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Reductive, Selective Deoxygenation of Acylbenzo[b]furans, Aromatic Aldehydes and Ketones with $NaBH_3CN$-TMSCl

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Abstract

Aromatic aldehydes, ketones and acylbenzo[b]furans have been reductively deoxygenated with sodium cyanoborohydride and the mild electrophile chlorotrimethylsilane.

The Wolff-Kishner[1] reaction is employed traditionally for the deoxygenation of acylbenzo[b]furans to alkylbenzo[b]furans. The harsh conditions of the method limit its use to relatively unsubstituted compounds. Alternate reductive deoxygenation methods, including ionic and non ionic hydrogenation[2] methods, or lithium in ammonia,[3] are not applicable because of the reactivity of the furan ring double bond[2] and the facile polymerization[4] of the benzo[b]furan substrates under the acid or the Lewis acid catalysts employed.

The reagent $NaBH_3CN$ has been used for imine reduction, carbonyl reductive amination and reduction, and reductive displacement of halides and tosylates.[5] Deoxygenation of aldehydes and ketones has been reported to occur through the corresponding hydrazone derivatives.[5, 8] The transition metal modified reagent was used to convert acid halides to aldehydes[6], to reduce alkyl halides to hydrocarbons[7], carbonyl compounds to alcohols and imines to amines.[8] Direct deoxygenation[9, 10] of aldehydes and ketones, and reductive protective group cleavage[11] has been reported to take place using ZnI_2[9] and $BF_3{\cdot}Et_2O$[10, 11] catalysis. Carbohydrate benzylidene[12] and other acetals[13] were reduced to ethers with acid catalysts or other electrophiles.

Avoiding the use of acid and Lewis acids catalysts, we used $NaBH_3CN$ and the mild electrophile TMSCl to convert acyl to alkyl benzo[b]furan derivatives.

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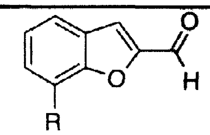
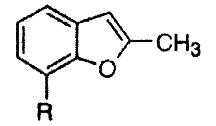
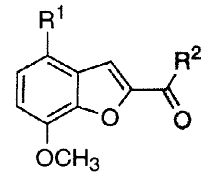
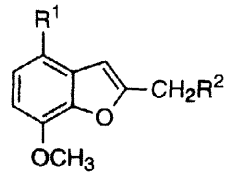
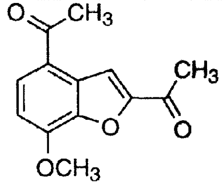
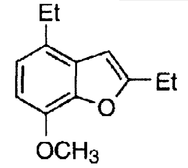
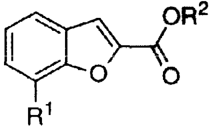
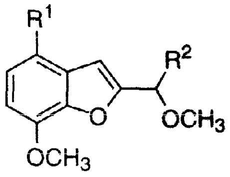
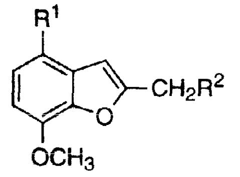
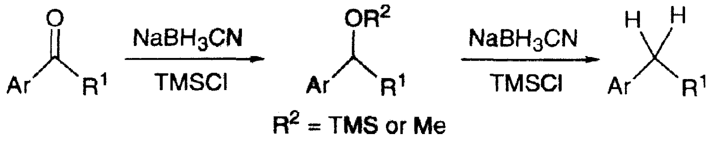
Table 1. Deoxygenation of acylbenzo[b]furan derivatives to alkylbenzo[b]furans

Entry	Substrate	Product		Yield (%)
a b	 1	 2	a: R = H b: R = OCH_3	77 79
c d e f	 3	 4	c: R^1 = H, R^2 = CH_3 d: R^1 = Br, R^2 = CH_3 e: R^1 = H, R^2 = Ph f: R^1 = Br, R^2 = Ph	80 78 81 76
g	 5	 6		83
h i	 7		h: R^1 = H, R^2 = C_2H_5 i: R^1 = OCH_3, R^2 = CH_3	No reaction
j k l	 8	 9	j: R^1 = H, R^2 = CH_3 k: R^1 = Br, R^2 = CH_3 l: R^1 = Br, R^2 = Ph	80 77 79

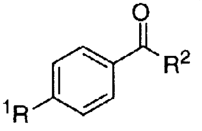
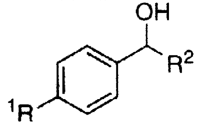
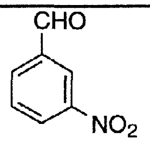
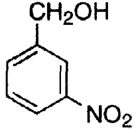
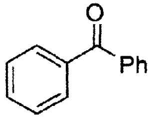
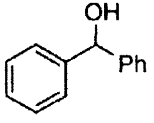
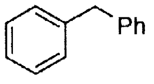
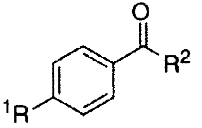
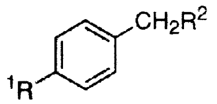
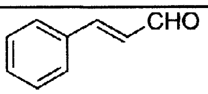
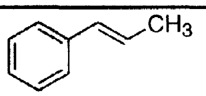
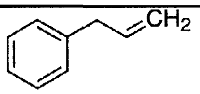
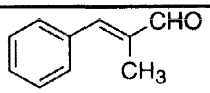
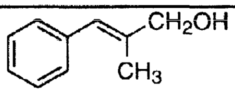
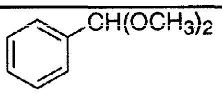
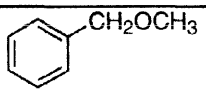
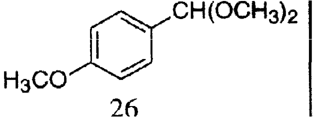
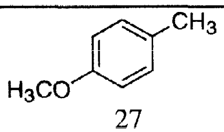
Under the typical experimental procedure[12e] benzo[b]furan aldehydes and 2-acyl-benzo[b]furan derivatives were smoothly deoxygenated to the corresponding alkyl benzofurans. Ethyl and methyl benzofuroate esters **7** did not react (table 1).[14]

The selectivity of the reagent was probed by applying the same experimental procedure on aryl aldehydes and ketone derivatives (table 2).[14] Aldehydes and ketones **17** with activated aromatic rings were deoxygenated. Carbonyl groups on nonactivated **10a, 10d** or deactivated **10b, 10c, 12** aromatic rings were reduced to alcohols. Benzophenone **14** under the standard reaction conditions afforded a mixture of the alcohol **15** and the diphenylmethane **16**. Cinnamaldehyde **19** was deoxygenated to 1-phenylpropene **20** and trace of 3-phenylpropene **21**. However the α-methylcinnamaldehyde **22** was only reduced to the alcohol **23**. The alcohols were formed from the desilylation of the presumed silylether intermediate[12d] (Eq. 1), during the aqueous experimental work up of the reaction mixture. Consequently, the benzo[b]furanyl methyl ethers **8** were demethoxylated at comparable yields to the precursor acylbenzo[b]furans. The dimethyl acetal of the benzaldehyde **24** was reduced to the methoxytoluene **25** and the dimethyl acetal of the 4-methoxy benzaldehyde **26** was reduced to the 4-methoxy-toluene **27**.



Eq. 1

Table 2. Deoxygenation of aromatic aldehydes and ketones.

Entry	Substrate	Product	Yield (%)
a b c d	 10	 11 a: $\mathrm{R^1 = H, R^2 = H}$ b: $\mathrm{R^1 = Cl, R^2 = H}$ c: $\mathrm{R^1 = NO_2, R^2 = H}$ d: $\mathrm{R^1 = H, R^2 = CH_3}$	77 81 85 83
e	 12	 13	83
f	 14	 15  16 15 16	51 33
g h i	 17	 18 g: $\mathrm{R^1 = OCH_3, R^2 = H}$ h: $\mathrm{R^1 = OCH_3, R^2 = CH_3}$ i: $\mathrm{R^1 = OCH_3, R^2 = Ph}$	88 85 78
j	 19	 20  21 (trace amount*)	89
k	 22	 23	79
l	 24	 25	78
m	 26	 27	84

*Detected by ^{1}H NMR

The reductive deoxygenation with the $\mathrm{NaBH_3CN}$-TMSCl combination is more selective than the $\mathrm{ZnI_2}$[9] and more reactive than the $\mathrm{ZnCl_2}$[8] catalyzed reactions. The chemoselectivity exhibited by the reagent is comparable to the selectivity reported for the $\mathrm{BF_3 \cdot Et_2O}$[10, 11] combination but with the added advantage that it can be applied to acid and Lewis acid sensitive substrates. In addition the sterically more demanding electrophile TMSCl in combination with the presumed silylether intermediate introduces another selectivity control. The steric effect is demonstrated by the deoxygenation of the cinnamaldehyde **19** while the α-methylcinnamaldehyde **22** was only reduced to the alcohol. In contrast to the deoxygenation of α, β-unsaturated carbonyl compounds with $NaBH_3CN$, BF_3[10] no significant migration of the double bond was observed.

Typical Experimental Procedure: $NaBH_3CN$ (18 mmol) was added to a cold (ice bath), magnetically stirred solution of the aryl ketone or aldehyde (3 mmol) and TMSCl (18 mmol) in dry acetonitrile (10 mL), containing powdered molecular sieves (3 Å), under nitrogen. The suspension was stirred at room temperature. After the completion of the reaction (monitored by TLC, usual reaction time 24 hours), the suspension was diluted with CH_2Cl_2 and filtered through celite. The filtrate was washed with NaCl solution, dried over $MgSO_4$ and concentrated under reduced pressure. ^1H NMR analysis of the crude products indicated that the conversion was practically quantitative. The products were isolated and purified by column chromatography (silica gel, $CHCl_3$).

References

1 a) Bisagni, M.; Buu-Hoi, N. P.; Royer, R. *J. Chem. Soc.* **1955**, 3688; b) Bisagni, M.; Buu-Hoi, N. P.; Royer, R. *J. Chem. Soc.* **1955**, 3693.

2 Mustafa A., Heterocyclic Compounds, Benzofurans, 29, New York: Wiley, 1974.

3 Darling, S. D.; Wills K. D. *J. Org. Chem.* **1967**, *32*, 2794.

4 a) Furukawa, J.; Kobayashi, E.; Nagata, S. *J. Polym. Sci., Polym. Chem. Ed.* **1978**, *16*, 2945; b) Furukawa, J.; Kobayashi, E.; Nagata, S. *J. Polym. Sci., Polym. Chem. Ed.* 1978, *16*, 2955.

5 Lane C. F., *Synthesis* **1975**, 135.

6 Hutchins, R. O.; Markowitz, M. *Tetrahedron Lett.* **1980**, *21*, 813.

7 Kim, S.; Kim, Y. J.; Ahn, K. H. *Tetrahedron Lett.* **1983**, *24*, 3369.

8 Kim, S.; Oh, C. H.; Ko, J. S.; Ahn, K. H.; Kim, Y. J. *J. Org. Chem.* **1985**, *50*, 1927.

9 Lau, C. K.; Dufresne, C.; Belanger, P. C.; Pietre, S.; Scheigetz, J. *J. Org. Chem.* **1986**, *51*, 3038.

10 a) Srikrishna, A.; Viswajanani, R.; Sattigeri, J. A.; Yelamaggad, C. V. *Tetrahedron Lett.* **1995**, *36*, 2347; b) Srikrishna, A.; Viswajanani, R.; Sattigeri, J. A.; Yelamaggad, C. V. *Synlett* **1995**, 93.

11 a) Srikrishna, A.; Sattigeri, J. A.; Viswajanani, R.; Yelamaggad, C. V. *J. Org. Chem.* **1995**, *60*, 2260; b) Srikrishna, A.; Viswajanani, R.; Sattigeri, J. A.; Vijaykumar, D. *J. Org. Chem.* **1995**, *60*, 5961.

12 a) Chapleur, Y.; Boquel, P.; Chretien, F. *J. Chem. Soc. Perkin Trans. I* **1989**, 703; b) Garegg, P. J.; Hultberg, H.; Wallin, S. *Carbohydr. Res.* **1982**, *108*, 97; c) Garegg, P. J.; Hultberg, H. *Carbohydr. Res.* **1981**, *93*, C10; d) Johansson, R.; Samuelsson, B. *J. Chem. Soc., Chem. Commun.* **1984**, 201; e) Johansson, R.; Samuelsson, B. *J. Chem. Soc. Perkin Trans. I* **1984**, 2371.

13 Horne, D. A.; Jordan, A. *Tetrahedron Lett.* **1978**, *19*, 1357.

14 All compounds were identified unequivocally by their UV, IR, NMR and mass spectra.