J. Chem. Research (S), 1999, 728–729†

Microwave Enhanced Deuteriations in the Solid State using Alumina Doped Sodium Borodeuteride†

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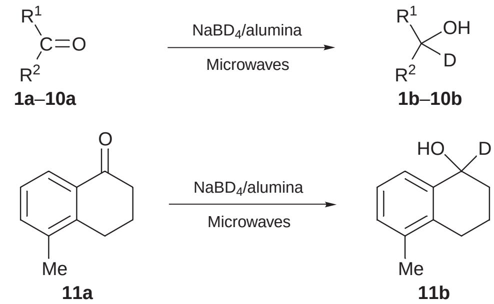
A number of deuteriated alcohols are rapidly (*ca.* 1 min) synthesised through the microwave enhanced solid state reduction of the corresponding aldehydes and ketones using alumina doped sodium borodeuteride ($NaBD_4$).

One of the important consequences of the development of ^{3}H NMR spectroscopy[1] has been the increased attention paid to the development of new tritiating reagents,[2] especially at carrier free levels. Until recently tritiated compounds at very high specific activity could only be obtained by hydrogenation or dehalogenation using T_2 gas or from the reduction of functional groups with tritide reagents. Unfortunately the only reducing agent then available at close to carrier free levels of radioactivity was sodium borotritide.[3] However, the observation[4] that extremely reactive hydrides can be prepared from alkyl lithium compounds and hydrogen under very mild conditions and near ambient temperatures has transformed the situation. Tritide reagents in which the tritium is attached to B, Al, Si, Sn and Zr are now available, covering a wide range of reactivity.[5]

In separate investigations[6,7] we have shown how microwaves can greatly increase the attractions of both hydrogen isotope exchange and hydrogenation reactions for labelling purposes, initially with deuterium, then tritium. Here we present our findings on reductive processes, benefiting from the recent observation of Varma *et al.*[8,9] that irradiation of a number of aldehydes and ketones in a microwave oven in the presence of alumina doped $NaBH_4$ for short periods of time led to rapid reduction (0.5–2 min) in good yields (62–93%).

In the present study seven aldehydes and four ketones were reduced (Scheme 1).



Scheme 1

The NMR spectra [^{1}H of the reactant, ^{1}H of the product and ^{2}H (^{1}H decoupled) of the product] showed, see *e.g.* Fig. 1, that (a) reduction was complete within 1 min of microwave irradiation; (b) the transformation was not accompanied by any side product formation so that the product purity was always $> 95\%$; (c) the degree of deuterium incorporation was similar to the original enrichment of the $NaBD_4$ reducing agent used (95%); (d) the reductions were completely selective and not affected by the presence of other functional groups and (e) the product yields were invariably high, the two exceptions refering to the more volatile products.

Acceleration of reactions through microwave irradiation coupled to the ability to perform them under solvent-less conditions are attractive features with considerable potential, not least in the radiosynthesis area where reduction of radioactive waste is an important consideration. Consequently these promising deuteriation findings can be seen as a precursor for corresponding tritium reduction processes, using the wider range of tritiated reducing agents refered to previously.

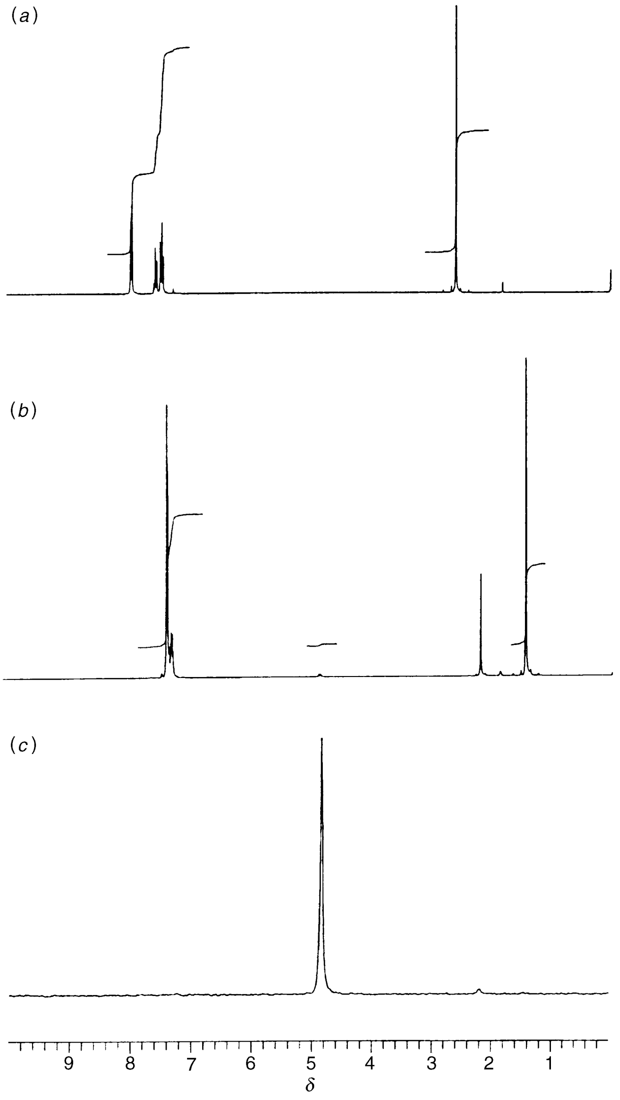


Fig. 1 ^{1}H NMR spectrum of (*a*) **8a**; (*b*) **8b** and (*c*) ^{2}H (^{1}H decoupled) NMR spectrum of compound **8b**

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Microwave enhanced deuteriation using alumina doped $NaBD_4$

Entry	R^1	R^2	Isolated yield(%)
1	Ph	H	37
2	*trans*-PhCH=CH	H	77
3	4-$NO_2C_6H_4$	H	37
4	2,4,6-$(MeO)_3C_6H_2$	H	83
5	$PhCH_2$	H	68
6	1-Naphthyl	H	85
7	2-Naphthyl	H	89
8	Ph	Me	82
9	4-$NO_2C_6H_4$	Me	68
10	3-ClC_6H_4	Me	86
11	5-Methyltetralone		87

Experimental

Microwave irradiation was carried out in a Matzui M167 BT microwave oven (750 W). ^1H (300 MHz, $CDCl_3$) NMR and ^2H (46 MHz, $CHCl_3$) NMR spectra are recorded on a Bruker AC300 spectrometer in the customary manner.

Alumina Doped $NaBD_4$.—10% alumina doped $NaBD_4$ was prepared by mixing $NaBD_4$ (0.5 g, 11.9 mmol) and neutral alumina (4.5 g) using a pestle and mortar under normal atmospheric conditions. The mixture was then transferred to a glass vial and stored in a silica gel dried dessicator for periods up to a week.

Typical Deuteriation Procedure.—For solid carbonyl compounds, the substrate *e.g.* *p*-nitroacetophenone (50 mg, 0.3 mmol) was thoroughly mixed with alumina doped $NaBD_4$ (0.126 g, 0.3 mmol of $NaBD_4$) using a pestle and mortar. The mixture was transferred to a loosely capped glass vial and irradiated in the microwave oven for 1 min at full power (750 W). The sample was allowed to cool to room temperature. The product was extracted using $CHCl_3$ (2 cm^3). The solvent was removed by rotary evaporation before being re-dissolved in $CHCl_3$ or $CDCl_3$ prior to NMR analysis. For liquid carbonyl compounds, thorough mixing was achieved by shaking the substrate with alumina doped $NaBD_4$ in the glass vial.

Received, 31st August 1999; Accepted, 10th September 1999
Paper E/9/06977A

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