

Synthesis of α -Aminoarylacetic Acids in the Presence of Phase Transfer Catalysts

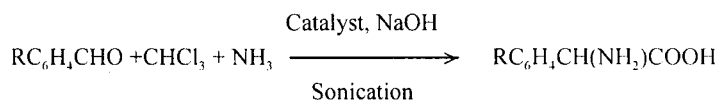
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Abstract: Synthesis of α -aminoarylacetic acids with good yield in the presence of phase transfer catalyst (PTC) under sonication has been studied. Results obtained are superior to those by other similar methods. The data show that β -cyclodextrin (β -CD) is a more efficient catalyst than other PTC. Optimum reaction conditions and a preliminary mechanism are also discussed.

Keywords: α -Aminoarylacetic acid, phase transfer catalyst, sonication.

In earlier publications^{1,2}, a one-step phase transfer catalyzed reaction for preparing α -aminoarylacetic acids from aryl aldehydes and chloroform, using quaternary salts or β -CD as phase transfer catalyst, was described; It was also reported that some reactions under sonication condition often occur more rapidly and easily³. We now find that this reaction can be advantageously realized by phase transfer catalysis under sonication.



R=H, *p*-Br, *m*-Br, *o*-Br, *p*-Cl, *m*-Cl, *o*-Cl, *p*-CH₃, *m*-CH₃, *p*-NO₂,
m-NO₂, *p*-OCH₃, *p*-N(CH₃)₂, *o*-OH

Optimum reaction conditions were determined with benzaldehyde. In the presence of lithium chloride, the yield noticeably decreases (see **Table 1**), but the same behavior has been observed in the absence of lithium chloride without the catalyst. The presence of a phase transfer catalyst is essential. β -CD proves to give the best results (see **Table 1**). The use of lithium chloride contradicts the effect of the catalysts. In contrast with the results obtained by Landini¹, lithium chloride is detrimental under sonication. These cases are consistent with the other report⁴.

Certain other variations in conditions are shown to affect the product yields. In the case of tetrabutyl ammonium bromide or β -CD, as more base was added in the system, the yields were increased 2-3 times (See **Figure.1**). However, when there is excess base in the system, it is not advantageous for the reaction as ammonia

tendency to escape. The reaction under sonication takes place more rapidly and it is easily to obtain some products, which can not be got previously², for example, *p*-nitrophenylglycine, *m*-nitrophenylglycine, *p*-dimethylaminophenylglycine, *o*-hydroxyphenylglycine, α -furanglycine. The yields were less under non-sonication condition because of side reactions, such as the Cannizzaro reaction occurring simultaneously or exclusively⁶.

Table 1. Reaction of Arylaldehydes with chloroform in the presence of different catalysts in a two-phase system

LiCl (mmol-equiv)	Catalyst (mmol-equiv)	Yield of α -Aminophenylacetic acid ^b (%)
0	0	13 ^a
2.8	0	16 ^a
0	(C ₄ H ₉) ₄ NBr (0.5)	41.
2.8	(C ₄ H ₉) ₄ NBr (0.5)	29
0	CH ₃ (CH ₂) ₁₅ N(CH ₃) ₃ Br (0.5)	56
2.8	CH ₃ (CH ₂) ₁₅ N(CH ₃) ₃ Br (0.5)	39
0	(C ₂ H ₅) ₃ C ₆ H ₅ CH ₂ NCl (0.5)	50
2.8	(C ₂ H ₅) ₃ C ₆ H ₅ CH ₂ NCl (0.5)	33
0	β -Cyclodextrin (0.5)	63
2.8	β -Cyclodextrin (0.5)	52
0	peracetyl- β -cyclodextrin (0.35)	41
2.8	peracetyl- β -cyclodextrin (0.35)	23

a. Reaction time 24h. b. Reaction time 2h.

Figure 1. Effect of the amount of NaOH on the yield in the presence of catalysts

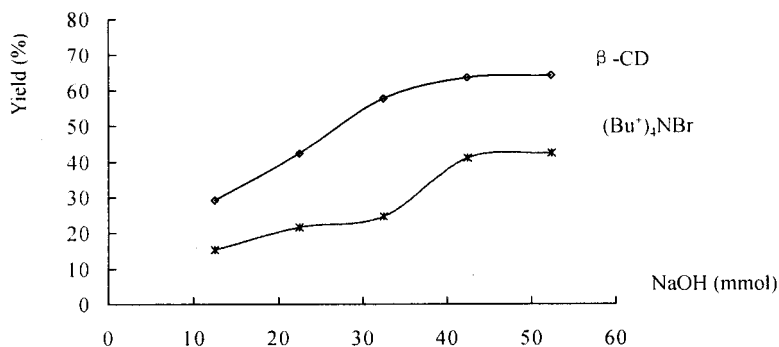


Table 2. Synthesis of α -aminoarylacetic acids in the presence of β -CD under sonication

No	ArCHOOH NH ₂	Yield ^a (%)	m.p. ^b (°C)		IR (KBr, cm ⁻¹)	Elemental Analysis Calcd (Found)		
						C	H	N
1	C ₆ H ₅	64	257-	3460 3000	1645-1600	63.51	6.00	9.27
			258	2680	1530 1410	(63.42)	(5.93)	(8.62)
2	<i>p</i> -Br C ₆ H ₄	43	255-	3420 2980	1640-1585	41.77	3.50	6.09
			257	2660	1530 1400	(41.72)	(3.42)	(5.83)
3	<i>m</i> -BrC ₆ H ₄	56	268-	3400 2940	1640-1585	41.77	3.50	6.09
			270	2660	1530 1400	(41.70)	(3.45)	(5.80)
4	<i>o</i> - Br C ₆ H ₄	64	254-	3400 2960	1640-1585	41.77	3.50	6.09
			257	2660	1530 1400	(41.75)	(3.42)	(5.88)
5	<i>p</i> -Cl C ₆ H ₄	70	262-	3450 2980	1640-1590	51.77	4.34	7.55
			264	2660	1530 1400	(51.54)	(4.21)	(7.11)
6	<i>m</i> -Cl C ₆ H ₄	53	244-	3450 2970	1640-1590	51.77	4.34	7.55
			246	2660	1530 1400	(51.70)	(4.30)	(7.46)
7	<i>o</i> - Cl C ₆ H ₄	62	273-	3450 2980	1640-1580	51.77	4.34	7.55
			275	2660	1530 1400	(51.62)	(4.40)	(7.23)
8	<i>p</i> -CH ₃ C ₆ H ₄	51	259-	3450 3000	1640-1600	65.44	6.71	8.48
			260	2680	1530 1409	(65.02)	(6.72)	(8.26)
9	<i>m</i> -CH ₃ C ₆ H ₄	76	243-	3440 2990	1640-1585	65.44	6.77	8.48
			244	2660	1520 1400	(65.43)	(6.91)	(8.45)
10	<i>p</i> -NO ₂ C ₆ H ₄	56	260-	3440 2960	1640-1590	48.98	4.08	14.28
			262	2670	1530 1405	(48.51)	(3.93)	(14.36)
11	<i>m</i> -NO ₂ C ₆ H ₄	48	251-	3440 2950	1640-1585	48.98	4.08	14.28
			252	2670	1530 1405	(48.67)	(4.21)	(14.02)
12	<i>p</i> -CH ₃ OC ₆ H ₄	42	238-	3450 3000	1640-1600	59.66	6.12	7.73
			240	2680	1530 1409	(58.93)	(6.14)	(7.67)
13	<i>p</i> -CH ₃) ₂ NC ₆ H ₄	41	262-	3440 2890	1640-1600	60.84	7.26	14.42
			263	2675	1520 1400	(61.53)	(7.10)	(14.51)
14	<i>o</i> -HOC ₆ H ₄	62	264-	3500 2940	1640-1580	57.48	5.43	8.38
			266	2660	1530 1409	(57.56)	(5.51)	(8.27)
15	α -furyl	31	273-	3440 2890	1680-1585	51.07	6.00	9.93
			275	2860	1500 1410	(51.01)	(5.12)	(9.85)

a. Yield of isolated product. b. In these cases the compound begins to melt at these temps., but incompletely; sintering and decomposition indicating color change followed melting.

β -CD can be used as phase transfer catalyst probably because arylaldehyde was bound to β -CD, transferred to the aqueous phase and condensed with dichlorocarbene⁵. However, in order to obtain any clear understanding of the phase transfer mechanism in the presence of β -CD and especially under sonication, further studies are necessary.

Experimental

The IR spectra were taken with PE-683 spectrophotometer. Elemental analysis was performed with Carbo Erba 1106 analyzer. Ultrasonic wave irradiates with SCQ50 (33KHz) ultrasonicator. All reported melting points were uncorrected. Arylaldehydes were freshly distilled.

General procedure. To an aqueous ammonia solution (6ml, 25%), 42.5mmol NaOH (solid), 2.8mmol LiCl (solid) and 0.5 mmol PTC or β -CD were added. The mixture was irradiated under sonication at -5° - 0° C. The aldehyde (10mmol) dissolved in a mixed solvent of CHCl_3 and CH_2Cl_2 (2ml : 2ml) were added dropwise with ultrasonic wave irradiating over two hours at -5° - 0° C, and gaseous ammonia was bubbled through the mixture frequently. The pH of the mixture was adjusted to 6-7 with concentrated hydrochloric acid and cooled to -10° C. The precipitated solid was collected, washed successively with water, ether and ethanol, recrystallized from diluted ethanol (H_2O :ethanol=5:1) and dried to afford α -aminoarylacetic acids. Positive ninhydrin tests were obtained on all compounds (see **Table 2**).

Acknowledgments

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