Conversion of the *N*-Benzylacetamido Group into the Acetamido Group by Autoxidation in Potassium t-Butoxide–Dimethyl Sulphoxide

Roy Gigg* and Robert Conant

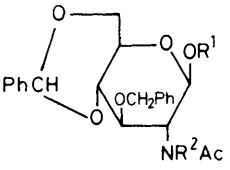
Laboratory of Lipid and General Chemistry, National Institute for Medical Research, Mill Hill, London NW7 1AA, U.K.

The *N*-benzylacetamido group is rapidly converted into the acetamido group at 20 °C by the action of molecular oxygen in a solution of potassium t-butoxide in dimethyl sulphoxide and a general route to acetylated amines by the alkylation of *N*-benzylacetamide and *N*-debenzylation by the above method is proposed.

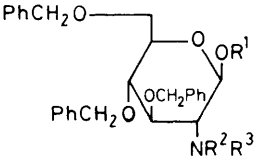
We reported in a preliminary communication[1] that attempts to isomerize allyl 3-*O*-benzyl-2-*N*-benzylacetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (**1**) into the corresponding prop-1-enyl glycoside (**2**) by the action of potassium t-butoxide in dimethyl sulphoxide at 20 °C led to the rapid formation of prop-1-enyl 2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (**3**) and that similar treatment of benzyl 3-*O*-benzyl-2-*N*-benzylacetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (**4**) gave the corresponding acetamido derivative (**5**).

In attempting to scale up the reaction and to generalise it into a preparative method for amines (see below) the reaction failed to go to completion. After consideration of various mechanisms it was concluded that the removal of the *N*-benzyl group was an oxidative reaction and that the limiting factor in the scaled up reactions was atmospheric oxygen, the reaction flask being stoppered to exclude moisture and carbon dioxide. By bubbling air through the reaction mixture the conversion was completed rapidly.

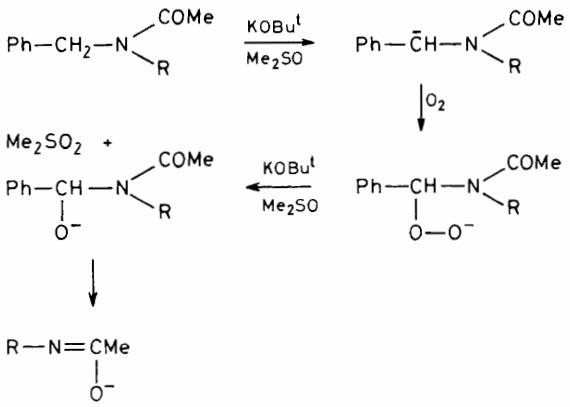
Dry carbon dioxide-free air was passed slowly into a stirred solution of benzyl 3,4,6-tri-*O*-benzyl-2-*N*-benzylacetamido-2-deoxy-β-D-glucopyranoside (**6**) [prepared by acetylation of (**7**)[2]] (1 g) in dry dimethyl sulphoxide (25 ml) containing potassium t-butoxide (1 g) and t.l.c. showed complete conversion into the acetamido derivative (**8**)[3] in 20 min. Similarly, prop-1-enyl 3,4,6-tri-*O*-benzyl-2-*N*-benzylacetamido-2-deoxy-β-D-glucopyranoside (**9**) [prepared by acetylation of (**10**)[2]] gave the acetamido derivative (**11**).[4]



(**1**) $R^1 = CH_2-CH=CH_2$; $R^2 = CH_2Ph$
(**2**) $R^1 = CH=CHMe$; $R^2 = CH_2Ph$
(**3**) $R^1 = CH=CHMe$; $R^2 = H$
(**4**) $R^1 = R^2 = CH_2Ph$
(**5**) $R^1 = CH_2Ph$; $R^2 = H$



(**6**) $R^1 = R^2 = CH_2Ph$; $R^3 = Ac$
(**7**) $R^1 = R^2 = CH_2Ph$; $R^3 = H$
(**8**) $R^1 = CH_2Ph$; $R^2 = H$; $R^3 = Ac$
(**9**) $R^1 = CH=CHMe$; $R^2 = CH_2Ph$; $R^3 = Ac$
(**10**) $R^1 = CH=CHMe$; $R^2 = CH_2Ph$; $R^3 = H$
(**11**) $R^1 = CH=CHMe$; $R^2 = H$; $R^3 = Ac$



Scheme 1

Thus the reaction appears to be an example of the autoxidation of carbanions studied in detail by Russell and his coworkers,[5] proceeding by the mechanism proposed in Scheme 1. Russell and his coworkers[5] have used oxygen and a mixture of dimethyl sulphoxide–t-butyl alcohol (4:1) as solvent to avoid the autoxidation of dimethyl sulphoxide to dimethyl sulphone which occurs with potassium t-butoxide in dimethyl sulphoxide. However, t-butyl alcohol reduces[6] the rate of isomerisation of allyl ethers to prop-1-enyl ethers and we have continued to use pure dimethyl sulphoxide since the *N*-debenzylation is rapid and dimethyl sulphone does not interfere with the isolation of the non-polar products.

The *N*-debenzylation of the *N*-benzylacetamido group by hydrogenolysis with Pd–C–H_2 in glacial acetic acid is a slow reaction and is therefore usually accomplished by the action of sodium in liquid ammonia,[1] but both methods also remove *O*-benzyl groups. The ability to remove the benzyl moiety from the *N*-benzylacetamido group, using the autoxidation procedure, without affecting *O*-benzyl groups should be of value in the chemistry of the amino-sugars when using the *N*-benzylacetamido group as a protected form of the acetamido group.[1] The method should also be useful for *N*-debenzylation of the *N*-benzylacetamido group produced during *O*-benzylation of acetamido-sugar derivatives under vigorous conditions (*e.g.* with benzyl bromide and sodium hydride in *N,N*-dimethylformamide).

The ease of removal of the *N*-benzyl group also suggested a new general route for the preparation of acetylated amines. Alkylation of *N*-benzylacetamide[7] with dodecyl bromide and sodium hydride in *N,N*-dimethylformamide readily gave *N*-acetyl-*N*-benzyldodecylamine which was rapidly *N*-debenzylated, as above, to give *N*-acetyldodecylamine.[8] This *N*-debenzylation was also achieved using Pd–C–H_2 in glacial acetic acid during 3 days.

Received, 14th January 1983; Com. 070

References

1 R. Gigg and R. Conant, *Carbohydr. Res.*, 1982, **100**, C5.
2 R. Gigg and R. Conant, *J. Carbohydr. Chem.*, in the press.
3 R. Harrison and H. G. Fletcher, *J. Org. Chem.*, 1965, **30**, 2317; J. R. Plimmer, N. Pravdić, and H. G. Fletcher, *ibid.*, 1967, **32**, 1982.
4 C. D. Warren, M. A. E. Shaban, and R. W. Jeanloz, *Carbohydr. Res.*, 1977, **59**, 427; M. A. Nashed, C. W. Slife, M. Kiso, and L. Anderson, *ibid.*, 1980, **82**, 237.
5 G. A. Russell and A. G. Bemis, *J. Am. Chem. Soc.*, 1966, **88**, 5491; G. A. Russell, A. J. Moye, E. G. Janzen, S. Mak, and E. R. Talaty, *J. Org. Chem.*, 1967, **32**, 137; G. A. Russell, A. G. Bemis, E. J. Geels, E. G. Janzen, and A. J. Moye, *Adv. Chem. Ser.*, 1968, **75**, 174.
6 C. C. Price and W. H. Snyder, *J. Am. Chem. Soc.*, 1961, **83**, 1773.
7 C. A. Buehler and C. A. Mackenzie, *J. Am. Chem. Soc.*, 1937, **59**, 421.
8 R. Goto, A. Watanabe, K. Hojo, and M. Kosaka, *Nippon Kagaku Zasshi*, 1966, **87**, 1220.