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HYDRATION OF CYANOHYDRINS IN WEAKLY ALKALINE SOLUTIONS OF BORIC ACID SALTS

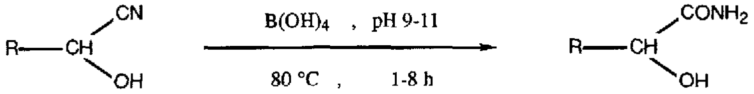
Jacqueline Jammot, Robert Pascal,*,¶ and Auguste Commeyras

U.A. C.N.R.S. n°1097 "Hétérochimies et aminoacides", Université des Sciences et Techniques du Languedoc,
Place E. Bataillon, 34060 Montpellier Cedex, France.

Summary : α-Hydroxyamides and α-hydroxyacids were prepared in satisfactory yield by heating aldehyde-derived cyanohydrins in aqueous solution in the presence of borax or alkaline borates.

The competing decomposition of cyanohydrins to cyanide and aldehydes or ketones[1] is a severe drawback during the hydration of these compounds in alkaline solution. Therefore acidic conditions are widely preferred.[2] However, a patent described a method involving the use of an aqueous solvent containing the carbonyl compound corresponding to the cyanohydrin (10-60 % by weight) and a catalytic amount of borate or perborate salts at weakly alkaline pH.[3] The hydration was carried out only from methylethylketone- and acetone-cyanohydrins, and the reaction of aldehyde derivatives was not described, despite the usefulness of the product. That is probably because there is little interest in a method involving high concentrations of aldehydes which are unstable in alkaline solution.

We found that the aldehyde-derived cyanohydrins give satisfactory yields of hydroxyamides by the simple addition of borate salts (Table). Typically, hydrations were carried out by heating (80°C) an aqueous solution containing the cyanohydrin (0.2-1 mol l^{-1}) and borate ion (0.2 mol l^{-1}, pH 9-11) until the nitrile had completely reacted (t.l.c., n.m.r.).



The preparation of hydroxyamides was achieved in 65-85% yield, except for the hydration of glycolonitrile. In that case, the yield of hydroxyacetamide is lower, probably due to the formation of polymers (as attested by the dark brown colour of the reaction medium). In spite of the moderate basicity of the solution, the subsequent hydrolysis to α-hydroxyacid (7-8% of the starting product by titration of carboxylic acids) reduces the yield of α-hydroxyamide (Table). The addition of a small quantity of cyanide to the reaction medium was shown to raise the yield and reduce the reaction time in the case of 2-hydroxy 4-methylthiobutyramide (Entry 8-9). α-Hydroxyacids were also prepared by the borate-catalyzed hydration of cyanohydrins. The synthesis of mandelic acid (in 76% yield) and 2-hydroxy 4-methylthiobutyric acid (90%) was achieved by addition of excess sodium hydroxide, when hydration is complete, and heating the medium under reflux 6 and 3 hours, respectively.

¶ Present address : C.R.B.M., C.N.R.S., Route de Mende, BP 5051, 34033 Montpellier Cedex, France.

Table. Hydration of cyanohydrins R-CH(OH)-CN at 80°C.

Entry	R	Concentration mol l^{-1}	Catalyst mol l^{-1}	Time	R-CH(OH)-CONH$_2$ % yield	m.p. °C	R-CH(OH)-COOH %
1	H-	0.2	NaB(OH)$_4$ 0.2	2 h 20	39[a,b]	114-5	7
2	CH$_3$(CH$_2$)$_5$-	0.5[c]	borax 0.1	2 h	67[d]	144-7	
3	CH$_3$-	1.0	borax 0.1	3 h 20	72[a,b]	74-6	
4	CH$_3$-	1.0	KB(OH)$_4$ 0.2	2 h 20	75[a,e]		
5	CH$_3$-	1.0 + KCN 0.2	KB(OH)$_4$ 0.2	2 h 20	75[a,e]		
6	C$_6$H$_5$-	0.5[c] + KCN 0.05	borax 0.1	2 h 20	73[d]	124	
7	(CH$_3$)$_2$CH-	0.5	borax 0.1	8 h	86[f]	102-3	
8	CH$_3$S(CH$_2$)$_2$-	0.5	borax 0.1	2 h 20	79[a,e]	85-7	8
9	CH$_3$S(CH$_2$)$_2$-	0.5 + KCN 0.05	borax 0.1	1 h 30	83[a,e]	88-9	8

Separation by circulation through a column filled with (a) a sulfonic acid, or (b) a quaternary ammonium hydroxide, ion exchange resin. (c) In methanol-water 1:1. (d) Crystallization in the medium. (e) Elimination of boric acid as B(OCH$_3$)$_3$ after addition of CH$_3$OH. (f) Extraction and liquid chromatography.

The present method avoids the disadvantages of the alkaline hydration of cyanohydrins. The lower pH reduces the degree of decomposition of the starting product, and consequently the extent of the subsequent side-reactions of the aldehyde. The addition of carbonyl compound, as recommended by Wechsberg and Schoenbeck,[3] is useless owing to the high stability of cyanohydrins derived from aldehydes compared to ketone derivatives.[1] This method should turn out to be particularly attractive for the preparation of α-hydroxyamides and α-hydroxyacids bearing acid-sensitive groups. These first results do not provide any explanation for the action of borate salts in the course of the hydration, but indicate that carbonyl compound probably plays no role, contrary to what was previously observed for α-aminonitriles.[4]

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References

1 G. Schlesinger and S. L. Miller, *J. Am. Chem. Soc.* 1973, **95**,3729.

2 C. L. Willis and L. H. Slaugh, U.S. Patent, 4,351,955; Mitsubishi Co., Jpn. Kokai Tokkio Koho, 82,128,658 (*Chem. Abstr.* 1982, **97**, 215565b); Asahi Chem. Ind. Co., Jpn. Kokai Tokkio Koho, 82,82,340 (*Chem. Abstr.* 1982, **97**, 144380z); H.T. Bucherer and W. Brandt, *J. Prakt. Chem.* 1934, **140**, 129; E. Erlenmeyer and O. Sigel, *Liebigs Ann. Chem.*, 1875, **177**, 102.

3 M. Wechsberg and R. Schoenbeck, Eur. Patent, 80, 0,006,140.

4 R. Pascal, J. Taillades, and A. Commeyras, *Tetrahedron*, 1978, 34, 2275; 1980, **36**, 2999.

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