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Poly(ethylene glycol)-Supported Tetrahydroxyphenyl Porphyrin: A Convenient, Recyclable Catalyst for Photooxidation Reactions

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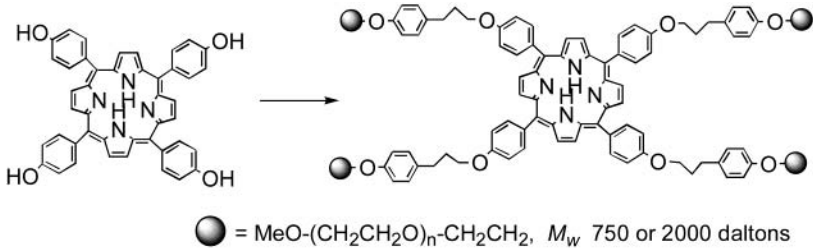
ABSTRACT



A new poly(ethylene glycol)-supported porphyrin has been prepared and its ability as a promoter in photooxidation reactions has been studied. The PEG-supported catalyst exhibits high activity, comparable to that of a nonanchored sensitizer, and it is easily removable by filtration from the reaction mixture. The polymer-bound porphyrin has been recycled up to six times with no loss of chemical and stereochemical efficiency.

Oxidation of unsaturated compounds with singlet oxygen is a common practice in organic synthesis.[1] To generate this labile reagent many methodologies have been developed, including decomposition of phosphite ozonides[2] and endoperoxides,[3] reaction of hydrogen peroxide with sodium hypochlorite,[4] subjecting gaseous oxygen to electrodeless discharge,[5] and dye-sensitized photooxidation of triplet oxygen.[6] The latter offers the advantage of producing byproduct-free reaction mixtures and employs a catalytic amount of the substance that promotes oxygen to its singlet state. However, the presence of the sensitizer, or its decomposition derivatives, can contaminate the reaction products and make the purification step really troublesome. A solution to this problem was proposed by DiMagno et al.,[7] by the use of the fluorous-phase approach to effectively remove the dye from the reaction mixture. In this paper we present a soluble polymer-supported catalyst as an alternative, easily removable, and recyclable promoter for the light-induced generation of singlet oxygen.

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(1) (a) Gollnick, K.; Shenk, G. O. In *1,4-Cycloaddition Reactions, The Diels−Alder Reaction in Heterocyclic Synthesis*; Hamer, J., Ed.; Academic: New York, 1967; pp 255−344. (b) Foote, C. S. *Pure Appl. Chem.* **1971**, *27*, 635. (c) *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Accademic: New York, 1979. (d) Frimer, A. A. *Chem. Rev.* **1979**, *79*, 359. (e) George, M. V.; Bhat, V. *Chem. Rev.* **1979**, *79*, 447.

(2) Murray, R. W.; Kaplan, M. L. *J. Am. Chem. Soc.* **1969**, *91*, 5358.

(3) Wasserman, H. H.; Sceffer, J. R.; Cooper, J. L. *J. Am. Chem. Soc.* **1972**, *94*, 4991.

(4) (a) Foote, C. S.; Wexler, S.; Ando, W.; Higgins, R. *J. Am. Chem. Soc.* **1968**, *90*, 975. (b) McKeown, E.; Waters, W. A. *J. Chem. Soc. (B)* **1966**, 1040.

(5) Corey, E. J.; Taylor, W. C. *J. Am. Chem. Soc.* **1964**, *86*, 3881.

(6) (a) Schenck, G. O. *Angew. Chem.* **1957**, *69*, 579. (b) Kautsky, H. *Biochem. Z.* **1937**, *291*, 271. (c) Adam, W.; Klug, P. *J. Org. Chem.* **1993**, *58*, 3416.

(7) DiMagno, S. G.; Dussault, P. H.; Schultz, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 5312.

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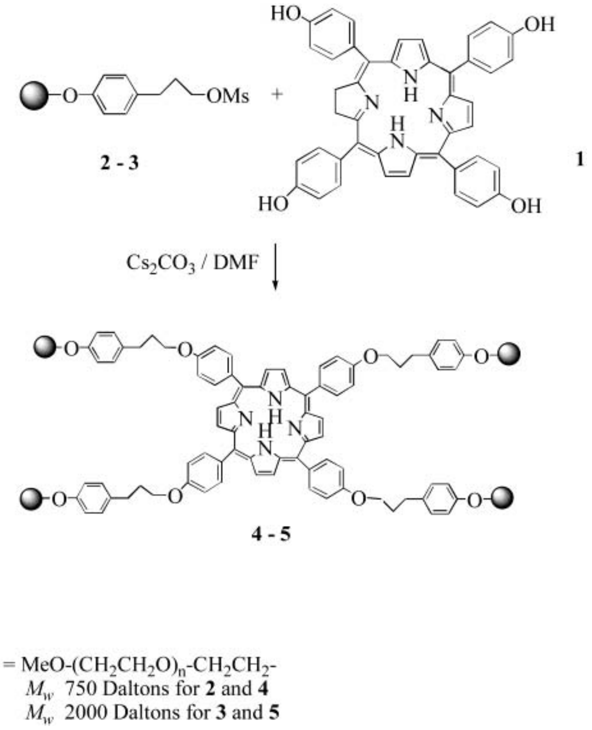
A polymer-bound catalyst can offer the possibility of simple recovery and recycling as well as easy product purification and isolation, and possibly shows higher stability toward the reaction environment.[8] For expensive and unstable catalytic species the immobilization on solid support may represent an additional bonus, provided that it does not affect the efficiency of the process.[9] In this context, soluble polymers have recently been the subject of an intense research activity; allowing the reaction to be carried out in homogeneous solution they would secure higher chemical and stereochemical efficiency than insoluble polymer.[10] Among the soluble polymeric matrixes employed, poly(ethylene glycol)s (PEGs) are the most successful. These inexpensive, readily functionalized polymers are soluble in many organic solvents but insoluble in a few others; because of this solubility profile PEG supports can combine the advantages of running a reaction under homogeneous conditions with those of recovering and recycling a heterogeneous catalyst.[11]

Recently, the monomethyl ether of PEG_{5000} (MeOPEG) has being used for anchoring achiral[12] and chiral[13] ligands, phase transfer,[14] and chiral organic catalysts.[15] As a part of these studies we decided to investigate the immobilization of a porphyrin on PEG.[16] Recently the first example of the use of a soluble polymer-supported ruthenium–porphyrin complex in epoxidation reactions was described.[17] We wish to report here the preparation and the use of a poly(ethylene glycol)-supported porphyrin as efficient, recoverable, and recyclable promoter for the photooxidation reaction.

On the basis of our experience in the PEG-supported synthesis of small organic molecules,[18] the mesylates **2** and **3**, MW 750 and 2000, respectively, were prepared in three steps and 95% overall yield from the commercially available monomethyl ether of PEG (MeOPEG) and attached to the commercially available, 5,10,15,20-tetrakis(4-hydroxyphenyl)porphyrin **1** (Scheme 1).

Scheme 1. Synthesis of PEG-Supported Porphyrin **5**



The reaction of 1 mol equiv of compound **1** with 4 mol equiv of the mesylates **2** and **3** in *N*,*N*-dimethylformammide (DMF) in the presence of 5.2 mol equiv of cesium carbonate afforded the desired supported porphyrin derivatives **4** and **5**. Unfortunately when the MeOPEG with MW 750 was used, the product **4** (obtained in 93% yield) could not be purified by precipitation from diethyl ether, but it was recovered as a very thick oil.[19] However, by employing the mesylate **3** of $MeOPEG_{2000}$ the expected PEG-supported porphyrin **5** was obtained as a solid readily precipitated with diethyl ether in 87% yield as a pure compound; the purity of the product was determined by ^1H NMR analysis in $CDCl_3$ at 300 MHz with presaturation of the methylene signals of the polymer centered at δ 3.63. The integrals of the signals of the PEG-CH_2OCH_3 fragment at δ 3.30 and 3.36 were used as internal standard.[20]

With porphyrin **5** in hand, we first investigated the photooxidation of the bisdialine **6** (see Figure 1).[21] The irradiation of a 0.01 M methylene chloride solution of the

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(8) *Chiral Catalyst Immobilization and Recycling*; De Vos, D. E., Vankelecom, I. F. J., Jacobs, P. A., Eds.; Wiley-VCH: Weinheim, Germany, 2000.

(9) Clapham, B.; Reger, T. S.; Janda, K. D. *Tetrahedron* **2001**, *57*, 4637–4662.

(10) For a recent report discussing the efficiency of soluble and insoluble polymer-supported catalysts see: Reger T. S.; Janda K. D. *J. Am. Chem. Soc.* **2000**, *122*, 6929.

(11) Review: (a) Gravert, D. J.; Janda, K. D. *Chem. Rev.* **1997**, *97*, 489. (b) Wentworth, P.; Janda, K. D. *Chemm. Commun.* **1999**, 1917.

(12) Yao, Q. *Angew. Chem., Int. Ed.* **2000**, *39*, 3896 and refereces cited therein.

(13) (a) Han, H.; Janda, K. D. *Tetrahedron Lett.* **1997**, *38*, 1527 and references therein. (b) Bolm, C.; Gerlach, A. *Eur. J. Org. Chem.* **1956**, 21 and references therein. (c) Flood, R. W.; Geller, T. P.; Petty, S. A.; Roberts, S. M.; Skidmore, J.; Volk, M. *Org. Lett.* **2001**, *3*, 683. (d) Fan, Q.-H.; Deng, G.-J.; Lin, C.-C.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2001**, *12*, 1241. (e) Guerreiro, P.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Dellis, P. *Tetrahedron Lett.* **2001**, *42*, 3423. (f) Kuang, Y.-Q.; Zhang, S.-Y.; Wei, L.-L. *Tetrahedron Lett.* **2001**, *42*, 5925. (g) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Pitillo, M. *J. Org. Chem.* **2001**, *66*, 3160. (h) Guo, H.; Shi, X.; Qiao, Z.; Hou, S.; Wang, M. *Chem. Commun.* **2002**, 118.

(14) (a) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Tocco, G. *Org. Lett.* **2000**, *2*, 1737. (b) Benaglia, M.; Cinquini, M.; Cozzi, F.; Tocco, G. *Tetrahedron Lett.* **2002**, *43*, 3391.

(15) (a) Benaglia, M.; F. Cozzi, F.; Celentano, G. *Adv. Synth. Catal.* **2001**, *343*, 171. (b) Benaglia, M.; Cozzi, F.; Celentano, G. *Adv. Synth. Catal.* **2002**, *344*, 149.

(16) A few metalloporphyrins linked to PEGs have been synthesized, mainly to tune their solubility properties for biomedical applications, see: Lottner, C.; Bart, K.-C.; Bernhardt, G.; Brunner, H. *J. Med. Chem.* **2002**, *45*, 2079 and references therein.

(17) Zhang, J.-L.; Che, C.-M. *Org. Lett.* **2002**, *4*, 1911.

(18) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F. *Eur. J. Org. Chem.* **2002**, 1184 and references therein.

(19) PEGs of MW > 2000 are solid, and they are known to be insoluble in Et_2O, hexanes, or 2-propanol; four chains of PEG_{750} bound to the molecule **1** should in principle provide a porphyrin anchored to a poly(ethylen glycol) moiety with MW > 3000, able to precipitate as solid in the proper conditions. Clearly the porphyrin residue plays a decisive role in preventing a cooperative effect of the PEG chains.

(20) For a detailed description of the isolation, purification, and yield determination of PEG-supported compounds see: Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F *Chem. Eur. J.* **2000**, *6*, 133.

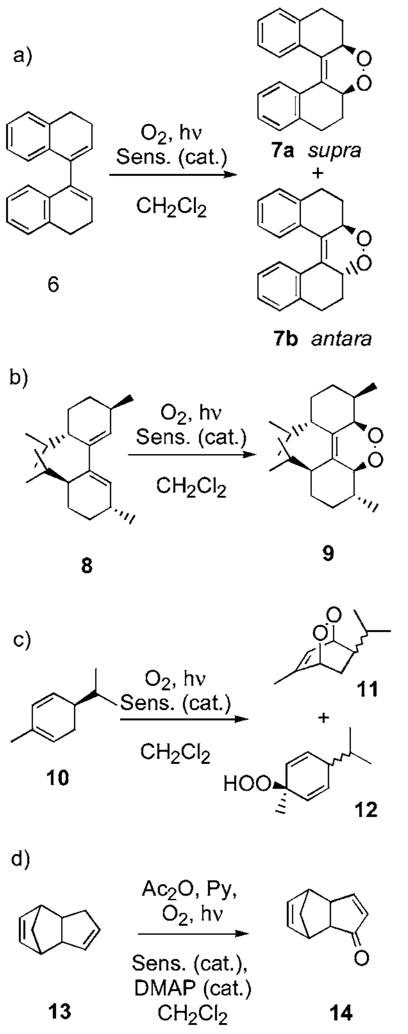

Figure 1. Photooxidation reactions promoted by PEG-supported porphyrin **5**.

starting material with a 100 W halogen lamp, in the presence of a 3% mol amount of tetraphenylporphyrin (TPP) as sensitizer gave a 80/20 mixture of *supra* and *antara* diastereoisomeric endoperoxides **7** in quantitative yield after 1 h (entry 1, Table 1). When the poly(ethylene glycol)-supported tetrahydroxyphenyl−porphyrin (PEG-TPP, **5**) was used to promote the reaction under the same conditions the product was formed after 1 h in > 98% yield, as a 82/18 mixture of the two stereoisomers (entry 2). The polymer-bound catalyst not only showed the same activity of the nonsupported species, but it greatly simplified the product isolation. At the end of reaction the solvent was concentrated in vacuum and diethyl ether was added to the PEG-supported porphyrin that was quantitatively recovered by filtration. From the concentrated filtrate solution the obtained endoperoxides were easily isolated by crystallization from ethanol.

The photooxidation of (+)-dimenthene **8** promoted by tetraphenylporphyrin (TPP)[22] was much slower and it required 15 h to give the endoperoxide **9** (see eq b in Figure 1) in 34% yield (entry 3). Also in these harsh conditions the PEG-supported catalyst behaved well and was showed to be stable even for prolonged reaction times, affording the product **9** in even better yields than the nonsupported species for comparable reaction conditions (entry 4).[23]

The immobilized catalyst showed its chemical and stereochemical efficiency also in very fast reactions, affording the desired products in yields and stereoselectivities comparable with those obtained with the nonsupported catalysts. For example, the photooxidation of *R*-(−)-α-phellandrene, **10**, promoted by different sensitizers, is known to generate mixtures of syn and anti endoperoxides **11** and hydroperoxydes **12** (eq c, Figure 1).[24] The reaction catalyzed by TPP produced after 10 min the endoperoxides in 67% yield, as a 55/45 mixture of *syn* and *anti* isomers. The use of PEG-TTP **5** under the same experimental conditions led to the formation of the product **11** in identical yield (65%) and stereoselectivity (*syn/anti* 56/44, entries 5 and 6).

The one-pot oxidation of olefin to α,*β*-unsaturated ketones[25] was applied to convert dicyclopentadiene **13** into the corresponding dicyclopentadienone **14**, a useful starting material for the preparation of enantiopure diols (eq. d, Figure 1). Once again, the soluble polymer-bound porphyrin **5** favorably compares with the nonsupported catalyst. The photooxidation of dicyclopentadiene promoted by tetraphenylporphyrin gave the ketone **14** in 80% yield after 6 h reaction (entry 7). The same result was obtained by using a 0.45% mol amount of PEG-TPP as sensitizer; after an aqueous workup, the organic phase was concentrated, diethyl ether was added, and the precipitated PEG-supported catalyst was separated by simple filtration; the evaporation of the organic phase afforded the final product in 82% yield (entry 8). It is worth mentioning that it is possible to run the reaction on a gram scale, using even a smaller amount of sensitizer; the oxidation of 13 mL of dicyclopentadiene, promoted by 220 mg of PEG-TPP **5** (0.025% mol equiv), gave 11 g of ketone **14**, isolated, after filtration of the supported catalyst, by simple evaporation of the organic solvent as analytically pure compound, which did not require further purification. In this case the catalyst was recovered in slightly lower yield (85% yield) probably because of the necessary extractive aqueous workup. The use of more powerful irradiation (500 W) was possible and allowed the reaction times to be shortened, affording the product in good yield (entry 9).

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(21) (a) Delogu, G.; Fabbri, D.; Fabris, F.; Sbrogiò, F.; Valle, G.; De Lucchi, O. *Chem. Commun.* **1995**, 1887. (b) Fabris, F.; Sbrogiò, F.; De Lucchi, O.; Delogu, G.; Fabbri, D.; Valle, G. *Gazz. Chim. Ital.* **1997**, *127*, 393.

(22) Fabris, F.; Leoni, L.; De Lucchi, O. *Tetrahedron Lett.* **1999**, *40*, 1223.

(23) The reaction was performed in the presence of NaHCO$_3$ to prevent a change of the color of the catalyst from purple to green that was observed after several hours of irradiation, probably due to the formation of protonated porphyrin species. However, it was also demonstrated that a simple addition of solid NaHCO$_3$ to the green catalyst is sufficient to restore the original purple color of **5** that was reused with no loss of chemical activity.

(24) (a) Trabanco, A. A.; Montalban, A. G.; Rumbles, G.; Barrett, A. G. M.; Hoffman, B. M. *Synlett* **2000**, *7*, 1010. (b) Suzuki, M.; Ohtake, H.; Kameya, Y.; Hamanaka, N.; Noyori R. *J. Org. Chem.* **1989**, *54*, 5292. (c) Matusch, R.; Schmidt, G. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 717.

(25) Mihelich, E. D.; Eickhoff, D. J. *J. Org. Chem.* **1983**, *48*, 4135.

Table 1. Photooxidation Reactions Promoted by Tetraphenylporphyrin (TPP) and PEG-TPP **5**

entry	sensitizer	substrate	lamp power, W	time[a]	yield, %	product ratio[c]
1	TPP	6	100	1.0 h	99	*antara/supra* 80/20
2	PEG-TPP	6	100	1.0 h	99	*antara/supra* 82/18
3	TPP	8	500	15 h	34	
4	PEG-TPP	8	500	15 h	42	
5	TPP	10	100	10 min	67[b,c]	*syn/anti* 55/45
6	PEG-TPP	10	100	10 min	65[b,c]	*syn/anti* 55/45
7	TPP	13	200	6.0 h	80	
8	PEG-TPP	13	200	6.5 h	82	
9	PEG-TPP	13	500	4.0 h	77	
10	PEG-TPP	6	100	1.0 h	98[d]	*antara/supra* 80/20
11	PEG-TPP	6	100	1.0 h	97[e]	*antara/supra* 81/19
12	PEG-TPP	6	100	1.0 h	97[e]	*antara/supra* 80/20
13	PEG-TPP	6	100	1.0 h	97[e]	*antara/supra* 82/18
14	PEG-TPP	6	100	1.0 h	97[e]	*antara/supra* 78/22
15	PEG-TPP	6	100	1.0 h	97[e]	*antara/supra* 80/20

[a] Required for consumption of the reagent. [b] Endoperoxydes. [c] Determined by ^{1}H NMR. [d] Reaction run with the catalyst employed in entry 2. [e] Reaction run with catalyst used in the previous entry.

Recycling of the PEG-bound porphyrin **5** was also studied. The catalyst already employed in entry 2 was reused a second time in the photooxidation of the bisdialine to give the product **7** in 97% yield and 80/20 diastereoisomeric ratio after 1 h of reaction (entry 10). The recovered PEG-TPP was recycled a third time without showing any decrease in the catalytic activity (entry 11); the PEG-supported sensitizer was recycled 6 times with no appreciable loss of chemical or stereochemical efficiency (entries 12−15).

In conclusion, a poly(ethylene glycol)-supported porphyrin was prepared as a promoter in photooxidation reaction. This soluble polymer-bound species was successfully employed in a different oxidation reaction, showing a catalytic activity comparable to that of a nonanchored promoter. The PEG-supported catalyst is easily removable by filtration from the reaction mixture, greatly simplifying the isolation of the products, which often do not require further purification. Moreover, the PEG-TPP is recyclable and has been reused up to six times without any appreciable loss of catalytic activity.

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Supporting Information Available: Synthesis and characterization of polymer-supported compound **5**, general procedures for the photooxidation reactions, and NMR data of compound **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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