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ASYMMETRIC REACTIONS.1. ASYMMETRIC SYNTHESIS OF METHYL α-PHENYLPROPIONATE BY MEANS OF OPTICALLY ACTIVE POLYMERS

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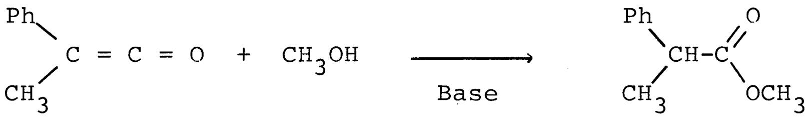
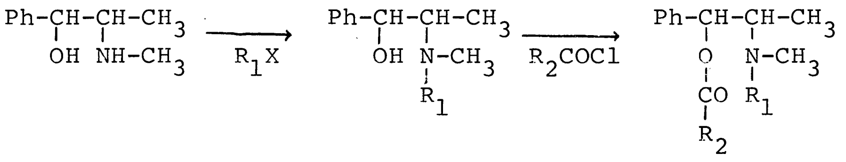
Asymmetric addition of methanol to phenylmethylketene was attempted with optically active low molecular weight and polymeric amines. Both of them were derived from quinine, N-alkylprolinol and ephedrine as propionyl and poly-acryloyl esters. Quinine and N-alkylprolinol catalysts showed a type of remarkable polymer effect with regard to stereoselectivity.

There have been some works concerning asymmetric reactions catalyzed by optically active synthetic polymers because it is interesting to use synthetic polymers as enzyme models of biological asymmetric syntheses. In those works, optically active poly-ethyleneimines1),2), poly-lysine-Cu(II)-complex3) and poly-amino acids-Pd(II)-complex4),5) were used as asymmetric catalysts. Though most of such polymers have not possessed as high stereoselectivity as enzymes, it is also important to use synthetic polymers for the studies of stereochemistry, polymer effect and new catalysts. This paper describes the syntheses and asymmetric catalysis of optically active basic polymers and their corresponding monomer unit model compounds, starting from some amino alcohols.

Pracejus6) previously reported asymmetric addition of alcohols to dissymmetric ketenes in the presence of optically active amines. In the present works, we examined the asymmetric addition of methanol to phenylmethylketene(PMK) with the catalysts obtained above.

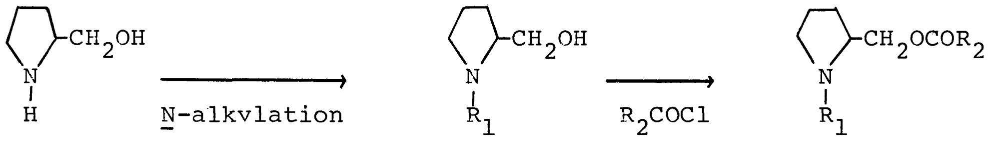


The syntheses of catalysts were carried out by the use of proline, ephedrine and quinine as starting materials. O-Acyl-N-alkylephedrines(1) and (2) were derived through O-acylation of N-alkylephedrine obtained via the reaction of (-)ephedrine with benzyl bromide or methyl iodide.



(1a) R_1, CH_3 ; R_2, $CH=CH_2$. (1b) R_1, CH_3 ; R_2, CH_2CH_3. (2a) R_1, CH_2Ph ; R_2, $CH=CH_2$. (2b) R_1, CH_2Ph ; R_2, CH_2CH_3.

Prolinol was prepared from *L*-proline by Karrer's method[7], and was *N*-methylated or benzylated to give *N*-alkylated prolinols. *O*-Acyl-*N*-alkylprolinols (3) and (4) were prepared by *O*-acylation of the above *N*-alkylprolinols.



(3a) R_1, CH_3 ; R_2, $CH=CH_2$. (3b) R_1, CH_3 ; R_2, CH_2CH_3. (4a) R_1, CH_2Ph ; R_2, $CH=CH_2$. (4b) R_1, CH_2Ph ; R_2, CH_2CH_3.

O-Acylquinines were synthesized by the method[8] reported earlier by Imoto *et al*.

Quinine-OCOR (5a) R, $CH=CH_2$. (5b) R, CH_2CH_3.

Table 1 shows the physical data of acryloyl and propionyl esters of amino alcohols obtained above. The polymerization of acryloyl esters(1a)-(4a) was performed, by the use of azo-bis-isobutyronitrile as an initiator, without solvents in a sealed tube at 80°C for 20-60 hours. (5a) was polymerized with the same initiator in dry benzene under refluxing. The physical data and yields of polymers are shown in Table 2.

Table 1.

	Acryloyl esters		Propionyl esters	
Amino alcohols	$[\alpha]_D$(benzene)	BP(°C)	$[\alpha]_D$(benzene)	BP(°C)
N-methylephedrine	-43.5	106-7(1mm)	-67.5	99-101(1mm)
N-benzylephedrine	-23.6	157-8(1mm)	-39.7	156-7(1mm)
N-methylprolinol	-20.3	93-4(14mm)	-18.7	89(12mm)
N-benzylprolinol	-32.5	132-3(1mm)	-41.3	127-8(1mm)
Quinine	+16.1($CHCl_3$)	mp.88-90*	-24.1($CHCl_3$)	mp.134-6

* Acryloylquinine[8] was reported to be an oily material, $[\alpha]_D$ = +13.3°($CHCl_3$).

Table 2. The physical data and yields of polymers

Polymers	$[\alpha]_D$(benzene)	$[\eta]$ dl/g(benzene)	MW	Yields(%)
Poly-1a	-42.0	0.075	6900	70.0
Poly-2a	-18.6	0.075	7800	66.5
Poly-3a	-17.8	0.036	3300	65.8
Poly-4a	-43.4	0.053	5300	50.5
Poly-5a	-14.7($CHCl_3$)	0.077	14000	56.4

Addition reaction of methanol to PMK was carried out under an argon atmosphere in a similar manner to Pracejus$^{6)}$. Freshly distilled PMK(2.5 m mol) was dissolved in a solution of catalyst(0.01 molar equivalent amount of PMK) in 25 ml of dry toluene at a fixed temperature. To the solution was added dry methanol(2.75 m mol), and the mixture was stirred at the same temperature until the reaction was over. The end point of the reaction was confirmed by the absence of yellow color of PMK.

After removing the basic catalyst with dilute hydrochloric acid, the solvent was evaporated under reduced pressure to leave a residual oil. The residue was distilled to give a colorless oil(bp.69-71°C at 2mm. Yield, 68%). The tlc and glc of the oil showed it to be a single material. The ir and nmr spectra of this product were completely in agreement with those of authentic methy α-phenylpropionate. The results of addition reactions tried with various catalysts at -78°, 0° and +25°C are given in Table 3.

Table 3. Results of asymmetric addition reaction with basic catalysts

T(°C)	-78		0		+25		
Catalysts	$[\alpha]_D$	O.Y(%)^{*1}	$[\alpha]_D$	O.Y(%)	$[\alpha]_D$	O.Y(%)	Conf.^{*2}
Poly-1a	+ 7.1	6.5	+ 6.1	5.5	+ 4.1	3.7	S
1b	+26.7	24.4	+11.5	10.5	+ 8.5	7.8	S
Poly-2a	+ 1.0	0.9	+ 1.3	1.1	+ 0.4	0.3	S
2b	+ 2.7	2.4	+ 0.9	0.8	+ 0.6	0.5	S
Poly-3a	+ 2.2	2.0	+ 0.3	0.2	+ 1.0	0.9	S
3b	+ 1.7	1.5	+ 0.6	0.5	+ 0.8	0.7	S
Poly-4a	- 5.5	5.0	- 1.6	1.4	- 0.4	0.3	R
4b	+ 1.1	1.0	+ 1.3	1.1	+ 1.2	1.1	S
Poly-5a	-18.6	17.0	-12.1	11.1	-10.5	9.6	R
5b	-34.0	31.1	- 3.7	3.3	- 3.8	3.4	R

*1, Optical yield was calculated from the specific rotation of the product and that of optically pure methyl α-phenylpropionate$^{6)}$ (S-form, $[\alpha]_D^{22}$ = +109°).

*2, Configuration of predominant isomer.

Table 3 shows that polymeric catalysts, poly-4a and poly-5a, gave the distinct polymer effect on the asymmetric addition of methanol to PMK. The effect was examined in more detail at wider range of temperatures(+50~-95°C), and the measured specific rotations were plotted against the reaction temperatures(T°C) in Figures 1 and 2. Figure 1 indicates that poly-4a gave products of specific rotation of opposite sign and higher optical yields in comparison with its monomeric model 4b, especially at lower temperatures. An approximately linear correlation between $[\alpha]_D$ and T(°C) was also observed with poly-4a, but only an irregular correlation was shown in the case of 4b.

Poly-5a revealed higher stereoselectivity than its model compound 5b above -50°C, and the optical yield with the former was about three times as high as that with the latter at 0°C(Figure 2).

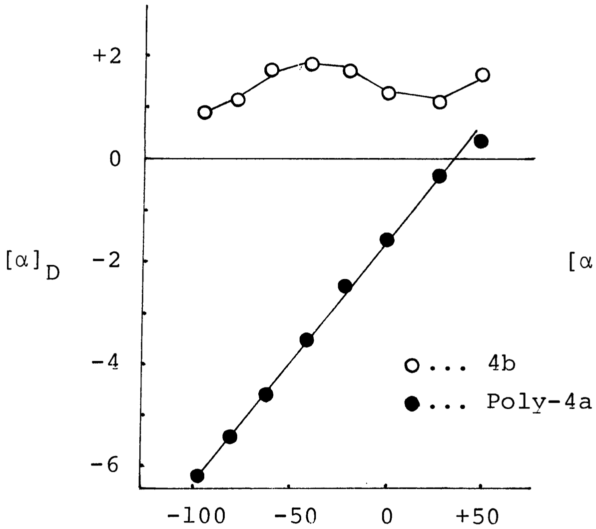


Figure 1. Plots of [α]$_D$ against T(°C) in case of 4b and poly-4a

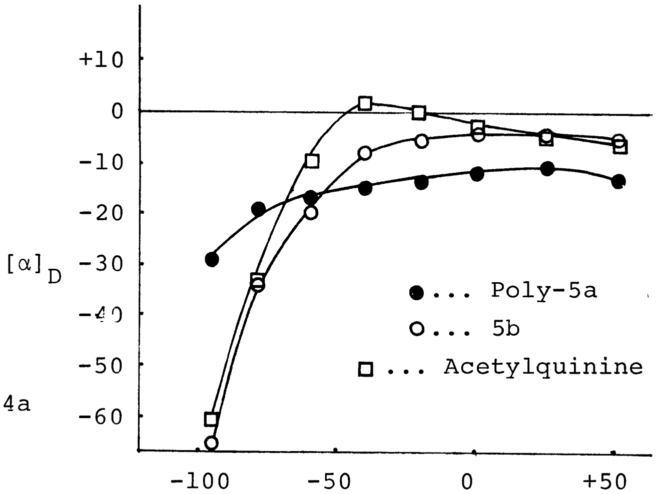


Figure 2. Plots of [α]$_D$ against T(°C) in case of 5b, poly-5a and acetylquinine$^{6)}$

These results clarified that the action of polymeric catalysts was quite different from that of their corresponding monomeric models in the stereochemistry of this addition reaction.

However, further work and consideration are required to explain fully these observations.

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