This article was downloaded by: [McMaster University] On: 02 April 2015, At: 08:13 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lsyc20

Low-Valent Titanium Mediated Deprotection of N-Allyl/Benzyl Amines: A New Approach

Sanjay Talukdar^a & Asoke Banerji^a ^a Bio-Organic Division, Bhabha Atomic Research Centre Trombay, Bombay, 400085 Published online: 23 Sep 2006.

To cite this article: Sanjay Talukdar & Asoke Banerji (1995) Low-Valent Titanium Mediated Deprotection of N-Allyl/Benzyl Amines: A New Approach, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 25:6, 813-818, DOI: <u>10.1080/00397919508013417</u>

To link to this article: http://dx.doi.org/10.1080/00397919508013417

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages,

and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

LOW-VALENT TITANIUM MEDIATED DEPROTECTION OF N-ALLYL/BENZYL AMINES : A NEW APPROACH

Sanjay Talukdar and Asoke Banerji*

Bio-Organic Division Bhabha Atomic Research Centre Trombay, Bombay-400085

Abstract: A novel low-valent titanium (LVT) mediated cleavage of N-allyl/ benzyl amines is reported. Regio- and chemo-selective cleavages were also observed.

Selective protection/deprotection of reactive sites in multifunctional compounds remains an area of active research in the chemical manipulation of synthetic as well as natural products¹. Protection of amino function is called for in the synthesis of many compounds and particularly in peptides. Amongst different protective groups for amines, N-benzylation is most frequently used. Classically, debenzylation of N-benzyl amines is achieved by high pressure catalytic hydrogenation ^{2,3}, by using hydrogen donors^{4,5,6} or by β-trimethylsilyl chloroformate⁷. Photo-sensitised single electron transfer (SET) mediated protocols⁸ have also been used successfully for N-debenzylation reactions. Recent report on zirconocene complex mediated deallylation of O-allyl/N-allyl amines⁹ prompted us to communicate our results on the cleavage of N-allyl/benzyl bonds by low valent titanium (LVT) reagents.

[•] To whom correspondence should be addressed.

Copyright @ 1995 by Marcel Dekker, Inc.

In continuation of our work on LVT mediated synthetic transformations, a novel approach to selective deprotection of allyl, benzyl¹⁰ and propargyl¹¹ ethers of alcohols and phenols was described. The selectivities in the cleavages could be explained by the differential stabilities of the intermediate Ti-complexes. Based on these findings, it could be argued that N-benzyl/allyl bonds should also undergo cleavages through similar mechanism though at comparatively slower rates. In order to verify this hypothesis, a systematic study on the effects of LVT on different N-benzyl/allyl amines was undertaken.

When a reaction was carried out with N-allyl diphenylamine (1b) and LVT (TiCl₂-Li-THF, reflux, 20 h), smooth deprotection occurred furnishing diphenylamine (2b) in 65% yield (Table, entry 1). Compared to N-deallylation, O-deallylation was much faster and required only 2.5 h¹⁰. The N-CH₂ group remains unaffected under these conditions as evidenced by the formation of Nmethylaniline (2a) from N-methyl-N-allylaniline (1a) (Table, entry 2). Similarly, selective N-debenzylation could be carried out in the presence of N-Me group. Thus, when N-benzyl-N-methyl aniline (3a) and N-(4-N,N-dimethylaminobenzyl) aniline (3b) were treated with LVT, N-methyl aniline(2a) (Table, entry 4) and p-N,N-dimethylamino toluene (4'b) (Table, entry 3) were obtained respectively. The scope of this methodology has been illustrated by the deprotection of a variety of N-allyl/benzyl amines. As an example of alicyclic compounds, deallylation of N-allyl dicyclohexylamine (1c) (Table, entry 5) was carried out successfully. This protocol could be used for substituted benzyl amines also. Thus, in the cases of N-(2-hydroxybenzyl)aniline (3c) and N-(4-N,N-dimethylamino benzyl)aniline (3b), aniline was obtained in both the cases. In addition to aniline, p-N,N-dimethylamino toluene (4'b) (Table, entry 3), ocresol (4'c) (Table, entry 6) were also isolated.

Selective cleavage of allyl group could be shown by using substrates containing both N-allyl and N-benzyl groups. Thus, N-allyl-N-benzylaniline (1d) furnished N-benzylaniline (2d) (Table, entry 7). O-Benzyl bond could be selectively cleaved in preference to N-benzyl bond. Thus, 2-hydroxybenzyl aniline (6a) was obtained as the sole product when 2-benzyloxy-N-benzyl aniline (5a) was used as substrate (Table, entry 8). N-Cinnamyl group could be cleaved at a faster rate possibly due to the additional stability of cinnamyl radical. 2-Methoxyaniline (8a) was obtained from N-cinnamyl-2-methoxyaniline (7a) (Table, entry 9). This reaction also shows the compatibility of methoxy groups under the present reaction condition. Mechanistically, the reaction probably proceeds via Single Electron Transfer (SET) process where LVT species donate electrons to amine (I) giving radical intermediate (II) which undergoes regioselective cleavage leading to stable allyl or benzyl radical and the amine complex (III); the free amine is liberated during the aqueous work-up.



This is the first report of LVT-mediated deprotection of N-benzyl or N-allyl amines which holds considerable promise in both aliphatic and aromatic domain. Regioselectivity and chemoselectivity have been demonstrated by the selective cleavage of N-allyl bond in the presence of N-benzyl bond and cleavage of Obenzyl bond in the presence of N-benzyl bond respectively. N-Methyl or Omethyl groups remain unaffected under the reaction conditions. This along with our earlier reports offer several protocols for the protection of alcohols, phenols and amines in multistep organic synthesis.

General Procedure for the N-deallylation/debenzylation

A mixture of TiCl₃ (3.47 g, 22.5 mmol) and lithium (0.525 g, 75 mmol) in dry THF (70 ml) was refluxed (3 h, argon). After cooling, an appropriate Nallyl or N-benzyl compound (5 mmol, 5 ml THF) was added and refluxed (monitored by TLC). After completion, the reaction mixture was cooled, diluted with petroleum ether-ethyl acetate mixture and passed through celite, the organic layer was washed with water, brine and dried (Na₂SO₄). Concentration gave crude product which was purified by preparative thin layer chromatography (SiO₂) to furnish desired amino derivative.



N-ALLYL/BENZYL AMINES

Entry	Substrate	Conditions	Product(s) ^a	Yield(%)
1	1b	20 h reflux	2b	65
2	1a	18 h "	2a	48
3	3b	22 h "	4b	49
			4'b	47
4	3a	22 h "	2a	55
5	1c	20 h "	2c	47
6	3c	22 h "	4b	47
			4°c	47
7	1 d	18 h "	2d	49
8	5a	16 h "	6a	48
9	7a	5h "	8a	53

Table : Cleavage of N-Allyl and N-Benzyl Amines with LVT

^a Products were characterised by comparison with authentic samples (IR, ¹HNMR, TLC and M.P.)

References:

- Green, T. W. and Wuts, P. G. M., "Protective Groups in Organic Synthesis," John Wiley & Sons, New York, 1991, 2nd edn.
- Velluz, L., Amiard, G. and Heymes, R., Bull. Soc. Chim. Fr., 1954, 1012.
- 3. Hartung, W.H. and Simonoff, R., Organic Reactions, 1953, VII, 263.
- ElAmin, B., Anantharamaiah., G. Royer, G. and Means, G., J. Org. Chem., 1979, <u>44</u>, 3442.
- 5. Ram, S. and Spicer L.D., Synth. Commun., 1987, 17, 415.
- 6. Adger, B.M., Farrel, C.O., Lewis, N.J. and Mitchel, M.B., Synthesis, 1987, 53.
- 7. Compbell, A.L., Pilipanskas, D.R., Khanna, I.K. and Rhodes, R.A., *Tetrahedron Lett.*, **1987**, <u>28</u>, 2331.

- 8. Pandey, G. and Sudha Rani K., Tetrahedron Lett., 1988, 29, 4157.
- 9. Ito, H., Taguchi, T. and Hanzawa, Y., J. Org. chem., 1993, 58, 774.
- 10. Kadam, S.M. Nayak, S.K. and Banerji, A., *Tetrahedron Lett.*, **1992**, <u>33</u>, 5129.
- 11. Nayak S.K., Kadam, S.M. and Banerji, A., Synlett, 1993, 581.

(Received in the UK 24 August 1994)