(6) The model dioxystilbenes **23-25** all have modest energetic differences between triplet and singlet states, showing that coupling between radical centers in these molecules is not very strong. We intend to extend our model to larger polyradicals, in order to examine ground-state spin multiplicity as a function of oligomer size.

Overall, the reasonable agreement between our results and ab initio results for several smaller cases shows the usefulness of this method when ab initio computations are not practical.

Acknowledgment. This work was supported by the Office of Naval Research and by the National Science Foundation (Grants CHE-8712319 and CHE-8506590). Partial support for a computer graphics workstation was provided by a University of Massachusetts Faculty Research Grant. Acknowledgement is also made for partial support by the donors of the Petroleum Research Fund, administered by the American Chemical Society. We acknowledge helpful and interesting discussions with Dr. Silas Blackstock.

Registry No. 1, 32714-83-3; 2, 71946-86-6; 3, 76984-35-5; 4, 88017-87-2; 5, 16893-57-5; 6, 118319-53-2; 7, 118319-54-3; 8, 118319-55-4; 9, 118319-56-5; 10, 118319-57-6; 11, 95406-55-6; 12, 118334-59-1; 13, 118319-58-7; 14, 118319-59-8; 15, 118319-60-1; 16, 24976-21-4; 17, 250-30-6; 18, 250-31-7; 19, 35834-36-7; 20, 118319-62-3; 21, 118334-60-4; 23, 118319-63-4; 24, 118319-64-5; 25, 118319-65-6; OA, 61518-27-2; OBQ, 32796-95-5; PBQ, 502-86-3.

Supplementary Material Available: ORTEP-type diagrams for all MNDO-UHF triplet optimized geometries, showing important bond lengths and angles (16 pages). Ordering information is given on any current masthead page.

Polymer-Supported Cation Radicals

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Reaction of chloromethylated polystyrene (3.90 mequiv/g) beads with triphenylamine and diethylchloroalane resulted in a highly cross-linked polymer. The chloromethylated polystyrene was modified by reaction with 2,6-dibromocarbazole (**4**) and K_2CO_3 in DMF at 100 °C to give an excellent yield of polymer-supported 2,6-dibromocarbazole (**5**) without concomitant cross-linking. The polymer-bound 2,6-dibromocarbazole was nonreactive toward $SbCl_5$, whereas the homogeneous counterpart 9-*N*-benzyl-2,6-dibromocarbazole (**6**) was found to readily generate the aminium cation radical upon reaction with $SbCl_5$. Attachment of phenothiazine to a polystyrene support yielded a reagent that would react very rapidly with $SbCl_5$ in dichloromethane. The polymer-bound phenothiazine cation radical was found to readily oxidize the metal-metal bond in $[C_5H_5Fe(CO)_2]_2$ and undergo anion exchange with Bu_4NPF_6 to afford a more synthetically useful reagent.

Introduction

Polymer-bound organic reagents often have one or more advantages over their homogeneous counterparts.[1] One primary advantage to polymer-bound reagents is the facile removal of expended or excess reagent at the completion of the reaction. This can lead to recovery and regeneration of the reagent. We recently demonstrated such a use with polymer-supported 2,6-di-*tert*-butylpyridine, which was shown to be easily recovered and fully regenerated for further reaction.[2]

For over two decades aminium cation radicals have been known to be very efficient one-electron transfer reagents.[3] A more recent use of aminium cation radicals for the mild stoichiometric oxidation of metal-metal bonds in transition-metal complexes[4] prompted us to report our work in the area of polymer-supported cation radicals. Bauld et al. has recently demonstrated that polymer-bound aminium cation radicals were efficient catalysts for certain Diels-Alder reactions;[5,6] however, because of low loading levels of the aminium cation radicals, the utility of the polymer-bound reagents has thus far been limited to catalytic applications.

In this paper we describe our efforts leading to the successful development of polymer-supported cation radical reagents having an equivalent weight that is practical for use as stoichiometric, one-electron oxidants. The polymeric reagent is simply filtered after the oxidation reaction to yield a product that is not contaminated by the expended oxidant or excess reagent.

Results and Discussion

Our initial approach attempted to load triphenylamine onto chloromethylated polystyrene (3.90 mequiv/g) with Lewis acid catalysis. This approach is known to work for chloromethylated polystyrene having 1.09 mequiv of active CH_2Cl per gram of polymer.[5] We find reaction of the more heavily chloromethylated (3.90 mequiv CH_2Cl/gram of polymer, i.e. 50% of the phenyl rings modified) polystyrene with triphenylamine in the presence of diethylchloroalane

(1) For reviews on polymer-supported reagents see: (a) *Polymer-supported Reactions in Organic Synthesis*; Hodge, P., Sherrington, D. C., Eds.; Wiley: New York, 1980. (b) Akelah, A.; Sherrington, D. C. *Chem. Rev.* **1981**, *81*, 557. (c) Frechet, J. M. J. *Tetrahedron* **1981**, *37*, 663. (d) Akelah, A. *Synthesis* **1981**, 413. (e) Mathur, N. K.; Narang, C. K.; Williams, R. E. *Polymers as Acids in Organic Chemistry*; Academic Press: New York, 1980. (f) Kraus, M. A.; Patchornik, A. *Macromol. Rev.* **1980**, *15*, 55. (g) Daly, W. H. *Makromol. Chem., Suppl.* **1979**, *2*, 3. (h) Leznoff, C. C. *Acc. Chem. Res.* **1978**, *11*, 327. (i) Heitz, W. *Adv. Polym. Sci.* **1977**, *23*, 1.

(2) Wright, M. E.; Pulley, S. R. *J. Org. Chem.* **1987**, *52*, 5036.

(3) (a) Walter, R. I. *J. Am. Chem. Soc.* **1955**, *77*, 5999. (b) Walter, R. I. *Ibid.* **1966**, *88*, 1923. (c) Bell, F. A.; Ledwith, A.; Sherrington, D. C. *J. Chem. Soc. C.* **1969**, 2719. (d) Hammerich, O.; Parker, V. D. *Adv. Phys. Org. Chem.* **1984**, *20*, 55.

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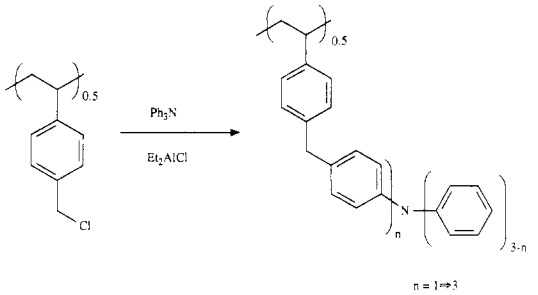
(6) For examples of radical-catalyzed Diels-Alder reactions, see: Bellville, D. J.; Wirth, D. D.; Bauld, N. L. *J. Am. Chem. Soc.* **1981**, *103*, 718. Gassman, P. G.; Singleton, D. A. *J. Am. Chem. Soc.* **1984**, *106*, 7993.

0022-3263/89/1954-0965$01.50/0

gives complete reaction of the CH_2Cl sites (i.e. 0% Cl analysis for modified polymers). Weight gain and nitrogen analysis both confirm extensive cross-linking is occurring (eq 1).

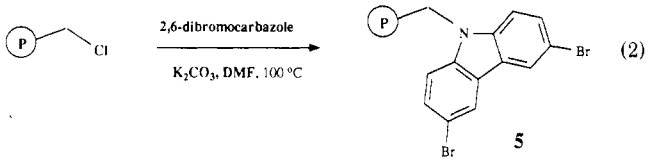


(1)

We also explored the synthesis of a triphenylamine monomer with a polymerizable vinyl group for eventual copolymerization with styrene (see paragraph at the end of the paper about supplementary material). The synthesis of 1-[4-bis[(4-bromophenyl)amino]phenyl]ethene (**3**) was accomplished; however, the purification of **3** proved to be very difficult. We then shifted over attention to other potential cation radical molecules and means of polymer modification.

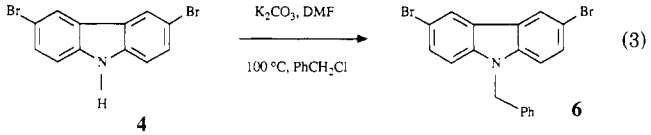
We find that by starting from the commercially available 2,6-dibromocarbazole (**4**) we can modify the chloromethylated polystyrene in high yield and without any cross-linking. Carbazole aminium cation radicals[7] are well documented in the literature and have an oxidation potential only slightly more positive than triphenylamine derivatives. The methods available for the N-alkylation of carbazoles vary from phase-transfer catalysis[8] to the generation of the N-metalated derivatives in organic solvents.[9]

Reaction of **4** and ⓅCH_2Cl with K_2CO_3 in dimethylformamide (DMF) gives an excellent (based on the ⓅCH_2Cl) conversion to the polymer-bound 2,6-dibromocarbazole (**5**) (eq 2). Both nitrogen and halide analyses



(2)

confirm clean incorporation of the carbazole, giving a polymer with 1.83 mequiv of carbazole per gram of polymer. The K_2CO_3/DMF combination also works quite well with benzyl chloride and **4** to give 9-*N*-benzyl-2,6-dibromocarbazole (**6**) in 81% isolated yield (eq 3).



(3)

(7) (a) Vincow, G. *Radical Ions*; Wiley: New York, 1968; p 202. (b) Bard, A. J.; Ledwith, A.; Shine, H. J. *Adv. Phys. Org. Chem.* **1976**, *13*, 155–278. (c) Liu, Y.; Liu, Z.; Wu, L.; Chen, P. *Tetrahedron Lett.* **1985**, *26*, 4201.

(8) (a) Nishi H.; Kohno, H.; Kano, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1897. (b) Sukata, K. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 280. (c) Davidson, R. S.; Patel, A. M.; Safdar, A. *J. Chem. Res. Synop.* **1984**, 88. (d) Schmolka, S. J.; Zimmer, H. *Synthesis* **1984**, 29. (e) Davidson, R. S.; Patel, A. M.; Safdar, A.; Thornthwaite, D. *Tetrahedron Lett.* **1983**, *24*, 5907.

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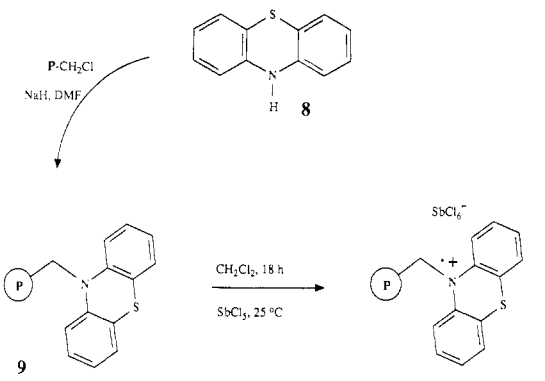
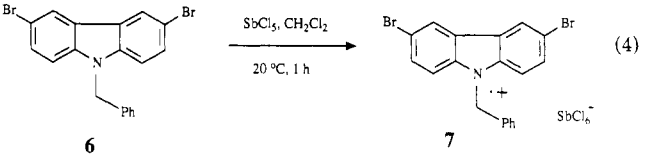
Scheme I



Compound **6** reacts with antimony pentachloride in dichloromethane to generate a deep green solution of the aminium cation radical **7** (eq 4). The aminium cation radical is easily isolated by precipitation with diethyl ether. This latter reaction is certainly not surprising but does unambiguously demonstrate that indeed the 9-*N*-benzyl-2,6-dibromocarbazole readily forms the cation radical and is seen as a model for the polymer-bound version.



(4)

Treatment of **5** with $SbCl_5$ in dichloromethane causes a color change to occur in the beads while the solution remains clear and colorless. Isolation of the polymer beads after several washes and drying under reduced pressure shows little, if any, weight gain. The conversion of the cation radical must be occurring to a very small extent. Reaction of **5** with $SbCl_5$ in refluxing CH_2Cl_2 for 12 h gives similar results. The conclusion to be drawn from these results is that the apparent oxidation potential for the polymer-bound version of the carbazole is more positive than the homogeneous counterpart. This could also explain why Bauld et al.[5] had difficulty in oxidizing the polymer-bound triphenylamine derivatives.

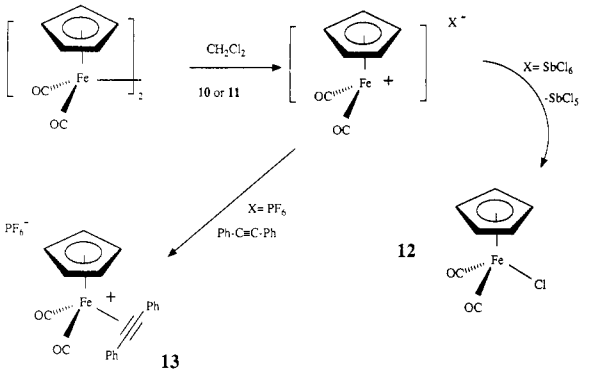
If the reluctance toward oxidation is one of potential, then going to a more easily oxidized system such as phenothiazine (**8**) should solve the problem.[10] Compound **8** is treated with ⓅCH_2Cl and NaH in DMF to give the polymer-supported phenothiazine **9** in excellent yield. The use of K_2CO_3 failed to give modification of the polymer. Treatment of **9** with $SbCl_5$ in dichloromethane for 18 h gives complete conversion to the cation radical as indicated by combustion analysis (Cl) and weight gain in the reaction (Scheme I).

Reaction of the polymer-bound cation radical **10** with $[C_5H_5Fe(CO)_2]_2$ (Fp_2) gives an immediate color change, and after 5 min of reaction the *only* carbonyl bands in the infrared spectrum that can be found are attributed to $C_5H_5Fe(CO)_2Cl$ (**12**).[11] From the results of Cummins and Kegley[4] this is not surprising since they also observed that $SbCl_6^-$ serves as a source of nucleophilic chloride. The results do clearly demonstrate that oxidation is rapid and complete with the polymer-bound phenothiazine. The polymer was collected, washed, and regenerated to give fully usable **10**.

(10) See ref 3d, p 105, for examples of relative oxidation potentials.

(11) Spectroscopic data was identical with that of an authentic sample prepared by the method of Piper, T. S.; Cotton, F. A.; Wilkinson, G. *J. Inorg. Nuc. Chem.* **1955**, *1*, 165.

Scheme II



Treating polymer **10** as an ion-exchange resin, metathesis with the less nucleophilic anion PF_6 for the $SbCl_6$ is readily accomplished to afford polymer **11**. The latter reagent reacts with $[C_5H_5Fe(CO)_2]_2$ in dichloromethane to give oxidative cleavage of the iron–iron bond. The iron cation can be trapped with diphenylacetylene to form the stable η^2-alkyne compound. Cationic iron–olefin and –alkyne complexes have been shown to be synthetic value by Rosenblum et al.[12] and Reger et al.,[13] respectively. The synthesis presented in Scheme II represents a fairly efficient synthetic route to these type of complexes from the readily available iron dimer.

It appears from our study that when the amines are placed in a polymer matrix the chemical oxidation becomes more difficult. This is evidenced quite clearly in the case of 2,6-dibromocarbazole. For successful generation of a polymer-bound cation radical we supported phenothiazine, which did under a rapid and clean conversion to the cation radical by treatment with $SbCl_5$ in dichloromethane. The polymer-bound cation radical has an equivalent weight of approximately 600, which is reasonable for stoichiometric syntheses. We have demonstrated that **10** readily oxidizes the metal–metal bond in Fp_2 and then can be easily isolated and fully regenerated. Use of a less nucleophilic anion such as PF_6 permits the synthesis of functionalized iron complexes. Further work exploring the synthetic potential of these new polymer-supported cation radicals is under way.

Experimental Section

General Procedures. All manipulations of compounds and solvents were carried out by using standard Schlenk techniques. Solvents were degassed and purified by distillation under nitrogen from standard drying agents.[14] Spectroscopic measurements utilized the following instrumentation: ^1H NMR, Varian XL 300; ^{13}C NMR, Varian XL 300 (at 75.4 MHz). NMR chemical shifts are reported in δ vs Me_4Si in ^1H NMR and assigning the $CDCl_3$ resonance at 77.00 ppm in ^{13}C spectra. The chloromethylated polystyrene beads (SX-1) were purchased from Bio-Rad Laboratories and used as received. The 2,6-dibromocarbazole, lithium aluminum hydride, potassium *tert*-butoxide, sodium hydride, antimony pentachloride, cyclopentadienyliron dicarbonyl dimer, and tetrabutylammonium hexafluorophosphate were purchased from Aldrich Chemical Co. and used as received. The triphenylamine and phenothiazine were purchased from Lancaster Synthesis Co. and used as received. The acetyl chloride was freshly distilled before use. Elemental analyses were performed by Atlantic Microlab, Atlanta, GA.

Polymer-Bound 9-N-Substituted 3,6-Dibromocarbazole (5). To a solution of **4** (1.80 g, 5.6 mmol) in DMF (80 mL) was added K_2CO_3 (2.07 g, 15.0 mmol). The mixture was stirred at room temperature for 20 min, and then the chloromethylated polystyrene beads (1.08 g, 3.90 mequiv/g) were added. The mixture was heated to ca. 100 °C and allowed to react for 10 h. The heat was removed, and the mixture was allowed to cool to ambient temperature. The mixture was then quenched with H_2O (50 mL) and stirred for an additional 10 min. The DMF/water mixture was removed by filtration on a glass frit, and the beads were washed with water (2 × 50 mL), THF/H_2O (2 × 100 mL, 1/1, v/v), and finally with methanol (100 mL) and then dried under reduced pressure at 65 °C for 24 h to yield **5** (2.44 g, 100% based on ⓅCH_2Cl). Nitrogen Anal. Calcd 2.57. Found: 2.55.

9-*N*-Benzyl-3,6-dibromocarbazole (6). To a DMF (20 mL) solution of **1** (2.0 g, 6.15 mmol) was added K_2CO_3 (1.5 g, 10.0 mmol) and benzyl chloride (0.78 g, 6.15 mmol). The mixture was heated to ca. 100 °C and allowed to react for 12 h. The heat was removed, and the mixture allowed to cool to ambient temperature. The mixture was diluted with H_2O (50 mL) and CH_2Cl_2 (30 mL). The organic layer was separated and then washed with H_2O (2 × 50 mL) and brine (50 mL). The organic layer was dried (K_2CO_3) and filtered, and the solvents were removed under reduced pressure. The residue was recrystallized from $EtOH/CH_2Cl_2$ to afford pure **6** (2.1 g, 81%) as white needles (mp 159 °C): ^1H NMR δ 8.07 (d, J = 2.0 Hz, 2 H), 7.42 (dd, J = 2.0, 8.7 Hz, 2 H), 7.15 (m, 5 H), 6.97 (t, 3.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 139.5, 136.2, 129.3, 127.8, 126.2, 123.6, 123.3, 112.5, 110.6, 46.7. Anal. Calcd for $C_{19}H_{13}Br_2N$: C, 54.9; H, 3.1. Found: C, 55.0; H, 3.2.

9-*N*-Benzyl-3,6-dibromocarbazole Aminium Hexachloroantimonate (7). Compound **6** (1.0 g, 2.4 mmol) was dissolved in CH_2Cl_2 (5 mL), and a CH_2Cl_2 (4 mL) solution of $SbCl_5$ (0.9 g, 3.0 mmol) was slowly added. The mixture was stirred for an additional 1 h and then diluted with diethyl ether (10 mL). The precipitate was collected and washed with anhydrous diethyl ether, and the solid was dried at room temperature under reduced pressure to yield **7** (0.93 g, 52%) as a dark green solid. Anal. Calcd for $C_{19}H_{13}Br_2Cl_6NSb$: C, 30.42; H, 1.73. Found: C, 30.56; H, 1.83.

Polymer-Bound 10-N-Substituted Phenothiazine (9). To a solution of **8** (2.0 g, 10 mmol) and the chloromethylated polystyrene beads (2.05 g, 3.90 mequiv/g) in DMF (40 mL) was slowly added NaH (0.29 g, 12 mmol). The mixture was stirred at ambient temperature for 6 h. The mixture was then quenched with H_2O (30 mL) and stirred for an additional 5 min. The DMF/water mixture was removed by filtration on a glass frit, and the beads were washed with CH_2Cl_2 (3 × 50 mL) and methanol (50 mL) and then dried under reduced pressure at 65 °C for 24 h to yield **9** (3.35 g, 100% based on ⓅCH_2Cl). Nitrogen Anal. Calcd N, 3.34. Found: N, 3.36.

Polymer-Bound 10-N-Substituted Phenothiazine Aminium Hexachloroantimonate (10). Compound **9** (1.0 g, 2.38 mmol) was suspended in CH_2Cl_2 (10 mL), and $SbCl_5$ (0.8 g, 2.7 mmol) was slowly added. The mixture was stirred at ambient temperature for an additional 18 h. The beads were collected on a glass frit and washed with CH_2Cl_2 (30 mL) and diethyl ether (3 × 50 mL) and then dried under reduced pressure at 65 °C for 24 h to yield **10** (1.8 g, 100% based on **9**). Chlorine Anal. Calcd Cl, 28.2. Found: Cl, 28.0.

Polymer-Bound 10-N-Substituted Phenothiazine Aminium Hexafluorophosphate (11). A dichloromethane (120 mL) solution of tetrabutylammonium hexafluorophosphate (5.00 g, 12.9 mmol) was passed through a column packed with **10** (1.00 g, 1.3 mmol) in dropwise fashion. The polymer beads were then washed with dichloromethane (3 × 4 mL) and dried under a stream of nitrogen gas at ambient temperature to yield **11** (0.71 g, 95% based on ⓅCH_2Cl).

Preparation of $C_5H_5Fe(CO)_2(\eta^2$-PhC≡CPh)PF_6 (13). A flask was charged with cyclopentadienyliron dicarbonyl dimer (0.075 g, 0.21 mmol), CH_2Cl_2 (6 mL), and **11** (0.31 g, 1.77 mequiv/g) and then allowed to stir at ambient temperature for 30 min. The polymer beads were removed by filtration and washed with dichloromethane (6 mL), and the filtrate was treated with diphenylacetylene (0.14 g, 0.79 mmol). The mixture was stirred for an additional 40 min and then diluted with Et_2O (40 mL) and

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(14) *The Chemists Companion*; Gordon, A. J., Ford, R. A., Eds.; Wiley: New York, 1972.

chilled to −78 °C. Complex 13 was collected, washed with cold Et_2O (10 mL), and finally dried under reduced pressure to yield 0.080 g (53%) of product. Spectroscopic data was identical with literature values.[13]

Acknowledgment. M.E.W. wishes to thank the Office of the Vice President for Research at Utah State University for generously funding this research. M.E.W. wishes to thank Prof. Vernon D. Parker for several meaningful and helpful discussions of this work prior to publication.

Supplementary Material Available: Full experimental details concerning the synthesis of 3 (4 pages). Ordering information is given on any current masthead page.

Notes

Product Enantioselectivity in the Microsomal Epoxide Hydrolase Catalyzed Hydrolysis of 10,11-Dihydro-10,11-epoxy-5*H*-dibenzo[*a*,*d*]-cycloheptene

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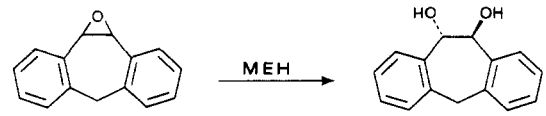
10,11-Dihydro-10,11-epoxy-5*H*-dibenzo[*a*,*d*]cycloheptene (1) is a product of considerable biological interest, its parent structure being present in the metabolites formed by the cytochrome P-450 catalyzed oxidation of the 10,11 double bond of several important tricyclic drugs used against central nervous system (CNS) diseases.[1-4]

Epoxides are usually biotransformed into the corresponding vicinal diols by a trans addition of water catalyzed by epoxide hydrolases, key enzymes of the xenobiotics detoxifying system.[5] The microsomal epoxide hydrolase (MEH) is endowed with a low substrate specificity, as required for an enzyme involved in the metabolism of a very broad range of exogenous compounds, but often exhibits a remarkable capability of chiral recognition, enabling it to discriminate between enantiomers of racemic epoxides[6-15] and between enantiomeric carbons of meso epoxides.[16-19] In most reported cases MEH catalyzes ring opening preferentially at *S* oxirane carbons to give the *R* or *R,R* enantiomers of the corresponding diols.[20] In particular, *cis*-stilbene oxide (5), a meso epoxide that is a close analogue of 1, was reported to be hydrolyzed to nearly optically pure (*R,R*)-(+)-1,2-diphenyl-1,2-ethanediol.[17]

In the course of an investigation of its MEH-catalyzed hydrolysis,[21] epoxide 1 was found to be a much worse substrate for this enzyme than 5, its lower reaction rate being due to a much lower V_S rather than to a higher K_m with respect to 5, thus pointing to a difficulty in the nucleophilic attack by water at the oxirane carbons of 1. It appeared therefore interesting to check if this large decrease in the rate of nucleophilic attack by water produced by the closure of a seven-membered ring through a methylene bridge between the ortho positions of the two phenyl rings of 5 was also accompanied by a change in the steric course of the reaction.



1 2

The enzymatic hydrolysis of 1 was carried out with rabbit liver microsomes at 37 °C and pH 7.4. Owing to the slow rate, it was necessary to incubate 50-mg samples of 1 for at least 24 h, with repeated addition of microsomal preparation, in order to achieve an about 25% conversion into the diol. No spontaneous hydrolysis of 1 occurred during this time, as shown in a blank experiment with inactivated enzyme. HPLC analysis revealed, by comparison with authentic samples of the (±)-*trans*-dihydrodiol 2 and of the diastereomeric *cis*-dihydrodiol, the

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