CHEMISTRY LETTERS, pp. 731-732, 1991

Asymmetric Hydrocyanation of 3-Phenoxybenzaldehyde Catalyzed by Poly(cinchona alkaloid-co-acrylonitrile)s

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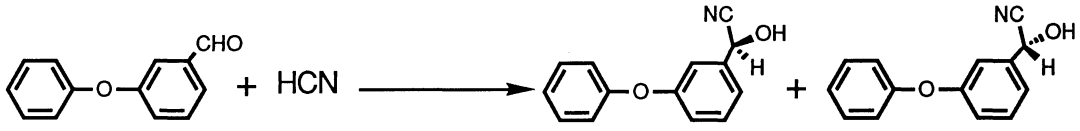
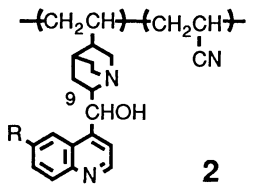
Asymmetric addition of hydrogen cyanide to 3-phenoxybenzaldehyde catalyzed by poly(quinidine-co-acrylonitrile) affords (S)-2-hydroxy-2-(3'-phenoxyphenyl)-acetonitrile in a moderate optical yield.

(S)-2-Hydroxy-2-(3'-phenoxyphenyl)acetonitrile (**3**) is an important alcohol moiety of optically active pyrethroid insecticides.[1] In conjunction with the synthesis of this cyanohydrin, the catalytic activities of alkaloids in asymmetric addition of hydrogen cyanide to carbonyl groups have been extensively studied, but the enantioselectivities have been disappointing.[2] The principal drawbacks in the use of the alkaloids seem to be due to their solubility and relatively less rigid structure. Kobayashi *et al* have reported the synthesis and properties of new poly(cinchona alkaloid-co-acrylonitrile)s (**2**), and discussed asymmetric Michael reaction catalyzed by **2**.[3] Herein, our interest has been focussed on the relationship between the structures and properties of **2** and the enantioselectivities in asymmetric hydrocyanation. Four kinds of copolymers(**2a-d**) were prepared and their catalytic activities in the asymmetric hydrocyanation were examined. Among them, **2a** exhibited a moderate enantioselectivity. In this communication, we wish to exemplify the asymmetric addition of hydrogen cyanide to 3-phenoxybenzaldehyde (**1**) using **2** as catalysts.

The catalyst (**2**) was prepared by the method of Kobayashi *et al*.[3,4] The reaction was carried out by using 1.1 mmol of **2**, 99 mmol of hydrogen cyanide, 50 mmol of **1** and 40 mL of toluene at 10 ℃ for 1h. After usual work-up, the crude product was chromatographed on silica gel to give a mixture of the enantiomers, **3** and **4**.[5] The optical purity of the resulting cyanohydrin was determined by HPLC, in which the optically active column, SUMIPAX OA-4100, was used.[6]



1 **3** **4**



2

2a : R=OMe, poly (quinidine-co-acrylonitrile)
2b : R=OMe, poly (quinine-co-acrylonitrile)
2c : R=H , poly (cinchonidine-co-acrylonitrile)
2d : R=H , Poly (cinchonine-co-acrylonitrile)

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The results of asymmetric additon of hydrogen cyanide to **1** catalyzed by cinchona alkaloids and **2** are summarized in Table 1. Cinchonidine, cinchonine and their copolymers with acrylonitrile (**2c** and **2d**) gave the racemic products in 98% yield. Quinine and its copolymer with acrylonitrile (**2b**) gave (R)-cyanohydrin (**4**) as a major product in low optical yields (entries 2 and 4). Quinidine and its copolymer with acrylonitrile (**2a**), on the other hand, gave (S)-cyanohydrin (**3**) preferentially in moderate optical yields (22% ee, entry 1 and 46% ee, entry 3). The configuration at C (9) of **2** would play an important role in this asymmetric hydrocyanation. Higher optical yields were obtained when **2a** and **2b** were employed as catalysts, compared with those of the corresponding monomeric alkaloids. The reaction mixture is gel-like in cases of **2a** and **2b**, whereas it is homogeneous in case of the corresponding monomer, quinidine and quinine. This gelation would be preferable both to increase the enantioselectivity and to decrease the racemization of the products. Thus, the present method with polymeric catalysts would be useful for asymmetric hydrocyanation. A further study on the improvement of optical yields and the mechanism of the asymmetric induction is in progress.

Table 1. Asymmetric Addition of Hydrogen Cyanide to **1** Catalyzed by Cinchona Alkaloids and **2**[a)]

Entry	Catalyst	Yield / %[b)]	% ee[c)]
1	quinidine	97	22[d)]
2	quinine	93	5[e)]
3	**2a**	98	46[d)]
4	**2b**	97	20[e)]

a) The reactions were carried out by using 1.1 mmol of the catalyst as a cinchona alkaloid, 99 mmol of hydrogen cyanide, 50 mmol of **1** and 40 mL of toluene at 10 °C for 1 h. b) Determined by HPLC, in which Lichrosorb SI-60 was used as a column. c) Determined by HPLC, in which SUMIPAX OA-4100 was used as a column. d) (S)-isomer (**3**) was preferentially obtained. e) (R)-isomer (**4**) was preferentially obtained.

References

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4) The ^{1}H NMR and IR spectra of this co-polymer (**2**) were found to be identical with those of the literature.[3)] The molar ratio of the corresponding cinchona alkaloid and acrylonitrile in the co-polymer (**2**) was calculated on the basis of the elementaly analysis.[3)] **2a** : 10.2 mol% of quinidine, $[\alpha]^{25}_D$ 48.2° (c 1.01, DMF) [lit. : 9.8 mol% of quinidine, $[\alpha]^{25}_D$ 48.8° (c 1.0, DMF).[3)]]. **2b** : 9.5 mol% of quinine, $[\alpha]^{25}_D$ -39.2° (c 1.00, DMF). **2c** : 10.6 mol% of cinchonidine, $[\alpha]^{25}_D$ -28.6° (c 1.01, DMF). **2d** : 14.6 mol% of cinchonine, $[\alpha]^{25}_D$ 65.9° (c 1.01, DMF).

5) The ^{1}H NMR and IR spectra of this mixture were found to be identical with those of the authentic sample : K.Tanaka, A.Mori, and S.Inoue, J.Org. Chem., **55**, 181 (1990) ; Y.Kobayashi, S.Asada, I.Watanabe, H.Hayashi, Y.Motoo, and S.Inoue, Bull. Chem. Soc. Jpn., **59**, 983 (1986).

6) HPLC conditions : UV 254 nm ; hexane / 1,2-dichloroethane / acetic acid /ethanol = 2000 / 500 / 10 / 25 (retention time : 24 min for **3** and 23 min for **4**). The isomers (**3** and **4**) on HPLC were confirmed with the authentic samples, respectively.[5)]

(Received February 8, 1991)