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A GENERAL PROCEDURE FOR THE CATALYTIC HYDROGENOLYSIS OF N-BENZYLAMINES UNDER EXTREMELY MILD CONDITIONS.

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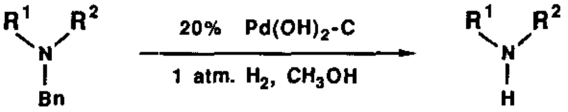
Abstract---A general procedure for debenzylation of N-benzylamines, which contain acid sensitive functional groups, by the catalytic hydrogenolysis using 20% $Pd(OH)_2$-C is reported.

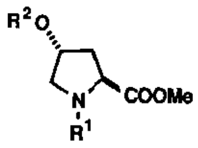
Despite of the importance of the benzyl group in the protection of amines,[1] deprotection of the N-benzyl group is still most often carried out by the traditional catalytic hydrogenolysis using Pd-C under high pressure and/or in the presence of the acid catalyst.[2]

Recently, Adger[3] and Ram[4] reported independently the Pd-C catalyzed hydrogen transfer hydrogenolysis of N-benzylamines with ammonium formate as a hydrogen donor. In the present paper, we wish to describe a general procedure for the catalytic hydrogenolysis of N-benzylamines under the extremely mild conditions using 20% $Pd(OH)_2$-C which has been discovered by Pearlman.[5] To the best of our knowledge, a few examples of the debenzylation of N-benzylamines using $Pd(OH)_2$-C have appeared in the literature.[6, 7] However, none of scope and limitations has been reported.

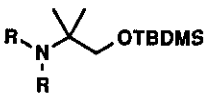
Scheme 1



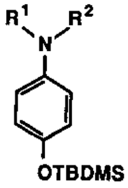
General Procedure: To a solution of an appropriate N-benzylamine (1.00 mmol) in 10 ml of dry methanol was added 50 mg of 20% $Pd(OH)_2$-C[5] in one portion. The mixture was hydrogenated under 1 atm hydrogen and the reaction was monitored by TLC analysis. After completion of the reaction, the catalyst was removed by filtration through celite and was washed with 20 ml of methanol. The filtrate and washing were combined and concentrated under reduced pressure to afford pure product.



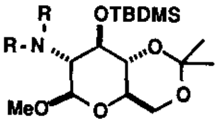
1a ; R^1=Bn, R^2=TBDMS
1b ; R^1=H, R^2=TBDMS
1c ; R^1=Bn, R^2=SiEt$_3$
1d ; R^1=H, R^2=SiEt$_3$
1e ; R^1=Bn, R^2=THP
1f ; R^1=H, R^2=THP
1g ; R^1=Bn, R^2=Tr
1h ; R^1=H, R^2=Tr



2a ; R=Bn
2b ; R=H



3a ; R^1=R^2=Bn
3b ; R^1=Bn, R^2=H
3c ; R^1=R^2=H



4a ; R=Bn
4b ; R=H

Table Catalytic Hydrogenolysis of N-Benzylamines

Entry	Substrate	Product^a	Reaction Time	Yield (%)^b
1	**1a**	**1b**	1.5 h	99
2	**1c**	**1d**	1.0 h	81^c
3	**1e**^{d}	**1f**	15 min	100
4	**1g**	**1h**	4.0 h	60
5	**2a**	**2b**	1.0 h	100
6	**3a**	**3c**	0.5 h	100
7	**3b**	**3c**	10 min	100
8	**4a**^{e}	**4b**	6.0 h	94

a) Characterized by NMR, IR, and Mass spectra; b) the purity of the product (>98%) was determined by NMR analysis; c) isolated yield; d) mixture of the diastereoisomers (1 : 1.6); e) reference 8.

In most cases, the reaction was fast and the product was obtained in excellent yield. Under these conditions, the acid sensitive protective groups of alcohol (triethysilyl, *tert*-butyldimethylsilyl, tetrahydropyranyl, acetonide) were not damaged. Exceptionally, in the case of **1g** (entry 4), the reaction was slow and several polar by-products possibly derived from detritylated compound were detected by TLC.

In conclusion, we wish to emphasize that N-benzylamines are now readily cleaved under the extremely mild conditions.

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REFERENCES AND NOTES

1) T. W. Greene, *Protective Groups in Organic Synthesis*, John Wiley & Sons, Inc., pp 272-273 (1981).

2) W. H. Hartung and R. Simonoff, *Organic Reactions*, VII, 263 (1953).

3) B. M. Adger, C. O'Farrell, N. J. Lewis, and M. B. Mitchell, *Synthesis*, **1987**, 53.

4) a) S. Ram and L. D. Spicer, *Tetrahedron Lett.*, **1987**, 28, 515. b) idem, *Synthetic Commun.*, **1987**, 17, 415.

5) W. M. Pearlman, *Tetrahedron Lett.*, **1967**, 1663. The catalyst was prepared according to the reported procedure and finally washed with distilled water until pH of the washing became neutral. The catalyst was dried over P$_2$O$_5$ under high vacuum at 60 °C for 24 h before use.

6) M. Furukawa, T. Okawara, Y. Noguchi, and Y. Terawaki, *Chem. Pharm. Bull.*, **1979**, 27, 2223.

7) Y. Yamamoto, W. Ito, and K. Maruyama, *J. Chem. Soc., Chem. Commun.*, **1985**, 1131.

8) Compound **4a** was prepared from methyl N-carbobenzyloxy-β-D-glucosaminide. T. Suami and T. Machinami, *Bull. Chem. Soc. Japan*, **1970**, 43, 3013.

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