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A Poly(ethylene glycol)-Supported Quaternary Ammonium Salt: An Efficient, Recoverable, and Recyclable Phase-Transfer Catalyst

Rita Annunziata,[†] Maurizio Benaglia,*,[†] Mauro Cinquini,[†] Franco Cozzi,[†] and Graziella Tocco[‡]

Centro CNR and Dipartimento di Chimica Organica e Industriale, Universita' degli Studi di Milano, via Golgi 19, I-20133 - Milano, Italy, and Dipartimento Farmaco Chimico Tecnologico, Universita' degli Studi di Cagliari, via Ospedale 72, I-09124 - Cagliari, Italy

franco.cozzi@unimi.it

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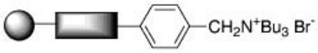
ABSTRACT



A quaternary ammonium salt readily immobilized on a soluble poly(ethylene glycol) polymer support efficiently catalyzes different reactions carried out under phase-transfer catalysis conditions; the catalyst, easily recovered by precipitation and filtration, shows no appreciable loss of activity when recycled three times.

One of the major problems associated with the use of soluble catalysts lies in the recovery of the catalyst from the reaction medium. Immobilization of the catalyst on a polymeric matrix can provide a simple solution to this problem.[1] In this context, the ideal polymer support should be soluble in some solvents, for the catalyzed reaction to be carried out under optimum conditions, and insoluble in other solvents, so that the supported catalyst can easily be isolated and recovered by precipitation and filtration.[2]

Poly(ethylene glycol)s (PEGs) of M_w greater than 2000 Da are readily functionalized, inexpensive polymers that feature these convenient solubility properties.[3] Recently, the mono methyl ether of PEG_{5000} (MeOPEG) has successfully been used for the immobilization of cinchona alkaloid-derived ligands for the asymmetric dihydroxylation reaction.[4] To the best of our knowledge, however, a whole catalytic system has never been attached to PEG.

Here we report that a quaternary ammonium salt can be easily synthesized on a modified MeOPEG, and this supported catalyst is an efficient and recoverable promoter of several reactions carried out under phase-transfer catalysis (PTC) conditions.[5]

[†] Universita' di Milano.

[‡] Universita' di Cagliari.

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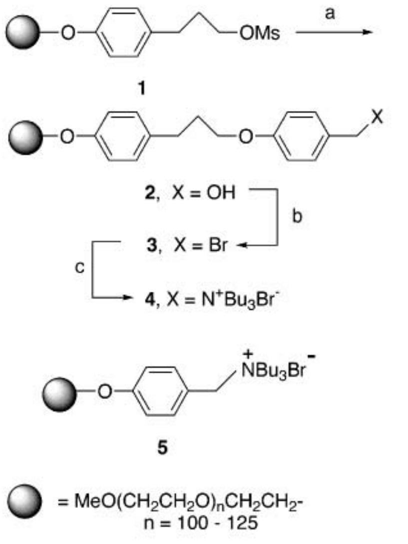
The preparation of the immobilized catalyst is described in Scheme 1. On the basis of our previous experience in the synthesis of small organic molecules bound to modified PEG,[6] ethereal bonds were selected for connecting the polymer core to the reactive functionality. Mesylate **1** (obtained in quantitative yield from MeOPEG)[6b] was reacted with the Cs salt of commercially available 4-hydroxybenzyl alcohol (3 equiv, DMF, 50 °C, 15 h) to afford alcohol **2** in nearly quantitative yield.[7] Reaction of **2** with PBr_3 (3 equiv, CH_2Cl_2, 0 °C to room temperature, 15 h) gave bromide **3** in 95% yield. This was converted into ammonium salt **4** by reaction with tributylamine (10 equiv) in toluene (65 °C, 72 h, 85% yield).

Scheme 1



[a] Cs_2CO_3 (3 mol equiv), 4-hydroxybenzylalcohol (3 mol equiv), DMF, 50°C, 15 h. [b] PBr_3 (3 mol equiv), CH_2Cl_2, 0°C to RT, 15 h. [c] *n*-Bu_3N (10 mol equiv), toluene, 65°C, 72 h.

Compound **4** was then used as catalyst in a series of standard transformations carried out under PTC conditions. The results are reported in Table 1. For sake of comparison, the yields of the same reactions promoted by nonsupported and structurally related catalysts were also included.[8]

The reported data indicate that **4** showed a catalytic activity that was similar to, or even better than that of the nonsupported catalysts. Remarkably, the benzylation of phenol and pyrrole (entries 7−10) required only 0.01 equiv of catalyst **4** to occur in ≥95% yield. Dichloromethane, in which the catalyst is readily soluble, was found to be the organic solvent of choice, but the reaction could satisfactorily be carried out also in the absence of organic solvent (entries 3 and 4). Generally the use of solid/liquid conditions led to higher yields than those observed under liquid/liquid conditions (entries 2 vs 1, 7 vs 5, 10 vs 9). As shown by entries 11−13 and 15, catalyst **4** could be recovered by precipitation and filtration, and recycled three times to run the same (entries 11 and 12) or a different reaction (entry 13) without any appreciable loss of the catalytic activity.[9]

It is also worth mentioning that compound **4** favorably compares as catalyst to other quaternary ammonium salts immobilized on insoluble polystyrene supports.[10] The use of these catalysts generally required higher reaction temper-

Table 1. Phase-Transfer Reactions Catalyzed by Ammonium Salt **4**

entry	substrate	reagent	conditions[a]	product	time (h); °C	yield (%)[b]	lit. yield (%)
1	*n*-$C_8H_{17}Br$	KI	H_2O	*n*-$C_8H_{17}I$	5; 40	56	93[c]
2	*n*-$C_8H_{17}Br$	KI	solid/liquid	*n*-$C_8H_{17}I$	4; 40	75	−
3	*n*-$C_8H_{17}Br$	KCN	H_2O[d]	*n*-$C_8H_{17}CN$	8; 85	85	93[c]
4	BnBr	KCN	H_2O[d]	BnCN	2; 25	97	97[e]
5	phenol	BnBr	NaOH aq	PhOBn	22; 25	18	86[f]
6	phenol	BnBr	NaOH solid	PhOBn	3; 25	90	−
7	phenol	BnBr	NaOH solid	PhOBn	22; 25	95	−
8	pyrrole	BnBr	NaOH aq	*N*-Bn-pyrrole	3; 40	95	−
9	pyrrole	BnBr	NaOH aq	*N*-Bn-pyrrole	24; 40	99	67[g]
10	pyrrole	BnBr	NaOH solid	*N*-Bn-pyrrole	0.25; 25	99	−
11	pyrrole	BnBr	NaOH solid	*N*-Bn-pyrrole	0.25; 25	95[h]	−
12	pyrrole	BnBr	NaOH solid	*N*-Bn-pyrrole	0.25; 25	93[i]	−
13	phenol	BnBr	NaOH solid	PhOBn	22; 25	92[j]	−
14	styrene	$CHCl_3$	NaOH aq[k]	−[l]	2.5; 40−60	95	88[m]
15	styrene	$CHCl_3$	NaOH aq[k]	−[l]	2.5; 40−60	90[n]	−

[a] All the reactions were carried out in a two-phase system. Under liquid/liquid and solid/liquid conditions, the organic solvent was CH_2Cl_2 unless otherwise stated. NaOH aq was a 0.1 M solution in H_2O unless otherwise stated. The amount of catalyst was 0.04 equiv in entries 1−4, 11, and 15 assuming an average MW of 6250 g/mol, and 0.01 equiv in entries 5−10 and 12−14. [b] Isolated yields, except for entries 1−3 (GC yields; the remainder was starting material). [c] 0.05 mol equiv of (*n*-$C_8H_{17})_4N^+Br^-$; toluene/H_2O; 5 h, 90 °C; GC yield (ref 8a). [d] No organic solvent was added. [e] 0.05 mol equiv of Aliquat 336; H_2O; 2h, rt (ref 8b). [f] 0.01−0.10 mol equiv of n-$Bu_3BnN^+Br^-$; NaOH 0.3 M in H_2O; 2−12 h, rt (ref 8c). [g] 0.10 mol equiv of $Et_3BnN^+Br^-$; NaOH 19 M in H_2O; 20 h, 40 °C (ref 8d). [h] Reaction carried out with a sample of **4** recovered after use in entry 10. [i] Reaction carried out with a sample of **4** recovered after use in entries 10 and 11. [j] Reaction carried out with a sample of **4** recovered after use in entries 10−12. [k] The organic solvent was $CHCl_3$.NaOH aq was 9 M in H_2O. [l] The product is 1,1-dichloro-2-phenylcyclopropane. [m] 0.05 mol equiv of catalyst; NaOH was 19 M in H_2O; 2.5 h, 40−60 °C (ref 8e). [n] Reaction carried out with a sample of **4** recovered after use in entry 14.

atures and/or longer reaction times than those employed here. For instance, the reactions of entries 2 and 4 required 15 h heating at 110 °C to occur in 81[10b] and 85[10a] % yield, respectively, in the presence of catalysts similar to compound **4** anchored on microporous polystyrene cross-linked with 2% divinylbenzene. In addition, solid supported phase-transfer catalysts required a preliminary, long conditioning time (up to 15 h) to ensure bead swelling and optimum accessibility of substrate and reagent to the catalytic site.[10c] Finally, the high stirrring rate necessary with these catalysts resulted in extensive mechanical degradation of the polymer beads, that were difficult to recover by filtration.[11]

Since PEG itself is known to be a phase-transfer catalyst,[5,12] the catalytic activity of alcohol **2** was tested in the benzylation of pyrrole under the conditions of entries 8 and 10.

In these reactions the product was obtained in 27 and 32% yield, respectively, thus showing that the ammonium moiety of catalyst **4** decisively contributed to the catalytic activity. Remarkably, the ammonium salt **5**, featuring a shorter spacer between the PEG core and the quaternary nitrogen atom is a catalyst less efficient than **4** (60 vs 75% yield in the reaction of entry 2).

In conclusion, the immobilization of an ammonium salt on a modified PEG provided an efficient phase-transfer catalyst that could easily be recovered and recycled. The possibility of exploiting enantiopure ammonium salts attached to modified PEG in asymmetric phase-transfer catalyzed reactions is currently under active investigation in our laboratories.

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Supporting Information Available: Full experimental details for the preparation of catalyst **4** and its use in phase-transfer catalyzed reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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[9] The catalyst employed in reaction 10 when recovered by precipitation and filtration contained undetermined amounts of NaOH and was used as such in reactions 12−14 (see Supplementary Information). These were carried out on the same scale as reaction 10.

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