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Asymmetric Reactions. IV. Asymmetric, Catalytic Activity of Poly(2-quinuclidinylmethyl acrylate)

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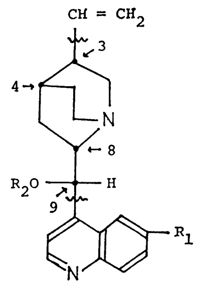
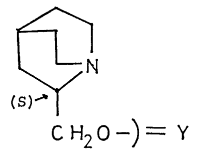
Synopsis. The asymmetric addition of methanol to phenylmethylketene has been conducted in the presence of poly(2-quinuclidinylmethyl acrylate) and 2-quinuclidinylmethyl propionate derived from (*S*)-2-quinuclidinylmethanol. The asymmetric functions of the above catalysts were similar to those of poly(*O*-acryloylquinine) and *O*-propionylquinine, which contain a quinoline ring and a vinyl group as additional groups to the quinuclidine ring.

Several workers[1–3] have recently studied asymmetric, catalytic reactions using chiral polymers derived from cinchona alkaloids. Cinchona alkaloids (**A**) consist of four asymmetric carbons (C_3, C_4, C_8, and C_9) and three main functional groups (a quinuclidinyl, a vinyl and a quinolyl group). In this paper, poly(2-quinuclidinylmethyl acrylate) (**HB**) and 2-quinuclidinylmethyl propionate (**LB**) were used to clarify the role of the quinuclidinyl group as an active site in cinchona alkaloid catalysts.



(A)

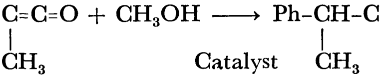


HB; -(CH_2-CH)$_n$-CO-Y
MB; CH_2=CH-CO-Y
LB; CH_3CH_2-CO-Y

(B)

High- or low-molecular-weight catalysts (**HB** or **LB**) have been prepared by the acylation of (*S*)-2-quinuclidinylmethanol, which was obtained by reduction of (*S*)-2-(ethoxycarbonyl)quinuclidine with lithium aluminum hydride; (*S*)-2-(ethoxycarbonyl)quinuclidine was obtained by optical resolution[4] of the racemic mixture[5,6] derived from 4-methylpyridine.

(*S*)-2-Quinuclidinylmethanol was allowed to react with propionic anhydride or acryloyl chloride giving 2-quinuclidinylmethyl propionate (**LB**) or 2-quinuclidinylmethyl acrylate (**MB**) respectively. A soluble polymer (**HB**) was obtained by the polymerization of **MB** using a catalytic amount of azobisisobutyronitrile as initiator. The catalytic activities of **LB** and **HB** have been examined for the asymmetric synthesis of methyl 2-phenylpropionate. The addition of methanol to phenylmethylketene has been conducted according to an earlier report.[1]



$$\underset{\displaystyle CH_3}{\text{Ph-C}}\text{=C=O} + CH_3OH \xrightarrow[\text{Catalyst}]{} \text{Ph-}\underset{\displaystyle CH_3}{\text{CH}}\text{-COOCH}_3$$

Figure 1 shows plots of the optical purities (O.P.) of the addition products against reaction temperatures (T °C) for **HB** and **LB**. The results[1a] obtained previously with poly(*O*-acryloylquinine) (**HA**) and *O*-propionylquinine (**LA**) are also shown in Fig. 1 [Quinine catalysts (**A**): C_8, *S*-configuration; R_1=OCH_3; R_2= acyl group].

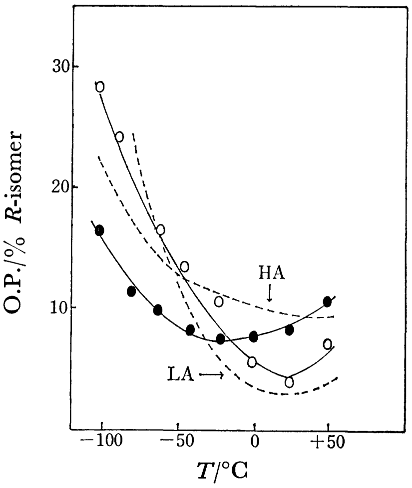


Fig. 1. Plots of optical purities[a] (O. P.) against reaction temperatures (T °C) in case of **HB** (●) and **LB** (○) (catalyst[b]: 0.025 mmol, phenylmethylketene: 2.500 mmol, methanol: 2.600 mmol, solvent: 25 ml of dry toluene).
a) The optical purity was calculated from the specific rotation of the product and that of optically pure methyl 2-phenylpropionate[1a] (*S*-form, $[\alpha]_D^{22}$ +109° in toluene). b) The molar equivalent amount of the polymeric catalyst was calculated on the basis of that of the monomer used in the polymerization.

All of the catalysts described above gave the addition products showing preference to the *R*-isomer in the range from −100 °C to +50 °C. Figure 1 also indicates that **HB** yielded a higher predominance of addition products with *R*-configuration than did **LB** above 0 °C. This sort of polymer effect was similar to that observed with quinine catalysts (**HA** and **LA**) above −50 °C.

Figure 1 suggests that the asymmetric functions of 2-quinuclidinylmethanol catalysts do not greatly differ from those of the quinine catalysts.

These results suggest that the configuration at C_8 of the quinuclidinyl group in cinchona alkaloid catalysts is very important in determining the configuration of products.

Experimental

A JASCO IRA-1 (IR) apparatus, a JEOL-60 MC (NMR) apparatus, a Hitachi M52 (MS) apparatus, a Rex-automatic polarimeter (optical rotation, 10 cm cell) and a Knauer vapor pressure osmometer (molecular weight) were used.

(S)-2-Quinuclidinylmethyl Acrylate (**MB**). Powdered sodium hydroxide (2.25 mmol) was suspended in a solution of (*S*)-2-quinuclidinylmethanol⁶⁾ (1.50 mmol) in dry dichloromethane (15 ml) in argon at −10 °C. To the mixture was added a solution of acryloyl chloride (1.80 mmol) in dry dichloromethane (5 ml). The reaction mixture was stirred for 20 h at the same temperature and the precipitate filtered. The filtrate was dried and evaporated to dryness and the residue subjected to column chromatography on alumina (2×10 cm, 200 mesh, neutral). Elution with chloroform gave **MB** as an oily material which was distilled to give a colorless oil. Yield, 60%. Bp 100 °C at 1 mmHg. $[\alpha]^{24}_{D}$ −60° (*c* 1.23, benzene); IR (neat): 1727, 1632, 995 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=5.64—6.46 ppm; MS *m/e* 195 (M$^+$).

Poly(2-quinuclidinylmethyl acrylate) (***HB***). A solution of 2-quinuclidinylmethyl acrylate (80 mg) and azobisisobutyronitrile (3 mg) in dry benzene (0.4 ml) was polymerized at 80 °C for 40 h in a sealed tube filled with argon. The product was poured into ether, and the precipitate filtered and washed with ether. Yield, 60%. $[\alpha]^{16}_{D}$ −47° (*c* 1.3, benzene); mol wt 5850 (benzene).

(S)-2-Quinuclidinylmethyl Propionate (***LB***). **LB** was obtained in 75% yield as a colorless oil by the reaction of (*S*)-2-quinuclidinylmethanol with propionic anhydride in the presence of triethylamine. Bp 105 °C at 3 mmHg. $[\alpha]^{20}_{D}$ −50.8° (*c* 0.96, benzene); IR (neat): 1740, 1188, 1058 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=2.37, 1.13 ppm; MS *m/e* 197 (M$^+$).

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