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RADICAL DEAMINATION REACTIONS OF RELEVANCE TO AMINOGLYCOSIDE CHEMISTRY

by

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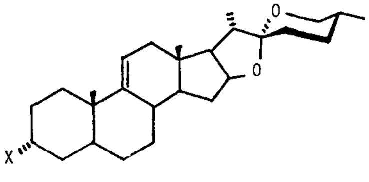
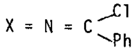
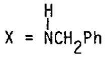
Abstract.— Reduction of tert.-, sec.- and prim.- isonitriles with tributylstanne affords in good yields, but at progressively higher temperatures, the corresponding hydrocarbons. Sec.-thiocyanates and selenocyanates are also smoothly reduced but via the isonitriles. All reactions are radical in character.

We have recently described a new method for the radical deoxygenation of secondary alcohols[1]. Since the reaction proceeds via a radical chain mechanism it is especially useful in carbohydrate chemistry. The selective removal of an amino group by a conceptually similar mechanism was also considered to be a worthwhile objective. An isolated report in the literature indicated that the isonitrile moiety could be reduced to the corresponding hydrocarbon by tri-n-butylstannane[2]. However, yields were low and isonitriles bearing a unactivated primary alkyl chain were not reported to be reactive. In view of the demonstrated affinity of tin radicals for sulphur and selenium containing substrates, we envisaged that the isothiocyanate or isoselenocyanate grouping might prove to be a better precursor for radical induced fragmentation[3].



1 $X = NH_2$
2 $X = N = C:$
3 $X = N = C = Se$
4 $X = N = C = S$
5 $X = H$
6 
$X = N = C\begin{smallmatrix}Cl\\Ph\end{smallmatrix}$
7 
$X = \overset{H}{\overset{|}{N}}CH_2Ph$

The steroidal amine (1), derived from Δ^9-tigogenin, was selected for preliminary studies. Formylation (formyl acetic anhydride) and dehydration (p-toluenesulphonyl chloride in pyridine) readily afforded the isonitrile[4] (2) and subsequent reaction with elemental selenium gave the corresponding isoselenocyanate (3). The isothiocyanate (4) was prepared by reaction of the amine with carbon disulphide and dicyclohexyl-carbodiimide. Reaction of each derivative with tri-n-butyl stannane in refluxing benzene in the presence of radical initiator (AIBN) gave the hydrocarbon (5) in excellent yields.(Table). However reduction of the imidoyl halide derivative (6) gave the benzylamine (7) (64%) indicating that fragmentation of the stabilised intermediate radical did not occur. In the case of the isothiocyanate (4) and isoselenocyanate (3) reductions, careful monitoring of the reaction by infrared spectroscopy indicated that the isonitrile (2) was formed as an intermediate.

Table

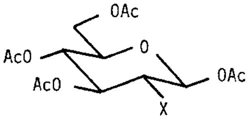
$$R - N = X \xrightarrow{nBu_3SnH} RH$$

AMINE ($R-NH_2$)	DERIVATIVE (X)	REACTION CONDITIONS	PRODUCT	YIELD (%)
3α-cholestanylamine	= C:	B	cholestane	55
	= C = S	B		83
3α-amino-5α: 22α - spirostane (1)	= C:	C	5α: 22α spirostane (5)	89
	= C = S	C		90
	= C = Se	C		88
n-octadecylamine	= C:	A	n-octadecane	81
	= C = S	A		80
2-methyl-2-amino-nonadecane	= C:	C	2-methylnonadecane	91
2-amino-2-deoxy β-D-glucose tetraacetate	= C:	C	2-deoxy-β-D-glucose tetraacetate	72
glycylglycine ethylester	= C:	C	n-acetylglycine ethylester	71
dl 1,2-diamino-1,2-diphenylethane	= C:	C	bibenzyl	56
meso 1,2-diamino-1,2-diphenylethane	= C:	C	bibenzyl	53

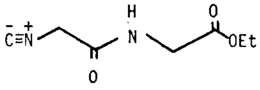
A : reflux in xylene , B : reflux in toluene , C : reflux in benzene

This was confirmed by an examination of n-octadecylamine derivatives. As anticipated, cleavage of the carbon nitrogen bond to give a primary alkyl radical required a considerably higher activation energy. Acceptable yields of n-octadecane were obtained only in refluxing xylene with periodic additions of initiator. At lower temperatures it was possible to isolate the isonitrile as an intermediate from the reaction of the isothiocyanate.

Contrastingly, an isonitrile bearing a tertiary carbon atom α to the nitrogen atom underwent smooth fragmentation in refluxing benzene solution and even at 60° C.



8 X = NC
9 X = H



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We have investigated the applicability of this sequence in the carbohydrate field. Formylation of α-D-glucosamine tetraacetate and dehydration using p-toluenesulphonyl chloride in pyridine gave the isonitrile (8) (60%) which was readily reduced by tri-n-butylstannane to the 2-deoxyglucose derivative (9) in 71% yield. The successful deamination of the relatively unstable isonitrile (10) prepared from the ethyl ester of glycylglycine indicates potential utility in the peptide area.

In view of our reported conversion of vicinal diols into olefins *via* the derived *bis* dithiocarbonates[5] it was of interest to examine the reaction of *meso* and *dl* 1,2-dipnenyl-1,2-diisocyanoethanes. Tri-n-butyl stannane reduction in refluxing benzene afforded bibenzyl. The outcome of the reaction was not altered by increasing temperature.

It is thus apparent that the radical induced deamination of isonitriles is a considerably more useful process than initially indicated. Yields are high and the reaction is tolerant to a large number of functional groups. It thus offers a complementary technique to recently described deamination reactions involving ionic-[6,7] and radical-[8] type intermediates.

REFERENCES

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3. Aryl isothiocyanates are reported to react with stannanes to give *either* (a) the product of addition across the thiocarbonyl group (J.G. Noltes and M.J. Janssen, *J. Organometal. Chem.* 1, *346* (1964) *or* (b) a mixture of the corresponding isonitrile and anilines (D.H. Lorentz and E.J. Becker, *J. Org. Chem.*, *28*, 1707(1963)) . The obtention of deaminated products was not described.

4. All new compounds have been completely characterised by analytical and spectroscopic methods.

5. A.G.M. Barrett, D.H.R. Barton, R. Bielski and S.W. McCombie, J.C.S. Chem. Comm., 866(1977).
6. G.E. Niznik and H.M. Walborsky, J. Org. Chem., 43, 2396(1978).
7. G.A. Doldouras and J. Kollonitsch, J. Amer. Chem. Soc., 100, 341(1978).

8. Professor A.R. Katritzky has kindly sent us a copy of his manuscript (A.R. Katritzky, K. Horvath, and B. Plau, J.C.S. (Chem. Comm.), in press.)) which describes the radical deamination of non-hindered primary amines by pyrolysis at 180-200° of 1,4-dihydropyridines.

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