Table II. Regioselectivity in Deprotonation of Ketimines of 3-Pentanone[a]

R in (Z)-2	base	deprotonation temp, °C	rel % yield[b,e] 5	6
t-C_4H_9	LDEA	3	22	78[c]
t-C_4H_9	LDA	3	30	70[c]
$CH_2C_6H_5$	LDA	25	74	26[d]
c-C_6H_{11}	LDEA	0	53	47[d]
C_6H_5	LDA	25	25	75[d]
C_6H_5	LDEA	25	38	62[d]

[a] Deprotonations of (Z)-2 (ca. 0.25 M) were carried out at the indicated temperature by using ca. 2 equiv of the specified lithium dialkylamide base (ca. 0.5 M) in THF. Methylation was carried out at −78 °C. [b] Ratios of 5 to 6 were measured by comparison of $^{13}CH_3$-labeled isopropyl groups to ^{13}C-labeled ethyl groups (cf. ref 6). For R = benzyl, signals from 3 and 4 were resolved, and their ratio as measured from $^{13}CH_3$ peak areas of labeled methyl groups agreed with the ratio of 5 to 6 determined after methylation. [c] These ratios are the corrected ratios of the products 5 and 6. [d] These ratios are the uncorrected ratios of the areas of the ^{13}C NMR signals ascribed to 5 and 6; we typically observed in this work and previously[4] that the peak area ratios differ by less than 10% from the corrected 5 to 6 ratios. [e] Yields of isopropyl ethyl ketimines measured in comparable methylations of the unlabeled azaallyllithium reagent derived from diethyl ketimine with unlabeled methyl iodide were measured by GC using an internal standard and are >95%.

largest steric demands, were studied in some detail to confirm the syn stereochemistry of the intermediate azaallyllithium reagents. When unlabeled 2 was deprotonated and the resulting intermediate (unlabeled 3) was treated with ^{13}C-labeled methyl iodide, we obtained (Z)-5 (δ 18.8) which isomerized on standing to give predominantly (E)-5 (δ 20.5). Further, when N-(tert-butyl)-3-methyl-2-butanimine was deprotonated and subsequently treated with ^{13}C-labeled methyl iodide, we obtained only (E)-6 (δ 10.9); on standing some (Z)-6 (δ 10.6) formed, but (E)-6 always predominated. It is apparent from our results that the previously described preference for syn structures in cyclic azaallyllithium reagents obtains in these acyclic cases as well but that this anion stability has little influence on the transition state for the deprotonation reaction. Indeed, the transition state for this type of exothermic reaction is not likely to be very productlike, and other factors such as steric accessibility of the weakly acidic protons are apparently as important as the stability of the incipient azaallyllithium reagent.

The results described above suggest a complicated picture for regioselectivity in imine deprotonations. Previously, deuterium incorporation (KO-t-Bu, Me_2SO-d_6) into N-benzyl-2-propanimine had suggested that deprotonation occurred only syn to the nitrogen alkyl group,[9] but a recent report that protonation of azaallyllithium reagents by methanol produces nearly quantitative yields of secondary enamines shows that H/D exchange experiments may not provide reliable information concerning deprotonation regioselectivity.[10] The work reported herein and our previous studies of regioselectivity in ketone dimethylhydrazone deprotonations[4,6] clearly show that regioselectivity in deprotonation of nitrogen derivatives of carbonyl compounds is not subject to any simple generalizations. More extensive kinetic and NMR studies to determine the factors responsible for regioselectivity in imine deprotonation are in progress and are certainly necessary for a complete understanding of the effects seen above. Nevertheless, it is clear from our present studies that regioselectivity in formation of azaallyllithium reagents from imines is variable to a greater extent than previously expected and that such regioselectivity is significantly affected by relatively minor experimental changes.

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Registry No. 1 (R = *tert*-Bu), 78004-43-0; 1 (R = c-C_6H_{11}), 6125-75-3; 1 (R = C_6H_5), 40296-03-5; 1 (R = $CH_2C_6H_5$), 31776-80-4; (E)-2 (R = *tert*-Bu), 78004-44-1; (Z)-2 (R = *tert*-Bu), 78004-45-2; (E)-2 (R = c-C_6H_{11}), 78004-46-3; (Z)-2 (R = c-C_6H_{11}), 78004-47-4; (E)-2 (R = C_6H_5), 78004-48-5; (Z)-2 (R = C_6H_5), 78004-49-6; (E)-2 (R = $CH_2C_6H_5$), 78004-50-9; (Z)-2 (R = $CH_2C_6H_5$), 78004-51-0; (E)-5 (R = *t*-Bu), 78004-52-1; (Z)-5 (R = *t*-Bu), 78004-53-2; (E)-5 (R = c-C_6H_5), 78004-54-3; (Z)-5 (R = c-C_6H_5), 78004-55-4; (E)-5 (R = C_6H_5), 78004-56-5; (Z)-5 (R = C_6H_5), 78004-57-6; (E)-5 (R = $CH_2C_6H_5$), 78004-58-7; (Z)-5 (R = $CH_2C_6H_5$), 78004-59-8; (E)-6 (R = *t*-Bu), 78004-60-1; (Z)-6 (R = *t*-Bu), 78004-61-2; (E)-6 (R = c-C_6H_{11}), 78004-62-3; (Z)-6 (R = c-C_6H_{11}), 78004-63-4; (E)-6 (R = C_6H_5), 78004-64-5; (Z)-6 (R = C_6H_5), 78004-65-6; (E)-6 (R = $CH_2C_6H_5$), 78004-66-7; (Z)-6 (R = $CH_2C_6H_5$), 78004-67-8.

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Synthesis of *N*-Glycosides. Formation of Glucosylamine by Reaction of 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose with Acetonitrile in the Presence of Trifluoromethanesulfonic Anhydride

Summary: The synthesis of glucosylamine by reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose with acetonitrile in the presence of trifluoromethanesulfonic anhydride was shown to proceed through an intermediate oxazoline.

Sir: We reported recently a new method for the synthesis of glycosylglycosides[1] and *O*-glycosyl amino acids,[1,2,4] based on the peculiar property of trifluoromethanesulfonic (triflic) acid to form a stable, insoluble hydroxonium trifluoromethanesulfonate $F_3CSO_3^-H_3O^+$, which provides a very efficient trapping of the water liberated during the glycosylation reaction.[3] In this communication we show that, when 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (1) was allowed to react at 0 °C for about 1 h in acetonitrile instead of dichloromethane in the presence of triflic anhydride, 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosylamine (3)

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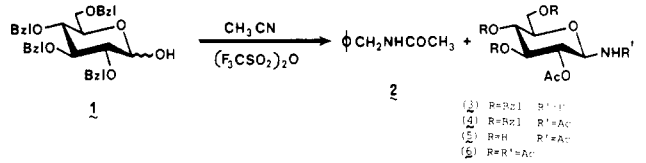
Table I. Physical and Spectroscopic Data for Compounds 2-6

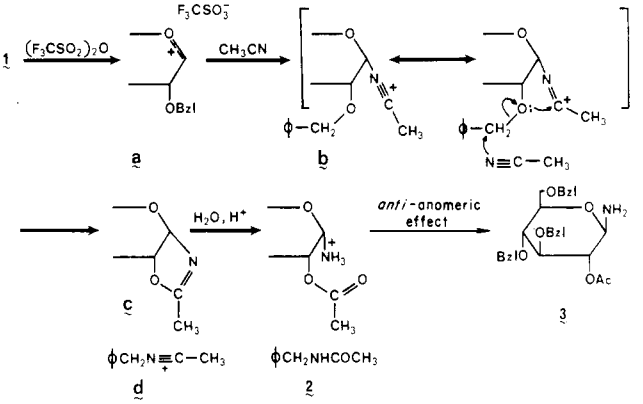
compd	mp, °C	$[\alpha]^{22}_D$, deg	IR, cm^{-1}	^1H NMR ($CDCl_3$),[a] δ[c]	^{13}C NMR (Me_4Si, $CDCl_3$),[a] δ
2	61		1680 (CO), 3480 (NH)	1.92 (CH_3), 4.35 (d, J = 6, CH_2), 6.55 (m, NH), 7.35 (s, 15 H, Ph)	23.09 (CH_3), 43.80 (CH_2), 170.24 (CO)
3	110	+23	1740 (CO), 3400, 3510 (NH)	1.92 (2 H exchangeables, NH_2), 1.97 (CH_3), 4.05 (d, $J_{1,2}$ = 9.2, H-1), 7.27 (15 H, C_6H_5)	20.99 (CH_3), 69.22 (C-6), 83.85 (C-3), 85.10 (C-1)
4	118	+35	1680, 1740 (CO), 3440 (NH)	1.95 (CH_3), 4.95 (t, H-3), 5.15 (t, $J_{1,2}$ = $J_{1,NH}$ = 9.2, H-1), 6.30 (d, J = 9.2, NH), 7.30 (15 H, C_6H_5)	20.76, 23.26 (CH_3), 68.40 (C-6), 77.8 (C-1), 83.41 (C-3), 70.47, 171.33 (CO)
5				1.92, 2.1 (CH_3), 4.72 (t, $J_{1,2}$ = $J_{2,3}$ = 9.5, H-2), 5.10 (d, $J_{1,2}$ = 9.5, H-1), 3.25-3.90 (m, 5 H, H-3, H-4, H-5, H-6's)	20.99, 22.87 (CH_3), 61.38 (C-6), 70.09, 73.88, 75.25 (C-2, C-3, C-4), 78.40, 78.64 (C-1, C-5), 174.03, 175.77 (CO)
6	152[b]	+28[b]		3.85 (octet, $J_{4,5}$ = 9.5, $J_{5,6}$ = 4.5, $J_{5,6'}$ = 2.2, H-5), 4.08 (q, $J_{6,6'}$ = -12.5, H-6'), 4.34 (q, H-6), 4.91 (t, J = 9.3, H-2), 5.05, (t, J = 9.3, H-4), 5.3 (t, J = 9.5, H-1), 5.35 (t, J = 9, H-3), 6.6 (d, J = 9.5, NH)	20.53, 23.32 (1:4, CH_3), 61.92 (C-6), 68.49, 70.91, 73.00, 73.78 (C-2, C-3, C-4, C-5), 78.39 (C-1), 169.69, 169.92, 170.47, 170.7, 171.11 (CO)

[a] Except for compound 5 whose NMR spectra have been recorded in D_2O solution. [b] Lit. F = 160 °C, $[\alpha]^{22}_D$ +17.7° (see ref 5 and 14). [c] Multiplicities, J values (in hertz), and assignments are given in parentheses.

Scheme I



Scheme II



and *N*-benzylacetamide (**2**) were obtained together with the expected octa-*O*-benzyltrehalose. Compound **3** was converted into its hydrochloride derivative by bubbling hydrogen chloride into a chloroform solution of **3**. After treatment with a 0.5 N sodium hydroxide solution, followed by acetylation of the resulting product with a mixture of acetic anhydride–methanol, compound **4** was obtained as crystalline material. Hydrogenolysis with H_2 in the presence of 10% Pd/C and subsequent acetylation in pyridine yielded *N*-acetyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (**6**). The reaction was repeated and provided in each case compound **3** with a yield ranging from 20 to 45% (Scheme I).

Physical and spectroscopic data of compounds **2**–**6** are given in Table I.

Particular noteworthy is the absence of a signal in the region of O-linked anomeric carbons (93–110 ppm) in the ^{13}C NMR spectra. In contrast, we observe the expected large upfield shift of anomeric carbon resonance upon formation of the N-glycosidic linkage[6] (C-1 at 85:10 ppm in **3**, ~78.5 ppm in other compounds).

The chemical shift and coupling constant for H-1 are indicative of a β-anomeric configuration. It is worth noting that the value for $J_{1,2}$ (9.2–9.5 Hz) which is characteristic of a vicinal diaxial coupling is substantially higher than usually found in O-glycosidic structures (7–8.5 Hz). The signal for the anomeric proton at 4.05 ppm in **3** is shifted downfield upon acetylation and appears as a nice well-resolved triplet at 5.15, 5.10, and 5.30 ppm, respectively, in **4**, **5**, and **6**. Deuterium exchange of the NHAc proton, in compound **5** for instance, changes the triplet signal into a doublet with a 9.3-Hz spacing. The chemical shift of the anomeric proton lies in the region usually found for the equatorial anomer. A comparison of data for **3** with those observed for **4**–**6** shows that this feature must be ascribed to the electron—withdrawing effect of the acetamide group attached to C-1 as assumed earlier.[7]

^1H NMR data reported in Table I provide an unambiguous assignment for the α-configuration of the 2-acetyl group. Spectra of compounds **5** and **6** are particularly clear in this respect: both show a well-resolved triplet ($J_{1,2} \simeq J_{2,3} \simeq$ 9.3–9.5 Hz) at, respectively, 4.72 and 4.91 ppm, assigned to H-2.

Compounds **2** and **3** might possibly be formed through the reaction course depicted in Scheme II. The formation of nitrilium salts by nucleophilic attack on an electrophilic carbon by a nitrile has already been reported.[8] With a strong electrophile such as the glycosyl cation a, a nitrile may act as a nucleophile, thus leading to the nitrilium ion intermediate b. Such a scheme has recently been suggested with carbohydrate substrates.[9,10] The formation of a 2-

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O-acetyl derivative with a gluco configuration implies an oxazoline of the same configuration as the intermediate. Subsequent hydrolysis of the oxazoline c is possible since the medium contains both the acid catalyst and water ($F_3CSO_3^-H_3O^+$).[1,3] Such cleavage has been previously observed[11] by Sinäy et al. in the presence of perchloric acid. The reverse anomeric effect[12] must be responsible for the β-anomeric configuration of the amino group in **3**.

Alternatively one might envisage another reaction course in which the key step would be the conversion of the acetonitrilium cation b in the *N*-acetamide derivative followed by the formation of the oxazoline ring c. Cyclization is accompanied by the removal of benzylic alcohol which, in the presence of a strong acid such as F_3CSO_3H, represents a source of benzylic cation. Compound **2** would be the result of the hydrolysis of the *N*-benzylacetonitrilium cation, $PhCH_2N^+{\equiv}CCH_3$, considered to arise by nucleophilic attack on the benzylic cation by the nitrogen atom of acetonitrile.

However this hypothesis seems to be less likely since it involves a cis nucleophilic displacement of the substituent on carbon-2.

In connection with this second possibility, an oxazoline resulting from an acetonitrilium ion with a β-configuration would be more plausible mechanistically. However, a β-oxazoline would produce a compound with a manno configuration, inconsistent with the physical and NMR data reported in Table I.

The above result shows that an acetonitrilium ion can adopt at least temporarily an α-anomeric configuration. (It must be mentioned that Lemieux and co-workers[13] obtained *N*-acetyl-3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosylamine during the azidonitration of tri-*O*-acetyl-D-galactal.) In similar circumstances formation of a β-nitrilium ion was suggested[9,10] as a consequence of the so-called reverse anomeric effect.

The reaction reported herein is interesting in many aspects. (a) It represents one of the rare examples in the field of carbohydrate chemistry of an oxazoline being cleaved hydrolytically. (b) It confirms our earlier suggestion[1,3] that, in the presence of trifluoromethanesulfonic anhydride as a condensing agent, the reaction proceeds through a glycosyloxocarbanion intermediate (a). (c) It could be a useful synthetic procedure to obtain glycosylamines and other *N*-glycosides, such as nucleosides.

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