

ASYMMETRIC INDUCTION BY PHASE-TRANSFER CATALYSIS USING CHIRAL CATALYSTS.  
SYNTHESIS OF 1,2-DICHLOROALKANES AND ACETYLCYANOHYDRINS

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**SUMMARY.** Asymmetric induction is observed in the addition of chlorine to alkenes as well as in the synthesis of *O*-acetylcyanohydrins under phase-transfer conditions using (-)-benzylcinchonidinium chloride and (-)-*N*-dodecyl-*N*-methylephedrinium bromide as chiral catalysts.

Phase-transfer catalysis (PTC) is a practical tool to perform organic reactions in heterogeneous media<sup>1)</sup>. The use of chiral quaternary ammonium salts (usually derived from naturally occurring amines like ephedrine or quina alkaloids) as phase-transfer catalysts, enables in some cases optically active products to be obtained under phase-transfer conditions.

However, although it is a matter of current interest, only a few examples of asymmetric induction or kinetic resolution by the said phase-transfer method have been reported. For example synthesis of oxiranes<sup>2)</sup>, alcohols<sup>3)</sup>, 2-phthalimidoesters<sup>4)</sup> and alkylations of C-anions<sup>5)</sup> have been described. The synthesis of asymmetric dichlorocarbene adducts<sup>6)</sup> was originally claimed but has been subsequently disproved<sup>7)</sup>. Chiellini<sup>8)</sup> has claimed to attain products with optical activity in the same reaction using 'onium' salts anchored on a polymeric support, but in this work experimental details are not given.

We wish to report two new examples of asymmetric synthesis under PTC conditions, by means of chiral catalysts:

a) Addition of chlorine to alkenes and b) synthesis of *O*-acetylcyanohydrins (Fig. 1).

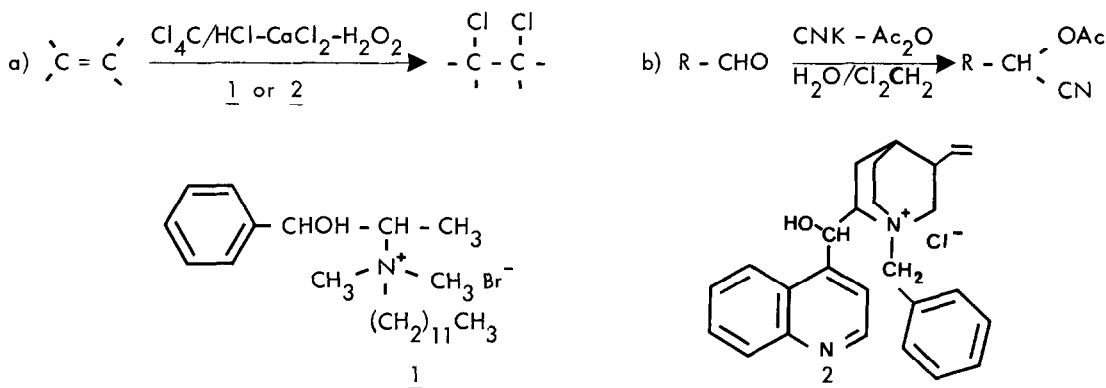


Fig. 1

Both reactions have been previously described under PTC conditions. The first one by G. Olah et al.<sup>9)</sup> and the second by Mc Intosh et al.<sup>10)</sup>. The catalyst used in both cases was triethylbenzylammonium chloride (TEBAC).

In our experiments we have followed the same procedures used by these authors, changing the conventional phase-transfer catalyst by a chiral one: i.e. N-Dodecyl-N-methyl ephedrinium bromide (1) and benzylicinchonidinium chloride (2) (Fig. 1).

The results obtained are listed in Tables 1 and 2. Products have been carefully isolated and purified in order to eliminate impurities from the catalysts (or their products of degradation) which are capable of giving misleading rotation measurements (see footnotes in Tables 1 and 2).

TABLE 1

EXP. No.	Starting Product	Final Product	Catalyst	Yield % <sup>a</sup>	$\alpha_{546}^b$	Remarks
1			<u>1</u>	30	+0.480	c, d
2			<u>2</u>	25	-0.019	
3			<u>1</u>	38	+0.021	c, e
4			<u>2</u>	31	-0.026	
5	$\text{CH}_3-(\text{CH}_2)_5-\text{CH}=\text{CH}_2$	$\text{CH}_3-(\text{CH}_2)_5-\text{CHCl}-\text{CH}_2\text{Cl}$	<u>1</u>	54	+0.125	f
6			<u>2</u>	44	+0.149	
7			<u>1</u>	50	-0.401	g, h
8			<u>2</u>	64.5	-0.170	

a) All the products show IR,  $^1\text{H-N.M.R.}$  spectra and physical constants ( $n_D$ , b.p., m.p.) identical to those reported in the literature.

b) Pure liquid.  $l = 1 \text{ dm.}$

c) Isolated by vacuum distillation and column chromatography over silica gel. Eluant: n-hexane.

d) 3-5% of E-1-chloro-2-phenyl-ethylene was isolated.

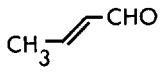
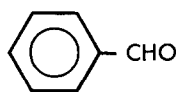
e) 14-16% of 2-chloro-cyclohexanol was isolated,  $(\alpha)_{546} = -0.09$  ( $c = 12.8$ , EtOH).

f) Isolated by vacuum distillation.

g) Purified by crystallization from methanol or by column chromatography over silica gel (Eluant: Toluene-n-hexane 2:1). The optical purity is in both cases the same. Chemical yield is 40% if column chromatography is employed.

h)  $(\alpha)_{546} c = 10$ , acetone

TABLE 2

EXP. No.	R - CHO	CATALYST	YIELD $\alpha, b$ %	$\alpha_{546}^c$
9	CH <sub>3</sub> -CH <sub>2</sub> -CHO	<u>1</u>	46	-0.335
10	$\begin{array}{c} \text{CH}_3 \diagdown \\ \text{CH-CHO} \\ \text{CH}_3 \diagup \end{array}$	<u>1</u>	63	-0.144
11	$\begin{array}{c} \text{CH}_3 \diagdown \\ \text{CH-CHO} \\ \text{CH}_3 \diagup \end{array}$	<u>2</u>	71	-0.095
12		<u>1</u>	44	0
13		<u>1</u>	53	-0.042

a) Isolated by vacuum distillation.

b) All the products show IR, <sup>1</sup>H-N.M.R. and physical constants ( $n_D$ , b.p.) identical to those reported in the literature.

c) Pure liquid.  $l = 1$  dm.

As it can be seen from the tables, the use of phase-transfer chiral catalysts, for both 1,2-dichloroderivatives and acetylcyanohydrins, gives reaction products with small rotations but perceptible. In experiments (5 and 6, 7 and 8, 10 and 11) a predominance of the same enantiomer is obtained with both catalysts, while for experiments (1 and 2, 3 and 4) the prevailing enantiomer is opposite to that obtained with the other catalyst.

The zero or low rotations of the acetylcyanohydrins derived from crotonaldehyde (experiment 12) and benzaldehyde (experiment 13), if compared with the results for aliphatic aldehydes (experiments 9-11) can be attributed to the increasing acidity of the  $\alpha$ -cyano proton of the acetylcyanohydrin due to the  $\pi$ -system, which enables racemization in the basic reaction media.

In some cases catalyst 1 (N-Dodecyl-N-metil-ephedrinium bromide) shows slightly higher stereoselectivity (experiments 1 and 2, 7 and 8, 10 and 11). The opposite effect occurs in experiments 3 and 4, 5 and 6. Consequently, it seems that stereoselectivity is closely related to the structures of the catalysts and substrate<sup>3,11</sup>. Further work is in progress on this aspect in order to improve asymmetric induction by phase-transfer methods.

### Acknowledgement

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