

Some novel polymer-supported optically active phase transfer catalysts: 2. Use in displacement, reduction, epoxidation and addition reactions

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The performance of 27 novel polymer-supported chiral phase transfer catalysts in a range of phase separated reactions has been studied. The later include a number of displacement reactions, sodium borohydride reductions of prochiral ketones, the epoxidation of chalcone, the addition of nitromethane to chalcone and the addition of thiophenol to cyclohexenone. Some of the reactions were performed under liquid/liquid conditions and others using solid/liquid. No systematic difference emerged between these. In general many of the catalysts provided fast reactions and good chemical yields of products. However, in no case was any significant enantiomeric excess achieved. The latter observation is discussed in the light of the reported behaviour of analogous non-supported catalytic systems, and suggestions proposed to explain these differences.

(Keywords: asymmetric; induction; phase transfer catalysis)

INTRODUCTION

The possibility of achieving enantioselectivity has been examined in a number of phase transfer catalysed (PTC) reactions using, in the main, low molecular onium salts of ephedrine and its relatives and the cinchona alkaloids, notably quinine, as the chiral catalyst¹⁻¹¹. The use of these materials has also been reviewed recently by Wynberg¹². Cram¹³ has employed chiral crown ethers for the same purpose and his results are vitally important because his catalysts represent one of the first attempts to develop novel structures without the inherent disadvantages of ammonium salts. Chiral onium salts derived from methionine have also been reported by Colonna and his coworkers¹⁴.

Among the reactions which have been studied are S_N2 displacements on racemic secondary halides^{3,6,8}, sodium borohydride reductions of prochiral ketones^{3,7}, epoxidations of prochiral α, β unsaturated ketones¹¹, and nitromethane and thiol Michael additions to α, β unsaturated ketones^{2,5,9}. Some confusion still remains in the literature concerning the effectiveness of asymmetric induction using chiral ammonium salts in these and other reactions, and Dehmlow and his coworkers¹ have made a careful appraisal of the situation. The results using polymer-supported chiral ammonium salts are far fewer and the effectiveness of these catalysts seems even more problematical. In this paper we report on the use of a wide range of novel polymer-supported catalysts in a cross-section of PTC reactions. In addition to those catalysts described in the previous paper, we have also used a few

low molecular species to provide a baseline for comparing the chemical activity of our systems.

EXPERIMENTAL

Materials

All materials were obtained from routine sources and in general were used as supplied. When required dry, toluene was distilled from calcium hydride. Potassium phenoxide was prepared as described by Kornblum *et al.*¹⁵. 2-Phenylethanol was made by a standard reduction of acetophenone using sodium borohydride in ethanol.

Catalysts

The catalysts tetrabutylphosphonium chloride, tetrabutylammonium bromide, 2(2-(2-methoxyethoxy)ethoxy)ethanol, MEEE, triethylene glycol dimethyl ether (triglyme) and dibenzo-18-crown-6-ether (D-18-C-6) were used as supplied (Fluka). Benzylquininium chloride (BQC) was prepared by quarternization of quinine with benzyl chloride in toluene/ethanol and was recrystallized from ethanol. M.p. 169°–171°C (literature m.p.¹⁶ 169°–172°C). $[\alpha]_D^{20} = -210$ (c 0.5 EtOH) [literature¹⁶ $[\alpha]_D^{20} = -212$ c 0.5 EtOH].

The various resin catalysts used were synthesized as described in the preceding paper and the same designations are employed in this report.

Synthesis of chromatographic standards

Ethyl 2-phenoxypropionate. Ethyl 2-bromopropionate (9 g, 49.6 mmol), potassium phenoxide (11 g, 83.3 mmol) and polymer catalyst (resin VIa, 0.9 g) were added to toluene (100 ml) in a 250 ml flask. This mixture was

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agitated at room temperature overnight and after filtration the crude product was recovered by evaporation of the filtrate. Vacuum distillation of this yielded pure ethyl-2-phenoxypropionate (7.2 g, 75%) which gave one peak in gas liquid chromatographic (g.l.c.) analysis.

Ethyl 2-azidopropionate. Ethyl 2-bromopropionate (5 g, 27.6 mmol), sodium azide (1.8 g, 27.7 mmol) and tetrabutylphosphonium chloride (0.6 g, 0.2 mmol) were added to water (10 ml) in a 100 ml conical flask. The solution was stirred at room temperature for 16 h after which it was extracted with methylene chloride (3 × 100 ml). The organic phase was then dried over anhydrous sodium sulphate and the solvent evaporated to yield the crude product. Vacuum distillation yielded pure ethyl-2-azidopropionate (2.9 g, 69%) which gave one peak in g.l.c. analysis.

Chalcone epoxide. Chalcone (5 g, 24 mmol), hydrogen peroxide (30 vol., 5 ml in 25 ml water) and potassium carbonate (1.7 g, 16 mmol) were added to ethanol (30 ml) and the mixture stirred for 18 h at room temperature. The mixture was then filtered and the filtrate cooled to ~5°C. This caused precipitation of the crude product which was collected. Column chromatography on silica using methylene chloride as the eluent yield the pure epoxide (4.4 g, 82%). M.p. = 79–80°C (literature¹⁷ 79–79.5°C). ¹H n.m.r. (CDCl₃): 4.1δ, d, 1H; 4.3δ, d, 1H; 7.4δ, m, 8H; 8.0δ, m, 2H.

3-Phenyl-4-nitro-1-phenylbutan-2-one. Chalcone (7.5 g, 36 mmol), nitromethane (33 g, 0.5 mol), anhydrous potassium fluoride (3.4 g, 58.6 mmol) and tetrabutyl phosphonium chloride (0.5 g, 1.7 mmol) were added to dry toluene (300 ml). This mixture was stirred at room temperature for 3 days, after which chloroform (150 ml) was added and the solution extracted with hydrochloric acid (2 M) and water. The organic phase was dried over anhydrous sodium sulphate and the solvent evaporated to yield the crude product. This was chromatographed on silica using diethyl ether/light petroleum (B.pt. 40–60°C) (1/9 then 3/7) to yield pure product (6.4 g, 66%). M.pt. = 101°C (literature¹⁸ M.pt. = 101–102°C). ¹H n.m.r. (CDCl₃): 3.3δ, d, 2H; 3.4δ, m, 1H; 4.6δ, m, 2H; 7.3δ, m, 8H; 7.9δ, m, 2H.

3-Phenylthiocyclohexanone. Thiophenol (5.5 g, 0.05 mol), cyclohexen-2-one (6.0 g, 0.067 mol), anhydrous potassium fluoride (4.4 g, 0.075 mol) and tetrabutyl phosphonium chloride (0.06 g, 0.2 mmol) were added to dry toluene (125 ml). This mixture was stirred at room temperature overnight, then diluted with methylene chloride (50 ml). The organic layer was washed well with aqueous sodium hydroxide (10%) and water, and was evaporated to dryness after initial drying with anhydrous sodium sulphate. The crude residue was chromatographed on silica using diethyl ether/light petroleum (b.p. 40–60°C) (1/9 then 1/1) as the eluent. The yield of pure product was 5.7 g, 56%. ¹H n.m.r. (CDCl₃): 1.5–2.5δ, m, 9H; 3.2–3.6δ, m, 1H; 7.2–7.6δ, m, 5H.

Phase transfer catalysed reactions studied Displacement reactions.

(i) **Phenoxide displacement on 2-bromobutane.** Typically a 2-bromobutane (0.48 mmol) solution in toluene (2 ml) was heated to 110°C with catalyst (0.075 mmol) and powdered solid potassium phenoxide (2.0 mmol). The mixture was vigorously stirred using a small magnetic follower and the loss of 2-bromobutane was monitored by quantitative gas-liquid chromatography (g.l.c.) (Table 1). The polymeric catalyst was filtered off and the optical rotation of the reaction mixture measured.

(ii) **Phenoxide displacements on ethyl 2-bromopropionate.** These were carried out using the same quantities of reagents as above, in this case, however, the temperature was maintained at 30°C. Both substrate and product were monitored by g.l.c.

(iii) **Azide displacements on ethyl 2-bromopropionate.** Typically an ethyl 2-bromopropionate (0.48 mmol) solution in tetrahydrofuran (2 ml) and catalyst (0.075 mmol) were heated at 65°C with powdered sodium azide (2.5 mmol) with vigorous stirring. Analysis of the reaction mixture was carried out as before (Table 1).

The liquid/liquid phase separated modification of this, tetrahydrofuran was replaced by toluene (2 ml) and the azide salt was dissolved in water (2 ml). The reaction temperature was also restricted to 25°C.

Table 1 G.l.c.^a and h.p.l.c.^b conditions used for analysis of substrates and products

Substrate	Product	Internal standard	Stationary phase	Oven temp (°C)	Column temp (°C)	Carrier gas lb/in ²	Eluent H ₂ O: CH ₃ OH	Flow rate ml min ⁻¹	Detector wave-length (nm)
2-Bromobutane	Not detected ^c	Nonane	2.5% E301	130	90	15	—	—	—
Ethyl 2-bromo propionate	Ethyl 2-phenoxy propionate	Decane	2.5% Apiezon	130	100	20	—	—	—
Ethyl-2-bromo propionate	Ethyl-2-azido propionate	Decane	2.5% Apiezon	130	90	10	—	—	—
Octan-2-one	Octan-2-ol	1,2-Dichloro-benzene	2.5% E301	150	110	15	—	—	—
Acetophenone	2-Phenyl-ethanol	1,2-Dichlorobenzene	2.5% E301	150	110	15	—	—	—
Chalcone	Chalcone epoxide	Acenaphthylene	ODS Pellosil	—	r.t.	—	63:35	1.5	354
Chalcone	3-Phenyl-4-nitro-1-phenylbutan-2-one	Acenaphthylene	ODS Pellosil	—	r.t.	—	60:40	1.4	354
Cyclohexen-2-one	3-Phenylthiocyclohexanone	Cumene	ODS Pellosil	—	r.t.	—	65:35	0.6	354

^a Perkin Elmer F11

^b Altex 110 pump, Cecil 212A detector

^c Phenyl ether product did not appear in the g.l.c. trace

Sodium borohydride reductions

Typically octan-2-one or acetophenone (0.48 mmol) in 1,2-dichloroethane (2 ml) and water (0.1 ml, usually) were stirred with catalyst (0.075 mmol) and sodium borohydride (4.2 mmol). Reactions were performed at both 75°C and 30°C. The loss of ketone and formation of alcohol were monitored by quantitative g.l.c. (Table 1) and the optical rotations of reaction mixtures were measured after filtering off the polymeric catalyst.

Chalcone epoxidations

Typically a chalcone (10.2 mmol) solution in toluene (15 ml), hydrogen peroxide (10 ml, 30 vol), sodium hydroxide (18.8 mmol) and catalyst (0.375 mmol) were stirred together with cooling for an initial period of 15 min, and thereafter at room temperature for 3 days. The reaction was followed by high pressure liquid chromatography (Table 1) and optical rotations of reaction mixtures were measured as before.

Nitromethane additions to chalcone

Typically a chalcone (7.7 mmol) solution in toluene (25 ml), nitromethane (18.6 mmol), anhydrous potassium fluoride (9.9 mmol) and catalyst (0.37 mmol) were stirred together at room temperature for 3–10 days (see Table 8). The reaction mixture was monitored as for the epoxidation reaction (Table 1).

Thiophenol additions to cyclohexen-2-one

Typically a cyclohexen-2-one (5 mmol) solution in cumene (15 ml), thiophenol (4 mmol), anhydrous potassium fluoride (6 mmol) and catalyst (0.01 mmol) were stirred together at room temperature under an atmosphere of nitrogen for 6 h. The reaction was monitored as for the nitromethane additions (Table 1).

RESULTS AND DISCUSSION

The results of phenoxide displacements on 2-bromo-

butane and ethyl 2-bromopropionate are shown in Table 2, while Tables 3 and 4 summarize the results for the azide displacements under solid/liquid and liquid/liquid conditions respectively. Table 5 shows the results of the sodium borohydride reductions of octan-2-one and Table 6 analogous reductions of acetophenone. Tables 7 and 8 summarize the results of the epoxidations and nitromethane additions to chalcone, and Table 9 the thiophenol additions to cyclohexen-2-one. In view of the large number of resin catalysts prepared and the wide range of reactions chosen for study it was impossible to use all catalysts in all reactions, and as a result an attempt was made to use representatives of each catalytic group in the different reactions, subject to their availability.

Table 3 Sodium azide displacements on ethyl 2-bromopropionate under solid/liquid conditions^a

Catalyst	Weight of catalyst (mg)	Time (h)	Loss of substrate (%)	Yield of product (%)
None	—	6	3	3
Bu ₄ P [⊕] Cl [⊖] ^c	23	1.5	90	90
Resin VIa ^c	32	6	74	72
Resin XIa ^c	44	6	81	80
Resin IVa	48	7.5	36	36 ^d
Resin IVf	75	6	46	44 ^d
Resin Va	90	5	50	47 ^d
Resin Vb	65	5.5	50	48 ^d
Resin Vd	50	7	14	12 ^d
Resin Ve	98	5	44	44 ^d
Resin VIb	40	6	30	26 ^d
Resin VIc	43	3	58	57 ^d
Resin IXb	62	6	60	56 ^d
Resin XIb	84	7	20	22 ^d

^a See Experimental for conditions

^b Corresponds to 0.075 mmol of the phase transfer catalytic moiety

^c Non-chiral

^d Literature³² [α]_D^{r.t.} = 18.7°, found ~0.1°, corresponding to <1% enantiometric excess

Table 2 Phenoxide displacements on 2-bromobutane and ethyl 2-bromopropionate^a

Substrate	Catalyst	Weight of catalyst (mg) ^b	Time (h)	Loss of substrate (%)	Yield of product (%)
2-Bromobutane	None	—	6	0	— ^d
	MEEE ^c	15	3	70	—
	Resin XIa ^c	195	3	93	—
	Resin IIIa	30	6	92	— ^e
	Resin IIIb	33	6	87	— ^e
	Resin IIIc	28	6	69	— ^e
	Resin IIId	15.6	6	68	— ^e
	Resin IIIe	15.5	6	80	— ^e
Ethyl 2-bromopropionate	None	—	24	8	5
	Pu ₄ P [⊕] Cl [⊖] ^c	23	3	77	75
	Resin VIa ^c	33	7	41	—
			24	76	75
	Resin XIa	44	7	76	73
	Resin IVd	50	24	31	28 ^f
	Resin IVf	75	6.5	54	51 ^f
	Resin Ve	97	7.5	45	43 ^f
	Resin VIb	39	24	28	27 ^f
	Resin VIc	58	24	20	18 ^f

^a See Experimental for conditions

^b Corresponds to 0.075 mmol of the phase transfer catalytic moiety

^c Non-chiral

^d Not detected by g.l.c. technique

^e Literature³¹ [α]_D^{r.t.} = 27.3°, found ~0.1°, corresponding to <1% enantiometric excess

^f Literature⁶ [α]_D^{r.t.} = 44.0°, found ~0.1°, corresponding to <1% enantiometric excess

Table 4 Sodium azide displacements on ethyl 2-bromopropionate under liquid/liquid conditions^a

Catalyst	Weight of catalyst ^b (mg)	Time (h)	Loss of substrate (%)	Yield of product (%)
None	—	{ 8 24	{ 7 12	{ 7 10
Resin XIa ^c	44	5	84	82
Resin IVa	97	{ 7 24	{ 17 56	{ — 56 ^d
Resin IVf	75	7.5	53	49 ^d
Resin Va	90	{ 7 24	{ 25 63	{ — 61 ^d
Resin Ve	98	6	53	54 ^d
Resin VIb	39	7	35	33 ^d
Resin VIc	43	6	59	56 ^d
Resin VIId	25	{ 7 24	{ 15 33	{ — 32 ^d

^a See Experimental for conditions

^b Corresponds to 0.075 mmol of the phase transfer catalytic moiety

^c Non-chiral

^d See footnote d in Table 3

Table 5 Sodium borohydride reductions of octan-2-one^a

Catalyst	Weight of catalyst (mg)	Temp. (°C)	Water (ml)	Time (h)	Yield of (%)
None	{ — — — —	{ 75 75 75 30	{ — 0.1 0.5 0.1	{ 7 7 7 24	{ ~0 ~0 4 3
Triglyme ^c	100	75	—	7	~100
Bu ₄ P [⊕] Cl [⊖] ^c	23	{ 75 30	{ 0.1 0.1	{ 3 7	{ ~100 59
Resin VIa ^c	33	{ 75 30	{ 0.1 0.1	{ 7.5 24	{ 96 78
Resin XIa	40	75	0.1	6.5	59 ^d
Resin IIIId	46	75	—	7	42 ^d
Resin IVa	97	30	0.1	24	47 ^d
Resin IVd	50	30	0.1	24	51 ^d
Resin IVf	75	30	0.1	24	68 ^d
Resin Vc	50	30	0.1	24	21 ^d
Resin Ve	98	30	0.1	24	83 ^d
Resin VIb	40	{ 75 30	{ 0.1 0.1	{ 7.5 24	{ 54 ^d 67 ^d
Resin VIc	58	75	0.1	7.5	87 ^d
Resin VIId	27	{ 30 75	{ 0.1 0.1	{ 24 7.5	{ 82 ^d 56 ^d

^a See Experimental for conditions

^b Corresponds to 0.075 mmol of phase transfer catalytic moiety

^c Non-chiral

^d Literature³³ [α]_D^{r.t.} = 19.4°, found, ~0.1°, corresponding to <1% enantiomeric excess

Chemical yields

In all the reactions studied the experimental conditions were carefully chosen to ensure virtually no reaction in the absence of a phase transfer catalyst (PTC) and the first entry in each of Tables 2–9 confirms this. Such a blank reaction is very important not only in assessing chemical yields but also in interpreting any enantioselectivity observed, and unfortunately some authors do not report such controls. In the case of the displacement reactions (Tables 2, 3 and 4) the starting substrate in each case was a racemic mixture and the aim was to select kinetically one of these enantiomers, in preference to the other, for conversion to product. In these reactions, therefore, there was a positive attempt made to limit chemical conversions to 50% to maximize enantiomeric excesses.

All of the resin catalysts examined proved to be effective to varying degrees. Many were as active as conventional low molecular weight species such as Bu₄P[⊕]Cl[⊖], while simultaneously being experimentally much more convenient. The only significant exception to this was in the epoxidation of chalcone (Table 7) where resins generally performed very poorly. Attempts to improve the situation by using only finely crushed polymers did meet with some success, and indeed the results quoted refer to catalysts used in this condition. This reaction was one in which there was a discrete aqueous phase (i.e. a liquid/liquid system) and this might have been a factor in the poor performance of resin catalysts. However, in the case of the

Table 6 Sodium borohydride reductions of acetophenone^a

Catalyst	Weight of catalyst ^b (mg)	Water (ml)	Time (h)	Yield of 1-phenyl-ethanol
None	—	{ 0.1 0.1	{ 6 24	{ ~0 4
Bu ₄ P [⊕] Cl [⊖] ^c	23	0.1	2	~100
Triglyme ^c	50	—	6	63
D-18-C-6 ^c	50	—	1	85
Resin XIa ^c	39	0.1	4	94
Resin IIIa	50 ^d	—	72	84 ^f
Resin IIIb	50 ^d	—	24	94 ^f
Resin IIIc	50 ^d	—	72	84 ^f
Resin IIId	50 ^e	—	24	97 ^f
Resin IIIe	50 ^e	—	24	98 ^f
Resin IVa	97	0.1	7	99 ^f
Resin IVd	50	0.1	24	61 ^f
Resin Vc	50	0.1	24	79 ^f
Resin VIb	39	0.1	24	99 ^f
Resin VIc	58	0.1	7.5	81 ^f
Resin VIId	25	0.1	24	96 ^f

^a See Experimental for conditions

^b Corresponds to 0.075 mmol of phase transfer catalytic moiety

^c Non-chiral

^d Fixed weight comparison (mmol of catalyst 0.13)

^e Fixed weight comparison (mmol of catalyst 0.23)

^f Literature⁷ [α]_D^{r.t.} = 42.2°, found, ~0.1°, corresponding to <1% enantiomeric excess

Table 7 Epoxidation of chalcone^a

Catalyst ^b	Weight of catalyst ^c (g)	Time (days)	Loss of chalcone (%)	Yield of epoxide (%)
None	—	3	2	1
Bu ₄ P [⊕] Cl [⊖] ^c	0.11	3	~100	98
Bu ₄ N [⊕] Br [⊖] ^d	0.12	3	44	40
Resin VIa ^d	0.14	3	23	21
Resin IVa	0.24	3	6	6 ^f
Resin IVb	0.35	3	5	5 ^f
Resin IVc	0.36	3	5	3 ^f
Resin IVf	0.37	3	3	2 ^f
Resin Va	0.45	3	9	6 ^f
Resin Vb	0.33 ^e	3	69	63 ^f
Resin Ve	0.50	3	10	7 ^f
Resin VIc	0.17	3	20	25 ^f
Resin VIe	0.15	3	16	15 ^f
Resin VIId	0.19	3	8	8 ^f
Resin IXb	0.31	3	22	21 ^f

^a See Experimental for conditions

^b All resin catalysts were crushed before use

^c Corresponds to 0.37 mmol of phase transfer catalytic moiety

^d Non-chiral

^e 0.18 mmol catalyst

^f Literature¹¹ [α]_D^{r.t.} minimum value = 51.0°, found ~0.01°, corresponding to <0.1% enantiomeric excess

Table 8 Nitromethane addition to chalcone^a

Catalyst ^b	Weight of catalyst ^c (g)	Time (days)	Loss of chalcone (%)	Yield of product (%)
None	—	{ 3 10	2 9	~0 6
Bu ₄ P [⊕] Cl [⊖] ^d	0.12	3	~100	96
Bu ₄ N [⊕] Br [⊖] ^d	0.12	3	68	64
BQC ^d	0.33	3	74	68
Resin VIa ^d	0.14	3	89	86
Resin IVa	0.16	3	~100	98 ^e
Resin VIc	0.17	{ 3 10	30 ~100	26 ^e ~100 ^e
Resin VIId	0.13	10	71	67 ^e
Resin VIIf	0.18	10	87	82 ^e
Resin IXb	0.31	3	15	10 ^e
Resin IXc	0.25	7	~100	96 ^e

^a See Experimental for conditions^b All resin catalysts were crushed before use^c Corresponds to 0.37 mmol of phase transfer catalytic moiety^d Non-chiral^e Literature² [α]_D^{r.t.} = 40.8°, found ~0.1° corresponding to ~0.1% enantiomeric excess

azide ion displacements on ethyl 2-bromopropionate, resin catalysts were effective both in the solid/liquid (Table 3) and liquid/liquid (Table 4) systems.

The majority of reactions were performed under solid/liquid PTC conditions with no discrete aqueous phase present. Reports of 'solid' resin catalysts being active under such conditions are few in number¹⁹, but this wide range of reactions and PTC moieties confirms that such catalysis can be extremely effective and experimentally most convenient.

A comparison of the non-chiral species resin VIa and resin XIa is possible from Tables 2, 4 and 5. These are both closely related to Bu₄P[⊕]Cl[⊖], with the phosphonium ion centre in XIa being attached to the macromolecular backbone by a spacer arm. In the two displacement reactions the spacer arm has a clear advantageous effect, whereas in the octan-2-one reductions the reverse seems to be the case.

Another interesting comparison arises with resins IVf, Ve and VIb. All of these contain phosphonium ion derived from DIOP, with IVf in addition carrying galactose derivatives, and Ve, fructose derived species. Generally the effectiveness of IVf and Ve are similar, and both are more active than VIb. A number of factors may play a role in this. The overall polarity of the first two resins is likely to be higher, and the balance between the overall polar and non-polar character of polymer-supported PTC species (as opposed to purely microenvironmental features) is now widely believed to be a significant factor in controlling activity^{20,21}. A concurrent feature concerns the reaction of DIOP with polymer chloromethyl groups. In VIb the density of chloromethyl groups available for reaction with DIOP is high and as mentioned in the previous paper significant reaction almost certainly occurs with both phosphine groups, effectively creating additional crosslinks. In IVf and Ve many chloromethyl groups are consumed in the initial attachment of the sugar residues, hence the likelihood of additional crosslinking on reaction with DIOP will be reduced. Thus VIb is likely to be a more impenetrable with lower PTC activity.

Asymmetric induction

The effectiveness of optically active PTC in achieving asymmetric induction is still a matter of debate¹. However, the positive results of a number of Michael additions^{3,5} seem to be genuine and have been reproduced in more than one laboratory. Thus chemical yields of ~100% have been accompanied by optical yields of ~25–35%^{2,9}. Another unambiguous case appears to be PTC epoxidations of chalcone using alkaline hydrogen peroxide and benzylated cinchona alkaloids as the optically active catalyst^{11,22}. Successful kinetic racemate resolutions have also been reported in displacement reactions on (\pm)ethyl 2-bromopropionate^{3,6,8} although confirmation from other laboratories does not appear to have emerged yet. Similarly asymmetric sodium borohydride reduction of ketones using chiral PTC^{3,7} would benefit from further investigation. Probably the most optimistic result, however, has been from Cram and his coworkers¹³ who have reported optical purities up to ~99% in Michael additions catalysed by chiral crown ethers.

In the case of polymer-supported analogues some encouragement was provided by Colonna and his coworkers²³ who reported that in the Darzens reaction enantiomeric excesses rose from ~2.5% in the case of low molecular weight chiral catalysts, to ~20–25% when analogous catalysts were attached to resins. In general, this early optimism has not been followed by any significant success. There have been reports of small levels of induction^{24,25} but how significant these are is difficult to say. Certainly in the case of chiral onium salts derived from methionine, attachment to a polymer support did not improve the zero enantioselectivity displayed by the low molecular weight analogue²⁶.

In the present work, despite a wide range of novel catalysts being employed in a cross-section of PTC reactions, no significant inductions were observed. In general, the high chemical yields achieved produced solutions with only very low optical rotations. (Tables 2–9) corresponding typically to <1% enantiomeric excesses and in general this augurs pessimistically for the future of such resin catalysts. Thus in the epoxidation of chalcone catalysed by the resin bound quinium species, VIIf (Table 7) in contrast to a previous report²⁴, we observed no induction. The attachment of the same species via a spacer

Table 9 Thiophenol addition to cyclohexen-2-one^a

Catalyst	Weight of catalyst ^b (mg)	Time (h)	Yield of product (%)
None	—	6	9
Bu ₄ P [⊕] Cl [⊖] ^c	30	6	96
Bu ₄ N [⊕] Br [⊖] ^c	32	6	94
Resin VIa ^c	39	6	69
Resin Va	105	6	62 ^d
Resin VIb	72	6	53 ^d
Resin VIc	46	6	60 ^d
Resin VIId	35	6	37 ^d
Resin VIe	42	6	38 ^d
Resin VIIf	60	6	79 ^d
Resin IXb	84	8	97 ^d
Resin IXc	70	6	43 ^d

^a See Experimental for conditions^b Corresponds to 0.1 mmol of phase transfer catalytic moiety^c Non-chiral^d Literature² [α]_D^{r.t.} = 64.6°, found ~0.1°, corresponding to <0.1% enantiomeric excess

arm, Resin XIb also produced no induction in the case of azide ion displacements (Table 3).

On the positive side, however, the lack of any significant optical rotation in the solutions of products seems to show that our optically active resin catalysts are generally stable under the conditions employed. In some instances, however, it can be argued that the decomposition of phosphonium salt species might release optically inactive materials, possibly accounting for the low enantiomeric excesses. However, this argument cannot be applied to all the catalytic species examined.

Thus at the present time the only systems with synthetic potential are the chalcone epoxidations catalysed by polyaminoacids reported by Colonna and Julia and their coworkers²⁷⁻²⁹. With these, optical yields up to ~96% have been reported²⁸. At the moment, however, asymmetric induction appears to arise in this reaction exclusively, and is complicated by the fact that the catalysts are partially degraded by hydrolysis under the reaction conditions²⁹. To what extent these systems are simple polymer-supported phase transfer catalysts therefore appears open to conjecture.

Why asymmetric induction is generally inhibited in polymer-supported systems is an interesting question. It is preferable for significant enantioselection, for the chiral catalyst to be involved in the transition state of the rate controlling process. With some resin catalysts the reaction might be controlled by diffusional processes within the matrix. The intervention of such a more highly activated process might facilitate reversibility during the potentially enantioselective process and hence effectively eliminate asymmetric induction. However, this does not seem to be an adequate explanation in most cases. The transition state should involve a specific interaction between the substrate and a tight ion-pair formed between the optically active phase transfer catalytic onium cation and the achiral nucleophilic anion. Such a tight ion pair would create in effect a pseudo chiral anion. This has been demonstrated by the appearance of induced circular dichroism in the absorption bands of achiral anions bound to chiral cations, in the case of both low molecular weight cations and polymer-bound analogues³⁰. Thus polymer-supported optically active PTC do in principle have the potential to form ion pairs capable of acting as chiral entities. The main problem, therefore, may involve the level of interaction within the ion pair, i.e. the 'tightness' of its conformation, or the specificity of interaction with the substrate. The latter factor might well be adversely influenced in polymer-supported systems versus non-supported ones and work directed towards defining more precisely this interaction may prove the most fruitful way forward.

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