Transglycosylation of N-*Aryl-mannosyl-, -galactosyl-, and -lactosyl-amine, and Tetra-*O-*acetyl*-N-*arylglucosylamine.*

By. R. BOGNÁR, P. NÁNÁSI, and É. NEMES-NÁNÁSI.

[Reprint Order No. 5397.]

The transglycosylation reaction has been extended to the mannose, galactose, and lactose series, and to a glucosylamine tetra-acetate. It seems to be governed by the relative basicities of the amine components.

IN extension of previous work (preceding paper) on the transglycosylation reaction experiments with D-mannosyl-, D-galactosyl-, and lactosyl-amine, and with D-glucosylamine tetra-acetate are recorded. Conversion of *N-p*-sulphamylphenyl-D-glucosylamine tetra-acetate by *p*-bromoaniline into *N-p*-bromophenyl-D-glucosylamine tetra-acetate and of the latter tetra-acetate into the former by sulphanilamide proves the reaction be reversible (cf. preceding paper).

A pure anomeric form of any of the *N*-arylglucosylamine tetra-acetates gives an anomeric mixture in warm alcoholic hydrogen chloride, equilibrium being rapidly reached.

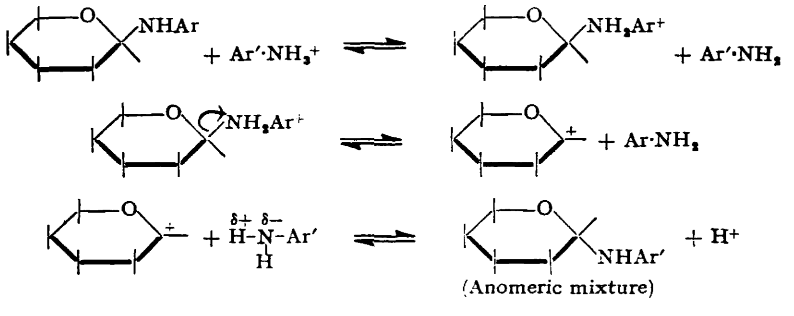
Transglycosylation of the tetra-acetates in anhydrous solvents supports the view that the reaction does not involve hydrolysis, and this is confirmed by the following facts : (*a*) (*a*) D-Glucose tetra-acetate does not react, at least not to a practicable extent, under the usual conditions of the reaction. (*b*) In the absence of another amine the acetylated glycosylamines mutarotate, under the conditions of transglycosylation, to equilibrium within 2 minutes, and the anomeric mixtures can be isolated in 50—60% yields. Further heating causes strong coloration and a reaction which has not been explained. However, if a proton-acceptor, *e.g.*, pyridine, is added, no coloration occurs and after 6—8 minutes' heating a yield exceeding 90% of the anomeric mixture is recovered, so the hydrolysis, if any, is very slight.

The less basic amines are best suited to transglycosylation, since the proton-affinity of the stronger amine will govern the reaction.

The pure anomeric tetra-acetates separated from the mixture obtained by transglycosylation correspond to those prepared as described in the preceding paper.

This represents a new method for preparation of *O*-acetylglycosylamines and further supports the pyranoside structure of these compounds.

The results suggest a proton-catalysed mechanism for transglycosylation (see annexed scheme).



EXPERIMENTAL

N-p-*Tolyl*-D-*mannosylamine from* N-p-*Sulphamylphenyl*-D-*mannosylamine*.—*N*-*p*-Sulphamylphenyl-D-mannosylamine (1·0 g., 1 mol.) and *p*-toluidine (0·5 g., 1·3 mols.) were boiled in methanol (8 ml.) and water (4 ml.) containing 3 drops of concentrated hydrochloric acid. Dissolution took place after 15 min. Crystallisation set in at room temperature, yielding 0·7 g. (87%) of crude product. Recrystallised twice from aqueous methanol (yield, 70%) this had m. p. 182° alone or mixed with *N*-*p*-tolylmannosylamine, $[\alpha]_{\rm D}^{22}$ $-178°$ (*c* 0·9 in pyridine), $-99·1°$ (*c*, 1·0 in MeOH) (Found : C, 57·4, 57·2; H, 6·9, 6·7; N, 5·4. Calc. for $C_{13}H_{19}O_5N$: C, 58·0; H, 7·1; N, 5·2%). Weygand (*Ber.*, 1939, **72**, 1663) gives m. p. 183—184°; Ellis and Honeyman (*J.*, 1952, 1496) give $[\alpha]_{\rm D}^{22}$ $-181°$ in pyridine.

N-p-*Sulphamylphenyl*-D-*galactosylamine from* N-(4-*Carboxy*-3-*hydroxyphenyl*)-D-*galactosylamine*.—*N*-(4-Carboxy-3-hydroxyphenyl)-D-galactosylamine (0·7 g., 1 mol.) and sulphanilamide (0·4 g., 1·05 mols.) were boiled for 5 min. in 80% methanol containing 0·004 g. of hydrogen chloride. Ether was added to the cooled solution. The precipitated product crystallised from aqueous ethanol (yield 50%) and had m. p. 174° alone or mixed with *N*-*p*-sulphamylphenylgalactosylamine, $[\alpha]_{\rm D}$ $-95°$ (*c*, 1·5 in pyridine) (Found : N, 7·8; S, 9·2, 9·3. Calc. for $C_{12}H_{18}O_7N_2S,H_2O$: N, 8·0; S, 9·1%). Bognár and Nánási (*J.*, 1953, 1703) gave m. p. 174—175°, $[\alpha]_{\rm D}$ $-97°$ in pyridine. Hydrolysis of 0·3 g. by acid gave 0·145 g. of sulphanilamide, m. p. 164°.

N-p-*Sulphamylphenyl-lactosylamine from* N-(4-*Carboxy*-3-*hydroxyphenyl*)-*lactosylamine*.—*N*-(4-Carboxy-3-hydroxyphenyl)-lactosylamine (1·6 g., 1 mol.) and sulphanilamide (0·6 g., 1·05 mols.) were boiled for 5 min. in 70% ethanol (12 ml.) containing hydrogen chloride (0·007 g.). The crude product (1·4 g., 85%) was precipitated from the cooled solution by ether and, crystallised from 83% alcohol (yield 55%), had m. p. 208° alone or mixed with *N*-*p*-sulphamylphenyllactosylamine trihydrate (m. p. 210°), $[\alpha]_{\rm D}^{22}$ $-66·1°$ (*c*, 1·5 in pyridine) (Found : N, 5·0. Calc. for $C_{18}H_{28}O_{12}N_2S,3H_2O$: N, 5·1%). Bognár and Nánási (*loc. cit.*) give m. p. 210—212°, $[\alpha]_{\rm D}^{22}$ $-69·0°$ (*c*, 1·7 in pyridine).

Anomeric Mixture of N-p-*Sulphamylphenyl*-D-*glucosylamine Tetra-acetates*.—(a) *From* α-N-*phenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*tetra-acetate*. *N*-Phenyl-D-glucosylamine 2 : 3 : 4 : 6-tetra-acetate ([α] +150° in $CHCl_3$; 2·1 g., 1 mol.) and sulphanilamide (0·9 g., 1 mol.) were boiled for 15 min. in absolute ethanol (15 ml.) containing concentrated hydrochloric acid (0·05 ml.). The crude product separating on cooling {0·72 g., 64%; m. p. 185°, $[\alpha]_{\rm D}^{22}$ $+60·0°$ (*c*, 1·0 in pyridine)} crystallised from ethanol and then had m. p. 188—192°, $[\alpha]_{\rm D}^{24}$ $+95·0°$ (*c*, 0·9 in pyridine), being a mixture of the anomeric *N*-*p*-sulphamylphenyl-D-glucosylamine 2 : 3 : 4 : 6-tetra-acetates.

Similar reaction in 96% ethanol gave a 70% yield of a mixture, m. p. 190°, $[\alpha]_{\rm D}^{22}$ $+26·2°$ (*c*, 0·7 in pyridine) (Found : N, 5·6. Calc. for $C_{20}H_{26}O_{11}N_2S$: N, 5·6%), which contains more of the lævorotatory anomer. This product yielded, with acetic anhydride and zinc chloride (Bognár and Nánási, *loc. cit.*), the hexa-acetate, m. p. 115°, $[\alpha]_{\rm D}$ $+75°$ (*c*, 0·7 in pyridine). Bognár and Nánási give m. p. 115°, [α] +77°.

(b) *From* β-N-*phenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*tetra-acetate*. The dry tetra-acetate ($[\alpha]_{\rm D}$ $-37°$ in $CHCl_3$; 1·0 g., 1 mol.) and sulphanilamide (0·43 g., 1 mol.) were boiled for 15 min. in absolute ethanol containing hydrogen chloride (0 007 g.). The crude product, recrystallised from alcohol, gave a mixture of anomers (yield 60%), m. p. 185°, $[\alpha]_{\rm D}^{22}$ $+49·4°$ (*c*, 0·6 in pyridine) (Found : N, 5·4%).

Anomeric Mixture of N-p-*Sulphamylphenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*Tetra-acetates from* β-N-p-*Tolyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*Tetra-acetate*.—The *p*-tolyl compound ($[\alpha]_{\rm D}$ $-58·5°$ in pyridine; 0·5 g., 1 mol.) and sulphanilamide (0·2 g., 1 mol.) were heated in absolute ethanol (2 ml.) containing hydrogen chloride (0·004 g.) for 7 min. The product (yield 80%) precipitated on addition of water (10 ml.) and crystallised from ethanol (0·22 g.) had m. p. 185—192°, $[\alpha]_{\rm D}^{22}$ $-30·0°$ (*c*, 0·9 in pyridine). The product (0·15 g.) precipitated from the mother-liquor had m. p. 180°, $[\alpha]_{\rm D}^{22}$ $+58·0°$ (*c*, 0·9 in pyridine) (Found : N, 5·6%). Both the α- and the β-isomer of *N*-*p*-tolyl-D-glucosylamine 2 : 3 : 4 : 6-tetra-acetate gave equilibrium mixtures under these conditions, even during the first 1—2 minutes' boiling, and only 47% of the unchanged compound was recovered after 7 minutes' boiling. On addition of small quantities of pyridine no appreciable hydrolysis takes place during 7 minutes' boiling and 91% of the compound can be recovered.

Mixed Anomeric N-p-*Bromophenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*Tetra-acetates from* β-N-p-*Tolyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*Tetra-acetate*.—The tolyl compound ($[\alpha]_{\rm D}$ $-48°$; 0·5 g., 1 mol.) and *p*-bromoaniline (0·4 g., 2 mols.) were boiled in absolute ethanol (2 ml.) containing hydrogen chloride (0·004 g.) for 5 min. then cooled and diluted with water (10 ml.). A crude oil separated which was twice crystallised from ethanol. The product (0·3 g.) separating from the solution had m. p. 158° alone or mixed with the pure β-anomer and $[\alpha]_D^{22}$ −68° (*c*, 0·9 in pyridine). The mother-liquor, on addition of water, afforded a substance (0·1 g.), m. p. 123°, $[\alpha]_D^{22}$ +86° (*c*, 0·9 in pyridine), +45° (*c*, 1·1 in $CHCl_3$) (Found : N, 2·9. Calc. for $C_{20}H_{24}O_9NBr$: N, 2·8%). Bognár and Nánási (*J.*, 1954, 189) give m. p. 150—152°, $[\alpha]_D$ +168° in pyridine and m. p. 162°, $[\alpha]_D$ −65° for the anomers. The yield of recrystallised products amounts to 50%.

N-p-*Bromophenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*Tetra-acetate*.—(a) *From* β-N-p-*sulphamylphenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*tetra-acetate*. The sulphamyl compound ($[\alpha]_D$ −54°; 0·5 g., 1 mol.) and *p*-bromoaniline (0·4 g., 2·15 mols.) were dissolved in hot absolute ethanol (2 ml.) containing hydrogen chloride (0·004 g.). The mixture was boiled for 5 min. after complete dissolution and then cooled. The amorphous product separating on addition of water (10 ml.) crystallised from ethanol (yield 0·3 g.), then having m. p. 161°, $[\alpha]_D^{22}$ −56·5° (*c*, 0·9 in pyridine), −31·6° (*c*, 0·7 in $CHCl_3$). A mixture with the pure dextrorotatory compound melted at 161—162°. The yield of recrystallised product is 60% (Found : N, 3·2%).

(b) *From* α-N-p-*sulphamylphenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*tetra-acetate*. This anomer, $[\alpha]_D$ +155°, gave similar results in methanol (yield, 0·3 g., 60%; m. p. and mixed m. p. 162°, $[\alpha]_D^{22}$ −56·5° in pyridine) (Found : N, 2·9%).

Both the α- and the β-sulphamyl compound are equilibrated under the conditions of transglycosylation, and after 7 minutes' boiling only 58% of unchanged compound was recovered. On addition of small amounts of pyridine 89% was recovered after 7 minutes' boiling.

N-p-*Sulphamylglucosylamine* 2 : 3 : 4 : 6-*Tetra-acetate from* N-p-*Bromophenyl*-D-*glucosylamine* 2 : 3 : 4 : 6-*Tetra-acetate*.—The bromo-compound, $[\alpha]_D$ −42° (1 mol.) and sulphanilamide (2·15 mols.) in absolute ethanol containing a small amount of hydrogen chloride gave a mixture of anomers (recrystallised from ethanol), m. p. 184—190°, $[\alpha]_D^{22}$ −35·0° (*c*, 0·9 in pyridine) (Found : N, 5·5%). A different mixture was isolated from the mother-liquor; this had $[\alpha]_D^{22}$ +48·8° (*c*, 0·9 in pyridine). The yield of recrystallised products was 60%.

INSTITUTE OF ORGANIC CHEMISTRY, KOSSUTH UNIVERSITY,
DEBRECEN, HUNGARY.

[*Received, May* 19*th*, 1954.]