

Polymer-Supported Tripyridylmethane Derivatives: Lewis Acid Catalyzed Ring Opening of Styrene Oxide

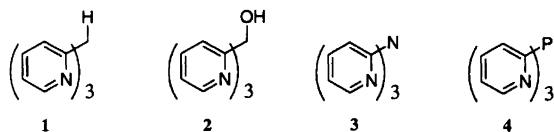
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Tri(2-pyridyl)methanol was allowed to react with 1% crosslinked gel-type chloromethylated polystyrene in the presence of a base to yield a polymeric tridentate ligand. A macroporous chloromethylated polymer was unreactive under the same conditions. In this case, grafting was accomplished after reaction of tri(2-pyridyl)methanol with a spacer containing a phenolic group, which after deprotonation readily reacted with the polymer. An Fe(III) complex of the polymeric ligand was used as a Lewis acid in the methanolysis of styrene oxide.

Metal complexes of tri(2-pyridyl)methane (**1**),^{1,2} tri(2-pyridyl)methanol (**2**),^{1,3} tri(2-pyridyl)amine (**3**) and tri(2-pyridyl)phosphine (**4**) have been extensively



studied in recent years.⁴ The ligands allow studies of metal complexes having uncommon coordination geometries, for example Hg(II) complexes.⁵ Complexes of these ligands with metal ions favoring tetrahedral coordination, in particular Zn(II), have been shown to serve as useful models for the action of carbonic anhydrase,⁶ whereas complexes with Ru(II) have been studied as possible photosensitizers in reductive processes.⁷ Recently, it was also demonstrated that complexes with electron-deficient metal centers may act as versatile Lewis-acid catalysts.⁸ Molybdenum and tungsten nitrosyl complexes were thus shown to give adducts with aldehydes, ketones and esters. The tungsten complex was shown to be the stronger Lewis acid, catalyzing Diels–Alder cyclizations, addition of silyl enol ethers to aldehydes, and hydrocyanations. With most metal ions the ligands have been shown to prefer *N*₃-coordination,⁴ although in some cases tripyridylmethanol prefers to take part in *N*₂*O*-coordination.⁹

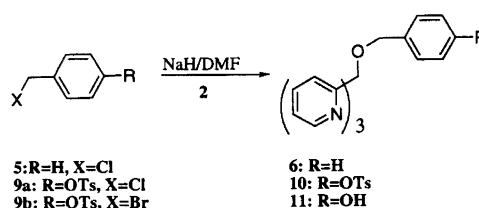
To enable more efficient use of the ligands in catalytic reactions, we considered the possibility to use complexes of the ligands bound to solid supports, thus facilitating

work up procedures and permitting repeated use of the reagents,¹⁰ which may be of special importance when chiral analogues of the ligand are employed.¹¹ To allow for various types of applications, we investigated methods for the grafting of metal complexes of tripyridylmethane derivatives on gel-type as well as on macroporous styrene–divinylbenzene polymers. The results of this study are presented here, along with results from the use of Fe(III) complexes of the polymer-bound ligands as Lewis-acid catalysts in the ring opening of styrene oxide.

Results and discussion

Grafting on polymeric supports. In order to find appropriate conditions for the reaction of tri(2-pyridyl)methanol (**2**) with chloromethylated polymers (Scheme 1), we first studied the reactivity of the ligand towards benzyl chloride (**5**). The reaction performed in DMF in the presence of sodium hydride yielded 74% of compound **6**, whereas the same reaction performed in THF in presence of potassium hydride and 18-crown-6 gave only 40% yield of the same compound.

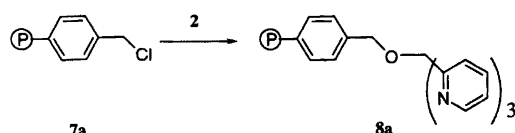
These different reaction conditions were tried on chloromethylated SX-1 (**7a**), which is a 1% cross-linked geltype polymer, affording polymer **8a** (Scheme 2). In



Scheme 1

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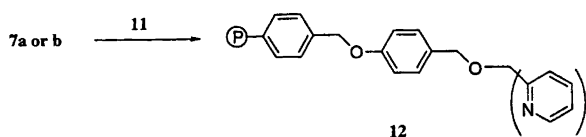
Scheme 2

both cases the amount of grafting was estimated to 1.2 mmol of ligand per gram of resin, corresponding to 61% conversion. It should be noted that no reaction took place in THF in the presence of potassium hydride without 18-crown-6 ether.

It is occasionally desirable to use column operation for reactions involving polymeric reagents. For such applications, macroporous polymers have advantageous properties, since swelling in organic solvents is less important. However, attempts to functionalize macroporous polymers with tripyridylmethanol in the same manner as employed for the gel-type polymer were unsuccessful, resulting only in recovered starting materials. This is probably due to both the steric hindrance of the tri(2-pyridyl)methanol and the low reactivity of highly cross-linked polystyrenes.

It was therefore necessary to modify the ligand in order to increase its reactivity. We have demonstrated that phenols are good candidates for reaction with chloromethylated polystyrenes¹² and that chloromethyl-4-tosyloxybenzene (**9a**) serves as a useful spacer.¹³ This spacer was initially allowed to react with the compound to be grafted. Deprotection liberates a phenol which subsequently can be grafted on various types of chloromethylated styrene-divinylbenzene polymers. A compound with higher reactivity was desired in the present case, therefore chloride **9a** was transformed into bromide **9b** prior to further modification.

Reaction of compound **2** with this spacer (**9b**) yielded the desired compound **10** (91%). Deprotection using sodium hydride/*tert*-butyl alcohol in DMF afforded phenol **11** (90%), which could be used for reaction with the gel-type polymer (**7a**) as well as with a macroporous chloromethylated polymer (**7b**), resulting in polymers **12a** (gel) and **12b** (macroporous) (Scheme 3). It was found, however, that the procedure could be simplified, since deprotection and grafting could be performed by a one-pot procedure using sodium hydride/*tert*-butyl alcohol in DMF. Attempts to employ sodium hydroxide as a base resulted in cleavage of the benzylic ether, whereas use of ethanol in place of *tert*-butyl alcohol gave an ethyl ether.



Scheme 3

Preparation of metal complexes. A yellow Fe(III) complex, thought to have a symmetrical (C_{3v}) structure and a ligand:metal ratio of 1:1, was obtained by treatment of **6** with iron(III) chloride. The addition of 3 equiv. of silver triflate to this complex in MeOH/CH₃NO₂ 2:3 afforded a cationic complex. An analogous polymeric cationic complex was obtained by treatment of iron(III) chloride with silver triflate, followed by addition of the polymeric ligand **12a**.

Ring opening of epoxides. To exploit the efficiency of the present metal complexes as Lewis acids, the nucleophilic ring opening of epoxides was investigated. For this purpose, catalytic amounts of the above Fe(III) complexes were added to styrene oxide (**13**) in methanol. The monomeric FeCl₃ complex was quite unreactive, with 5% catalyst leading to merely 45% conversion to 2-methoxy-2-phenylethanol (**14**) after 17 h (Scheme 4). In contrast, complete conversion was observed after 5 min using only 1% of the cationic monomeric complex.

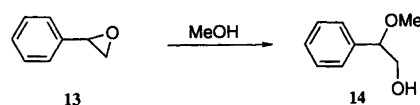
The polymeric complex obtained from **12a** turned out also to serve as an efficient catalyst for the same reaction, although with slightly lower reactivity than the monomeric analogue. In this case, complete conversion using 0.6% of the catalyst was observed within 30 min. In reactions with polymers, a 1:2 mixture of MeOH and CH₂Cl₂ was used as solvent in place of MeOH/CH₃NO₂, in order to allow for more efficient swelling of the polymer. The polymer could be reused, although with somewhat decreasing activity. In the third cycle, complete conversion to the ring-opened compound was observed after 45 min, whereas 1 h reaction time was required to obtain 90% conversion in the fifth cycle. The choice of solvent turned out to be important, since the use of THF in place of CH₂Cl₂ led to rapidly decreasing activity of the catalyst, probably due to leakage of the metal ion from the polymer into solution. The nucleophilic ring cleavage in the catalytic reactions was found to proceed with total regioselectivity at the benzylic position, as observed by ¹H NMR spectroscopy.

Conclusion

Methods are described for efficient grafting of sterically hindered alcohols to gel-type as well as macroporous styrene-divinylbenzene polymers. A cationic Fe(III) complex of a polymeric ligand efficiently catalyzes the ring opening of styrene oxide in the presence of methanol.

Experimental

General. The following compounds were prepared by literature methods: Tri(2-pyridyl)methanol,^{1,14} chloro-



Scheme 4

methylated polystyrenes **7a** and **7b**,¹⁵ chloromethyl-4-tosyloxybenzene.¹³ Commercially available reagents were used unless otherwise stated. The polymer SX-1 was purchased from Bio Rad. DMF was distilled over CaH₂ before use. ¹H and ¹³C NMR spectra were recorded in CDCl₃ with TMS as an internal standard at 250 and 62.9 MHz, respectively. Melting points are uncorrected.

Tri(2-pyridyl)benzyloxymethane (6). A solution of tri(2-pyridyl)methanol (100 mg, 0.38 mmol) and sodium hydride (as an 80% suspension in oil, 12 mg, 0.40 mmol) in DMF (1 mL) was stirred for 10 min under N₂. Benzyl chloride (32 μ L, 0.40 mmol) was added via a syringe. After being stirred overnight, water (3 mL) was added and the resulting solution was extracted with CH₂Cl₂ (3 \times 10 mL). The combined dichloromethane phases were washed with 0.1 N aq HCl (2 \times 20 mL). The organic layer was dried (MgSO₄) and then evaporated under vacuum affording 100 mg (70%) of the desired product **6**, m.p. 145–146 °C. ¹H NMR (CDCl₃) δ 8.61 (ddd, 3H, *J*=4.8, 1.8 and 1.1 Hz), 7.76 (dt, 3H, *J*=7.9, 1.1 Hz), 7.68 (td, 3H, *J*=7.9, 1.8 Hz), 7.39–7.24 (m, 5H), 7.16 (ddd, 3H, *J*=7.9, 4.8, 1.4 Hz), 4.53 (s, 2H). ¹³C NMR δ 161.6, 148.5, 139.0, 136.0, 128.1, 127.3, 127.1, 123.75, 122.0, 88.4, 66.85. IR (KBr, cm⁻¹): 1583, 1574, 1462, 1430, 1110, 1085, 1074. Anal. Calcd. for C₂₃H₁₉N₃O: C, 77.77; H, 5.19; N, 11.38. Found: C, 77.60; H, 5.30; N, 11.50.

1-Tosyloxy-4-(bromomethyl)benzene (9). To a solution of lithium bromide (8.52 g, 98.1 mmol) in acetone (30 mL) was added 1-tosyloxy-4-(chloromethyl)benzene (2.91 g, 9.8 mmol). The resulting solution was stirred for 24 h at r.t. After evaporation of acetone and addition of water (70 mL) to the residue, the resulting aqueous layer was extracted with CH₂Cl₂ (2 \times 60 mL). Drying (MgSO₄) and evaporation of CH₂Cl₂ under vacuum yielded 3.3 g (99%) of **9** as a white solid, m.p. 88 °C. ¹H NMR (CDCl₃) δ 7.70 (d, 2H, *J*=8.3 Hz), 7.32 (d, 2H, *J*=8.3 Hz), 7.31 (d, 2H, *J*=8.6 Hz), 6.95 (d, 2H, *J*=8.6 Hz), 4.43 (s, 2H), 2.45 (s, 3H). ¹³C NMR δ 149.26, 145.46, 136.67, 132.10, 130.25, 129.75, 128.34, 122.57, 32.07, 21.60.

Tri(2-pyridyl)-[4-(tosyloxy)benzyloxy]methane (10). A solution of tri(2-pyridyl)methanol (2 g, 7.6 mmol) and sodium hydride (as an 80% suspension in oil, 340 mg, 11.3 mmol) in dry DMF (12 mL) was stirred for 15 min at r.t. under N₂ giving a yellow suspension. After adding compound **9** (2.6 g, 7.6 mmol), the solution was stirred for a further 48 h to give a clear yellow solution. DMF was evaporated under vacuum at 50 °C. The resulting residue was chromatographed on neutral alumina (eluent: EtOAc/hexane 1/3) affording 3.6 g (91%) of compound **10** as a white solid, m.p. 161 °C. ¹H NMR (CDCl₃) δ 8.58 (app dt, 3H, *J*=4.7, 1.4 Hz), 7.74–7.63 (m, 10 H), 7.31 (d, 2H, *J*=8.4 Hz), 7.16 (ddd, 3H, *J*=6.5, 4.7, 2.3 Hz), 6.90 (d, 2H, *J*=8.6 Hz), 4.52 (s, 2H), 2.46 (s,

3H). Anal. Calcd. for C₃₀H₂₅N₃O₄S: C, 68.81; H, 4.82; N, 8.03. Found: C, 68.69; H, 4.60; N, 7.89.

Tri(2-pyridyl)-[4-(hydroxy)benzyloxy]methane (11). A suspension of NaH (as an 80% suspension in oil, 290 mg, 9.7 mmol) in dry DMF (10 mL) and *tert*-BuOH (3 mL) was stirred for 15 min at r.t. Compound **10** (1 g, 1.90 mmol) was added, and the resulting yellow solution was stirred for 3 h at r.t. which became brown during this period. An aqueous solution of HCl (0.2 M, 200 mL) was added. After washing with CH₂Cl₂ (4 \times 40 mL), the aqueous phase was made neutral with 10% aq. NaHCO₃. The resulting white suspension was extracted with CH₂Cl₂ (3 \times 40 mL). Drying (MgSO₄) and evaporation of CH₂Cl₂ afforded 634 mg (90%) of **11** as a white solid, m.p. 63 °C. ¹H NMR (MHz, CDCl₃) δ 8.57 (ddd, 3H, *J*=4.8, 1.8, 1 Hz), 8.20 (br s, 1H), 7.78 (dt, 3H, *J*=8.0, 1 Hz), 7.67 (td, 3H, *J*=8, 1.8 Hz), 7.15 (ddd, 3H, *J*=7.6, 4.8, 1.1 Hz), 7.07 (d, 2H, *J*=8.5 Hz), 6.65 (d, 2H, *J*=8.5 Hz), 4.30 (s, 2H). ¹³C NMR δ 161.31, 156.16, 148.45, 136.27, 129.35, 128.96, 123.69, 122.20, 115.32, 88.20, 66.74.

Polymer-supported ligand 2 (8a). A solution of tri(2-pyridyl)methanol (**2**) (131 mg, 0.50 mmol) and sodium hydride (as an 80% suspension in oil, 30 mg, 1 mmol) in dry DMF (5 mL) was stirred for 30 min at r.t. under N₂. Chloromethylated polystyrene (**7a**) (SX1, 4.91 mmol of chloromethyl groups/g of polymer, 100 mg, 0.49 mmol) was added, and the resulting mixture was stirred for 3 d, at r.t. The polymer was removed by filtration and washed successively with MeOH, THF–H₂O (1/1), H₂O, acetone, CH₂Cl₂ and MeOH. The polymer was dried at r.t. under vacuum for 12 h. Weight gain: 40 mg corresponding to 1.25 mmol of ligand **2**/g of polymer (%N=4.95 corresponding to 1.2 mmol of ligand **2**/g of polymer). IR (KBr, cm⁻¹): Characteristic peaks appearing at the same frequency as in the monomeric model **6**: 1583, 1574, 1430, 1110, 1085.

Polymer-supported ligand 11 (12b)

A solution of ligand **11** (37 mg, 0.10 mmol) and sodium hydride (as an 80% suspension in oil, 15 mg, 0.50 mmol) in dry DMF (1.0 mL) was stirred for 30 min at r.t. under N₂. Chloromethylated polystyrene **7b** (DVB) (1.7 mmol of chloromethyl groups/g of polymer, 62.5 mg, 0.1 mmol) was added, and the resulting mixture was stirred for 4 d at r.t. The polymer was removed by filtration and washed successively with MeOH, THF–H₂O (1/1), H₂O, acetone, CH₂Cl₂ and MeOH. The polymer was dried at r.t. under vacuum for 12 h. Weight gain: 10 mg corresponding to 0.42 mmol of ligand **11**/g of resin (%N=1.8 corresponding to 0.43 mmol of ligand **11**/g of polymer).

An alternative method employs reacting ligand **10** (210 mg, 0.4 mmol) with *tert*-butanol (0.5 mL) and NaH (as an 80% suspension in oil, 60 mg, 2.0 mmol) in dry DMF (2.5 mL). Chloromethylated polystyrene **7b**

(1.7 mmol of chloromethyl groups per g of polymer, 250 mg, 0.42 mmol) was added and the resulting suspension was stirred for 3 d at r.t. The polymer was removed by filtration and washed successively with MeOH, THF-H₂O (1/1), H₂O, acetone, CH₂Cl₂ and MeOH. The polymer was dried at r.t. under vacuum for 12 h giving 290 mg of a white polymer. Weight gain: 40 mg corresponding to 0.41 mmol of ligand **12b**/g of resin.

Tri(2-pyridyl)benzyloxymethane-iron(III) trichloride. A solution of tri(2-pyridyl)benzyloxymethane (**6**) (50 mg, 0.14 mmol) in acetone (1 mL) was added to iron(III) chloride (23 mg, 0.14 mmol) in dry acetone (1 mL). Yellow crystals formed upon standing. Yield: 60 mg (82%).

12a-Iron(III) triflate. To a solution of iron(III) chloride (52 mg, 0.32 mmol) in acetone (5 mL) was added silver(I) triflate (247 mg, 0.96 mmol). Silver chloride precipitated immediately, and after 30 min the mixture was filtered into a suspension of polymer **12a** (0.8 mmol of ligand/g of polymer, 100 mg, 0.08 mmol) in acetone (10 mL). The reaction mixture was stirred for 3 h at r.t. The polymer was filtered off and washed with acetone (20 mL) affording 108 mg of polymer. Weight gain: 8 mg corresponding to 0.15 mmol of Fe(III) complex/g polymer [%Fe = 1.42 corresponding to 0.25 mmol of iron(III) complex/g of polymer].

Methanolysis of styrene oxide using monomeric catalyst. **6-Iron(III) triflate** (0.01–0.05 equiv.) was prepared prior to the catalytic reaction by addition of 3 equiv. of silver(I) triflate to **6-iron(III) chloride** in nitromethane. The mixture was stirred for 30 min, filtered (celite), the filtrate was diluted with methanol [CH₃NO₂-MeOH (2:1)] and styrene oxide (114 μL, 1 mmol) was added. The reaction mixture was stirred at r.t. and the reaction was monitored by GLC.

Methanolysis of styrene oxide using a polymer-supported catalyst. To a slurry of polymer **12a-iron(III) triflate** (0.006 equiv. Fe) in CH₂Cl₂-MeOH (2:1) was added styrene oxide (114 μL, 1 mmol). The reaction mixture was stirred at r.t. and the reaction was monitored by

GLC. When all of the epoxide was consumed, the reaction mixture was centrifuged, and the supernatant was carefully removed. Dichloromethane and methanol were added to the polymer, and the reaction was reinitiated by addition of more styrene oxide. The procedure was repeated for five cycles.

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