

Cyanoborohydride Supported on an Anion Exchange Resin as a Selective Reducing Agent

By ROBERT O. HUTCHINS,* NICHOLAS R. NATALE, and IRA M. TAFFER
(Department of Chemistry, Drexel University, Philadelphia PA 19104)

Summary Ion-exchange resin bound cyanoborohydride provides a successful and convenient reagent for a variety of reductions with the added advantages of ease of work up and resin retention of cyanide.

THE immobilization of reagents on polymeric supports has been investigated extensively¹ primarily because insoluble polymeric reagents expand the range of applicable solvents, increase the ease of work-up and product purification, and, conceivably at least, provide for recovery and regeneration of the supported reagent.

Cyanoborohydride anion^{2,3} is efficiently incorporated into quaternary ammonium cation exchange resin (Amberlyst 26) by passing an aqueous solution through a column of acid- and base-washed resin followed by rinsing with water and drying *in vacuo*.[†] Resin prepared in this fashion typically contains *ca.* 3.3 mequiv. of $\text{BH}_3\text{CN}^-/\text{g}$ (as determined by acid hydrolysis) and apparently is stable indefinitely in a closed container at room temperature.

Preliminary investigations indicate the resin to be effective in a variety of reductive applications including reductive amination,^{2a,4} amine dimethylation,⁵ reduction of conjugated enones to allylic alcohols,^{2c} dehalogenations,^{2a,b} and conversion of pyridinium ions into tetrahydro derivatives (Table).[‡] In addition, the polymeric resin offers important advantages over NaBH_3CN since the spent insoluble reagent can be removed and recovered by simple filtration and washing, and toxic cyanide residues are retained on the polymer and not extracted into organic or aqueous phases. Furthermore, the resin may be reused by rinsing the spent material with dilute acid followed by regeneration with NaBH_3CN . The reductions are slower with the resin probably because substrate contact is less efficient with this particular polymer and, moreover, tetra-alkylammonium cations appear to temper the reduction rates of most functional groups by cyanoborohydride.^{2a,b} Thus, while reductive amination with NaBH_3CN proceeds well at ambient temperature, more vigor-

TABLE

| Compound | Solvent (ratio $\text{MBH}_3\text{CN}/\text{Compd.}$) | $T/^\circ\text{C}$ | Time/h | Product | % Yield ^a (% with NaBH_3CN) |
|--|---|--------------------|--------|--|--|
| PhCOMe | EtOH (0.726) [†] | 78 | 48 | PhCH(NH ₂)Me | 53—66 (58—71) ^b |
| Cyclo-octanone | EtOH (0.726) [†] | 78 | 48 | Cyclo-octylamine | 49 (48) ^c |
| PhCH(Me)NH ₂ | MeCN (2) [§] | 25 | 20 | PhCH(Me)NMe ₂ | 84 (81) ^d |
| PhNH ₂ | MeCN (2) [§] | 25 | 16 | PhNMe ₂ | 78 (92) ^d |
| α -Ionone | EtOH (2) | 78 | 3 | α -Ionol | 70 (72) |
| 4-Cyano- <i>N</i> -(<i>p</i> -nitrobenzyl)-pyridinium bromide | 1:1 H ₂ O EtOH (2) | 78 | 15 | 4-Cyano- <i>N</i> -(<i>p</i> -nitrobenzyl)-1,2,5,6-tetrahydropyridine | 71 (75) |
| 4-Cyano- <i>N</i> -(<i>p</i> -bromophenacyl)-pyridinium bromide | 1:1 H ₂ O EtOH (2) | 78 | 17 | 4-Cyano- <i>N</i> -(<i>p</i> -bromophenacyl)-1,2,5,6-tetrahydropyridine | 50 |
| Me[CH ₂] ₁₁ I | HMPA (2) | 90 | 5 | Me[CH ₂] ₁₀ Me | 89 ^e (88—90) ^{2b} |
| Me[CH ₂] ₁₁ Br | HMPA (2) | 90 | 8 | Me[CH ₂] ₁₀ Me | 77 ^e (97) ^e |

^a Yields are for isolated products purified by distillation or recrystallization. ^b Reported 77%^{2a} as the HCl salt with NaBH_3CN . ^c Reported as the HCl salt.⁴ ^d In MeOH, 25 °C; reported as the picrate.⁵ ^e G.l.c. yield.^{2b} [†] With NH_4OAC . [§] With CH_2O .

[†] Excess of NaBH_3CN may be recovered by evaporation of the aqueous effluent, extraction of the residue with tetrahydrofuran (THF) followed by either concentrating the THF solution to dryness or precipitation of the NaBH_3CN with dioxan (see ref. 2a); U.S.P. 4,107,099(1978).

[‡] NaBH_3CN in protic solvents selectively converts 4-substituted pyridinium salts into the corresponding 1,2,5,6-tetrahydro derivatives (unpublished results).

ous conditions (refluxing ethanol) are required for adequate conversions with the resin. However, this does not adversely affect the attractiveness of the reagent since other functional groups (*i.e.* NO₂, CN, carbonyl, alkenes) remain unaltered at this temperature in neutral or basic media.

The procedure for the dimethylation of 1-phenylethylamine is typical. A slurry of resin (6.0 g, 20 mmol BH₃CN⁻) in a solution of 1-phenylethylamine (1.21 g, 10 mmol) and 37% formalin (4 ml, 50 mmol) in 15 ml of acetonitrile was stirred at 25 °C for 45 min, 1 ml of acetic acid was added, and stirring continued for 20 h total.

The solution was decanted, and the resin slurried with 25 ml of acetonitrile and filtered. The solvent was removed under reduced pressure, 20% NaOH added, and the solution extracted (×3) with ether, from which was isolated (distillation) 1.25 g (84%) of *NN*-dimethyl-1-phenylethylamine.

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⁵ R. F. Borch and A. I. Hassid, *J. Org. Chem.*, 1972, **37**, 1673.