REDUCTION WITH POLYMER-BOUND NADH MODELS
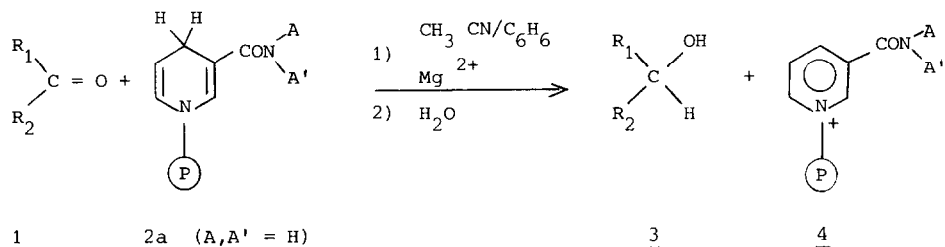
by G DUPAS, J BOURGUIGNON, C RUFFIN et G QUEGUINER [*]

Laboratoire de Chimie Organique Hétérocyclique, Institut National Supérieur de
Chimie Industrielle de Rouen et Faculté des Sciences et Techniques de Rouen,
76130 MONT SAINT-AIGNAN (France)

Abstracts   We have performed numerous reductions with a NADH model grafted
on a Merrifield resin The yields are generally excellent and in all cases
always superior to those obtained with "free" models

In a previous paper, we reported the first truly reactive polymer-
bound NADH model (1) This model grafted on a partially halogenomethylated
copolymer of styrene and divinyl benzene (Merrifield polymer resin   2 % DVB,
200-400 mesh, 4-5 % Cl) gives us quantitative yields in the reduction of some
carbonyl compounds Moreover, the products can be easily isolated from the reaction
mixture and the insoluble immobilized NADH model can be recycled and reused
The appearance of a recent paper (2) of Zicmanis and Nalivaiko has prompted us
to publish new results concerning our system

In view of exploring the field of applications of our model, we now
describe new results obtained in the reduction of various carbonyl substrates

$$\begin{array}{c} R_1 \\ \diagdown \\ C = O \\ \diagup \\ R_2 \end{array} + \; \underset{\underset{\underline{2a} \; (A,A' = H)}{}}{\text{2a}} \quad \xrightarrow[\; 2) \; H_2O \;]{\; 1) \; CH_3CN/C_6H_6, \; Mg^{2+} \;} \quad \begin{array}{c} R_1 \\ \diagdown \\ C \\ \diagup \diagdown \\ R_2 \quad H \end{array} \!\!\! \begin{array}{c} OH \end{array} + \; \underset{\underline{4}}{\text{4}}$$

$\underline{1}$ $\underline{2a}$ (A,A' = H) $\underline{3}$ $\underline{4}$

Standard conditions are the following   all reactions are conducted
in sealed tubes under argon , substrates 1 mmole, bounded NADH polymer, 1,2 milli-
equivalent (meq) , solvent   7 ml of CH_3CN, 7 ml of C_6H_6 , Mg $(ClO_4)_2$ 1 mmole ,
temperature   usually 80°C , time   5 days After 5 days, the reaction mixture
is treated with water, filtered from the NAD^+ polymer-bound $\underline{4}$ (which can be
reduced by sodium dithionite and reused) The aqueous phase is extracted with
solvents and then treated in the usual manner Yields are given in product $\underline{3}$
isolated, the structure of which is determined by N M R.

The results are summarized in the tables below

TABLE 1   Reduction of benzaldehydes

Substituent		Yields of alcohols 3		
		with the grafted model 2a	with "free" models (a)	
H	1a	12 (b)	2	(3)
o NO$_2$	1b	100	~	
m NO$_2$	1c	100	29	(3)
p NO$_2$	1d	100	56	(3)
p.Cl	1e	100	6	(3)
o.OH	1f	56 (b)	traces	(4)
m.OH	1g	21 (b)		
p OH	1h	21		

(a) "free" model is generally the 1-benzyl-1,4 dihydro nicotinamide (BNAH).

(b) carbonyl compound which does not react is fully recovered

TABLE 2   Reduction of p nitro-benzaldehyde (PNBA) with various grafted models of NADH 2

A,A' in 2		Yield in 3
H,H	2a	100
Me,Me	2b	94
Et,Et	2c	80
[hexagon]	2d	93
[hexagon with O]	2e	90
[hexagon]	2f	90
C$_6$H$_5$,C$_6$H$_5$	2g	45

TABLE 3   Reduction of other aldehydes
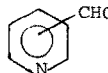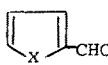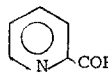
Sub-strates	Sub-stituent		Yields of alcohols 3 with the grafted model 2a
[pyridine-CHO]	2-CHO	1i	100
	3-CHO	1j	94
	4-CHO	1k	100
[ring X-CHO]	X=O	1l	45
	X=S	1m	9

TABLE 4   Reduction of ketones

Sub-strates	Subs tituent		Yields of alcohols 3	
			with the grafted model 2a	with "free" models
[pyridine-COR]	R=CH$_3$	1n	100	100 (7)
	R=C$_6$H$_5$	1o	100	97 (7)
⌀COCOOEt		1p	100 (c)	100 (7)
⌀COCF$_3$		1q	100 (c)	79 (7)
MeCOCOOMe		1r	100	~

(c) reactions performed at room temperature

Under the standard conditions the following ketones are not reduced o, m, p nitroacetophenones , o,p hydroxyacetophenones , 3 and 4-acetyl pyridines , 3 and 4-benzoyl pyridines

Tables 1, 3 and 4 show that with the grafted model the yields are generally excellent and in almost cases better than with the "free" models One reason for these features is that the work up of the reaction mixture is probably easier with polymer bounded NADH.
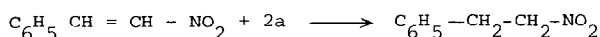
Table 2 shows that with various substituents on the amide part the yields of reduction of PNBA decrease slowly excepted in the case of A and A' = C_6H_5 where the yield is much lower

In the literature, it is said that with 1-benzyl-N,N diakyl-1,4 dihydronicotinamide, the yields and the kinetics of the reduction of aldehydes are greater than with BNAH (3 and 5) In the case of grafted models, we can think that the polymeric structure of the support modifies the conditions of the reductions when the amide part of the reactive model changes it is possible that the access to the active site is more difficult Moreover, in the case of 2g, the electronic effect of the phenyl groups lowers the reactivity of the reactant

In the case of the reduction of hydrobenzaldehyde 1f, 1g and 1h (table 1) we can notice that the higher reactivity of the ortho compound caused by the hydrogen bound is confirmed (4)
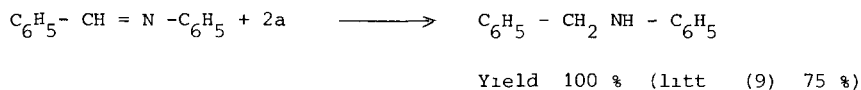
Compound 1i is reduced in 100 % yields both with the "free" model (6) or with the grafted model the carbonyl group is activated by the catalyst which is fixed in its neighbourhood by coordination with the nitrogen atom of pyridine ring (6). The same phenomenon explains the reactivity of 2-acetyl and 2-benzoyl pyridine (7) It is interesting to notice that with our model we have reduced the two other pyridine carbaldehydes 1j and 1k which are not or difficulty reduced by "free" model (6) in other conditions

Other reductions with the grafted model are actually performed For example excellent results have been obtained with nitrostyrene 5 and Schiff's base 6

$$C_6H_5\ CH = CH - NO_2 + 2a \longrightarrow C_6H_5 - CH_2 - CH_2 - NO_2$$

5   Yield 100 % (litt (8) 22 %)

$$C_6H_5 - CH = N - C_6H_5 + 2a \longrightarrow C_6H_5 - CH_2 NH - C_6H_5$$

Yield 100 % (litt (9) 75 %)

REFERENCES AND FOOTNOTES

1   R MATHIS, G DUPAS, A DECORMEILLE and G QUEGUINER, Tetrahedron Letters, 59, (1981)

2   A ZICMANIS and R NALIVAIKO, Latvijas PSR Zinatnu Akademijas Vestis Kimijas serija, 3, 351, (1982)

3   Y OHNISHI and M KITAMI, Tetrahedron Letters, 4033, (1978) In the same conditions, the yields of reduction of various benzaldehydes are greater with 1-benzyl-N,N-dimethyl-1,4 dihydronicotinamide (BMNAH)

4   U K PANDIT, F R MAS CABRE, Chem Comm , 552, (1971) In other conditions, (Hantzsch ester as reducing agent and various solvents), these authors obtained only traces of reduction product with o hydroxybenzaldehyde

5   R A HOOD and R.H PRINCE, J C S , Chem Comm , 163, (1979).
The rate of reduction of pyridine-2 carboxaldehyde with NN' diethyl-N-benzyl-1,4 dihydronicotinamide is 200 times greater than with BNAH The reactions are drawn with $ZnBr_2$ catalysis

6   M SHIRAI, T CHISHINA and M TANAKA, Bull Chem Soc Japan, 48, 1079, (1975)
The solvent is methanol, the catalysts are Zn^{2+} or various salts

7   A OHNO, M IKEGUCHI, T KIMURA and S OKA, J Am Chem Soc , 101, 7036, (1979)
In this case, the reductions are performed at room temperature with chiral models of NADH which induce asymetry

8   S SHINKAI, Y. KUSANO, T IDE, T SONE and O MANABE, Bull Chem Soc. Japan, 51, 3544, (1978)

9   S SINGH and V K SHARNA, Tetrahedron Letters, 2733, (1979)