

Synthesis of a new chiral phase-transfer catalyst: Chemical activity in alkylation reactions

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Received 3rd March 1989; accepted 24th October 1989

A new chiral phase-transfer catalyst (3*S*,4*S*)-1-benzyl-1-methyl-3,4-pyrrolidin-diol-onium iodide (**2**) synthesized, is found to be more active than the conventional tetraalkylammonium salts in alkylation reactions on active methylene compounds under usual solid-liquid phase-transfer conditions.

In the last few years growing attention has been focused on the synthesis of chiral phase-transfer catalysts to obviate difficulties encountered in asymmetric synthesis¹⁻⁴. In spite of growing importance, very few

such catalysts are known, derived from ephedrine¹ and cinchonidine²⁻⁴. Herein, we report the synthesis and the chemical activity of a new chiral phase-transfer catalyst **2**, prepared by quaternization of the known intermediate **1** which was prepared from D-(+)-tartaric acid⁵ (Scheme 1).

Alkylation of active methylene compounds under usual solid-liquid phase-transfer conditions* were carried out at room temperature using catalyst **2**. All the reactions listed in the Table 1 led exclusively to monoalkylated products with good yields in presence of 1 mole % catalyst. This catalyst is more active than the conventional tetraalkylammonium salts, which require higher temperatures when bases like K₂CO₃ or Na₂CO₃ were used⁶. Further, alkylation of benzyl cyanide with dimethyl sulphate could also be effected, which required simple work-up operation compared to conventional tetraalkylammonium salts. As an example in asymmetric alkylation the efficacy of the pre-

Table 1—Alkylation reactions using new chiral phase-transfer catalyst.

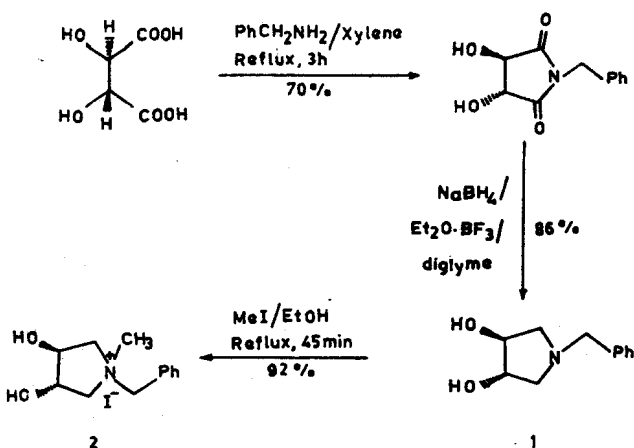
Sl. No.	Substrate	RX	Product	Time (hr)	Yield (%)	m.p or b.p/mm Hg (°C) ^d	
						Found	Lit.
1.		MeI		2.5	96	79-80/10mm	78-80/10mm
2.		EtBr		2	78	202	--
3.		n-BuBr		4	86	238	235-40
4.		PhCH ₂ Br		8	88	107/0.1mm	105/0.1mm
5.				3.5	79	178	--
6.		MeI		2.5	92	80-82/11mm	79-81/11mm
7.	PhCH ₂ CN	Me ₂ /SO ₄		12	82	228	230-32
8.	Ethylcyclopentanone-2-carboxylate	MeI		1.5	79	181	--

¹H-NMR(CDCl₃): a. 0.87-1.5(t,3H), 1.17-1.35(t,6H), 1.83-2.02(m,2H), 3.32-3.5(t,1H), 4.06-4.33(q,4H)

b. 1.18-1.35(t,6H), 2.81-2.98(dd,1H), 3.34(d,2H), 3.5-3.7(t,1H), 4.09-4.35(q,4H).

c. 1.4(s,3H), 1.92-2.6(m,6H), 3.7(s,3H).

d. Uncorrected.



Scheme 1

sent catalyst was tested with alkylation of ethyl cyclopentanone-2-carboxylate, where the product ethyl cyclopentanone-2-methyl-2-carboxylate has $[\alpha]_D = +0.92$ (C=1 in methanol) (Table 1; entry 8).

Further work to extend the application of present catalyst for other type of substrates and to modify the catalyst to induce higher asymmetric induction is in progress.

Experimental

Preparation of 2

A solution of 1 (0.1 mole, 19.3 g) in ethanol was cooled and methyl iodide (0.125 mole, 17.75 g) was added dropwise during 15 min. The reaction mixture was refluxed for 30-45 min, cooled and treated with

ether. The separated solid was filtered and washed twice with ether to give 2 as a white powdery solid; yield 24.8 g (92%); m.p. 132; $[\alpha]_D = 2.28$ (C=4.2, methanol) (Found : C, 42.9; H, 5.3; N, 4.2; I, 37.9. C₁₂H₁₈NO₂I requires C, 43.0; H, 5.4; N, 4.2; I, 37.9%); ¹³C NMR (CD₃OD) : 57.35, 73.36, 74.48, 75.12, 79.81, 80.16, 132.54, 133.02, 134.51, 136.65.

General alkylation procedure

A mixture of diethyl malonate (10 mmole), alkyl halide (13 mmole), catalyst 1 (0.1 mmole) in DMF (15 ml) was treated with anhydrous K₂CO₃ (32 mmole) and allowed to stir at room temperature. After completion of the reaction (see Table 1), the mixture was extracted with dichloromethane, washed with water, brine and dried (Na₂SO₄). The solvent was evaporated and the residue was further purified by column chromatography.

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