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ASYMMETRIC ALKYLATION REACTION BY MEANS OF A CHIRAL PHASE TRANSFER CATALYST.

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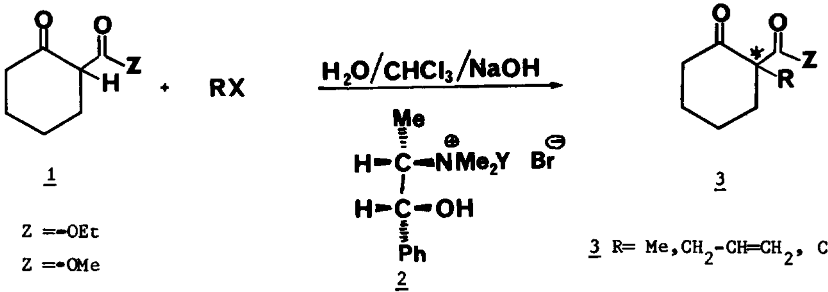
HIYAMA's recent work on enantioselective oxirane synthesis with the aid of a chiral phase transfer catalyst (2) prompted us to report our results on an alkylation reaction performed via the asymmetric catalyst (-)-N-benzyl,N-methyl ephedrinium bromide 2 (3), according to the equation:



1

1a Z = -OEt

1b Z = -OMe

1c Z = -Me

2

2d Y = $-CH_2$-Ph

2e Y = -Me

3

3 R= Me, CH_2-CH=CH_2, CH_2-C≡CH.

In a standard experiment, the cyclic β-keto ester or β-diketone 1 (20 mmol) dissolved in chloroform or dichloromethane (20 ml) together with the alkylating reagent (22 mmol) was vigorously stirred overnight with a mixture of 10% aqueous sodium hydroxyde (20 ml) and 2 (0.2g), at room temperature. The organic phase was separated, washed with water and the solvent removed. The residue was taken up into ether, whereby the catalyst 2 cristallised (and could be further recovered). Removal of the solvent gave the crude product, a purification of which by column chromatography (silica gel, n-hexane:ethyle acetate 20:1) afforded pure compound 3.

The main results are collected in the table.

The enantiomeric excess values were not estimated as the optical rotation of the enantiomerically pure samples had not been known. However, it could be evaluated to 5-6% in run 1 by n.m.r. spectroscopy of 3 (Z =OMe; R =$-CH_2$-CH=CH_2) with the aid of a chiral shift reagent Eu(tfacCam)$_3$ (5).

An increase in the amount of catalyst used did not raise the value of asymmetric induction.

The use of hexane instead of chloroform as a solvent afforded the products 3 with a satisfactory yield but without any trace of optical rotation.

Table

run	Z in 1	RX	Catalyst	$[\alpha]_D^{25}$ (CHCl$_3$, c 1.5) of 3	Yield (%) of 3
1	-OEt	CH_2=CH-CH_2Br	2d	-8.2°	85
2	-OMe	CH_2=CH-CH_2Br	2d	-12.8°	75
3	-OMe	CH C-CH_2Br	2d	-3.8°	75
4	-Me	MeI	2d	-4.6°	85
5	-Me	CH_2=CH-CH_2Br	2d	-23.5°	90
6	-Me	CH_2=CH-CH_2Br	2e	-1.2°	80

With the quaternary ammonium salt 2e used as a catalyst (2) the reaction did proceed but with lower degree of induction (comparison of runs 5 and 6).

This is the first asymmetric alkylation reaction performed by a phase transfer catalysis, i.e. in mild conditions: weakly alkaline aqueous medium, room temperature.

Other new asymmetric phase transfer catalysts are presently under investigation, in order to increase the asymmetric inductions.

Acknowledgement.

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References and notes.

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3) The ammonium salt 2e was prepared by quaternisation of (-)-N-methylephedrine with benzyl bromide in toluene; the precipitated salt was washed with n-hexane and dried: mp. 222°C, $[\alpha]_D^{25}$ - 5.1° (c 6.5, methanol).
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