'One-pot' Conversion of Mannich Bases *via* Quaternary Ammonium Salts into the Corresponding Methyl Compounds with Sodium Cyanoborohydride in Hexamethylphosphoramide

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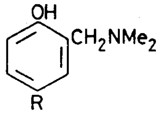
Summary Sodium cyanoborohydride in hexamethylphosphoramide reduces quaternary ammonium salts of Mannich bases to give the corresponding methyl compounds in good yields.

It is well known that sodium cyanoborohydride, $NaBH_3CN$, is a milder and more selective reducing agent than sodium borohydride, and its properties and uses have been reviewed recently.[1,2] We now report a new method for the reduction of quaternary ammonium salts of Mannich bases to the corresponding methyl compounds in the presence of other functional groups including halogeno, ester, nitrile, and nitro by $NaBH_3CN$ in hexamethylphosphoramide (HMPA) in good yields [equation (1)].

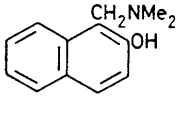
$$\begin{array}{l} ArCH_2NMe_2 \xrightarrow{\text{i}} ArCH_2NMe_3^+\ MeSO_4^- \\ \qquad\qquad\qquad\quad\ \downarrow \text{ii} \\ \qquad\qquad\qquad\quad ArMe \end{array} \qquad (1)$$

i, Me_2SO_4 in ether or tetrahydrofuran; ii, $NaBH_3CN$ in HMPA

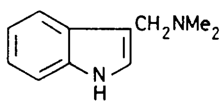
The results are summarized in the Table. Sodium borohydride in dimethyl sulphoxide[3] also reduced the Mannich base (**6**) of β-naphthol to α-methyl-β-naphthol in high yield (2 equiv.; room temp.; 0·5 h; 80%), but not the Mannich base (**5**) of *p*-nitrophenol to 4-nitro-*o*-cresol (4 equiv.; 50 °C; 3 h).



(1) R = H
(2) R = Cl
(3) R = CO_2Et
(4) R = CH_2CN
(5) R = NO_2



(6)



(7)

Table. Reduction of Mannich bases (0·3—0·5 M) *via* quaternary ammonium salts with $NaBH_3CN$ (0·6—1·8 M) in HMPA.

Mannich base	$NaBH_3CN$/ amine	Temp./ °C	Time/ h	% Reduction (isolated)
(**1**)	2	70	3	71·3
(**2**)	2	70	5	83·3
(**3**)	2	70	5	91·4
(**4**)	2	70	3	72·3
(**5**)	2	70	3	35·3
	4	70	12	89·8
	6	100	0·5	87·5
(**6**)	2	70	4	73·7
(**7**)	2	70	1	77·0

The procedure involves conversion of the Mannich base into the quaternary ammonium salt with Me_2SO_4 (10 equiv.)

in ether at room temperature followed by addition of $NaBH_3CN$ in HMPA, and stirring at 70 °C for the lengths of time in the Table.

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[1] C. F. Lane, *Synthesis*, **1975**, 135.

[2] Recently, Hutchins *et al.* reported that $NaBH_3CN$ in HMPA provides a convenient system for the removal of RX (X = Br, I, *p*-$MeC_6H_4SO_3$, *etc.*) to the corresponding hydrocarbons (RH); R. O. Hutchins, D. Kandasamy, C. A. Maryanoff, D. Masilamani, and B. E. Maryanoff, *J. Org. Chem.*, 1977, **42**, 82.

[3] R. O. Hutchins, D. Hoke, J. Keogh, and D. Koharski, *Tetrahedron Letters*, 1969, 3495.