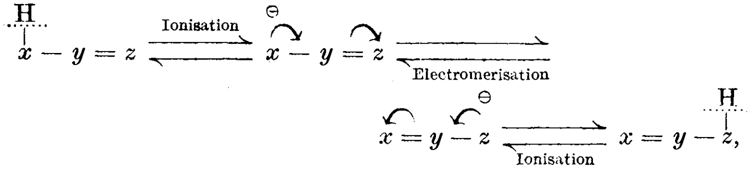
# CCVI.—*The Mechanism of Tautomeric Interchange and the Effect of Structure on Mobility and Equilibrium. Part II. Ring-Chain Tautomerism in its Relation to the Mutarotation of the Sugars.*

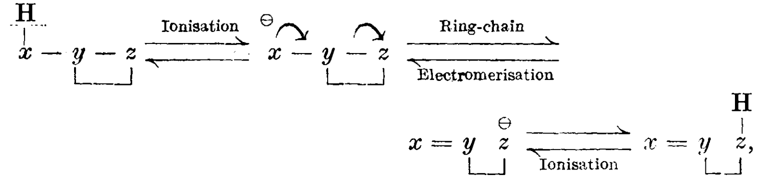
By JOHN WILLIAM BAKER.

IN view of the correlation which has been established [E. H. Ingold (Usherwood), *Chem. and Ind.*, 1923, **42**, 1246; Cooper, Ingold, and Ingold, J., 1926, 1868] between triad tautomerism, ring-chain tautomerism, and additive reactions (as keto-enol change, keto-cyclol change, and the aldol reaction), the inclusion of the chemical transformations underlying the mutarotation of sugars within the general phenomenon of ring-chain tautomerism (Jacobsen and Stelzner, Meyer and Jacobsen's " Organische Chemie," 2 Afl., 1, **2**, pp. 886, 910, 915, 927; Baker, Ingold, and Thorpe, J., 1924, **125**, 268) has paved the way for the application of new analogies. There is, in fact, no reason to doubt that the mutarotation of sugars is dependent on prototropy (compare Kuhn and Jacob, *Z. physikal. Chem.*, 1924, **113**, 389; Lowry, *Chem. Rev.*, 1927, **4**, 231) and not on anionotropy, that is, a phenomenon analogous to that exhibited by pseudo-bases.

Ingold, Shoppee, and Thorpe (J., 1926, 1477) have examined the effect of structural influences on triad prototropy on the basis of the mechanism



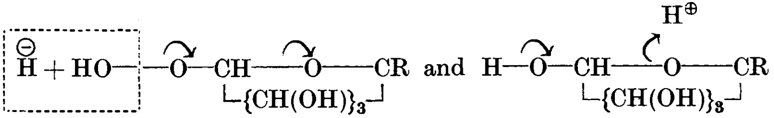
the assumed function of catalysts being the facilitation of the preliminary ionisation. This paper contains a study of structural effects on ring-chain tautomerism in its application to the mutarotation of sugars, and the results are considered in the light of the corresponding mechanism



which is the electronic interpretation of that previously upheld by Baker, Ingold, and Thorpe (*loc. cit.*).

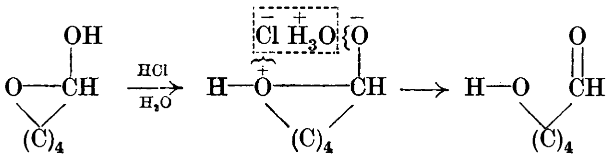
Lowry (J., 1925, **127**, 1371) has developed the conception of prototropy in relation to mutarotation and has advanced a mechanism in which *two* catalytic molecules (or ions) are assumed to attack the sugar molecule, at the points corresponding with $x$ and $z$, simultaneously. One acts as a proton-donator and the other as a proton acceptor, and the result is to produce a bipolar ion which undergoes internal neutralisation with a change of structure. This theory of duplex action differs from the above theory of unitary action in certain consequences, some of which will be considered below.

The detailed consideration of the mechanism divides itself into two parts : the history of the ionised proton and the history of the electrons from which it separates; or, in other words, the functions of catalysts, and the function of structural influences in the sugar molecule. Catalysts are expected to be of two kinds : (1) those which attack the ionising proton directly, such as the anions of weak acids, water, and all other bases; (ii) those which facilitate its liberation indirectly, such as the cations of weak bases, water, and all other acids. The respective mechanisms may be represented by the examples :



and in the second illustration it is not necessary to suppose that the attacking proton is free or that the eliminated one remains in that condition; nor does the illustration represent the only possible method of indirect action, another type of which is elaborated below (p. 1586). The essential function of a catalyst of this class is regarded as that of bringing a positive potential into the molecule in positions which will facilitate the electromeric changes necessary to the reaction. The nature of the sugar molecule itself is of importance in this connexion. Glucose is a definite, although very weak, acid ($k = 3{\cdot}6 \times 10^{-13}$) and should obviously be capable of catalysing its own mutarotation, either through its anion by the first of the mechanisms indicated, or by means of the molecule according to the second mechanism. Dawson's work has shown that catalytic coefficients differ by enormous ratios, and it would therefore be dangerous to conclude that the " arrests " of mutarotation observed (Lowry and Richards, J., 1925, **127**, 1385) in organic solvents at the ordinary temperature demonstrate a condition *qualitatively* different from the ordinary dynamic condition of a dissolved sugar which has not attained equilibrium. Evidence is recorded in this paper indicating that specimens of tetramethyl- and tetra-acetyl-glucose, which show an " arrest " in purified solvents at the ordinary temperature and even at 44°, mutarotate rapidly at a suitable higher temperature; in particular, in the fused condition in silica apparatus, the cleanliness of which had previously been demonstrated by the repeated production of " arrests." These results completely confirm the work of Irvine and Gilmour (J., 1908, **93**, 1440) on the relative nature of so-called arrests, and favour the inclusion of the sugars themselves within the category of catalysts, as is required by the theory of mechanism indicated above.

Turning to structural influences, Lowry's theory of duplex catalytic action is expressed as follows, simultaneous attack by an acid and water being taken as an example :



and a similar mechanism presumably applies to the mutarotating nitrogen sugars in which the ·OH group of the cyclol form is replaced by NHR. In these compounds the group R can, of course, be varied, and the facility of the change would thus appear to depend on the extent to which it collaborates with the proton acceptor. This may be deduced from the strengths as acids of the compounds $R{\cdot}CO_2H$ or R·OH, and for the groups R indicated should be as follows :

$$C_6H_4Br(Cl)(p) > C_6H_5 > C_6H_4Me(p) > C_6H_4{\cdot}OMe(p)$$

On the other hand, the mechanism derived from analogy with triad tautomerism presumes that the attack of an acid catalyst would be indirect and would operate at the most basic part of the molecule, and thus the strengths as bases of the compounds $R{\cdot}NH_2$ or $R{\cdot}NR^1R^2$ should determine the relative velocities of isomerisation, a sequence which is the reverse of that given above :

$$C_6H_4{\cdot}OMe(p) > C_6H_4Me(p) > C_6H_5 > C_6H_4Cl(p) > C_6H_4Br(p)$$

The experimental results which relate to a series of nitrogen sugars, prepared from tetra-acetylglucosidyl bromide, correspond with this deduction. The strengths of the five primary bases $R{\cdot}NH_2$ vary over a range of 1 : 15, and the coefficients for the velocities of mutarotation of the corresponding sugars under constant conditions of temperature and acid catalysis vary as 1 : 23, but the ratios of the two constants are grouped in a striking manner round a common value (p. 1593).

An unexpected point of considerable interest has emerged during the study of sugars derived from secondary bases. If the attack of the acid catalyst on one of the sugars considered in the preceding paragraph were to result in actual co-ordination of a proton to give an ammonium complex which then became the actual individual responsible for mutarotation, it is evident that, since the nitrogen atom in the latter would bear two equivalent hydrogen atoms, the replacement of one of them by methyl should not fundamentally affect the situation, because the other still remains available to act as the mobile hydrogen atom. Tetra-acetylglucosemethylanilide was prepared and examined, but no signs of mutarotation could be detected, either at the ordinary temperature under conditions varying from those conducive to "arrests" to those in which considerable concentrations of acid were employed, or in the fused state. It is concluded that the attack of the catalyst does not involve co-ordination,* but merely the augmentation of

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* This may not necessarily be the case with sugar derivatives of very strong bases, examples of which are at present under investigation.

the positive field in the region of the electrons binding the original hydrogen atom by an electrostatic mechanism which may be correlated with the modern theory of electrolytes. In short, it is the hydrogen atom already present in the system $\mathrm{H{-}X{-}\underbrace{C{-}O{-}C}}$ which is the mobile one, and the recognition of this circumstance by Baker, Ingold, and Thorpe was one of the principal reasons for grouping mutarotation phenomena within the general category of ring-chain tautomeric changes. The stronger the basic properties of the unshared nitrogen electrons, the closer will the polar reagent approach; the greater the field thus induced, the smaller will be the reaction of the valency electrons on the nucleus of the mobile hydrogen. Thus the effect of structural changes on the velocity of mutarotation should run parallel with their effect on basic character, as is found to be the case.

In the absence of acid catalysts, however, it is obvious from the scheme given on p. 1584 that the velocity of mutarotation should depend on the tolerance of the atom $x$ (from which in the cyclol form the proton separates) for a negative charge, and hence, under such conditions, it is to be expected that the velocity of mutarotation should be greater when $x$ is an oxygen atom than when it is nitrogen. This is actually the case. The velocity coefficient of tetra-acetyl glucose $(\mathrm{H{-}O{-}\underbrace{C{-}O{-}C}})$ in 90% alcohol at 44° is 1·07 $\mathrm{hrs.}^{-1}$, whereas in the same solvent at the same temperature the velocity of mutarotation of tetra-acetylglucoseanilide $(\mathrm{H{-}\underset{|}{N}{-}\underbrace{C{-}O{-}C}})$ is too slow to measure, the initial value $[\alpha]^{44^\circ}_{5461}$ $-73{\cdot}7^\circ$ being unchanged after 24 hours. Mutarotation of the anilide does, however, proceed fairly rapidly in the fused condition; a sample which had m. p. 98° and $[\alpha]^{24^\circ}_{5461}$ $-75{\cdot}2^\circ$ in "arrest" ethyl acetate, had m. p. 60° and $[\alpha]^{24^\circ}_{5461}$ $+45{\cdot}7^\circ$ in the same solvent after previous heating at 100—105° for 1 hour.

The matter will be developed further in future papers.

## EXPERIMENTAL.

### I. *Experiments on "Arrest" Specimens.*

A. *Materials used.*—A pure specimen of tetra-acetyl *d*-glucose supplied by Messrs. Boots Pure Drug Co. was dried for 12 months over phosphoric oxide in a vacuum desiccator. A specimen of tetramethyl glucose, m. p. 80°, prepared by The British Drug Houses, Ltd., was rapidly crystallised from a mixture of pure dry ether and ligroin (b. p. 30—40°) with the rigid exclusion of moisture. The process was repeated until a product of m. p. 103—104° (specimen put into a bath at 90° initially) was obtained. This specimen was stored over phosphoric oxide in a vacuum for 18 months without any change of m. p. being detected. Ethyl acetate was purified in the usual manner and finally distilled twice over phosphoric oxide. The latter operation seemed to give the sample a very slight acid reaction, and a better specimen was obtained by subsequent treatment with a little dry sodium, followed by slow distillation (twice) in a carefully purified apparatus made of pyrex glass throughout and protected from atmospheric moisture. The acetone used was purified through the sodium iodide compound by the method of Shipsey and Werner (J., 1913, **103**, 1255) employed by Lowry.

B. *Description of Apparatus.*—The apparatus, which was composed entirely of clear fused silica, consisted of a 2-dcm. polarimeter tube, 1 cm. in diameter, with optically ground end-plates fused on. At a distance of 2 cm. from each end were fused in two side-tubes, 0·5 cm. in diameter, bent at right angles and connected by ground joints to two flasks of about 25 c.c. capacity, each of which had a wide fused-in side-tube bent at right angles. In this side-tube a small glass tube containing phosphoric oxide could be placed (thus making it possible to replenish the drying agent without soiling the side-tube with phosphoric acid) and it was connected during the actual arrest experiment to a large backing train of phosphoric oxide drying-tubes. The whole apparatus was constructed to specification by the British Thermal Syndicate, Newcastle. The apparatus was initially purified by prolonged steaming and dried by heating in a slow current of air (dried by phosphoric oxide) at reduced pressure. Subsequently, cleaning was effected simply by washing with the pure " arrest " solvent and drying in a stream of dry air.

The polarimeter tube was jacketed for temperature control. The temperature readings recorded are those of the jacket of the tube. Readings were made for the mercury green line, the source of light being a powerful Kelvin, Bottomley and Baird mercury vapour lamp.

*Arrest of Mutarotation.*—(a) *Tetra-acetyl glucose in ethyl acetate.* A solution containing 1·343 g. in 100 c.c. at 24° had $\alpha$ $+0{\cdot}18°$, ($[\alpha]_{5461}^{24°}$ 6·7°), unchanged for 23 hours. Thereafter, very slow mutarotation occurred, but it was not complete when observations were stopped (171 hours; $\alpha$ $+1{\cdot}82°$).

(b) *Tetramethyl glucose in ethyl acetate.* A solution containing 1·526 g. in 100 c.c. at 44° had $\alpha$ $+4{\cdot}34°$ ($[\alpha]_{5461}^{44°}$ 142·3°), unchanged for 6 hours. This value is considerably higher than that ($[\alpha]_{5461}$ 122·4°) recorded by Lowry (*loc. cit.*) in agreement with the higher

m. p. of the sample used. Mutarotation then proceeded slowly and was complete in about 198 hours.

(c) *Tetramethyl glucose in acetone.* A solution containing 1·482 g. in 100 c.c. had at 44° α +4·02° ($[\alpha]^{44°}_{5461}$ 135·6°), unchanged for over 3 hours, after which slow mutarotation set in.

C. *Mutarotation in the Fused State.—Tetra-acetyl glucose.* Fusion of the sugar (0·249 g.) at 130—135° for 30 minutes was effected in one bulb of the silica apparatus, the other containing the "arrest" ethyl acetate (15·75 g.) ultimately used to test the rotation. Solution was effected by tilting the apparatus. The initial value of α, measured 10 minutes after solution was effected, was 2·12°, whence $[\alpha]^{44°}_{5461} = 74·5°$. This value remained unchanged for 2 hours, after which the mutarotation was slowly completed, the final constant value ($[\alpha]^{44°}_{5461}$ 91·4°) being reached after 144 hours. The experiment was repeated with similar results.

*Tetramethyl glucose.* In a similar experiment, this sugar (0·2820 g.) was heated at 120° for 15 minutes in the arrest apparatus and after cooling was dissolved in "arrest" acetone (13·96 g.). The initial value of α was 3·04°, whence $[\alpha]^{41·5°}_{5461} = 95·0°$, which remained unchanged for 24 hours.

## II. *Relative Velocity Experiments.*

D. *Preparation of* p-*Substituted Anilides of Tetra-acetyl Glucose.*—These were obtained by the action of excess of the *p*-substituted aniline on tetra-acetylglucosidyl bromide, a little ether being used as a solvent in the case of the solid bases. The method of isolation varied slightly from case to case, since sometimes the required anilide and sometimes the hydrobromide of the base crystallised.

*Anilide.* Tetra-acetylglucosidyl bromide (8 g.) was dissolved in 5·6 g. of freshly distilled aniline (3 mols.) and kept for 24 hours at room temperature; precipitation of the partly separated aniline hydrobromide was then completed by addition of ether. The excess of aniline was removed from the filtered ethereal solution by shaking with dilute hydrochloric acid. The residue from the dried ethereal extract slowly crystallised. After several crystallisations from ether–ligroin (b. p. 40—60°) *tetra-acetylglucoseanilide* had m. p. 98° (Found: C, 56·6; H, 6·1. $C_{20}H_{25}O_9N$ requires C, 56·7; H, 6·0%).

The p-*toluidide* was obtained similarly from 8·2 g. of acetobromoglucose and 6·4 g. of *p*-toluidine dissolved in a little ether. After evaporation of the ether on a steam-bath the p-*toluidide* crystallised; after several recrystallisations from methyl alcohol it had m. p. 147° (Found: C, 57·4; H, 6·2. $C_{21}H_{27}O_9N$ requires C, 57·6; H, 6·2%).

p-*Anisidide.* On similar condensation of 8·2 g. of acetobromoglucose with 7·4 g. of *p*-anisidine a mixture of *p*-anisidine hydrobromide and the required anisidide crystallised, from which the latter was separated by crystallisation from aqueous methyl alcohol. A further quantity was obtained from the ethereal extract. After many crystallisations from methyl alcohol–ligroin (b. p. 60—80°) the p-*anisidide* had m. p. 129° (Found : C, 55·6; H, 6·1. $C_{21}H_{27}O_{10}N$ requires C, 55·6; H, 6·0%).

p-*Bromoanilide.* In this case a mixture of *p*-bromoaniline hydrobromide and the required *p*-bromoanilide crystallised. After dilution with ether, the insoluble residue was treated with cold 10% sodium hydroxide solution and extracted with chloroform. *p*-Bromoaniline was removed from the chloroform extract by shaking with dilute hydrochloric acid, and the dried extract concentrated to small bulk. On addition of ligroin and seeding, the product crystallised. A further quantity was obtained in the usual manner from the ethereal extract. After several crystallisations from pure methyl alcohol the p-*bromoanilide* had m. p. 160° (Found : C, 47·9; H, 4·9. $C_{20}H_{24}O_9NBr$ requires C, 47·8; H, 4·8%).

The p-*chloroanilide* was prepared in a similar manner. After many crystallisations from methyl alcohol–ligroin (b. p. 60—80°) it had m. p. 147° (Found : C, 52·1; H, 5·4. $C_{20}H_{24}O_9NCl$ requires C, 52·5; H, 5·3%). It is much more soluble in methyl alcohol than the *p*-bromo-compound.

N-*Methylanilide.* A mixture of acetobromoglucose (8·0 g.) and 6 g. of freshly distilled methylaniline (3 mols.) was warmed on the steam-bath to effect solution. After standing for 6 hours, it was again warmed on the steam-bath for 5 minutes to complete the reaction. The resulting dark green, viscous gum was largely diluted with dry ether, and the precipitated methylaniline hydrobromide filtered off. The ethereal extract was shaken with dilute hydrochloric acid, which removed the excess of methylaniline and nearly all the colour. The pale yellow syrup obtained from the dried ethereal solution slowly crystallised in a vacuum desiccator. After several crystallisations from ether–ligroin, the N-*methylanilide* had m. p. 102° (Found : C, 57·7; H, 6·5. $C_{21}H_{27}O_9N$ requires C, 57·7; H, 6·2%).

E. *Mutarotation in* 90% *Alcohol.*—The solvent used was prepared by the addition of 10% (by weight) of conductivity water to pure absolute alcohol, which had been carefully distilled several times. The water was added in order to prevent relatively large changes in the water content of the solvent owing to the hygroscopic character of absolute alcohol.

(a) *Tetra-acetyl glucose.* Strength of solution, 2·0956 g./100 c.c. Temp., 44°.

| Time (hrs.). | $\alpha$. | $[\alpha]_{5461}$. | $k$ (hrs.$^{-1}$). |
|---|---|---|---|
| 0·183 | +1·06° | 25·3° | — |
| 0·23 | 1·22 | 29·1 | (0·9488) |
| 0·25 | 1·31 | 31·2 | (0·9970) |
| 0·283 | 1·39 | 33·1 | 1·0720 |
| 0·333 | 1·54 | 36·7 | 1·1241 |
| 0·416 | 1·71 | 40·8 | 1·0993 |
| 0·50 | 1·89 | 45·1 | 1·0598 |
| 0·583 | 2·05 | 48·9 | 1·0569 |
| 0·666 | 2·21 | 52·7 | 1·0654 |
| 0·75 | 2·35 | 56·0 | 1·0681 |
| 0·833 | 2·48 | 59·1 | 1·0718 |
| 0·913 | +2·59° | 61·8° | 1·0709 |
| 1·0 | 2·68 | 63·9 | 1·0534 |
| 1·166 | 2·86 | 68·2 | 1·0320 |
| 1·416 | 3·11 | 74·2 | 1·0766 |
| 1·50 | 3·15 | 75·1 | 1·0966 |
| 1·75 | 3·32 | 79·2 | 1·0684 |
| 2·0 | 3·42 | 81·6 | 1·0442 |
| 2·50 | 3·62 | 86·4 | — |
| 3·50 | 3·79 | 90·4 | — |
| $\infty$ | 3·97 | 94·7 | — |
|  |  | Mean | 1·067 |

(b) *Tetra-acetylglucoseanilide.* A solution containing 1·5188 g. in 100 c.c. had $[\alpha]_{5461}^{44^\circ}$ − 73·7°, unchanged after 24 hours. Evaporation of this solution over phosphoric oxide in a vacuum at the ordinary temperature yielded a pure white solid, m. p. 97°, showing that the original material was unchanged.

*Mutarotation of tetra-acetylglucoseanilide on fusion.* A sample of the anilide having m. p. 98° and $[\alpha]_{5461}^{24^\circ}$ − 75·2° in " arrest " ethyl acetate was heated at 105—110° for 1 hour and then cooled. The product had m. p. (indefinite) about 60°; and a solution containing 0·7512 g. in 100 c.c. gave $\alpha$ + 0·69°, whence $[\alpha]_{5461}^{24^\circ} = +$ 45·7°, mutarotation having occurred during fusion.

*Comparative Velocities of Mutarotation of Tetra-acetylglucoseanilides in Ethyl Acetate with Acid Catalysts at* 24°.—Since it was only desired to determine the relative velocities of mutarotation of the anilides in the same solvent under the same conditions of catalysis, the solvent used was prepared empirically by addition of such small amount of hydrochloric acid to ethyl acetate as gave conveniently measurable velocities. The ethyl acetate used contained a little acetic acid (S), but it was shown that the catalytic activity of the acetic acid was only of the order of 1—2% of that produced by an equivalent concentration of hydrochloric acid. The order of the velocities of mutarotation was confirmed, for three of the five derivatives, in pure ethyl acetate to which only acetic acid in concentration 0·9*N* had been added (U). In certain cases, the standard catalytic solution was diluted with pure ethyl acetate (T) in order to reduce the velocities of mutarotation to measurable magnitudes, the two series of measurements being correlated by a determination of the velocity of mutarotation of the anilide in both solvents.

The value of $[\alpha]_0$ was obtained graphically by extrapolation of the straight line obtained by plotting $\log([\alpha]_\infty - [\alpha]_t)$ against $t$. Details of the optical measurements are recorded only in the first example.

*Mutarotation of tetra-acetylglucose-*p*-bromoanilide in S* : strength of solution, 1·1668 g./100 c.c. (0·0233 g.-mol./l.). $k = \frac{2\cdot 3}{t} \log \frac{[\alpha]_\infty - [\alpha]_0}{[\alpha]_\infty - [\alpha]_t}$ hrs.$^{-1}$.

| Time ($t$ hrs.). | $a$. | $[\alpha]_{5461}$. | $k$. | Time ($t$ hrs.). | $a$. | $[\alpha]_{5461}$. | $k$. |
|---|---|---|---|---|---|---|---|
| 0·033 | −1·11° | −47·55° | 2·258 | 0·833 | +0·50° | +21·42° | 2·025 |
| 0·083 | 0·96 | 41·13 | 1·835 | 0·917 | 0·55 | 23·57 | 1·986 |
| 0·166 | 0·68 | 29·14 | 1·890 | 1·00 | 0·60 | 25·71 | 1·974 |
| 0·25 | 0·40 | 17·14 | 2·039 | 1·25 | 0·70 | 29·99 | — |
| 0·333 | 0·21 | 9·00 | 2·003 | 1·75 | 0·82 | 35·14 | — |
| 0·417 | 0·02 | 0·86 | 2·050 | 2·50 | 0·88 | 37·70 | — |
| 0·50 | +0·10 | + 4·29 | 1·990 | 3·75 | 0·89 | 38·14 | — |
| 0·533 | 0·22 | 9·43 | 2·172 | ∞ | 0·90 | 38·56 | — |
| 0·699 | 0·40 | 17·57 | 2·115 | | | Mean | 2·028 |

*Tetra-acetylglucose-*p*-chloroanilide in S* : strength of solution, 1·0012 g./100 c.c. (0·0219 g.-mol./l.). Mean value of $k$ (11 observations), 2·77 hrs.$^{-1}$ ± 0·07.

*Tetra-acetylglucoseanilide in S* : strength of solution, 1·0092 g./100 c.c. (0·02385 g.-mol./l.). Mean value of $k$ (9 observations), 7·77 hrs.$^{-1}$. Maximum, 8·09; minimum, 7·21.

*Tetra-acetylglucoseanilide in T* : strength of solution, 1·0212 g./100 c.c. (0·0242 g.-mol./l.). Mean value of $k$ (12 observations), 4·06 hrs.$^{-1}$. Maximum, 4·34; minimum, 3·89.

*Tetra-acetylglucose-*p*-toluidide in T* : strength of solution, 0·8416 g./100 c.c. (0·0193 g.-mol./l.). Mean value of $k$ (6 observations), 15·6 hrs.$^{-1}$. Maximum, 17·6; minimum, 14·2.

*Tetra-acetylglucose-*p*-anisidide in T* : strength of solution, 1·0288 g./100 c.c. (0·0227 g.-mol./l.). Mean value of $k$ (8 observations), 24·3 hrs.$^{-1}$. Maximum, 26·3; minimum, 22·4.

*Mutarotation in ethyl acetate* 0·9N *with respect to acetic acid* (U). (a) *Tetra-acetylglucoseanilide* : strength of solution, 0·9408 g./100 c.c. Mean value of $k$ (11 observations), 0·209 hrs.$^{-1}$. Maximum, 0·248; minimum, 0·188.

(b) *Tetra-acetylglucose-*p*-toluidide* : strength of solution, 1·0224 g./100 c.c. Mean value of $k$ (10 observations), 0·577 hrs.$^{-1}$. Maximum, 0·604; minimum, 0·543.

(c) *Tetra-acetylglucose-*p*-anisidide* : strength of solution, 0·9800 g./100 c.c. Mean value of $k$ (9 observations), 1·69 hrs.$^{-1}$. Maximum, 1·88; minimum, 1·55.

## *Summary of Results.*

*Relative velocities of mutarotation of para-substituted anilides of tetra-acetyl glucose with acid catalysis* ($K_b$ is the dissociation constant of the *p*-substituted aniline as a base*).

| Substituent. | Anilide (g.-mol./l.). | $K_b$. | Velocity coefficient of mutarotation, $k$ hrs.$^{-1}$, (*a*) in S. | (*b*) in T. | (*c*) in U. | $k/K_b$ (for S). |
|---|---|---|---|---|---|---|
| Br | 0·023 | $1·0 \times 10^{-10}$ | 2·00 | — | — | )$2·0 \times 10^{10}$ |
| Cl | 0·022 | $1·5 \times 10^{-10}$ | 2·74 | — | — | $1·83 \times 10^{10}$ |
| H | 0·024 | $4·6 \times 10^{-10}$ | 7·76 | 4·05 | 0·209 | $1·69 \times 10^{10}$ |
| Me | 0·020 | $11—15 \times 10^{-10}$ | (29·6)† | 15·45 | 0·577 | $1·97 \times 10^{10}$ |
| OMe | 0·023 | $15 \times 10^{-10}$ | (45·9) | 23·92 | 1·69 | $3·06 \times 10^{10}$ |

*Attempt to cause Tetra-acetylglucose-*N*-methylanilide to exhibit Mutarotation.*—(a) *In "arrest" ethyl acetate.* A solution containing 1·0224 g. in 100 c.c. had $[\alpha]_{5461}^{24°}$ +49·0°, which remained unchanged for 24 hours, even after the addition of a trace of hydrochloric acid on a platinum wire. The residue obtained by evaporating this solution over phosphoric oxide at the ordinary temperature had m. p. 95—96° without purification.

(b) *In ethyl acetate containing hydrochloric acid.* A solution of 1·0380 g. in 100 c.c. of ethyl acetate about 0·03*N* with respect to acid had $[\alpha]_{5461}^{24°}$ + 51°, and one containing 1·040 g. in 100 c.c. with only about 1/10 this concentration of acid had $[\alpha]_{5461}^{24°}$ + 52·5°, both values being constant.

(c) *On fusion.* A sample of the methylanilide was heated at 105—110° for a short period and cooled. A solution containing 1·0432 g. in 100 c.c. in "arrest" ethyl acetate had $[\alpha]_{5461}^{24°}$ + 51·8°. In no case could any change in rotation be observed.

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* From Landolt-Börnstein. The values for *p*-toluidine and *p*-anisidine vary, but from theoretical considerations it would be expected that the latter is the stronger base.

† The values in parentheses are extrapolated on the assumption of direct proportionality from those found in T by means of the values obtained for the anilide in each solution.