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Reduction of Nitrostyrenes to Nitroalkanes with a NADH Grafted Model

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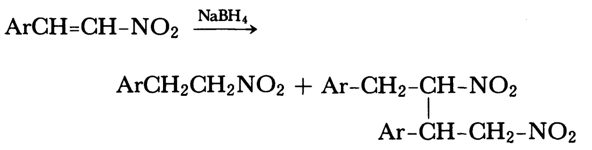
Synopsis. Grafting of the 1,4-dihydronicotinamide structure on a Merrifield type resin is described. With this reagent, arylnitroethanes have been obtained by regioselective reduction of β-nitrostyrenes. The yields are good and no dimeric compounds are formed. The role of magnesium ions in these reductions is different from that observed with classical NADH models.

Arylnitroethanes are compounds of special interest since they are useful synthetic intermediates. The nitro group can be converted to other functional groups such as carbonyl, nitrile oxides, or amino group.

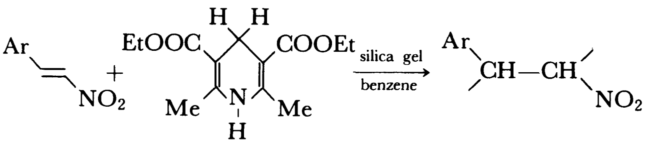
A widely used method to obtain 2-aryl-1-nitroethanes involves reduction of nitrostyrenes. Selective reduction of the ethylene double bound is rather difficult: borohydride reduction under various conditions often leads to contamination of the desired product by side reactions: for example a dimeric compound can be formed by Michael addition of the nitronate intermediate to the starting nitroalkene.[1)]

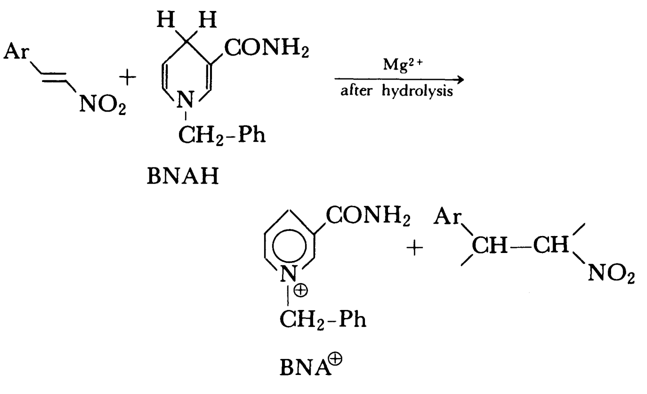


$$ArCH{=}CH\text{-}NO_2 \xrightarrow{NaBH_4} ArCH_2CH_2NO_2 + Ar\text{-}CH_2\text{-}\underset{\displaystyle Ar\text{-}CH\text{-}CH_2\text{-}NO_2}{\underset{|}{CH}}\text{-}NO_2$$

Recently some improvements to the usual procedure led the authors to better results.[2)]

Other reagents have been used to ensure selective reduction of the ethylenic double bond of nitrostyrenes, for example NADH models such as 1,4-dihydronicotinamide derivatives or Hantzsch ester. With this last reagent good results in the reduction of various nitroolefins in the presence or silica gel have been reported.[3)]





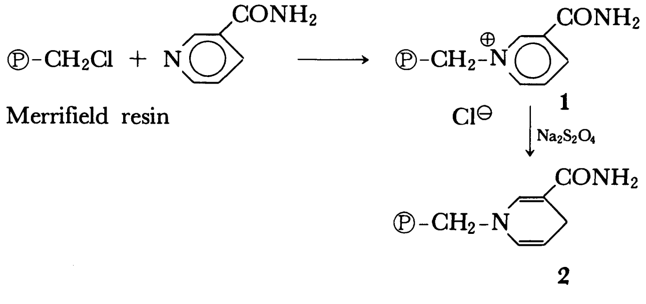
With 1,4-dihydronicotinamide derivatives there are few examples of such reductions[4)] and the yields are rather poor. Moreover it was established that β-nitrostyrene is not reduced in the absence of magnesium ions.[4a)]

The work-up of reactions performed with BNAH is not easy. It is rather difficult to isolate the desired product from starting reagents or other products formed during the reduction.

Grafting reagents on to an insoluble matrix can constitute an elegant way of resolving the practical problems encountered with free reagents.[5)] A few NADH grafted models have been studied.[6)] In our laboratory we have synthesized the first truly reactive polymer-bound NADH model.[7)] With this reagent excellent results are obtained in the reduction of activated carbonyl compounds.[7)]

In this publication we describe the optimisation of the synthesis of the grafted reagent on a Merrifield type resin and its use in the reduction of aryl nitro olefins.

Preparation of Grafted Reagent. The reagent is obtained by reaction of the halomethylated copolymer styrene and divinylbenzene resin with nicotinamide (Scheme 1). The pyridinium salt is just filtered, not dried, before being subjected to regioselective 1,4-reduction with $Na_2S_2O_4$. If the polymer-bonded pyridinium salt **1** is quite free of the solvent used during the quaternarization (CH_3CN), wetting of the polymer does not occur and reaction of $Na_2S_2O_4$ becomes impossible.



The reduction of **1** is complete as shown by the absence of chlorine in the analysis of **2**.

Reduction of Nitrostyrenes. With BNAH, reduction of a substrate in the presence of magnesium ions usually occurs in acetonitrile as solvent. With the reagent **2** we observed that in this solvent the polymer matrix did not swell and consequently no reduction occured. The access to the active site of the polymer bonded reagent is probably impossible. A swelling cosolvent is needed which also ensures the solubility of Mg^{2+} ions. Finally the best results were obtained in a benzene-acetonitrile (1/1) mixture. In typical conditions [grafted NADH model 1.2 milliequivalent, $Mg(ClO_4)_2$ 1 mmol, nitrostyrene 1 mmol, solvents 14 ml, 5 d, 80 °C] the results were as follows:

$$\underset{\mathbf{3}}{\mathrm{ArCH{=}CHNO_2}} + \mathbf{2} \longrightarrow \underset{\mathbf{4}}{\mathrm{ArCH_2CH_2NO_2}} + \mathbf{1}$$

Table 1. Reduction of β-Nitrostyrenes

Ar in starting nitrostyrene **3**		Yield in **4**	Ar in starting nitrostyrene **3**		Yield in **4**
Phenyl	**3a**	100	3,4-(Methylenedioxy)phenyl	**3e**	72
2-Naphtyl	**3b**	98	3-Pyridyl	**3f**	60
p-Methoxyphenyl	**3c**	77	2-Thienyl	**3g**	70
3,4-Dichlorophenyl	**3d**	90			

$$\underset{\beta}{\mathrm{ArCH_2}}\text{-}\underset{\alpha}{\mathrm{CH_2}}\text{-}\mathrm{NO_2} \qquad \mathbf{4}$$

	Ar=		NMR (Chemical shift)
4a	Phenyl	Oil (2b)	3.17 (t) $CH_2\beta$; 4.45 (t) $CH_2\alpha$; 6.93—7.4 (m) H arom.
4b	2-Naphthyl	Oil $C_{12}H_{11}NO_2$	3.42 (t) $CH_2\beta$; 4.65 (t) $CH_2\alpha$; 7.50 (m) H arom.
4c	*p*-Methoxyphenyl	Oil (2b)	3.21 (t) $CH_2\beta$; 4.53 (t) $CH_2\alpha$; 3.75 (s) CH_3O; 6.84 and 7.12 H arom.
4d	3,4-Dichlorophenyl	Oil $C_8H_7Cl_2NO_2$	3.30 (t) $CH_2\beta$; 4.60 (t) $CH_2\alpha$; 7.30 (m) H arom.
4e	3,4-(Methylenedioxy)phenyl	F=55 (2b)	3.20 (t) $CH_2\beta$; 4.52 (t) $CH_2\alpha$; 6.56—6.80 (m) H arom.
4f	3-Pyridyl	Oil $C_7H_8N_2O_2$	3.30 (t) $CH_2\beta$; 4.60 (t) $CH_2\alpha$; 7.10—7.60 (m) H_4 and H_5 arom.; 8.43 (m) H_2 and H_6 arom.
4g	2-Thienyl	Oil (3)	3.43 (t) $CH_2\beta$; 4.50 (t) $CH_2\alpha$; 6.70—7.20 (m) H arom.

The most interesting features of these reductions are: (i) Yields are good to quantitative. (ii) The work-up is easy; filtration followed by evaporation of the solvents gives the pure arylnitroethanes. Some of them (**3b**, **3d**, and **3f**) are new compounds. They have been identified by the usual spectroscopic methods. (iii) No dimeric compound was detected in the final product [absence of signals near δ 5.0 in the ^{1}H NMR spectra[1]].

Role of Magnesium Ions. The role of magnesium ions in BNAH reduction is to ensure an interaction between the substrate and the model through a ternary complex.[8] In the case of free models in the absence of Mg^{2+}, generally no reaction occurs. However the reduction of (α-methylbenzylidene)malonitrile with a BNAH derivative affords different product depending upon the presence or not of Mg^{2+} (9). We have performed the reduction of **3a** in the typical conditions described above but without the magnesium ion. A large quantity of polymeric compounds is obtained but after chromatographic purification we could isolate 10% of **4a**. To our knowledge it is the first partial reduction of 1-phenyl-2-nitroethene observed with a 1,4-dihydronicotinamide reagent in the absence of magnesium ions. We think that a "polymer effect" occurs: the redox potential of the reactants are changed and the transition state becomes different to that ocurring with a free model. The medium used (CH_3CN-C_6H_6) is less polar and the polymeric matrix contains numerous phenyl rings. The micro environment in the neighbourhood of the active site is less favorable to solvatation of the dihydronicotinamide by CH_3CN. So the interaction between the reagent and the substrate is forced. This phenomenon could be sufficient to induce a partial reduction.

Experimental

Nitrostyrenes derivatives were prepared according to the literature.[10] Merrifield resin was purchased from Merck (Art. 818178). NMR spectra were recorded with a Varian EM 360 L spectrometer (solvent $CDCl_3$, internal reference HMDS). Analyses have been performed with a Carlo Erba 1106 apparatus).

Grafted Reagent. Merrifield resin (50 g) nicotinamide (20 g) in 300 ml of dry acetonitrile were stirred at 90 °C during 6 d. The pyridinium derivative **1** was filtered, washed with acetonitrile then with hot water. The product was suitable for the next step.

Analysis of a dried sample gave the following typical values. C: 79.9; H: 7.0; N: 3.6; Cl: 5.0%.

The wet quaternarized resin (about 20 g) was treated with a mixture of $Na_2CO_3 \cdot 10H_2O$ (20 g) and $Na_2S_2O_4$ (40 g) in 200 ml of water. The mixture was stirred for 6 h at room temperature. The color of the resin turned from red-orange to yellow. After filtration the resin was dried for 2 d (40 °C/0.5 Torr (1 Torr=133.322 Pa)). The grafted NADH model was storred under argon in the refrigerator.

Typical analysis is as follows. C: 83.5; H: 3.5; N: 3.8% (absence of chlorine).

This corresponds to 1.3 meq of the 1,4-dihydronicotinamide moiety pergram (based on N percentage).

Reduction of Nitrostyrenes. In a dry glass tube 1.2 meq of grafted reagent **2**, 250 mg of $Mg(ClO_4)_2$ (1 mmol), 1 mmol of nitrostyrene, 7 ml of hyperdry benzene and 7 ml of hyperdry acetonitrile were introduced under an argon atmosphere. The tube was sealed, then heated at 80 °C for 5 d. After cooling the tube was broken. The resin is discarded, washed with acetonitrile, and water (1 ml) was added. The solvents were evaporated. The residue was extracted with water, then extrated with chloroform. After evaporation of the solvent the pure arylnitroethanes were recovered.

The aryl-2-nitroalkanes have the characteristics given on the precedent page.

References

1) A. I. Meyers and J. C. Sircar, *J. Org. Chem.*, **32**, 4134 (1967).

2) A. K. Sinhababu and R. T. Borchardt, *Tetrahedron Lett.*, **24**, 227 (1983); A. Bhattacharjya, R. Mulhopadhyay, and S. C. Pakrashi, *Synthesis*, **1985**, 886.

3) K. Nakamura, M. Fujii, S. Oka, and A. Ohno, *Chem. Lett.*, **1985**, 523.

4) S. Shinkai, Y. Kusano, T. Ide, T. Sone, and O. Manabe, *Bull. Chem. Soc. Jpn.* **51**, 3544 (1978); K. Wallenfels, W. Ertel, A. Hockendorf, J. Rieser, and K. H. Uberschar, *Naturwissenschaften*, **62**, 459 (1975); *Chem. Abstr.*, **84**, 84708g.

5) A. Akelah, *Synthesis*, **1981**, 413; A. Akelah and D. C. Sherrington, *Chem. Rev.*, **81**, 557 (1981).

6) A. S. Lindsey, S. E. Hunt, and N. G. Savill, *Polymer*, **7**, 479 (1966); B. Eling, G. Challa, and U. K. Pandit, *J. Polym. Sci., Polym. Chem. Ed.*, **23**, 2165 (1985).

7) R. Mathis, G. Dupas, A. Decormeille, and G. Quéguiner, *Tetrahedron Lett.*, **22**, 59 (1981); G. Dupas, J. Bourguignon, C. Ruffin, and G. Quéguiner, *Tetrahedron Lett.*, **23**, 5141 (1982).

8) R. A. Gase, G. Boxhoorn, and U. K. Pandit, *Tetrahedron Lett.*, **1976**, 2889; M. Hughes and R. H. Prince, *J. Inorg. Nucl. Chem.*, **40**, 703 (1978); A. Ohno, T. Kimura, A. Yamamoto, S. G. Kim, S. Oka, and Y. Ohnishi, *Bull. Chem. Soc. Jpn.*, **50**, 1535 (1977).

9) Y. Ohnishi, M. Kagami, T. Numakunai, and A. Ohno, *Chem. Lett.*, **1976**, 915.

10) J. Bourguignon, G. Le Nard, and G. Quéguiner, *Can. J. Chem.*, **63**, 2354 (1985).