Sand-supported Organic Reactions: $NaBH_4$ Reduction of Carbonyl Compounds

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Summary 'Fontainebleau sand' is an efficient support for the $NaBH_4$ reduction of carbonyl compounds in the absence of organic solvent.

CHROMATOGRAPHIC alumina and molecular sieve zeolites are efficient but expensive supports in the alkaline borohydride reduction of carbonyl compounds.[1] Because of the widespread interest in the use of inorganic supports in organic synthesis,[2] we looked for efficient and less sophisticated types of support. We report preliminary results on the use of the inexpensive 'Fontainebleau sand,' a slightly hydrolysed microcrystalline silica (from Prolabo: $SiO_2 > 98\%$; specific surface 1·4 m^2/g) as a support for the $NaBH_4$ reduction of carbonyl compounds in 'dry media',[3] *i.e.* in the absence of any organic solvent.

5 mmol of $NaBH_4$ dissolved in the minimum of water were adsorbed on 5 g of sand which was then dried for 4 h on P_2O_5 (0·5—1 Torr). To this sand-supported $NaBH_4$, 5 g of sand on which 5 mmol of the carbonyl compound had been adsorbed were added. After mechanical mixing and heating at 60 °C for various lengths of time, the products were eluted by diethyl ether and determined by g.l.c. The results are given in the Table. Under these conditions the yields of reduction products were quite good (expts. 4 and 5 excepted).

Table. Reduction experiments at 60 °C.

Expt.	Carbonyl compound	Product	Time/ h	Yield/ %
1[a]	Cyclohexanone	Cyclohexanol	0·5	82
2	4-t-Butylcyclohexanone	4-t-Butylcyclohexanol[b]	4	70
3	2-Decalone	Decan-2-ols	5	88
4	Norbornanone	Norbornanols[c]	48	30
5	3(α and β)-hydroxyandrostan-17-one	None	20	0
6	Octan-2-one	Octan-2-ol	3	96
7	Octan-1-al	Octan-1-ol	3	98
8	Acetophenone	1-Phenylethanol	4 20[a]	88 95
9	Benzaldehyde	Benzyl alcohol	3	98
10	*m*-Chlorobenzaldehyde	*m*-Chlorobenzyl alcohol	2	90
11[a]	Cyclohex-2-enone	Cyclohexanol (52%) Cyclohex-2-enol (48%)	0·1	97

[a] At 20 °C. [b] *cis*:*trans* = 20:80. [c] *exo*:*endo* = 33:67.

The reaction of cyclohex-2-enone (expt. 11) is even faster on sand than on alumina.[4]† We noted that regioselectivity (expt. 11) and observed stereoselectivities (expts. 2 and 4) for these ketones were close to those obtained from $NaBH_4$ reduction in tetrahydrofuran (THF).‡ The fact that 3(α and β)-hydroxyandrostan-17-one (expt. 5) is not reduced is in agreement with the 'evaporating hopping' concept;[5] the ketone should vaporise and then reach the supported $NaBH_4$ provided that the ketone vapour pressure is high enough, which is not the case for the steroids.

Finally, $NaBH_4$ adsorbed on sand is a stable reducing agent.§ In contrast, $NaBH_4$ adsorbed on chromatographic silica gel (amorphous and hydroxylated silica) has, in our hands, no reducing activity.[6] This can be explained by hydrolysis of the borohydride catalysed by the support and producing $NaB(OH)_4$, or by the formation of borates $\mathrm{Na(BO{-}Si}\leqslant\})_4$ by the reaction of BH_4^- with the $\{\geqslant\mathrm{Si{-}OH}$ groups of silica.

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† When solid $NaBH_4$ is mixed with neat cyclohex-2-enone, an exothermic reaction takes place leading to tarry material from which some 1,2 and 1,4 reduction compounds could be isolated in a lower yield (60%).

‡ E. d'Incan and A. Loupy, unpublished results. For $NaBH_4$ reduction in THF (0·08 M solution) 4-t-butylcyclohexanone(60 °C) yields *cis* and *trans*-alcohols in 20:80 ratio, norbornanone(60 °C) yields *exo* and *endo*-alcohols in 38:62 ratio, and cyclohex-2-enone-(20 °C) yields cyclohexanol and cyclohex-2-enol in 52:48 ratio.

§ No loss of activity of the sand-supported $NaBH_4$ is observed after 1 week.

[1] F. Hodosan and N. Serban, *Rev. Roum. Chim.*, 1969, **14**, 121; E. Santaniello, F. Ponti, and A. Manzocchi, *Synthesis*, 1978, 891; E. Santaniello, C. Farachi, and A. Manzocchi, *ibid.* 1979, 912; P. A. Risbood and D. M. Ruthven, *J. Org. Chem.*, 1979, **44**, 3969.

[2] G. H. Posner, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 487; A. McKillop and D. W. Young, *Synthesis*, 1979, 401; *ibid.*, p. 481.

[3] E. Keinan and Y. Mazur, *J. Org. Chem.*, 1978, **43**, 1020; G. Bram and G. Decodts, *Tetrahedron Lett.*, 1980, 5011, and references cited therein.

[4] G. Bram, E. d'Incan, and A. Loupy, unpublished results.

[5] A. W. Adamson and V. Slawson, *J. Phys. Chem.*, 1981, **85**, 116.

[6] For a description of the use of $NaBH_4$ on silica gel see F. Hodosan and V. Ciurdaru, *Tetrahedron Lett.*, 1971, 1997; V. Ciurdaru and F. Hodosan, *Rev. Roum. Chim.*, 1977, **22**, 1027.