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Synthesis of a poly(ethylene glycol)-supported tetrakis ammonium salt: a recyclable phase-transfer catalyst of improved catalytic efficiency

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Abstract—The immobilization of four quaternary ammonium groups on a poly(ethylene glycol) support provided an efficient and recyclable phase-transfer catalyst. © 2002 Elsevier Science Ltd. All rights reserved.

We recently reported[1] that immobilization of a benzyl tributylammonium salt on the monomethylether of poly(ethylene glycol) of M_w 5000 Da ($MeOPEG_{5000}$) by means of an inert spacer afforded compound **1** (Fig. 1), which proved to be an efficient and recyclable catalyst for some standard reactions carried out under phase-transfer catalysis (PTC) conditions.[2] Due to the high M_w of the polymeric support, catalyst **1** suffers from a low loading, i.e. a low number of catalytic sites per gram of polymer.[†]

We reasoned that an increase in the number and a proper spatial arrangement of the catalytic sites would likely provide a more efficient catalyst. Here, we report that loading expansion of PEG carried out exploiting the principles of dendrimer chemistry[3] led to the PEG-supported tetrakis ammonium salt **2**. This catalyst displayed a higher catalytic efficiency than **1**, while retaining the solubility properties peculiar of the PEG support,[4] that allowed simple catalyst recovery and recycling by precipitation and filtration.

Catalyst **2** was readily prepared (Scheme 1) from tetrakis benzylalcohol **3**, easily obtained from PEG_{4600},[5] via tetrakis bromide **4**. The overall yield from the commercially available, unfunctionalized polymer was 71% over five steps.[6,7] Catalyst **2** (loading = 0.679 mmol/g) was employed in some standard reactions carried out under PTC conditions. These included the *O*- and *N*-benzylation of phenol and pyrrole, respectively, the bis-benzylation of diethyl malonate, and the

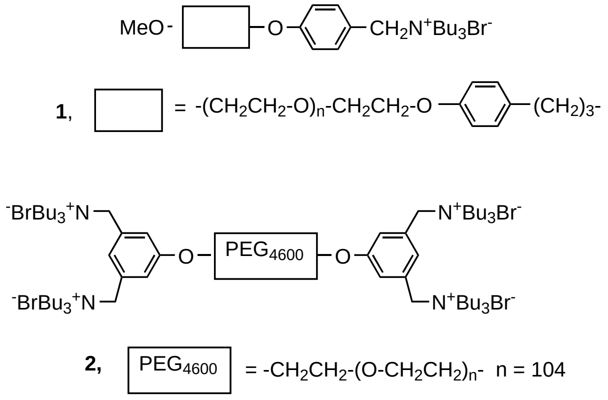
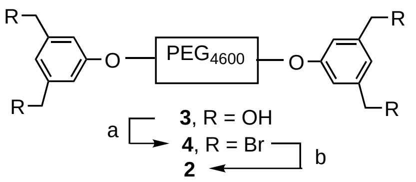


Figure 1.



Scheme 1. Legend: (a) PBr_3, DCM; (b) Bu_3N, toluene.

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[†] By assuming an average M_w of 5000 Da for the PEG fragment the calculated loading for compound **1** is 0.183 mmol/g.

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dichlorocyclopropanation of styrene. The activity of compound **2** was compared to that displayed by compound **1** in the same reactions (Table 1).

The reported data showed that, in all of the benzylation reactions examined, catalyst **2** afforded the products in yields similar to those obtained with catalyst **1** but with shorter reaction times (for *O*-alkylation see entries 2 and 3 versus 1, for *N*-alkylation see entry 6 versus 5 and for *C*-alkylation see entry 9 versus 8). The presence of a higher number of catalytic sites in **2** than in **1** allowed a ten-fold decrease of the catalyst loading (entry 7).

At this low catalyst concentration, however, a longer reaction time was required in order to obtain the product in a reasonably high yield. Catalyst **2** compared nicely to **1** also in the dichlorocyclopropanation of styrene performed under liquid/liquid PTC conditions (entry 16 versus 15), a process in which the latter was not particularly efficient.

One of the most important reasons for catalyst immobilization resides in the possibility of catalyst recovery and recycling. Recovery of catalyst **2** was conveniently performed by precipitation with diethyl ether directly from the reaction mixture, followed by filtration. Average recovery yields ranged from 80 to 95%. Catalyst recycling was studied for the bis-benzylation of diethyl malonate (entries 10–12) and the dichlorocyclopropanation of styrene (entries 17–20). In the alkylation of malonate, some decrease in chemical yield was observed when the catalyst was re-used for the third time (entry 11); however, when the twice-recycled catalyst was employed for a longer reaction time (15 min instead of 5 min), a yield as high as 91% was achieved (entry 12). In the cyclopropanation reaction catalyst **2** did not show virtually any erosion of activity up to the fifth cycle (entry 20), in which a yield as high as 95% was still observed.

The catalytic activity of the PEG-supported tetrakis ammonium salt **2** favorably compares to that of other ammonium salts supported on insoluble polymers such as cross linked polystyrenes.[8,9] The use of these catalysts generally required higher temperatures and catalyst concentrations, and longer reaction times than those employed here. In addition, optimum reaction conditions were observed for these insoluble polymer-supported catalysts only after long conditioning times, necessary to ensure the bead swelling that facilitates accessibility of substrate and reagents to the catalytic sites. It is also worth mentioning that catalysts such as **1** and **2** do not suffer from the extensive mechanical degradation experienced by polystyrene-supported catalysts after operating at the high stirring rates required by PTC conditions.[8] A useful comparison for catalyst **2** is also provided by the dendrimeric, poly(pentaerythrol)-based polyammonium salts synthesized by Ford,[7] featuring a surface containing up to 36 trimethyl

Table 1. Phase-transfer reactions catalyzed by ammonium salts **1** and **2**

Entry	Substrate	Reagent	Catalyst (mol%)	Conditions	Product	Time (min)	Yield (%)[a]
1	PhOH	BnBr	**1** (1)	NaOH solid	PhOBn	60	54
2	PhOH	BnBr	**2** (1)	NaOH solid	PhOBn	15	72
3	PhOH	BnBr	**2** (1)	NaOH solid	PhOBn	60	89
4	PhOH	BnBr	**2** (1)	NaOH solid	PhOBn	180	95
5	Pyrrole	BnBr	**1** (1)	NaOH solid	*N*-Bn pyrrole	30	99
6	Pyrrole	BnBr	**2** (1)	NaOH solid	*N*-Bn pyrrole	5	98
7	Pyrrole	BnBr	**2** (0.1)	NaOH solid	*N*-Bn pyrrole	400	85
8	$CH_2(COOEt)_2$	BnBr	**1** (3)	NaOH solid	$CBn_2(COOEt)_2$	30	99
9	$CH_2(COOEt)_2$	BnBr	**2** (3)	NaOH solid	$CBn_2(COOEt)_2$	5	99
10	$CH_2(COOEt)_2$	BnBr	**2** (3)[b]	NaOH solid	$CBn_2(COOEt)_2$	5	90
11	$CH_2(COOEt)_2$	BnBr	**2** (3)[c]	NaOH solid	$CBn_2(COOEt)_2$	5	75
12	$CH_2(COOEt)_2$	BnBr	**2** (3)[c]	NaOH solid	$CBn_2(COOEt)_2$	15	91
13	Styrene	$CHCl_3$	**1** (1)	NaOH solid	–[d]	30	93
14	Styrene	$CHCl_3$	**2** (1)	NaOH solid	–[d]	30	98
15	Styrene	$CHCl_3$	**1** (1)	NaOH aqueous[e]	–[d]	200	40
16	Styrene	$CHCl_3$	**2** (1)	NaOH aqueous[e]	–[d]	200	84
17	Styrene	$CHCl_3$	**2** (1)[f]	NaOH solid	–[d]	30	97
18	Styrene	$CHCl_3$	**2** (1)[g]	NaOH solid	–[d]	30	98
19	Styrene	$CHCl_3$	**2** (1)[h]	NaOH solid	–[d]	30	97
20	Styrene	$CHCl_3$	**2** (1)[i]	NaOH solid	–[d]	30	95

[a] Isolated yields after flash chromatography. Reaction solvent was DCM and the temperature 25°C for entries 1–12; reaction solvent was $CHCl_3$ and the temperature 30°C for entries 13–20.

[b] With a catalyst sample recovered after use in entry 9.

[c] With a catalyst sample recovered after use in entries 9 and 10.

[d] The product is 1,1-dichloro-2-phenylcyclopropane.

[e] NaOH was 9 M in water.

[f] With a catalyst sample recovered after use in entry 14.

[g] With a catalyst sample recovered after use in entries 14 and 17.

[h] With a catalyst sample recovered after use in entries 14, 17, and 18.

[i] With a catalyst sample recovered after use in entries 14, 17, 18, and 19.

ethylammonium groups. In this case, a strong catalytic activity was achieved only for dendrimers possessing a large number of catalytic sites (at least 12). Remarkably, the corresponding tetrakis ammonium salt did not show any rate enhancement with respect to non-catalyzed reaction conditions. The recycling of these dendrimeric catalysts was not reported.

In conclusion, a simple and high yielding synthesis of a new phase-transfer catalyst supported on poly(ethylene glycol) has been reported. The catalyst, that featured four quaternary ammonium groups located at the termini of the polymer backbone, displayed a remarkable efficiency in promoting different reactions carried out under PTC conditions at low catalyst concentrations (1–3 mol%) for short reaction times and under mild conditions. The polymer support allowed to easily recover and recycle the catalyst.[10]

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