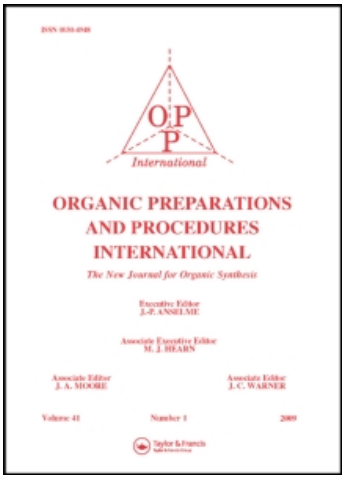

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ASYMMETRIC INDUCTIVE SYNTHESIS OF α-AMINOARYLACETIC ACIDS IN THE PRESENCE OF β-CYCLODEXTRIN

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ASYMMETRIC INDUCTIVE SYNTHESIS OF α-AMINOARYLACETIC ACIDS IN THE PRESENCE OF β-CYCLODEXTRIN

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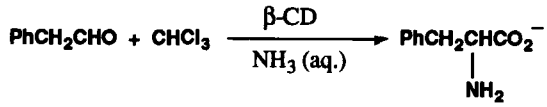
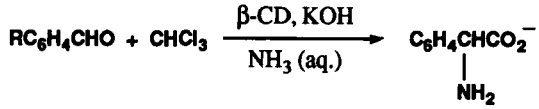
Landini[1] has reported the synthesis of α-aminoarylacetic acids in the presence of a quaternary salt TEBA as phase transfer catalyst from the reaction of chloroform with corresponding aldehydes. Optically active α-aminoarylacetic acids could be obtained in chiral micellar systems by a similar scheme[2,3]. We now report that asymmetric induction in this reaction occurs in the presence of β–cyclodextrin (β-CD).

The highest yield of pure products is 85% for α-amino(4-bromophenyl)acetic acid ($[\alpha]_D^{25}$ +9.08). The value of e.e. % is about 2.6% for α-aminophenylacetic acid and about 28.2% for phenylalanine. All of the amino acids obtained are optically active. Moreover, some yields of pure products are higher than those obtained from the phase-transfer or the chiral micellar conditions (Table 1). In particular, the synthesis of phenylalanine from phenylacetaldehyde in the presence of β-CD has not

been reported previously.





R = H, *m*-CH_3, *p*-CH_3, *m*-Br, *p*-Br, *p*-Cl, *p*-CH_3O

It is suggested that the substrate is captured by the β-CD in the chiral cavity thus favoring somewhat attack of CCl_3^- of carbonyl group in one direction, and the hydroxy group of β-CD plays an important role in the process. It can be seen that the S-form is enriched for α-aminophenylacetic acid and the R-form for phenylalanine. The favored configuration of other aminoacids cannot be determined because the absolute configuration and the $[\alpha]_{max}$ have not been reported in literature.

TABLE 1. Asymmetric Syntheses of α-Aminoarylacetic Acids and Phenylalanine in the Presence of β-Cyclodextrin

Cmpd No	ArCHO	Yield (%)	mp. (°C)	$[\alpha]_D^{25}$ (g/l) (in 1 M HCl)	e.e. %[a]
1	C_6H_5	51.7	257-258	+3.41 (c: 0.22)	2.6[b]
2	*m*-$CH_3C_6H_4$	19.4	243-245	+8.33 (c: 0.12)	
3	*p*-$CH_3C_6H_4$	25.4	259-260	+3.30 (c: 0.30)	
4	*p*-$CH_3OC_6H_4$	27.6	238-239	+8.59 (c: 0.16)	
5	*m*-BrC_6H_4	39.1	268-270	+8.25 (c: 0.08)	
6	*p*-BrC_6H_4	84.5	255-257	+9.08 (c: 0.34)	
7	*p*-ClC_6H_4	45.3	262-264	+15.83 (c: 0.12)	
8	$C_6H_5CH_2$	30.0	259-261	+1.26 (c: 1.45)[c]	28.2[c]

a) e. e. % = $([\alpha]_D/[\alpha]_{D,max})$ x 100%. b) $[\alpha]_{D,max}^{25}$ + 130.7 (c: 1.1M HCl)[4]. c) The value + 1.26 was measured in 5 M HCl. $[\alpha]_{D,max}^{25}$ +4.47(c: 1.5M HCl)[5]

EXPERIMENTAL SECTION

The optical rotations were measured with WZZ-1 polarimeter. The IR spectra were taken with PE-683 spectrophotometer. Microanalyses were performed with Carbo Erba 1106 analyzer. β-Cyclodextrin (>97%) was recrystallized from water. All reported melting points were uncorrected. All other materials were standard reagent grade.

General Procedure. -To an aqueous ammonia solution (20 mL, 25%), 214.3 mmol KOH (solid), 10 mmol LiCl (solid) and 1 mmol β-CD were added. The mixture was stirred at -10 to -5°. A solution of

TABLE 2. IR and Elemental Analysis of α-Amino Acids Synthesized

No.	IR(KBr) (cm^{-1})						Elemental Analysis Calcd (Found)		
							C	H	N
1	3460	3000	2680	1645-1600	1530	1410	63.57 (63.42)	6.00 (5.93)	9.27 (8.62)
2	3440	2990	2660	1640-1585	1520	1400	65.44 (65.43)	6.71 (6.91)	8.48 (8.45)
3	3450	3000	2680	1640-1600	1530	1409	65.44 (65.02)	6.71 (6.72)	8.48 (8.26)
4	3450	3000	2680	1640-1600	1530	1409	59.66 (58.93)	6.12 (6.14)	7.73 (7.67)
5	3400	2940	2660	1640-1585	1530	1400	41.77 (41.70)	3.50 (3.45)	6.09 (5.80)
6	3420	2980	2660	1640-1585	1530	1400	41.77 (41.72)	3.50 (3.42)	6.09 (5.83)
7	3450	2980	2660	1640-1590	1530	1400	51.77 (51.54)	4.34 (4.21)	7.55 (7.11)
8	3450	2980	2670	1635-1590	1525	1362	65.44 (65.06)	6.71 (6.80)	8.52 (8.10)

a) See Table 1.

the aldehyde (5 mmol) in 1-1.5 mL $CHCl_3$ was added dropwise with stirring over 3 hrs while the temperature was kept at -5-0°; then the mixture was stirred at room temperature overnight. The pH of the mixture was adjusted to 6-7 with conc. hydrochloric acid and cooled to 0°. The precipitated solid was collected, washed successively with water, ether and ethanol. Recrystallization from water:ethanol (5:1) and drying afforded pure α-aminoarylacetic acids or phenylalanine. Positive ninhydrin tests were obtained on compounds **1-8**.

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