A Novel One-pot Method for Reductive Conversion of Azides to Acyl Amines with Acetic Anhydride and Trimethyl Chlorosilane

Apurba Barua, Ghanashyam Bez, Nabin C. Barua*

Natural Products Chemistry Division, Regional Research Laboratory, Jorhat-785006, Assam, India
Fax +91-(0376) 321158

Received 26 February 1999

Abstract : A combination of acetic anhydride and chloro-trimethylsilane has been shown to effect the conversion of a variety of azides to the corresponding acetylated amines in excellent yields without affecting other functional groups such as ether, ester, halide etc.

Key words: azide, acyl amines, trimethyl chlorosilane, acetic anhydride

The reduction of azides to amines is of immense importance in organic synthesis as a general protocol for introduction of an amino group and quite a number of excellent methods are reported in the literature for bringing about this transformation.[1] Equally important is the protection of amines as acetyl or other acyl derivatives albeit there are only a few literature procedures[2] for converting azides directly to amides. Recently, Kotsuki et al.[3] reported a chemoselective procedure for conversion of azides to *N*-(*tert*-butoxy carbonyl)amines in one step using Et_3SiH and di-*tert*-butyl dicarbonate in the presence of a catalytic amount of 20% Degassa $Pd(OH)_2/C$ with moderate to excellent yields.

We earlier reported that the combination of acetic anhydride and chlorotrimethylsilane is an excellent reagent system for cleaving a variety of methyl and methylthiomethyl ethers to the corresponding acetates both in aliphatic and aromatic series.[4] The same reagent system has also been shown to be effective for converting a variety of ketones into their corresponding enol acetates in good yields.[5] The naked acylonium ion, which is believed to be formed on mixing acetic anhydride with chlorotrimethylsilane might be the reacting species in these transformations. We have recently observed that when azides are treated with this reagent under reflux the corresponding amides are formed in excellent yields. This observation has been generalised through entries 1-14 in Table 1.

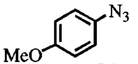
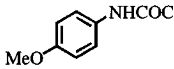
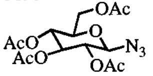
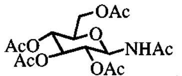
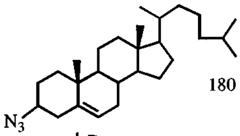
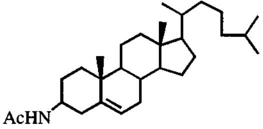
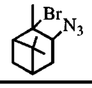
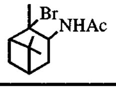
$$R{-}N_3 \xrightarrow[\text{R = alkyl, aryl}]{\text{CTMS/Ac}_2\text{O, }\Delta} R{-}NHAc$$

Typical Procedure:

To a stirred solution of the azide (1 equiv) in a minimum amount of acetic anhydride is added chlorotrimetylsilane (1 equiv.). The reaction was refluxed for 0.5-1 hr while monitoring the reaction on TLC. On completion of the reaction, the temperature of the reaction mixture was brought down to RT, quenched with cold water and extracted with dichloromethane. The dried extract on evaporation left a residue which was purified by preparative TLC or by crystallization.

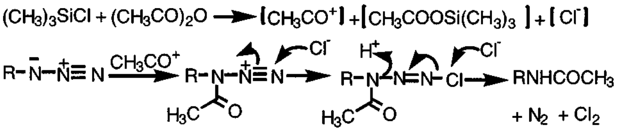
It is evident from Table-1 that the methyl ether group in **2** and the ethyl ester function in **5** remained unaffected. However, the phenolic hydroxyl group in **3** is converted into its acetate. It is interesting to note that treatment of anisyl azide with ClTMS and trifluoroacetic anhydride gave trifluoroacetyl *m*-anisidine in 82% yield.

Table 1. Reductive acylation of azides to acyl amines with CITMS/Ac_2O.

Entry	Azides[a]	Reaction time (min)	Product[b]	yield[c] (%)
1	Phenyl azide	10	acetanilide	90
2	3-Methoxy phenyl azide	60	m-acetanisidide	92
3	3-Hydroxy phenyl azide	60	3-acetamidophenol	85
4	4-Chloro phenyl azide	60	N-(4-chloro phenyl) acetamide	82
5	4-Azido ethyl benzoate	60	4-acetylamino ethyl benzoate	89
6	1,6-Dimethyl phenyl azide	60	N-(1,6-dimethyl phenyl) acetamide	87
7	Benzoyl azide	60	N-acetyl benzamide	80
8	Benzyl azide	60	N-(phenylmethyl)acetamide	78
9	Cetyl azide	60	N-acetyl cetyl amine	69
10	n-Octyl azide	30	N-acetyl octyl amine	79
11		60		82
12		150		62
13		180		67
14		90		81

[a]All the azides were prepared by following standard literature procedures and characterised by IR, ^1H NMR and MS before performing the reactions. [b]All the acyl amines were characterised by IR, ^1H NMR, MS and by direct comparison with authentic materials. [c]Yields refers to yields of pure isolated products.

As for the mechanism of reaction no definit statement can be made as yet. However, the most plausible mechanism might involve initial attack of acylonium ion to electron rich nitrogen atom of the azide with concomitant chloride ion assisted nitrogen gas elimination and protonation from the HCl associated with ClTMS to give the product as shown in the following mechanism.



Thus we have demonstrated a straight forward one pot procedure for conversion of azides to their corresponding acylated amines in excellent yields in a easy-to-carryout procedure.

Acknowledgement

Authors are grateful to Director, RRL Jorhat for providing facilities for this work. GB is grateful to CSIR for Senor Resrarch Fellowship (SRF).

References and Notes

(1) a)Scrivens, E.F.V.; Turnbull, K. *Chem.Rev.*,**1988**, *88*, 297 and references cited therein. b) Samano, M.C.; Rabins, M.J.; *Tetrahedron Lett.*, **1991**, *32*, 6293 c) Poopeiko, N. E.; Protica, T. I. and Mikhailopulo, I.A.; *Synlett*, **1991**,342. d) Ranu, B.C.; Sarkar, A.and Chakrabarty, R; *J. Org. Chem.*,**1994**, *59*, 4114. e) Corey, E.J.; Nicolaou, K.C.; Balanson, R.D.; Machida, Y.; *Synthesis*, **1975**, 590. f) Kirk, D.N.; Wilson, M.A.; *J. Chem. Soc. Chem.Commun.*, **1970**, 64 g) Konodo,T.; Nakai, H.; Goto, T.; *Tetrahedron*, **1973**, *29*, 1801. h) Rolla,E.; *J. Org. Chem.*, **1982**, *47*, 4327.

(2) a) Rosen, T.; Lico, I. M. and Chu, D.T.W.; *J. Org. Chem.*, **1988**,1580. b) Garcia, J.; Urpi, F.and Vilarrasa, *Tetrahedron Lett.*, **1984**, *25*, 4841.

(3) Kotsuki, H; Ohishi, T and Araki, T. *Tetrahedron Lett.*, **1997**, *38*, 2129.

(4) Barua, N C; Sharma, R P and Baruah, J N *Tetrahedron Lett.*, **1983**, *24*, 1189.

(5) Chowdhury, P K and Sharma, R P, Baruah, J N *Tetrahedron Lett.*,**1983**, *24*, 3383.

Article Identifier:
1437-2096,E;1999,0,05,0553,0554,ftx,en;L02699ST.pdf