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β-Cyclodextrin-TEBA: A New Catalyst System For Selective Synthesis of α-Hydroxyacids

Cheng-He Zhou [a], De-Qi Yuan [a] & Ru-Gang Xie [a]
[a] Department of Chemistry, Sichuan University, Chengdu, 610064, P. R. China
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β-CYCLODEXTRIN-TEBA: A NEW CATALYST SYSTEM FOR SELECTIVE SYNTHESIS OF α-HYDROXYACIDS

Cheng-He Zhou, De-Qi Yuan, Ru-Gang Xie*
Department of Chemistry, Sichuan University, Chengdu 610064, P. R. China

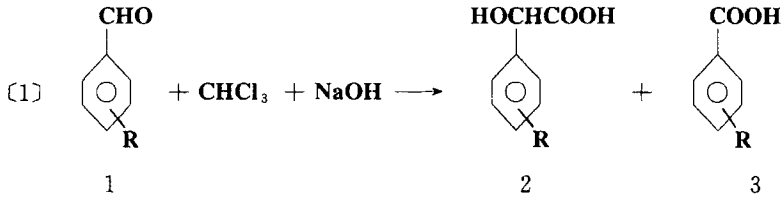
Abstract: The presence of β-cyclodextrin (β-CD) and triethylbenzyl ammonium chloride (TEBA) favors the one-pot reaction of aromatic aldehydes, chloroform and sodium hydroxide to give α-hydroxyarylacetic acids in 81%～89% yields.

Cyclodextrins (CDs), cyclicoligomer consisting of α-1, 4-linked D-glucopyranose, have been attracting growing attention because of their ability to form inclusion complexes and act as efficient catalysts in various reactions[1]. Recently, much effort has been directed to the selectivities of CD-catalyzed reactions. The regio-selectivity enhancement by CDs in substitutions of phenol or its derivatives[2,3] and assymetric induction of CDs in certain reactions[4] have been described. We now report the effect of β-cyclodextrin (β-CD) and triethylbenzylammonium chloride (TEBA) on the one-pot synthesis of α-hydroxyarylacetic acids from aromatic aldehydes, chlorofrom and sodium hydroxide.

The reaction was performed by adding aqueous sodium hydroxide to the mixture of aldehyde, chloroform and catalyst, and stirring the resulting mixture at 50℃ for 8 hours, The products were extracted from the reaction solution and

* To whom correspondence should be addressed

purified by columu chromatography on silica gel. All the results are described by equation〔1〕, and tables 1 and 2.



a. R=H; b. R=p-CH_3; c. R=m-CH_3; d. R=p-OCH_3; e. R=o-Cl.

In general, reaction 〔1〕 is either ineffective or gives practically none of the expected α-hydroxyacid because of side reactions, such as Cannizzaro reaction and so forth. Catalytic amount of β-CD enhances clearly the formation of α-hydroxyacid, especially in those cases which proceed poorly in the absence of catalyst (Table 1). TEBA also operates in this reaction and appears to be somewhat better than β-CD.

Of still more significance is that when β-CD is used in conjunction with TEBA, both the yield and selectivty of α-hydroxyacids can be further improved substantially. As an example, we examined in particular the formation of p-methylmandelic acid with TEBA fixed at 5 mol% (with respect to the initial amount of aldehydes) and β-CD varied from 0 to 20 mol%. Table 2 shows that both the yield and selectivity are obviously dependent on the amount of β-CD. Use of 2 mol% of β-CD results in suppression of side reactions to almost negligible extent, and formation of the expected product is significantly enhanced. Less than 0.1% or more than 10% of β- CD has little influence on the reaction.

By applying this binary catalyst system to the synthesis of other derivatives of mandelic acid, good yields (81-89%) are obtained with little by-products (table 1). These results indicate that the present new synthetic method is far superior to others with regard to its simplicity, selectivity and high yields. Further work on clarifying the details of this synthetic reaction is in progress.

Table 1 Yields of α-Hydroxyacids* in the Presence or Absence of Catalysts

hydroxyacid 2		2a	2b	2c	2d	2e
Catalyst	none	28	38.8	29.7	41.2	trace
	2mol%β-CD	32	41.7	41	56	32
	2mol%β-CD+ 5mol%TEBA	85.8	83.4	81	89	88
mp. (℃)		118−9	145.5−6.5	93−3.5	107.5−8	120.5−1
(Lit. Value[5])		(118−9)	(144)		(108−9)	(120−1)

* Separated and purified by column chromatography. Satisfactory IR spectra and microanalysis (C±0.32; H±0.25) were obtained for all the hydroxyacids.

Table 2 Effect of β-CD-TEBA Binary Catalyst System on the Reaction of p-Methylbenzaldehyde and Chloroform

Catalyst (mol%)	TEBA	0	0	5	5	5	5	5	5	5
	β-CD	0	2	0	0.1	1	2	4	10	20
yield (%)	2b	38.8	41.7	73.9	75.4	79.7	83.4	77.2	76.3	73.2
	3b	10.4	8.2	6.5	6.1	5.6	0.5	2.8	7.0	7.1
Selectivity*		64.6	70.1	85.0	86.1	87.7	98.8	93.2	84.5	83.8

* The percentage of α-hydroxyacid among the total reaction products.

Experimental

A mixture of 0.05 mol of aromatic aldehyde 1, 8.5 g of chloroform and required amount of β-CD and TEBA in a flask equipped with a magnetic stirrer and dropping funnel is stirred for 20 min at 50℃, then 10 g of sodium hydroxide dissolved in 10 ml of water are added dropwise to the flask with stirring. After completion of this addition, the reaction is continued for 8 h with the temperature maintatined at 50 ℃, Then appropriate amount of distiiled water is added to dissolve the precipitate formed during the reaction, and the resulting solution is thoroughly washed with ether, adjusted to pH 3 with dilute hydrochloric acid and extracted with 3×30 ml of ether. The extract is dried with anhydrous sodium sulfate, then evaporated to dryness and the remaining precipitate is subjected to culumn chromatography on silica gel using acetone-petroleum (60-90°) (1/2 ~2/3, v/v) as eluent affording pure α-hydroxyacetic acid 2 and benzoic acid 3.

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