Some novel polymer-supported optically active phase transfer catalysts: 1. Synthesis

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The synthesis and characterization of 27 novel polystyrene resin-supported optically active phase transfer catalysts is described. The first group of five catalytic species are essentially supported tetraethylene oxide derivatives each carrying a terminal chiral group. The second group consists of resins loaded with a protected galactose function along with a range of onium salt and oligoether catalysts. The third group are analogous to the second with a protected fructose residue replacing the galactose one. In the fourth group some attempt has been made to define the stereochemical relationship between the chiral species and the catalytic one, by attaching a chiral diphosphine to the support. Similarly, a phosphinated sugar, ephedrine and quinine have been attached. In the final group a chiral acetal function has been synthesized on the resin, and this function subsequently modified with a phosphonium salt and an oligoether each as the phase transfer catalytic species. In general good loadings were achieved as indicated by changes in elemental analyses and shifts in the infra-red absorption spectra of resins.

(Keywords: polymer-supported; chiral phase transfer; catalysts)

INTRODUCTION

Enantioselective reactions have become increasingly important in recent years because of the growing demand for optically pure compounds in the pharmaceutical and agro-chemical industries. The various areas of asymmetric synthesis have been reviewed recently[1,2]. A number of groups have been examining the possibility of achieving either asymmetric induction or kinetic racemate resolution in phase transfer catalysed (PTC) and related reactions[3], and a few polymer-supported systems have also been reported[4-15]. In principle, the latter have the advantage, in the long term, of efficiently retaining rare or expensive catalysts for re-use or re-cycling, or indeed for allowing reactions to be conducted continuously in columns.

To date virtually all the work reported has employed free or supported quarternary ammonium salts based either on ephedrine and its relatives, or the cinchona alkaloids, notably quinine, as the active chiral catalyst. Some confusion still remains in the literature concerning the effectiveness of these catalysts, and in the case of non-polymeric catalysts the situation has been admirably reviewed recently[3]. Because of the restricted number of catalytic structures which have been examined, and because many of these can decompose readily under the basic conditions often used in PTC, we felt that there was some scope for synthesizing alternative polymer-supported catalysts in order to explore the effectiveness of a wider range of chiral structures and also to provide a wider context in which the earlier results might be viewed.

This paper describes the synthesis of 23 novel polymeric optically active PTC, and is followed by a paper describing the application in a wide range of PTC reactions. A preliminary communication of our efforts has already been published[16].

EXPERIMENTAL

Materials

All materials were obtained from routine sources and in general were used as supplied. When required dry dioxane, tetrahydrofuran (THF) and toluene were distilled from calcium hydride. Pyridine was distilled from barium oxide.

Precursor resin **I** was Bio-Beads SX2 exhaustively chloromethylated using chloromethyl ethyl ether and $SnCl_4$ in a standard procedure[17]. Microanalysis yielded 5.2 mmol Cl per gramme of resin.

Precursor resin **II** was a nominally 2% crosslinked beaded copolymer made in-house by suspension copolymerization of chloromethyl styrene (FLUKA mixed isomers) (96%) with commercial divinylbenzene (4%)[18]. Microanalysis yielded 5.6 mmol Cl per gramme of resin. (*Note* in resin **II** the position of aromatic substitution is controlled by the isomeric mixture of the functional comonomer, whereas in resin **I** largely para-substitution is expected).

Precursor resin **III** (*Scheme 2*) was prepared as already reported in detail in the literature[19]. It was made from Bio-Beads SX2, ~40% chloromethylated. Tetraethylene glycol was attached by a single end to ~28% of aromatic groups, the remaining chloromethyl groups being consumed in the formation of doubly attached bridging oligoether residues. The sulphur content of resin **III** was 2.55% corresponding to 14% substitution of aryl groups.

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Precursor resins **X** and **XI** (*Scheme 6*) were prepared from resin **I** essentially as described by Montanari[20]. Amination to resin **X** was virtually quantitative and microanalysis of resin **XI** yielded 3.4 mmol Br per gramme of resin.

Analysis techniques

^{1}H n.m.r. spectra were recorded on a Perkin Elmer R32, 90 MHz. Elemental analyses were conducted on a Carlo Erba 1106 analyser. Infra-red spectra were recorded initially on a Perkin Elmer 257 using KBr discs. More informative spectra were obtained at the University of Ottawa, Department of Chemistry, using a Nicolet MX-1 Fourier transform infra-red spectrometer (*FT*i.r.). This was particularly useful for characterizing resins since the instruments computer could store and compare data on resins before and after a chemical modification. By appropriate nulling, polymer backbone signals were effectively eliminated providing a clear 'difference' spectrum. Optical rotations were measured on a Perkin Elmer 241 Polarimeter appropriately thermostatically controlled. Sample sizes down to ~1 ml were readily accommodated using a microcell.

Synthesis of chiral catalyst precursors

2(2-(2-Pyridinemethyleneoxyethoxy)-ethoxy) ethanol. This was prepared from triethylene glycol monochlorohydrin by adaption of a procedure described by Manecke[21]. Sodium hydride (1.47 g, 37 mmol), 2-pyridinemethanol (4.0 g, 37 mmol) and dry toluene (250 ml) were added to 250 ml flask. The solution was refluxed for 1 h then triethylene glycol monohydrin (6.3 g, 37 mmol) was added and refluxing continued for a further 3 days. The solution was cooled and toluene removed before water (200 ml) was added and the resultant residue and solution extracted with chloroform (3 x 100 ml). The combined extracts were dried over anhydrous sodium sulphate and the solvent removed under vacuum. Vacuum distillation yielded the pure product (5.1 g, 89%). ^{1}H n.m.r. ($CDCl_3$) 0.96, m, 2H; 1.4δ, m, 2H; 3.7δ, m, 10H; 4.7δ, s, 2H; 7.3δ, m, 3H; 8.4δ, m, H.

(−)-2,3,O,-Isopropylidene-2,3-dihydroxy-1,4-bis (diphenylphosphino)-butane [(−)-DIOP]. This was prepared from d-tartaric acid as shown in *Scheme 1*. The route is essentially as described in the literature[22–26]. In an alternative procedure the diethyl ester corresponding to **A** was prepared by replacing methanol with ethanol, and this diester was more effectively reduced to diol **B** using $NaBH_4$ in place of $LiAlH_4$.

The characterization of each product was as follows:

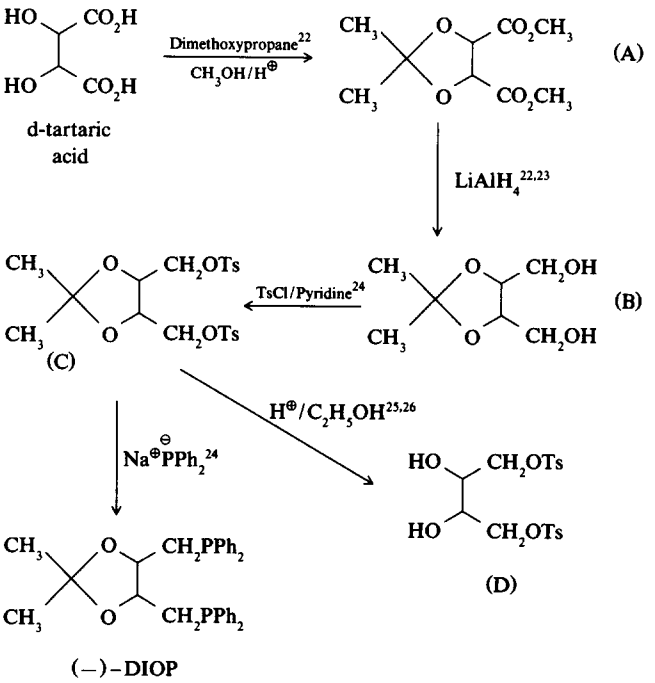
Dimethyl 2,3-O-isopropylidene-L-tartrate, **A**: yield after vacuum distillation, 75%; ^{1}H n.m.r. ($CDCl_3$): 1.5δ, s, 6H; 3.8δ, s, 6H; 4.8δ, s, 2H.

2,3,-O-Isopropylidene-L-threitol, **B**: yield after vacuum distillation, 66%; ^{1}H n.m.r. ($CDCl_3$) 1.4δ, s, 6H; 3.3δ, m, 2H; 3.8δ, m, 4H; 4.0δ, m, 2H.

1-4,Ditosyl-2,3-O-isopropylidene-L-threitol, **C**: yield after recrystallization from ethanol, 36%; m.p. 91°C (literature m.p.[24] 92°C). ^{1}H n.m.r. ($CDCl_3$). 1.3δ, s, 6H; 2.5δ, s, 6H; 4.1δ, m, 6H; 7.3δ, d, 4H; 7.8δ, d, 4H.

(−)-DIOP: yield after double recrystallization from ethanol, 19%; m.p. 88°C (literature m.p.[24] 88°–89°C). ^{1}H n.m.r. ($CDCl_3$) 1.3δ, s, 6H; 2.4δ, m, 4H; 3.9δ, m, 2H; 7.3δ, m, 20H. $[\alpha]_D^{20} = -11.6$ (c4.5 C_6H_6), [literature[24] $[\alpha]_D^{20} = -12.3$ (c4.6 C_6H_6)].

Scheme 1



(−)-1,4-Ditosylthreitol, **D**. This was prepared according to the literature[25] by intercepting the synthesis of (−)-DIOP as indicated in *Scheme 1*. The product analysed as follows: yield after recrystallization from chloroform, 89%; m.p. = 72°C (literature[25] m.p. = 73°C). ^{1}H n.m.r. ($CDCl_3$): 2.4δ, s, 6H; 4.0, m, 6H; 7.5δ, d, 4H; 7.8δ, d, 4H. $[\alpha]_D^{20} = 4.0$ (c 1.8 acetone), [literature[26] $[\alpha]_D^{20} = 4.6$ (c 2.06 acetone)].

1,2:3,4-di-O-Isopropylidene-α-D-galactopyranose (di-isopropylidene galactose). This was prepared from galactose according to a method described in the literature[27]. The product analysed as follows: yield 28%; ^{1}H n.m.r. ($CDCl_3$) 1.3δ, m, 12H; 2.8δ, s, 1H; 3.7–4.7δ, m, 6H; 5.5δ, d, 1H. $[\alpha]_D^{20} = -53.9$ (c 3.5 $CHCl_3$). [literature[27] $[\alpha]_D^{20} = -54.7$ (c 3.6 $CHCl_3$)].

1,2:4,5-di-O-Isopropylidene-β-D-fructopyranose (di-isopropylidene fructose). Again a literature method[28] was employed and the product analysed as follows: yield 22%, m.p. = 117°C (literature[28] m.p. = 118°–119°C). ^{1}H n.m.r. ($CDCl_3$): 1.3–1.6δ, m, 12H; 2.3δ, s, 1H; 3.7–4.3δ, m, 8H. $[\alpha]_D^{20} = -153$ (c 1.0 acetone). [literature[28] $[\alpha]_D^{25} = -155$ (c 1.0 acetone)].

6-Diphenylphosphino-6-deoxo-1,2:3,4-diisopropylidene-D-galactose (DPPDIG). This was prepared essentially as indicated in the literature[29] from the tosylated derivative of diisopropylidene galactose[30]. Characterization of the intermediate and the final product were as follows:

Tosyl derivative of diisopropylidene galactose: yield after recrystallization from cold chloroform, 69%; m.p. 88°–90°C (literature[30] m.p. = 88°–91°C); ^{1}H n.m.r. ($CDCl_3$): 1.3–1.6δ, m, 12H; 2.4δ, s, 3H; 4.0–4.6δ, m, 5H; 4.6δ, d, 1H; 5.4–5.5δ, d, 1H; 7.3δ, d, 2H; 7.8, d, 2H.

DPPDIG: yield after double recrystallization from ethanol, 38%; m.p. = 124°–125°C (literature[30] m.p. = 124°–125°C). ^{1}H n.m.r. ($CDCl_3$): 1.5δ, m, 12H; 2.4δ, d, 2H; 3.7δ, m, 1H; 4.2δ, m, 1H; 4.5δ, m, 1H; 5.5δ, d, 1H; 7.4δ, m, 10H. $[\alpha]_D^{20} = -111$ (c 1.0 C_6H_6) [literature[30] $[\alpha]_D^{20} = -111.5$ (c 1.0 C_6H_6)].

Synthesis of resin-supported catalysts

The various polymeric optically active catalysts were prepared as shown in *Schemes 2–6*.

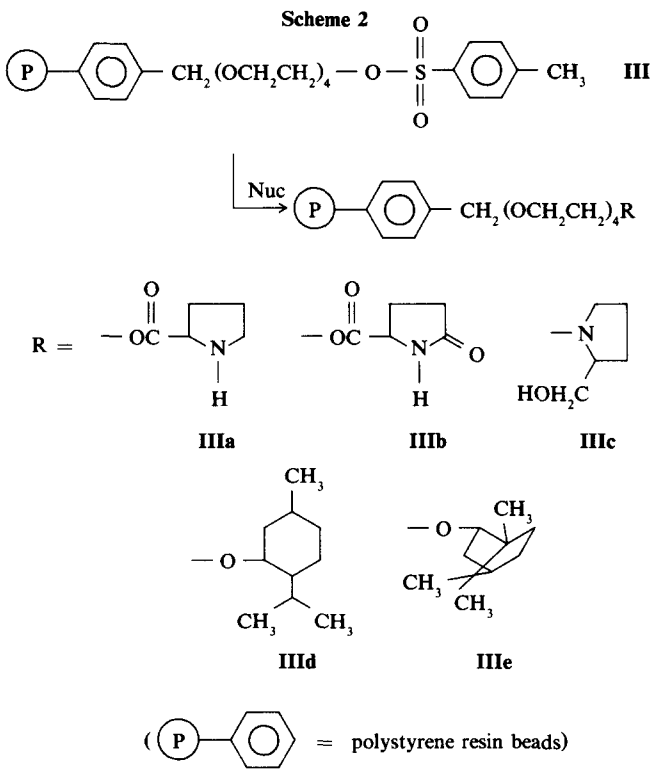
Resin **IIIa** (*Scheme 2*). To a baffled flask[31] (100 ml) resin **III** was added (0.62 g), l-proline (0.52 g, 4.5 mmol), triethylamine (0.6 ml, 4.3 mmol) and dimethylformamide (30 ml). This mixture was agitated[31] at 100°C for 48 h. The resin was filtered off and washed well with water, 50% tetrahydrofuran/water and tetrahydrofuran (THF). It was then extracted with the latter solvent for 6 h, and dried for a further 6 h in a vacuum oven at 60°C. Microanalysis: C, 70.7; H, 8.1; N, 1.65; S, ~0. *FT*i.r.: loss, 1360, 1177 cm^{-1}, S=0; gain, 1740, 1670 cm^{-1}, C=0.

Resin **IIIb** (*Scheme 2*). As above, resin **III** (0.56 g), 2-pyrrolidone-5-carboxylic acid (0.54 g, 4.2 mmol), triethylamine (0.5 ml, 3.6 mmol) in dimethylformamide (30 ml) were heated at 100°C for 48 h. The resin was similarly isolated, washed and dried. Microanalysis: C, 71.4, H, 7.4; N, 1.14; S, ~0. *FT*i.r.: loss, 1360, 1175 cm^{-1}, S=0; gain, 3300–3200 cm^{-1}, N–H, 1738, 1696 cm^{-1} C=0.

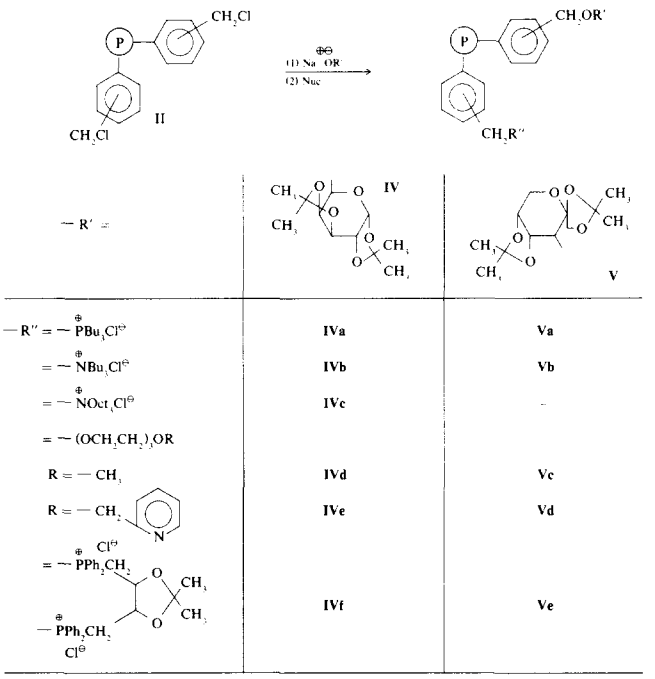
Resin **IIIc** (*Scheme 2*). Resin **III** (0.66 g) and 2-pyrrolidonemethanol (0.7 g, 6.9 mmol) were added to N_2 flushed acetone (50 ml) and the mixture heated under reflux for 24 h. The resin was collected and washed with sodium bicarbonate solution, water and acetone. Finally it was extracted with acetone and dried as for **IIIa** and **b**. Microanalysis: C, 73.4; H, 8.7; N, 2.06; S, ~0. *FT*i.r.: loss, 1362, 1176 cm^{-1}, S=0; gain, 3500–3300 cm^{-1}, O–H.

Resin **IIId** (*Scheme 2*). Sodium hydride (0.35 g, 7.3 mmol) and *l*-menthol (1.15 g, 7.3 mmol) were added to a solution of triglyme (5 ml) in dry tetrahydrofuran (25 ml). This mixture was heated under reflux for 1 h before resin **III** (1.0 g) was added. Refluxing was continued for a further 3 days under an N_2 atmosphere. The resin was then filtered off and washed with water, 50% THF/-water and THF. It was then extracted with THF for 6 h

Scheme 2



Scheme 3



and dried as before. Microanalysis: C, 75.8; H, 8.3; S, ~0. *FT*i.r.: loss, 1362, 1176 cm^{-1} S=0; gain, 2867 cm^{-1} C–H.

Resin **IIIe** (*Scheme 2*). The procedure was similar to that for **IIId** and employed *l*-borneol (1.58 g, 10.2 mmol), sodium hydride (0.49 g, 10.2 mmol) and resin **III** (1.1 g). Isolation, purification and drying were also the same. Microanalysis: C, 79.5; H, 8.2; S, ~0. *FT*i.r.: loss, 1362, 1175 cm^{-1}, S=0; gain, 2864 cm^{-1} C–H.

Resin **IV** (*Scheme 3*). 1,2:3,4-di-O-isopropylidene-α-D-galacto-pyranose (3 g, 23 mmol) and sodium hydride (0.9 g, 18.7 mmol) were added to dry THF (30 ml) in a 100 ml flask. The mixture was heated under reflux for 1 h then resin **II** (2 g, 11.7 mmol Cl) was added together with triglyme (0.5 ml). The resulting suspension was heated under reflux for 3 days. The resin was collected and washed, extracted and dried as described for **IIIa**. Two samples of **IV** were prepared in which slightly different loadings of the galactose derivative were obtained. This was apparent from the elemental microanalyses and the appropriate loading data appears in *Table 3*. Microanalyses: (i) C, 70.5; H, 6.96; Cl, 8.69. (ii) C, 69.8; H, 6.87; Cl, 8.56. *FT*i.r.: partial loss, 1267 cm^{-1}, CH_2Cl, 707 cm^{-1}, C–Cl; gain, 1382 cm^{-1}, $C(CH_3)_2$, 1211, 1103, 1070, 1005 cm^{-1}, 1,3 dioxolane ring.

Resin **IVa** (*Scheme 3*). Resin **IV** (1.4 g) and tributylphosphine (4 g, 20 mmol) were added to dimethylformamide (30 ml). The mixture was agitated at 60°C for 5 days. The resin was isolated, purified and dried as described for resin **IIIa**. Microanalysis: C, 68.3; H, 8.1; P, 4.8; Cl, 5.7. i.r. (KBr) decrease 1266 cm^{-1} CH_2Cl, 708 cm^{-1} C–Cl.

Resin **IVb** (*Scheme 3*). The same procedure was adopted as for resin **IVa**, employing resin **IV** (1.5 g) and tributylamine (3.5 g, 18.9 mmol) in dimethylformamide (35 ml). In this case the temperature was maintained at 45°C for 5 days. Isolation, purification and drying were again as for resin **IIIa**. Microanalysis: C, 73.1; H, 8.6; N, 1.5; Cl, 3.3. i.r. (KBr) decrease 1266 cm^{-1} CH_2Cl, 708 cm^{-1} C–Cl.

Resin **IVc** (*Scheme 3*). The same procedure was adopted as for resin **IVa**, employing resin **IV** (1.8 g) and trioctylamine (6.6 g, 18.7 mmol) in dimethylformamide (35 ml). The temperature employed was 60°C and the isolation and work-up procedures were as for resin **IIIa**. Microanalysis: C, 78.0; H, 8.5; N, 1.4; Cl, 2.3. i.r. (KBr) decrease 1265 cm^{-1} CH_2Cl, 708 cm^{-1} C–Cl.

Resin **IVd** (*Scheme 3*). 2(2-(2-methoxyethoxy)ethoxy)ethanol (8 g, 49 mmol) and sodium hydride (1.3 g, 27 mmol) were heated to 110°C for 30 min before dry toluene (30 ml) and resin **IV** (1.3 g) were added. The resulting mixture was refluxed for 2 days before the resin was isolated and worked-up as for resin **IIIa**. Microanalysis: C, 69.6; H, 7.9; Cl, ~0. *FT*i.r.: loss, 1266 cm^{-1} CH_2Cl, 708 cm^{-1} C–Cl, gain, 1103–1070 cm^{-1} C–O–C.

Resin **IVe** (*Scheme 3*). 2(2-(2-pyridinemethyleneethoxy)ethoxy)ethanol (2.3 g, 9.5 mmol) and sodium hydride (0.95 g, 39.6 mmol) were stirred together at room temperature for 30 min, before dry toluene (30 ml), resin **IV** (1.0 g) and a little tetrabutylphosphonium chloride (0.05 g, 0.17 mmol) were added. The mixture was refluxed for 4 days. The resin was collected and washed with water, THF/water (50%), THF, methylene chloride and toluene before being extracted and dried as for resin **IIIa**. Microanalysis: C, 74.0; H, 7.4; N, 2.1; Cl, 0.3. *FT*i.r.: loss 1267 cm^{-1} CH_2Cl, 710 cm^{-1} C–Cl, gain 1590, 1571, 1435 pyridine ring, 1353 cm^{-1} C–N, 1107–1085 cm^{-1}, C–O–C.

Resin **IVf** (*Scheme 3*). DIOP (0.75 g, 1.5 mmol) and resin **IV** (1.2 g) were reacted in dimethylformamide (30 ml) as described for resin **IVa**. The resin was isolated as described for resin **IIIa**. Microanalysis: C, 71.5; H, 6.9; P, 3.1; Cl, 4.7. *FT*i.r.: loss 1267 cm^{-1} CH_2Cl, 708 cm^{-1}, gain 1438 cm^{-1} P–Ph, 1384 cm^{-1} $C(CH_3)_2$, 1221, 1186, 1122 cm^{-1} 1,3-dioxlane ring.

Resin **V** (*Scheme 3*). This was prepared similarly to resin **IV** using 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (3.5 g, 13.4 mmol), sodium hydride (0.6 g, 12.5 mmol) and resin **II** (4 g, 23.2 mmol Cl). The isolation procedure was also the same. Three independent samples were prepared giving rise to different resin loadings of the fructose derivative (see *Table 3*). Microanalyses: (i) C, 70.0; H, 7.1; Cl, 3.4. (ii) C, 69.7; H, 7.3; Cl, 3.6. (iii) C, 70.9; H, 6.7; Cl, 8.9. *FT*i.r.: loss 1267 cm^{-1} CH_2Cl, 707 cm^{-1} C–Cl, gain 1381 cm^{-1} $C(CH_3)_2$, 1219, 1080, 1020 cm^{-1} 1,3 dioxolane ring.

Resins **Va–e** (*Scheme 3*). These were prepared from resin **V** essentially as described from **Va, b, d, e, f**. Microanalyses indicated a less favourable incorporation of each PTC residue (*Table 1*) and the loadings achieved appear in *Table 3*. I.r. spectra confirmed these changes.

Resins **VIa–f** (*Scheme 4*). These were all prepared from resin **II** by heating with the appropriate nucleophile in dimethylformamide. The conditions employed, and washing/extraction solvents used are summarized in *Table 2*. In each case the microanalysis (*Table 1*) indicated significant conversions and these were confirmed by *FT*i.r. spectral changes.

Resin **VII** (*Scheme 5*). Resin **I** (5.5 g, 32.3 mmol Cl) was added to sodium bicarbonate (8 g, 95 mmol) in dimethylsulphoxide (100 ml) contained in a 250 ml flask. The mixture was agitated at 155°C for 18 h. The resin was collected then washed well with water, dilute HCl, dilute HCl in THF, THF and toluene. Finally it was extracted with toluene for 10 h and vacuum dried at 100°C. Microanalysis: C, 78.3; H, 7.5; Cl, 0.75. *FT*i.r.: loss 1266 cm^{-1} CH_2Cl, 708 cm^{-1} C–Cl, gain 1698 cm^{-1} C=O.

Resin **VIII** (*Scheme 5*). Resin **VII** (2 g), 1,4-ditosylthreitol (4.5 g, 10.5 mmol) and *p*-toluenesulphonic acid (0.022 g, 0.12 mmol) were added to dry toluene (100 ml) in a 250 ml flask. The mixture was refluxed for 24 h with the continuous removal of the water formed using a Dean–Stark apparatus. The resin was filtered off and washed, extracted and dried as for resin **IIIa**. Microanalysis: C, 71.7; H, 6.3; S, 6.60. *FT*i.r.: loss 1695 cm^{-1} C=0, gain 1384 cm^{-1} $C(CH_3)_3$, 1364, 1177 cm^{-1} S=O.

Resin **IX** (*Scheme 5*). Resin **VIII** (2 g) and lithium bromide (6 g, 68.9 mmol) were heated to 60°C for 5 days in dry dimethylformamide (50 ml). The resin was collected and washed with water, water/THF (50%), THF and acetone. Finally it was extracted with acetone before vacuum drying as for resin **IIIa**. Microanalysis: C, 70.0; H, 6.0; Br, 18.9. I.r. (KBr) loss 1362, 1177 cm^{-1} S=O.

Resin **IXa** (*Scheme 5*). This was prepared similarly to resin **IVd** using resin **IX** (1.5 g), 2(2-(2-methoxy-

Table 1 Elemental microanalyses of resins **Va–e, VIa–f**

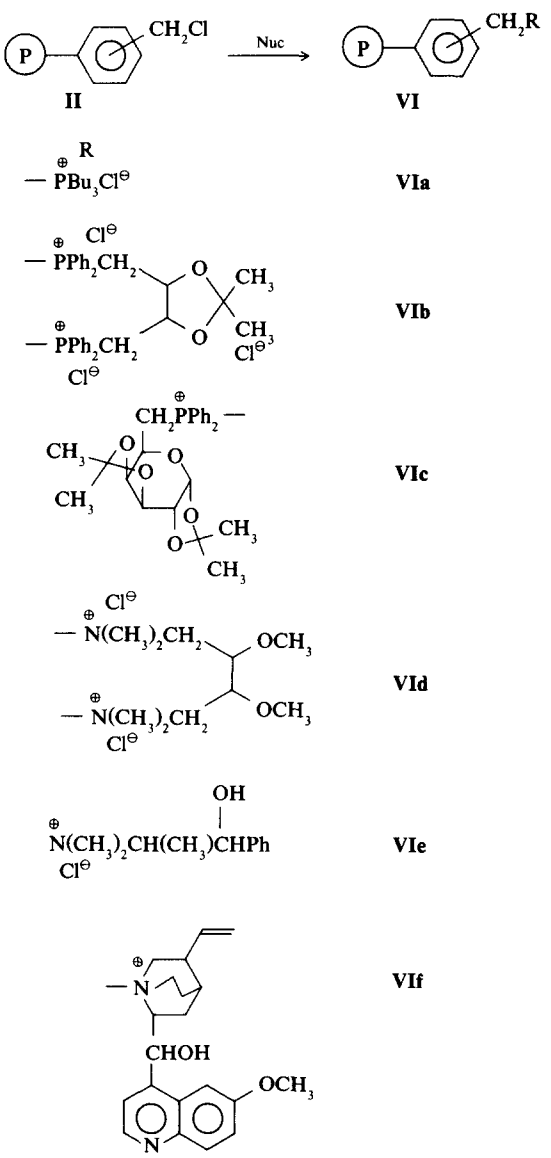
Resin	Carbon	Hydrogen	Phosphorus	Nitrogen	Chlorine
Va	67.6	8.9	1.6	–	1.8
Vb	71.7	7.5	–	0.8	2.8
Vc	68.9	8.6	–	–	~0
Vd	75.1	7.5	–	1.8	1.1
Ve	72.1	7.0	2.4	–	4.9
VIa	67.2	10.1	8.1	–	9.0
VIb	68.6	6.6	4.9	–	14.4
VIc	67.1	6.9	7.0	–	7.7
VId	59.2	7.6	–	4.2	10.4
VIe	69.8	8.2	–	3.4	7.9
VIf	68.2	12.7	–	12.6	8.7

Table 2 Syntheses[a] of resins **VIa–f** (Scheme 4)

Resin VI	Resin II (g/mmol)	Nucleophile employed (g/mmol)	Temperature (°C)	Washing sequence	Extraction solvent
a	2.5/13.5	PBu_3 3/17.4	60	THF, THF/H_2O (50%), THF	THF
b	0.5/5.9	DIOP[b] 3/6.0	60	Acetone, THF/H_2O (50%), THF, ethanol	ethanol
c	2.0/11.7	DPPDIG[b] 1.8/4.3	60	H_2O, THF/H_2O (50%), THF	THF
d	1.5/8.8	DMDAB[c] 1.5/7.3	45	H_2O, THF/H_2O (50%), THF, acetone, toluene	toluene
e	2.6/15.3	*N*-methylephedrine 2.9/16.2	55	H_2O, THF/H_2O (50%), THF, acetone, toluene	toluene
f	2.5/14.7	quinine 6.2/16.4	40	H_2O, acetone/H_2O (50%), acetone, CH_2Cl_2	acetone

[a]30-40ml dimethylformamide, 5 days
[b]DIOP, DPPDIG: see catalyst precursors
[c]DMDAB, (S,S)–(+)–2,3-dimethoxy-1,4-bis(dimethylamino)butane

Scheme 4



ethoxy)ethoxy)ethanol (10 g, 61 mmol) and sodium hydride (1.5 g, 62.5 mmol) in toluene. The mixture was heated for 4 days and the resin worked up as for resin **IIIa**. Microanalysis: C, 74.7; H, 6.6; Br, 4.9. I.r. (KBr) 1102 cm^{-1} C–O–C.

Resin **IXb** (*Scheme 5*). This was prepared from resin **IX** (1.2 g) using tributylphosphine (2.5 g, 12.4 mmol) as described for resin **IVa**. Microanalysis: C, 69.8; H, 7.7;, P, 3.7; Br, 12.3.

Resin **IXc** (*Scheme 5*). This was prepared from resin **IX** (1.3 g) using excess dimethylamino-1-propanol in dimethylformamide (30 ml). In this case the temperature

Scheme 5

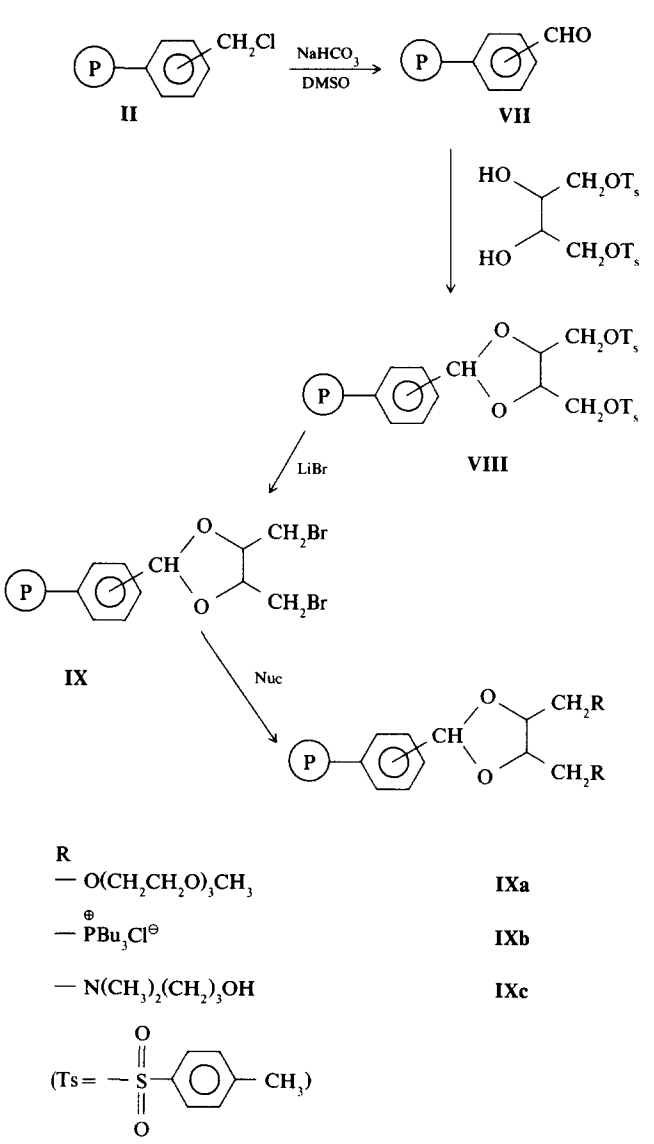


Table 3 Functional group content[a] or loading of resin catalysts **IVa–f** and **Va–e**

Resin	Galactose, G, or Fructose, F, content (%)		Phosphonium salt (%)	Ammonium Salt (%)	Oligoether (%)
IVi	G	31	–	–	–
IVii	G	32	–	–	–
IVa	G	32	40	–	–
IVb	G	31	–	28	–
IVc	G	32	–	52	–
IVd	G	32	–	–	52
IVe	G	32	–	–	44
IVf	G	32	13	–	–
Vi	F	59	–	–	–
Vii	F	56	–	–	–
Viii	F	31	–	–	–
Va	F	56	18	–	–
Vb	F	56	–	18	–
Vc	F	59	–	–	25
Vd	F	56	–	–	32
Ve	F	31	9	–	–

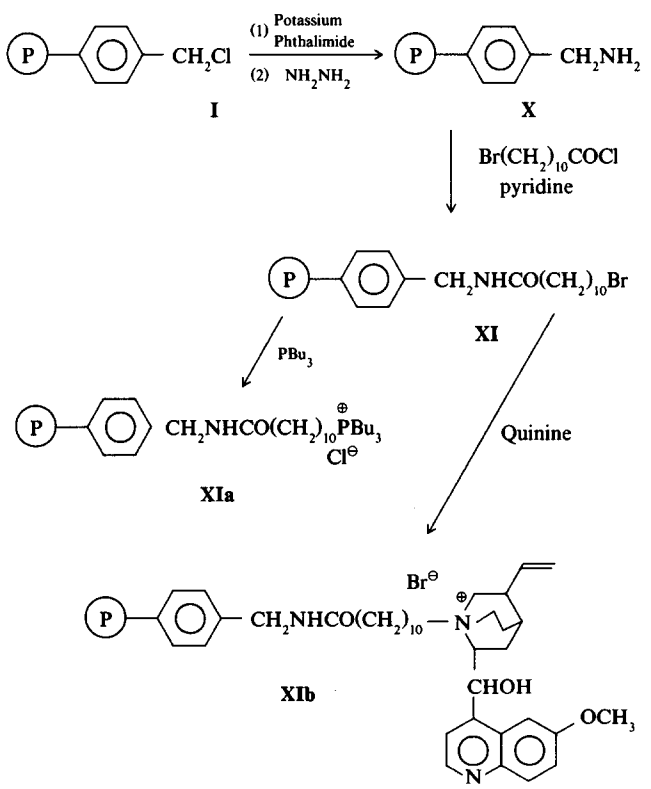
[a]% of resin aromatic groups; estimated from elemental microanalyses (P, N and Cl difference, as appropriate)

was restricted to 35°C for 5 days. Resin work-up was as before for resin **IIIa**. Microanalysis: C, 63.3; H, 7.1; N, 2.1; Br, 13.9. I.r. (KBr): 3400–3250 cm^{-1} OOH.

Resin **IXa** (*Scheme 6*). This was prepared from resin **XI** (1.5 g) using tributylphosphine (2.5 g, 12.4 mmol) in dimethylformamide as described for resin **IVa**. Microanalysis: C, 73.1; H, 8.7; N, 3.5; P, 2.6; Br, 7.8.

Resin **XIb** (*Scheme 6*). This was prepared similarly from resin **XI** (1.1 g) using quinine (1.6 g, 4.9 mmol) in dimethylformamide (40 ml). The work-up of the resin was the same but acetone was used in place of THF. Microanalysis: C, 69.4; H, 6.8; N, 3.7; Br, 5.2.

Scheme 6

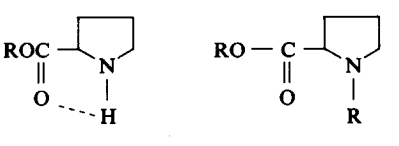


RESULTS AND DISCUSSION

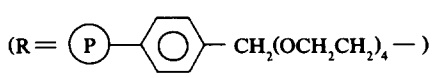
The syntheses of catalyst precursors was achieved with slight modifications to literature procedures. Each material yielded a consistent ^1H n.m.r. spectrum, and melting points and optical rotations were as expected within small errors.

Characterization of resin modifications is always difficult, and the present syntheses were no exception. In general considerable reliance was placed on the *FT*i.r. difference spectra and on elemental microanalyses. The appearance or disappearance of a heteroatom, e.g. Cl, Br, S, N and P, was taken as a good indication of success of a particular transformation, and quantitative analytical data on these were used to estimate the degree of chemical modification achieved.

In the case of resins **IIIa–e**, *Scheme 2*, virtually quantitative loss of sulphur was achieved, indicating a loading of ~14% of aromatic groups with oligoether chains terminally substituted with the required optically active group. One complication, however, arose with resin **IIIa**. The *FT*i.r. spectrum confirmed complete loss of the tosyl bands at 1360 and 1177 cm^{-1}. However, these were replaced by two independent carbonyl stretches at 1740 and 1670 cm^{-1}. The peak at 1670 cm^{-1} is quite low for a normal ester carbonyl and suggests some degree of hydrogen bonding, and indeed such a structure is the one anticipated (**E**). The peak at 1740 cm^{-1}, however, is more consistent with a normal ester possibly indicating that some of the amino groups have reacted further with a second tosylate to form the structure **F**.



(E) (F)

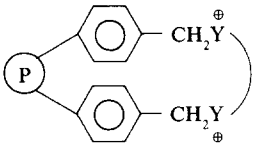


Previous experience with achiral catalysts similar to these[19] has indicated that in solid/liquid phase separated systems the polymer-bound oligoether is able to complex K^+ ions and transfer its attendant nucleophilic anion into an organic phase. In this instance such complexation would be expected to bring the terminal chiral group to the site of subsequent reaction, e.g. an S_{N_2} displacement.

In the case of resins **IVa–f**, *Scheme 3*, the approach was simply to introduce a chiral protected galactose residue onto a resin along with a number of different achiral groups known to function as effective phase transfer catalysts (PTC). In these the stereochemical relationship of the optically active species and the catalyst itself was not well defined. *Table 3* indicates the loadings of each species achieved as calculated from elemental microanalyses. An analogous group of catalysts, resins **Va–e**, were prepared with a fructose derivative and the results for these also appear in *Table 3*.

Protected monosaccharides have previously been successfully attached to polystyrene and styrene[32] and, as here, the reaction was efficient. In the present case, however, there was a possibility that the subsequent attachment of the PTC group might displace some or all of the saccharide. In practice, the *FT*i.r. spectra showed that the isopropylidene protecting groups, and hence the saccharides, were unaffected, confirming the stability of the bound sugar residues under the conditions employed.

In the case of resins **VIb–f**, the stereochemical relationship between the optically active species and the PTC residue is well-defined; indeed it can be argued that they are indeed a single structure. Species similar to **VIe** and **VIf** have been described before[6,7,10] but **VIb–d** are new. In each case an optically active amine or phosphine was reacted directly with chloromethylated resin and moderate to good loadings of each onium salt were achieved (*Table 4*). In the case of resin **VIb** synthesized from the diphosphine, DIOP, and resin **VId** from the commercial diamine (S,S)-(+)-2,3-dimethoxy-1,4-bis(dimethylamino) butane the analyses suggested the preferential formation of the bridging di-onium structures, **G**. No other structural evidence is to hand, however,



(G)

to confirm this. In the case of the quininium species, resin **VIf**, attachment to the resin is shown via the aliphatic ammonium ion. This is the structure indicated by previous workers[10]. However, if linear soluble poly(chloromethylstyrene) is reacted with quinine under similar conditions an insoluble gel results[33]. This is almost certainly a crosslinked material strongly indicating at least partial reaction with the aromatic nitrogen centre. The structure **VIf** indicated in *Scheme 4* is therefore almost certainly an over-simplification.

In synthesizing resins **IXa–c**, the aim was to introduce an optically active structure onto the support, and in a subsequent reaction attach specifically to that structure, groups capable of functioning as PTC. In this respect the approach was different to that used for resins **VIb–f**, but nevertheless the final catalysts had a definitive stereochemical relationship between their chiral centres and the PTC group. *Table 5* summarizes the loadings of the various groups which were achieved. Although conversion of chloromethyl groups to aldehydic ones was achieved in good yield, the subsequent attachment of (−)-1,4-ditosylthreitol to effectively protect the aldehyde function was much less successful. The subsequent modifications proceeded more satisfactorily to give acceptable final loadings of the required catalyst structures. Resin **IXa** might be regarded as an 'open-chain' chiral crown ether. Recently a chiral crown containing monomer has been described[34] providing an alternative route to polymeric catalysts of this type. Resin **IXb** might also be regarded as a chiral form of the 'multi-site' phase transfer catalysts recently reported[35].

Resin **XIb** was synthesized specifically to compare the activity of known supported quinium salts with that of a quinium salt bound by a 'spacer-arm' to the resin. The mobility and accessibility of catalyst residues may have a significant influence on the success or failure of asymmetric induction using optically active species and this point is discussed further in the following paper. During this work a similar 'spacer-arm' bound species was described by Kobayashi[10]. The loadings achieved in the present work are summarized in *Table 6*. The conversion of chloromethyl to aminomethyl groups was virtually quantitative and the spacer arm content achieved was also

Table 4 Functional group content of loading[a] of resins **VIa–f**

Resin	Chloromethyl	Phosphonium	Ammonium
II[b]	~84	–	–
VIa[b]	6	78	–
VIb	54	30	–
VIc	42	42	–
VId	12	–	72
VIe	22	–	62
VIf	32	–	52

[a] % of resin aromatic groups; estimated from elemental microanalyses
[b] non-chiral

Table 5 Functional group content of loading[a] of resins IXa–c and their precursors

Resin	Aldehydic as in **VI**	Tosylacetal as in **VIII**	Bromoacetal as in **IX**	Ammonium salt	Phosphonium salt	Oligoether
VII	81	–	–	–	–	–
VIII	60	21	–	–	–	–
IX	60	~1	20	–	–	–
IXa	60	~1	7	–	13	–
IXb	60	~1	5	15	–	–
IXc	60	~1	6	–	–	14

[a] % of resin aromatic groups; estimated from elemental microanalyses

Table 6 Functional group content or loading[a] of resins **XIa** and **b** and their precursors

Resin	Amine as in **X**	Bromide as in **XI**	Ammonium salt	Phosphonium salt
X[b]	84	–	–	–
XI[b]	20	64	–	–
XIa[b]	20	38	–	26
XIb	20	32	32	–

[a] % of resin aromatic groups; estimated from elemental
[b] Non-chiral

most satisfactory. Further modification of resin **XI** to yield resins **XIa** and **b** was achieved in ~50% yield providing good loadings of the required onium salts.

Since by design all of the resin-bound species synthesized were crosslinked it was impossible to characterize their overall optical activity into terms of optical rotation. However, in general the conditions employed to attach catalysts were no more stringent than those used in modifying optically active low molecular species with full retention of optical activity. Indeed in general the linkage reactions did not intimately involve the various chiral centres of the molecules in question except perhaps for resins **IIIa**, **b** and **c**. In the case of the monosaccharide containing species the presence of the isopropylidene protecting groups was confirmed by *FT*i.r., and confirms the chiral nature of these catalysts.

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