Simple Selective Reduction by Sodium Borohydride of an Ester or a Cyano Group of α -Cyano Epoxides

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Sodium borohydride reduced the ester group of epoxide (1) or one cyano group of (2) selectively within 5 min to give new hydroxy- or amino-functionalized epoxides.

The epoxides (1) and (2) substituted by at least one cyano group, are useful basic substances in heterocyclic chemistry since they react with a large number of dipolarophilic and nucleophilic reagents.¹ These epoxides are also of interest in the preparation of derivatives of α -halogenocarboxylic acids.² A selective reduction of the ester or one cyano group of the epoxides (1) and (2) respectively should lead to the hitherto unknown epoxides (3) and (4). Surprisingly this selective reduction is easily achieved using sodium borohydride.

NaBH₄ (5 mmol) was added to an ethanolic solution (30 ml) of the epoxide (1) (5 mmol). After 5 min stirring at room temperature the solution was acidified (0.4 M HCl; 100 ml) and the epoxide (3) extracted and purified (Table 1).

Epoxide (4) was obtained as follows. H_2O (5 ml) was added to a suspension of NaBH₄ (5 mmol) in tetrahydrofuran (THF) (15 ml) and after 30 s the epoxide (2) (5 mmol) was added to the solution. After 5 min at room temperature, the epoxide (4) (50-80% not optimized) and the epoxide (3), obtained as a byproduct (5-20%), were extracted and purified by standard methods (Table 2).

Sodium borohydride is a mild reducing reagent, the reactivity of which can be modified by a suitable choice of reaction conditions.³ Generally ester groups are not reduced by NaBH₄, however reductions have been observed in Bu⁴OH–MeOH⁴ or in poly(ethylene glycol).⁵ To the best of

our knowledge, the only reported reduction of a nitrile to an amine by NaBH₄ is the reduction of a poly-(fluoroalkylnitrile).⁶ Ethyl diphenylmethyl- β -alaninate was also reported as a byproduct in the reduction of ethyl α -cyano- β -phenylcinnamate.⁷

This simple selective reduction of a nitrile group on the epoxides (2) is unprecedented and contrasts with the reduction of 2-phenyl oxirane by $NaBH_4/Bu'OH$ -MeOH which appears to be selective reduction of the epoxide ring in the



Reagents: i, NaBH₄, EtOH; ii, HCl; iii, NaBH₄, THF-H₂O; iv, NaOH.

Table 1. Characterisi	ng data for epoxi	ides (3).			
R ¹ R ² M.p. or b.p./mbar % Yield		Ph H 46 84	<i>p</i> -NO ₂ C ₆ H ₄ H 91 80	Ph Me 100/210 ⁻² 88	Et H 60/10 ⁻² 80
¹ H n.m.r./δ (CDCl ₃) I.r./cm ⁻¹ (CCl ₄)	$\left\{ \begin{array}{c} R^{1} \\ R^{2} \\ CH_{2} \\ OH \\ \nu_{CN}(s) \\ \nu_{CN}(s) \end{array} \right.$	7.40 (m, 5H) 4.30 (s, 1H) 4.02 (s, 2H) 2.72 (s, 1H) 2240 3596	8.26 (d, 2H), 7.61 (d, 2H) 4.50 (s, 1H) 4.20 (AB, 2H) a 2236 3599	7.35 (m, 5H) 1.75 (s, 3H) 3.95 (s, 2H) 3.17 (s, 1H) 2234 3609	1.16 (t, 3H), 1.87 (m, 2H) 3.24 (t, 1H) 3.90 (AB, 2H) 3.50 (s, 1H) 2236 3590
^a Solvent $CDCl_3 + C$	F ₃ CO ₂ H.				
Table 2. Characterisir	ng data for epoxi	des (4).			
R ¹ R ² % Yieldª		Ph H 70	<i>p</i> -NO ₂ C ₆ H ₄ H 50	Ph Ph 60	Et H 70
¹ H n.m.r. ^{b/δ} (CDCl ₃)	$\left\{ \begin{array}{c} R^1 \\ R^2 \\ CH_2 \\ NH_2 \end{array} \right.$	7.37 (m, 5H) 4.15 (s, 1H) 3.12 (AB, 2H) 1.47 (s, 2H)	8.22 (d, 2H), 7.60 (d, 2H) 4.45 (s, 1H) 3.34 (AB, 2H) 1.81 (s, 2H)	7.25 (m, 10H) 2.87 (AB, 2H) 1.49 (s, 2H)	1.17 (t, 3H), 1.82 (m, 2H) 3.12 (t, 1H) 3.10 (AB, 2H) 2.27 (s, 2H)
I.r./cm ⁻¹ (CCl ₄)	$ u_{CN}(m) $ $ u_{NH_2}(s) $	2236 3402, 3330	2240 3418, 3350	2235 3405, 3340	2236 3400, 3340

^a Oil purified by silica gel chromatography. ^b The comparison between the $\delta(CH_2)$ of the epoxides (4) ($R^1 = Ph$, $R^2 = H$) and (4) ($R^1 = R^2 = Ph$) makes it clear that R^1 is *trans* relative to CH_2NH_2 .

The unexpected rapid reduction of an ester or a cyano group by NaBH₄ is noteworthy in that only one functional group is reduced: the ester group of the epoxide (1), or the cyano group of the epoxide (2) which is *trans* to the aryl or ethyl substituent.[†]

The epoxides (1) and (2) in ethyl acetate did not react with NaBH₄, therefore an alkoxyborohydride or hydroxyborohydride species may be the effective reducing reagent.

As a further example of this selective reduction we have also shown that $-CH_2(CN)CO_2Et$ is readily reduced by NaBH₄ and gives $-CH_2(CN)CH_2OH$.

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† Satisfactory analytical and spectroscopic data were obtained to support the structural assignments.

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