quad (11)$$

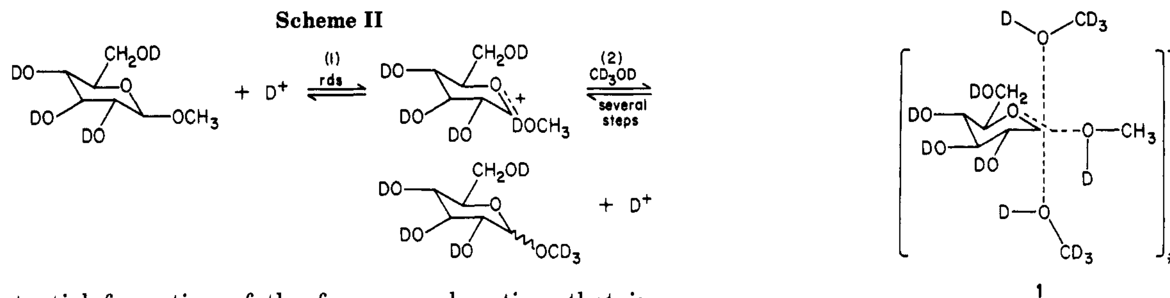
$$\log k_{obsd} = \log \frac{[PNAH^+]}{[PNA]} + \log \frac{\gamma_S\gamma_{PNAH^+}\gamma_{CH_3OH}}{\gamma_{tr}^+\ \gamma_{PNA}} + \log [CH_3OH] + (\log k)K_{PNAH^+} \quad (12)$$

When the data in Table I are fitted to eq 12, the slope and the correlation coefficient are decreased (to 0.24 and 0.89, respectively). Thus, the fit to eq 10 is clearly superior to 12, demonstrating that methanol functions as solvent only and does not function as a reagent in the kinetic sense; that is, under these conditions the anomerization process is zero order in methanol.

Discussion

The data in Table I clearly demonstrate that a fivefold change in methanol concentration has no effect on the rate constant other than affecting the effective acidity. Thus anomerization is zero order in methanol, consistent with Scheme I. Our ^1H NMR analyses, however, show that the nucleophilic specie R_2OH is involved in the anomerization process and that the free oxycarbocation shown in Scheme I does not exist on the reaction pathway. Our ^1H NMR results demonstrating this result are: At higher methanol concentrations, products consisted solely of the anomers of D-glucopyranoside; as the methanol concentration was reduced below that reported in Table I, peaks in the ^1H NMR spectrum appeared consistent with maltoside-type product formation. (Indeed, the same infinity ^1H NMR spectrum was obtained beginning with maltose, methyl α-, or methyl β-D-glucopyranoside. In no cases were peaks attributable to furanosides or open-chain acetals observed). In Me_2SO/methanol solutions and consistent with Scheme I, the results discussed thus far require R_2OH to be involved after the rate limiting step and prior to any po-

Scheme II



1

tential formation of the free oxycarbocation; that is, anomerization requires the presence of a nucleophilic agent other than R_1OH. Scheme II[4] summarizes this situation.

At higher methanol concentrations, step 1 would be rate-limiting and only anomerization would be observed; at reduced methanol concentrations, a hydroxyl group of a glucose molecule may react competitively with methanol (step 2) producing maltoside-type products.

Jencks and Sinnott[8] have recently presented evidence that in CH_3CH_2OH/CF_3CH_2OH mixed solvents, solvolysis products of D-glucopyranosyl derivatives cannot be explained on the basis of a mechanism such as Scheme II. One of our "control" experiments supports this conclusion for the Me_2SO/CH_3OH solvent system as well: when the ^1H NMR spectrum of pentamethyl β-D-glucopyranoside[9] was observed in Me_2SO containing 0.92 M D_2SO_4 and 1.2 M CD_3OD, there was no evidence of any reaction over 84.5 hours at 70 °C. This result demonstrates that methylation of the glucoside hydroxyls not only precludes the formation of maltoside-type products, as expected, but it also retards by about two orders of magnitude[10] the rate of anomerization utilizing the 1.2 M CD_3OD. Thus we conclude that not only is the external nucleophile (R_2OH in Scheme I, CD_3OD in Scheme II) involved subsequent to the rate-limiting step in Me_2SO/methanol solutions, but the glucoside hydroxyl groups participate in the reaction.

The mechanism proposed in the extensive study by Jencks and Sinnott[8] proceeds along the course of Scheme II, except the "intermediate" of Scheme II has specific interaction with two solvent molecules and has a lifetime less than 10^{-13} s; i.e., 1 is an activated complex. Our results require the two CD_3OD molecules to be interacting via solvational forces; i.e., these two molecules do not lie inside the solvent cavity, but rather are still part of the solvent cage. Our observation of the rate enhancement due to the glucopyranoside hydroxyls is accounted for, in part, by the interaction of a CD_3OD with the C_2–OD. The complete solvent cage organization established by the four glucopyranoside hydroxyls and how that relates to transition state stabilization is far too complex a subject for studies completed to date; however, the general structure of the transition state for methyl glucopyranoside anomerization seems clear. While reactions of glucopyranosyl derivatives in which the leaving group is poorer than CH_3OD may have more nucleophilic participation by the solvent, the exact mode of anomerization (and probably hydrolysis) of the glucopyranosides appears to involve the specific solvational forces depicted in 1. The recent study of the acetolyses of permethylated glucosides in acetic anhydride,[11] catalyzed by H_2SO_4, may well occur via a mechanism analogous to Scheme II (as proposed) because of the absence of the types of interactions proposed for 1. The results to date support an important interaction between the glycoside hydroxyls and hydroxylic solvent/nucleophiles. The exact details of these interactions (e.g., stereochemical requirements) have yet to be determined.

Acknowledgment. Support by the National Science Foundation, CHE-7907588 and CHE-8421082, is gratefully acknowledged.

Registry No. Methyl α-D-glucopyranoside, 97-30-3; methyl β-D-glucopyranoside, 709-50-2; sulfuric acid, 7664-93-9; methanol, 67-56-1.

Rates of Base-Catalyzed Hydrogen Exchange of Terminal Acetylenes in Aqueous Solution. Absence of a Resonance Interaction

A. J. Kresge* and M. F. Powell†

Department of Chemistry, University of Toronto, Scarborough College, Scarborough, Ontario M1C 1A4, Canada

Received August 13, 1985

Rates of detritiation of 13 monosubstituted acetylenes labeled at the acetylenic hydrogen position were measured in aqueous amine buffer solution at 25 °C, and hydroxide ion catalytic coefficients were evaluated. These rate constants, plus a few additional values from the literature, give a good correlation against inductive or field substituent constants: $\log (k_{HO^-}/M^{-1}\,s^{-1}) = 1.46 \pm 0.12 + (8.00 \pm 0.50)\sigma_I$. This correlation is not improved by addition of resonance substituent constants, and the coefficients of the resonance term in two different dual parameter (resonance plus field) treatments of the data are in fact zero.

It is commonly believed that the carbanionic electron pair of acetylide ions resides in an sp hybrid orbital.[1] Since this orbital is orthogonal to the acetylenic π-system, this pair of electrons cannot be delocalized by conjugation with the π-system, and the electron pair is consequently localized on a single atom. In this respect acetylide ions are similar to "normal"[2] oxygen and nitrogen bases, whose

† Present address: Institute of Pharmaceutical Sciences, Syntex Research, Palo Alto, CA 94304.

(1) See: for example, Morrison, R. T., Boyd, R. N. "Organic Chemistry", 4th, ed.; Allyn and Bacon: Boston, 1983; pp 567–568.
(2) Eigen, M. *Angew. Chem., Int. Ed. Engl.* 1964, 3, 1–19.

0022-3263/86/1951-0819$01.50/0 © 1986 American Chemical Society