Polystyrene-Anchored *Cinchona* Ammonium Salts: Easily Recoverable Phase-Transfer Catalysts for the Asymmetric Synthesis of α-Amino Acids

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Received: March 23, 2004; Accepted: June 7, 2004

Abstract: Cinchonidine, epicinchonidine, cinchonine or quinine have been *N*-anchored to cross-linked polystyrene (Merrifield resin) or grafted polystyrene (SynPhase™ Lanterns) affording polymer-supported chiral ammonium salts which are employed as phase-transfer catalysts in the asymmetric alkylation of *N*-(diphenylmethylene)glycine esters. These new polymeric catalysts can be easily recovered after the reaction by simple filtration and reused.

Keywords: alkylation; amino acids; ammonium salts; asymmetric synthesis; C–C bond formation; organic catalysis; phase-transfer catalysis

Introduction

Optically active α-amino acids are compounds of well-known interest, and their synthesis by simple and easily scalable procedures represents an important synthetic challenge that has boosted the development of numerous methodologies.[1] Amongst them, the enantioselective synthesis employing easily available and re-usable chiral catalysts presents clear synthetic advantages for large-scale procedures. Probably, the phase-transfer catalysis (PTC)[2] methodology applied to the asymmetric alkylation[1r] of glycine and alanine Schiff bases is the most simple and easy to scale-up. Thus, the advent in the early 1990 s of the enantioselective alkylation of amino acid imines under PTC conditions catalyzed by quaternized *Cinchona* alkaloids,[3] pioneered by O'Donnell[4] and improved by Corey[5] and Lygo,[6] allowed one to obtain impressive degrees of enantioselection using a very simple procedure. Moreover, dimeric,[7] trimeric[8] and even dendrimeric[9] *Cinchona* alkaloid-derived catalysts, as well as non-*Cinchona*-derived species such as spiro ammonium[10] and phosphonium salts,[11] TADDOL[12a, b] and other tartaric derivatives,[12c, d] guanidinium salts,[12e] binaphthyl-derived amines[12b,13] and salen-metal complexes[14] have also been used in this kind of asymmetric PTC alkylations.

Attaching the alkaloid-derived chiral catalyst to a solid support can be considered a step beyond in the development of the PTC methodology due to the easiness of its separation and possible recycling, the preparation and uses of all kinds of supported reagents being considered nowadays a fast-forward topic.[15] Thus, early in the 1970s *N*-methylephedrine and (*R*)-*N*,*N*-dimethyl-α-methylbenzylamine were immobilized on cross-linked chloromethylated polystyrene for different asymmetric transformations under PTC conditions, although with low ees.[16] *Cinchona* alkaloids allow different sites for polymer attachment. Thus, the bridgehead nitrogen of quinine was quaternized with cross-linked polystyrenes and the resulting polymers **1** (n = 1, 12; R = OMe; X = Cl, Br) were used in the enantioselective epoxidations of chalcone with poor results.[17] Moreover, cinchonidine was anchored to the Merrifield resin and the resulting polymeric ammonium salt **1** (n = 1, R = H, X = F) was used as PTC catalyst in Michael additions albeit also with low ees.[18]

The success of the mentioned O'Donnell-Corey-Lygo enantioselective PTC alkylation of glycinate imines[4–6] prompted the application of polymer-supported *Cinchona* alkaloid-derived ammonium salts to this protocol. Thus, our group[19] and others[20] have anchored cinchonidine to cross-linked polystyrene (**1**, n = 1, R = H, X = Cl) for the asymmetric alkylation of benzophenone

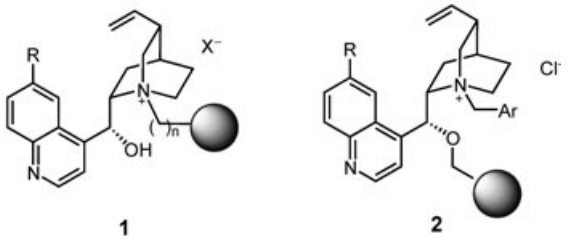


Figure 1.

  DOI: 10.1002/adsc.200404093

imine-derived glycine esters (up to 90% ee), whereas spacer chains of different lengths using cinchonidine and quinine (**1**, n = 4, 6, 8; R = H, OMe; X = Cl, I) have also been introduced achieving up to 81% ee.[21] In addition, *O*-supported polymeric derivatives such as **2**[22] (R = H, OMe; Ar = 9-anthryl) (up to 94% ee) as well as *N*- and *O*-alkylated polyethylene glycol (PEG) monomethyl ether ammonium salt derivatives such as **3**[23a] (R = H, OMe; Ar = 9-anthryl) (up to 71% ee) and **4** [R = H, OMe; Ar = 9-anthryl, oval = $MeOPEG_{5000}$-O_2C-;[23a] R = H, Ar = 9-anthryl, oval = $MeOPEG_{5000}$-O-C_6H_4-$(CH_2)_3O$-[23b]] (up to 81% ee), respectively, have been obtained. Furthermore, a quinine-derived *N*-methylanthrylammonium salt attached to a PEG chain at the 6-position of the quinoleine nucleus has been prepared,[23b] all these polymers being used for the asymmetric alkylation of glycinate imines although achieving only up to 12% ee.

In this context, and as part of our ongoing studies towards the synthesis of polymeric PTC catalysts for the asymmetric synthesis of α-amino acids,[19] we show in this paper the *N*-anchoring of some natural or modified *Cinchona* alkaloids to cross-linked or even grafted polystyrene, and the use of these supported ammonium salts as chiral PTC catalysts in the enantioselective alkylation of iminic glycine esters.

Results and Discussion

Resin-supported ammonium salts **1a** and **1c** were obtained by reaction of cross-linked chloromethylated polystyrene (Merrifield resin, Fluka, cross-linked with 1% of divinylbenzene, 200–400 mesh, 1.7 mmol Cl/g) with an excess (2 equivs.) of cinchonidine and quinine, respectively, in refluxing toluene. After filtration and washing thoroughly with ethyl acetate, polymer-supported quaternary ammonium chlorides **1a** and **1c** were obtained. The increase in the initial resin weight, the new bands in the IR spectra attributable to the alkaloid structure and the presence of nitrogen in the elemental analysis showed the incorporation of the alkaloids to the resin. In addition, and taking into account the influence of substituting a hydroxy group by an allyloxy group in the catalytic performance of ammonium *Cinchona*-derived ammonium salts in PTC reactions,[5] the polymer **1a** was *O*-allylated by reaction with allyl bromide in the presence of aqueous KOH,[5a] affording polymeric salt **1b**. Moreover, the cinchonine-derived Merrifield resin-supported ammonium salt **5** was also obtained, as cinchonine has been considered a *pseudoenantiomer* of cinchonidine, its use being therefore a simple way of achieving an opposite enantioselection.[4f]

All these polymers **1** and **5** were tested as insoluble PTC catalysts (0.1 equiv.) in the triphase alkylation reaction of *N*-(diphenylmethylene)glycine esters **6** in an organic solvent and using an aqueous base. The search for the optimum reaction conditions was performed using a model benzylation reaction of different iminic glycine esters **6**, and cinchonidine-supported salt **1a** as PTC catalyst (Table 1). The enantioselectivity of the reaction was measured by chiral GLC analysis (see Experimental Section) of the corresponding *N*-trifluoroacetamide esters from **7**.[24] In all cases (*S*)-**7** was obtained, its absolute configuration being determined by the sign of the specific rotation of the phenylalanine,[25] obtained by hydrolysis of **7** under refluxing 6 N HCl and treatment with propylene oxide.

Thus, when using the ethyl or isopropyl esters **6a** or **6b**, respectively, in a system formed by toluene and a 25% aqueous NaOH solution at room temperature, the corresponding benzylated derivatives **7aa** and **7ba** were obtained in 44 and 66% ee, respectively (Table 1, entries 1 and 2). However, when the reaction was carried out with the commercially available *tert*-butyl derivative **6c**, the reaction time was considerably longer and product **7ca** was obtained in only 58% ee (Table 1, entry 3). Thus, derivative **6b**[26a] was chosen as starting material for subsequent alkylation reactions.

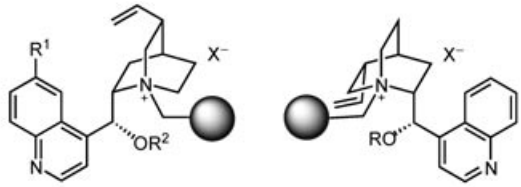


Figure 3.

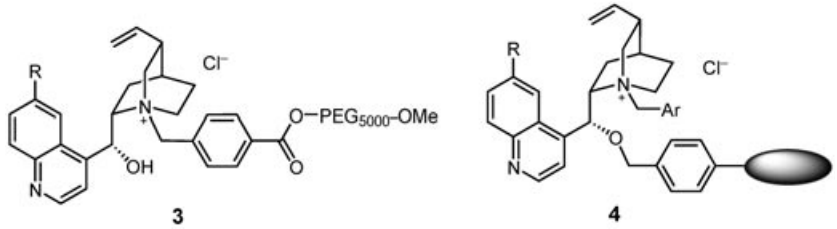


Figure 2.

Toluene proved to be the solvent of choice (Table 1, entry 2), the use of dichloromethane or *tert*-butyl methyl ether (Table 1, entries 4 and 5) giving rise to lower ees, whereas more polar solvents such as acetone or acetonitrile affording racemic **7ba** (Table 1, entries 6 and 7).

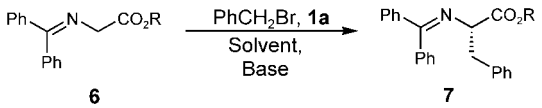
In addition, different aqueous alkaline bases in toluene as organic solvent at room temperature were examined (Table 1, entries 2 and 8–10), 25% aqueous NaOH affording the higher ee (Table 1, entry 2), whereas the use of LiOH, KOH or especially CsOH gave lower enantioselectivities. In addition, solid potassium carbonate was also employed as base in acetonitrile as solvent, although affording only 10% ee of compound **7ba** (Table 1, entry 11). Finally, lowering the reaction temperature gave place to a notable increment in the enantioselectivity. Thus, when the model benzylation reaction was performed at 0 °C (bath temperature) the enantioselection rose to 90% ee (Table 1, compare entries 2 and 12).

With all these optimized parameters, we performed the enantioselective model benzylation of **6b** using also polymeric PTC catalysts **1b**, **c** and **5** (Table 2). The *O*-allylation of the polymeric ammonium salt **1a** seemed to lower its capacity for enantioselection. Thus, when the polymeric *O*-allylated cinchonidine-derived ammonium salt **1b** was used as PTC catalyst in the benzylation reaction of **6b**, much lower ees were obtained of (*S*)-**7ba** compared to when the OH-intact polymeric catalyst **1a** was used (Table 2, compare entries 1 and 2 with entries 3 and 4). Moreover, the polymeric ammonium salt from quinine **1c** proved to be inferior to cinchonidine as PTC catalyst, as shown in the poor enantioselectivities achieved for (*S*)-**7ba** when **1c** was employed (Table 2, entries 5 and 6). Furthermore, the above-mentioned consideration of cinchonine as a *pseudoenantiomer* of cinchonidine[4f] proved to be true when the asymmetric benzylation reaction of **6b** was carried out using polymer-supported cinchonine-derived ammonium salt **5a**, affording now the corresponding (*R*)-**7ba**, although in a lower ee than when using its cinchonidine-derived counterpart **1a** (Table 2, compare entries 1 and 2 with entries 7 and 8). Similarly to when using the *O*-allylated cinchonidine-derived ammonium salt **1b**, the *O*-allylated cinchonine-derived polymer **5b** gave rise to a lower enantioselection of (*R*)-**7ba** than its OH-free counterpart **5a** (Table 2, compare entries 8 and 9).

Due to the low enantioselectivity achieved when using the cinchonine-derived polymeric catalysts **5**, we thought about the preparation of a polymeric ammonium salt derived from cinchonidine but with an opposite configuration on the carbon bearing the OH group in the alkaloid moiety. Thus, we prepare epicinchonidine by OH mesylation of cinchonidine and subsequent reaction with refluxing water, according to the reported procedure.[27] After *N*-quaternization of the epicinchonidine using the Merrifield resin, polymer-supported ammonium salt **8** was obtained and employed as PTC catalyst in the model benzylation reaction. However, the sense of the enantioselectivity was not the expected and (*S*)-**7** was the main enantiomer, the asymmetric induction being very low (Table 2, entry 10). In all cases, the polymers were recovered by filtration after the alkylation reaction and reused up to three times without any loss of activity.

We were also interested in anchoring the catalysts to a type of support where a more mobile polymer is grafted

Table 1. Enantioselective benzylation of glycine derivatives **6** using polymeric catalyst **1a** under PTC conditions.



6 **7**

Entry	R (No.)	Solvent	Base	T [°C]	t [h]	Product No.	Yield [%][a]	*S/R* ratio[b]	ee [%]
1	Et (**6a**)	PhMe	25% aq. NaOH	25	4	**7aa**	85	72/28	44
2	*i*-Pr (**6b**)	PhMe	25% aq. NaOH	25	4	**7ba**	90	83/17	66
3	*t*-Bu (**6c**)	PhMe	25% aq. NaOH	25	36	**7ca**	80	79/21	58
4	*i*-Pr (**6b**)	CH_2Cl_2	25% aq. NaOH	25	4	**7ba**	95	77/23	54
5	*i*-Pr (**6b**)	*t*-BuOMe	25% aq. NaOH	25	2	**7ba**	75	75/17	58
6	*i*-Pr (**6b**)	Acetone	25% aq. NaOH	25	1	**7ba**	86	50/50	0
7	*i*-Pr (**6b**)	MeCN	25% aq. NaOH	25	2	**7ba**	85	50/50	0
8	*i*-Pr (**6b**)	PhMe	25% aq. KOH	25	3	**7ba**	94	79/21	58
9	*i*-Pr (**6b**)	PhMe	25% aq. CsOH	25	10	**7ba**	80	68/32	36
10	*i*-Pr (**6b**)	PhMe	11% aq. LiOH[c]	25	23	**7ba**	90	80/20	60
11	*i*-Pr (**6b**)	MeCN	K_2CO_3 (s)	25	36	**7ba**	60	55/45	10
12	*i*-Pr (**6b**)	PhMe	25% aq. NaOH	0	17	**7ba**	90	95/5	90

[a] Crude yield determined by ^{1}H NMR (300 MHz).
[b] Determined by chiral GLC from the corresponding trifluoroacetamides (see text).
[c] Solubility of LiOH in water.[26b]

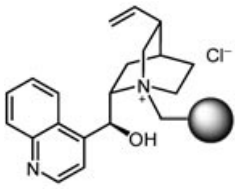


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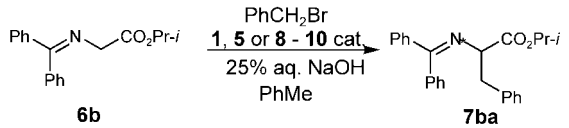
Figure 4.

Table 2. Enantioselective benzylation of glycine derivative **5b** using polymeric catalysts **1**, **5** or **8** – **10** under PTC conditions.



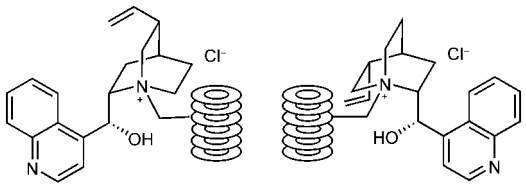
Entry	Catalyst	T [°C]	t [h]	Yield [%][a]	*S/R ratio*[b]	ee [%]
1	**1a**	25	4	90	83/17	66
2	**1a**	0	17	90	95/5	90
3	**1b**	25	10	62	67/33	34
4	**1b**	0	140	23	75/25	50
5	**1c**	25	8	76	59/41	18
6	**1c**	0	96	81	60/40	20
7	**5a**	25	4	88	30/70	40
8	**5a**	0	24	85	30/70	40
9	**5b**	0	24	45	34/66	32
10	**8**	0	31	60	54/46	8
11	**9**[c]	25	24	83	83/17	66
12	**9**[c]	0	160	55	68/32	36
13	**10**[c]	25	96	30	31/69	38

[a] Crude yield determined by ^{1}H NMR (300 MHz).
[b] Determined by chiral GLC from the corresponding trifluoroacetamides (see text).
[c] Reused up to three times with only 3% lowering in yield and ee between first and third run.

to a rigid plastic. Compared to cross-linked microporous beads, which dominate the field of solid supports,[15] the use of these materials would allow great flexibility of design, as plastics can be molded onto any particular shape.[28] We were interested in employing polystyrene-grafted polypropylene in a particular shape called "Lanterns",[28] inspired by its use for the *O*-anchoring of cinchonidine.[29] Thus, commercially available chloromethylated polystyrene-grafted polypropylene (chloromethylated SynPhase™ Lanterns)[30] were used for the *N*-quaternization of cinchonidine and cinchonine, affording supported ammonium salts **9** and **10**, respectively. These derivatized Lanterns were added to the reaction flask, being employed as PTC catalyst in the benzylation of **6b**. Thus, when the cinchonidine-supported Lantern **9** was used working at room temperature, the final (*S*)-**7ba** was obtained with an identical degree of asymmetric induction as when using its Merrifield resin-attached counterpart **1a** (Table 2, compare entries 1 and 11), although lowering the reaction temperature afforded lower ee and high reaction time (Table 2, entry 12). Moreover, a similar enantioselectivity for (*R*)-**7ba** was obtained using the cinchonine-supported Lantern **10** as catalysts aswhen using the Merrifield-derived analogue **5a** (Table 2, compare entries 7 and 13). These Lantern-attached ammonium salts **9** and **10** were tweezers-separated after the reaction and reused up to three times with almost no loss of activity (Table 2, see footnote[c]).

The next step was the use of other electrophiles in the alkylation reaction of **6b** using **1a** as the highest enantioselective supported PTC catalysts with 25% aqueous NaOH as base, toluene as solvent and at 0 °C. We performed then the alkylation reaction using electrophiles such as differently substituted benzyl bromides as well as allyl and propargyl bromides (Table 3).

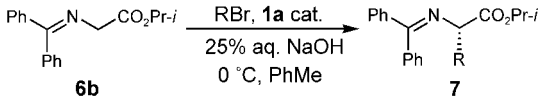
Interestingly, all other electrophiles afforded lower ees than the formerly employed benzyl bromide (Table 3, entry 1). Thus, a bulky *tert*-butyl group at the 4-position of the aromatic ring gave only 44% ee (Table 3, entry 2). In addition, when different halogens were also at the 4-position of the nucleus (Table 3, entries 3, 4, 7 and 8), a certain dependence of the electronegativity was observed, the presence of a fluorine atom giving place to 72% ee (Table 3, entry 3), whereas an iodine atom affording only 50% ee (Table 3, entry 8). The 2-, 3- or 4-position of the halogen on the aromatic ring also influences the enantioselection (Table 3, entries 5–7). Thus, the presence of a bromine atom at the 3- or 4-positions of the aromatic ring gave similar ees (Table 3, entries 6 and 7), whereas a bromine substituent at the 2-position lowered the enantioselectivity down to 20% ee (Table 3, entry 5). In addition, the presence of different groups on the aromatic ring did not seem to influence remarkably the enantioselection. Thus, when electron-withdrawing groups, such as nitro or cyano, or electron-donating groups, such as methoxy, were present the obtained ee was almost the same (Table 3, entries 9–11). Finally, the use of allyl bromide (Table 3, entry 13) or propargyl bromide (Table 3, entry 14) gave rise to rather low ees, the (*S*)-enantiomer being the main one in all cases.



9 10

Figure 5.

Table 3. Enantioselective alkylation of glycine derivative **6b** using polymeric catalyst **1a** under PTC conditions.



Entry	RBr	*t* [h]	No.	Yield [%][a]	*S/R* ratio[b]	ee [%]
1	$PhCH_2Br$	17	**7ba**	90	95/5	90
2	4-*t*-$BuC_6H_4CH_2Br$	7	**7bb**	86	72/28	44
3	4-$FC_6H_4CH_2Br$	10	**7bc**	76	86/14	72
4	4-$ClC_6H_4CH_2Br$	10	**7bd**	66	83/17	58
5	2-$BrC_6H_4CH_2Br$	13	**7be**	80	60/40	20
6	3-$BrC_6H_4CH_2Br$	12	**7bf**	80	80/20	60
7	4-$BrC_6H_4CH_2Br$	14	**7bg**	79	78/22	56
8	4-$IC_6H_4CH_2Br$	14	**7bh**	77	75/25	50
9	4-$O_2NC_6H_4CH_2Br$	26	**7bi**	22	82/18	64
10	4-$NCC_6H_4CH_2Br$	19	**7bj**	70	80/20	60
11	4-$MeOC_6H_4CH_2Br$	10	**7bk**	85	82/18	64
12	2-$C_{10}H_7CH_2Br$	6	**7bl**	45	74/26	48
13	CH_2=$CHCH_2Br$	19	**7bm**	75	66/34[c]	32
14	CH≡CCH_2Br	43	**7bn**	63	68/32	36

[a] Crude yield determined by ^{1}H NMR (300 MHz).
[b] Determined by chiral GLC from the corresponding trifluoroacetamides (see text).
[c] Assigned by the relative retention times of the (*R/S*)-isomers reported in the literature.[24]

Conclusion

We have prepared chiral polymeric ammonium salts by anchoring a number of *Cinchona*-derived alkaloids to different types of commercially available polystyrene-related supports, such as the Merrifield resin and polystyrene-grafted polypropylene (SynPhase™ Lanterns). All these ammonium salts have been employed as solid-supported chiral PTC catalysts for the asymmetric benzylation of *N*-(diphenylmethylene)glycine isopropyl esters achieving moderate enantioselectivities. The best ees of the (*S*)-enantiomer were achieved using a Merrifield resin-supported cinchonidinium salt, whereas cinchonine-derived salts gave rise to opposite (*R*)-enantioselectivity. In all cases higher ees were obtained when a hydroxy group was present in the alkaloid moiety, their *O*-allylated counterparts giving lower enantioselectivities. All these supported PTC catalysts could be easily separated from the reaction mixture and reused.

Experimental Section

General Remarks

All the reagents and solvents employed were of the best grade available and were used without further purification. IR spectra were recorded on a Nicolet 510 P-FT and only the structurally most important peaks are listed. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 at 300 and 75 MHz, respectively, using $CDCl_3$ as solvent and TMS as internal standard. Low-resolution electron impact (EI) mass spectra were obtained at 70 eV on a Shimadzu QP-5000. HRMS (EI) were recorded on a Finnigan MAT 95S. Microanalyses were performed by the Microanalyses Service of the University of Alicante. Merrifield resin (cross-linked with 1% of divinylbenzene, 200–400 mesh, 1.7 mmol Cl/g) was purchased from Fluka. Chloromethylated SynPhase™-PS Lanterns (A-Series, 17 × 6 mm, surface area = 7.2 cm^2, loading = 75 μmol) are available from Mimotopes Pty. Ltd.[30] Glycinimides **6a** and **6c** were commercially available (Aldrich), whereas **6b** was prepared according to the literature.[26a] The enantiomeric ratio of products **7** were determined by chiral GLC analyses (Crownpack Chirasil-L-Val column, 25 m × 0.25 mm i.d.; conditions A: P = 85 kPa, 1 min 85 °C, 2 °C/min to 180 °C; conditions B: P = 50 kPa, 1 min 85 °C, 10 °C/min to 180 °C) of their corresponding *N*-trifluoroacetamide esters.[24] GLC reference racemic samples were prepared from the corresponding racemic **7**, which were obtained using *n*-tetrabutylammonium bromide as PTC catalyst. Crude yields of compounds **7** were determined by weighing the reaction crude containing excess electrophile and measuring the ratio by ^{1}H NMR.

Preparation of Merrifield Resin-Supported Ammonium Salts 1a, 1c, 5a and 8

To a suspension of cinchonidine, quinine, cinchonine, or epicinchonidine[27] (2 mmol) in toluene (10 mL) was added the Merrifield resin (588 mg, 0.5 quivs.), and the mixture was stirred under reflux for 24 h. The reaction was cooled to room temperature and the solid was filtered, washed with AcOEt (3 × 15 mL) and dried under vacuum (15 Torr), affording the polymer-supported ammonium salts.

***Polymeric ammonium salt* 1a:** IR (KBr): ν = 3415 (br), 3060, 1596, 1430, 1220, 1100, 750 cm^{-1}; microanalysis: % N = 3.25; loading = 1.7 mmol g^{-1}.

***Polymeric ammonium salt* 1c:** IR (KBr): ν = 3398 (br), 3020, 615, 1497, 1455, 1241, 1012, 757 cm^{-1}; microanalysis: % N = 3.06; loading = 1.6 mmol g^{-1}.

***Polymeric ammonium salt* 5a:** IR (KBr): ν = 3409 (br), 3080, 1590, 1440, 1231, 1103, 760 cm^{-1}; microanalysis: % N = 3.25; loading = 1.7 mmol g^{-1}.

***Polymeric ammonium salt* 8:** IR (KBr): ν = 3362 (br), 3029, 1598, 1454, 1233, 1038, 769 cm^{-1}; microanalysis: % N = 3.25; loading = 1.7 mmol g^{-1}.

Preparation of *O*-Allylated Merrifield Resin-Supported Ammonium Salts 1b and 5b

To a suspension of **1a** or **5a** (0.5 mmol) in CH_2Cl_2 (3 mL) was added allyl bromide (1.5 mmol, 86.5 μL) and 50% aqueous KOH (2.5 mmol, 0.3 mL) and the mixture was stirred for 24 h at room temperature. The solid was filtered and washed with water (3 × 5 mL) and CH_2Cl_2 (3 × 5 mL), and dried under vacuum (15 Torr) affording the corresponding polymers.

***Polymeric ammonium salt* 1b:** IR (KBr): ν = 3080, 1590, 1440, 1231, 1103, 760 cm^{-1}; microanalysis: % N = 2.03; loading = 1.2 mmol g^{-1}.

***Polymeric ammonium salt* 5b:** IR (KBr): ν = 3016, 1607, 1487, 1454, 1110, 760 cm^{-1}; microanalysis: % N = 1.82; loading = 1.0 mmol g^{-1}.

Enantioselective Alkylation of Iminic Glycine Esters 6 using Polymers 1, 5 or 8 as Catalysts under PTC Conditions

To a stirred suspension of **6** (0.5 mmol), the polymeric catalyst **1**, **5** or **8** (0.1 equiv.) and the corresponding aqueous base (4 mL) in the appropriate solvent (5 mL) at the selected temperature (see Table 1), was added the corresponding bromide (0.6 mmol). When the reaction was considered finished (GLC), the mixture was filtered and the solid was washed with AcOEt (25 mL), consisting of the recovered polymeric catalyst. The filtrate was washed with water (3 × 15 mL) and the organic phase was dried ($MgSO_4$), filtered off and evaporated (15 Torr) to give compounds **7**. Data of known compounds are given from this mixture. In the case of new compounds, spectroscopic data are given from pure chromatographed or crystallized or analytical samples.

***Ethyl 2-(diphenylmethyleneamino)-3-phenylpropanoate* (7aa):**[4a] ^{1}H NMR: δ = 1.24 (3H, t, *J* = 7.1 Hz), 3.18 (1H, dd, *J* = 13.3, 9.2 Hz), 3.28 (1H, dd, *J* = 13.3, 4.4 Hz), 4.10–4.26 (3H, m), 6.59 (1H, d, *J* = 6.5 Hz), 7.03 (1H, m), 7.17 (2H, m), 7.23–7.39 (6H, m), 7.58 (2H, m), 7.80 (1H, m); GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 25.24 min, t_R (*S*) 26.41 min.

***Isopropyl 2-(diphenylmethyleneamino)-3-phenylpropanoate* (7ba):**[9b] ^{1}H NMR: δ = 1.20, 1.22 (6H, 2d, *J* = 6.5 Hz), 3.17 (1H, dd, *J* = 13.1, 9.2 Hz), 3.27 (1H, dd, *J* = 13.1, 4.3 Hz), 4.19 (1H, dd, *J* = 9.2, 4.3 Hz), 5.04 (1H, hept, *J* = 6.1 Hz), 6.62 (1H, m), 7.03–7.60 (13H, m), 7.79 (1H, d, *J* = 7.9 Hz); GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 24.72 min, t_R (*S*) 26.00 min.

tert-*Butyl* 2-(diphenylmethyleneamino)-3-phenylpropanoate (7ca):[6e] ^{1}H NMR δ = 1.4 (9H, s), 3.15 (1H, dd, *J* = 13.4, 9.2 Hz), 3.24 (1H, dd, *J* = 13.4, 4.8 Hz), 4.11 (1H, dd, *J* = 9.2, 4.8 Hz), 6.60 (1H, m), 7.04–7.59 (13H, m), 7.80 (1H, d, *J* = 7.9 Hz); GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 25.46 min, t_R (*S*) 27.03 min.

***Isopropyl 3-(4-*tert*-butylphenyl)-2-(diphenylmethyleneamino)propanoate* (7bb):** mp 137–138 °C; IR (KBr): ν = 3058, 3032, 1741, 1619 cm^{-1}; ^{1}H NMR: δ = 1.21, 1.23 (6H, 2d, *J* = 6.3 Hz), 1.28 (9H, s), 3.12 (1H, dd, *J* = 13.3, 9.2 Hz), 3.24 (1H, dd, *J* = 13.3, 4.3 Hz), 4.15 (1H, dd, *J* = 9.2, 4.3 Hz), 5.03 (1H, hept., *J* = 6.3 Hz), 6.56 (1H, d, *J* = 6.7 Hz), 6.97 (2H, d, *J* = 8.2 Hz), 7.19–7.60 (10H, m), 7.80 (1H, d, *J* = 8.3 Hz); ^{13}C NMR: δ = 21.7, 31.4, 34.3, 39.0, 67.6, 68.2, 124.9, 125.7, 127.6, 127.9, 128.0, 128.1, 128.2, 128.7, 129.5, 130.0, 130.1, 132.4, 135.0, 136.2, 137.6, 139.5, 149.1, 170.3, 171.3; MS: *m/z* = 427 (M^+, 0.4), 340 (28), 281 (20), 280 (100), 239 (11), 238 (65), 194 (17), 193 (66), 192 (42), 166 (18), 165 (60), 163 (13), 147 (14), 117 (15), 91 (13), 57 (19); HRMS: calcd. for $C_{25}H_{26}N$ ($M^+ - CO_2Pr$-*i*): 340.2065; found: 340.2036; GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 38.23 min, t_R (*S*) 39.18 min.

***Isopropyl 2-(diphenylmethyleneamino)-3-(4-fluorophenyl)propanoate* (7bc):** IR (film): ν = 3068, 1737, 1624, 1598, 1102 cm^{-1}; ^{1}H NMR: δ = 1.21, 1.23 (6H, 2d, *J* = 6.2 Hz), 3.14 (1H, dd, *J* = 13.4, 9.1 Hz), 3.23 (1H, dd, *J* = 13.4, 4.6 Hz), 4.15 (1H, dd, *J* = 9.1, 4.6 Hz), 5.04 (1H, hept, *J* = 6.2 Hz), 6.67 (1H, d, *J* = 6.6 Hz), 6.88 (2H, m), 7.01 (2H, m), 7.26–7.38 (5H, m), 7.48 (1H, m), 7.58 (2H, m), 7.80 (1H, d, *J* = 8.1 Hz); ^{13}C NMR: δ = 21.7, 38.7, 67.3, 68.5, 127.6, 128.0, 128.2, 128.2, 128.4, 128.7, 130.0, 130.3, 131.2, 131.3, 132.4, 133.8, 136.2, 137.6, 139.3, 160.0, 163.2, 170.8, 171.0; MS: *m/z* = 390 (M^+ + 1, 0.1), 303 (13), 302 (55), 281 (20), 280 (100), 238 (58), 194 (20), 193 (80), 192 (46), 166 (27), 165 (96), 164 (11), 121 (12), 109 (30), 77 (14); HMRS: calcd. for $C_{25}H_{23}NO_2F$ (M^+ + 1): 388.1713; found: 388,1738; GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 23.44 min, t_R (*S*) 24.87 min.

***Isopropyl 3-(4-chlorophenyl)-2-(diphenylmethyleneamino)propanoate* (7bd):** IR (film): ν = 3062, 3027, 1737, 1619, 1096 cm^{-1}; ^{1}H NMR: δ = 1.21, 1.23 (6H, 2d, *J* = 6.2 Hz), 3.12 (1H, dd, *J* = 13.4, 9.1 Hz), 3.22 (1H, dd, *J* = 13.4, 4.4 Hz), 4.15 (1H, dd, *J* = 9.1, 4.4 Hz), 5.04 (1H, hept, *J* = 6.2 Hz), 6.68 (2H, d, *J* = 6.3 Hz), 6.80 (1H, d, *J* = 8.1 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 7.15 (2H, d, *J* = 8.4 Hz), 7.25–7.51 (4H, m), 7.57 (2H, d, *J* = 8.1 Hz), 7.80 (1H, d, *J* = 8.1 Hz); ^{13}C NMR: δ = 21.7, 38.9, 67.1, 68.5, 127.6, 128.0, 128.2, 128.2, 128.4, 128.7, 128.9, 130.0, 130.3, 131.1, 131.9, 132.1, 132.4, 136.1, 136.7, 137.1, 137.9, 139.3, 170.8, 170.9; MS: *m/z* = 405 (M^+, 0.04), 320 (13), 318 (37), 281 (19), 280 (95), 238 (57), 194 (19), 193 (85), 192 (44), 166 (28), 165 (100), 164 (11), 124 (22), 77 (17); HMRS: calcd. for $C_{21}H_{17}NCl$ ($M^+ - CO_2Pr$-*i*): 318.1050; found: 318.1054; GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 35.84 min, t_R (*S*) 36.97 min.

***Isopropyl 3-(2-bromophenyl)-2-(diphenylmethyleneamino)propanoate* (7be):** IR (film): ν = 3062, 3026, 1733, 1665, 1100 cm^{-1}; ^{1}H NMR: δ = 1.22, 1.24 (6H, 2d, *J* = 6.1 Hz), 3.23 (1H, dd, *J* = 13.4, 9.8 Hz), 3.49 (1H, dd, *J* = 13.4, 4.2 Hz), 4.41 (1H, dd, *J* = 9.8, 4.2 Hz), 5.04 (1H, hept, *J* = 6.1 Hz), 6.61 (1H, d, *J* = 6.1 Hz), 7.01–7.59 (12H, m), 7.81 (1H, d, *J* = 7.9 Hz); ^{13}C NMR: δ = 21.8, 39.5, 64.6, 68.5, 125.2, 126.9, 127.6, 127.9, 128.0, 128.1, 128.2, 128.3, 128.8, 130.0, 130.2, 131.3, 132.3, 132.5, 132.7, 133.3, 136.0, 137.3, 139.3, 171.0; MS: *m/z* = 370 (M^+ – Br, 26), 364 (20), 362 (21), 281 (11), 280 (51), 238 (40), 194 (13), 193 (54), 192 (32), 180 (24), 179 (12), 166 (27), 165 (100), 164 (10), 77 (14); HRMS: calcd. for $C_{25}H_{24}NO_2$ (M^+ –

Br): 370.1807; found: 370.1809; GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 38.57 min, (*S*) 39.65 min.

***Isopropyl 3-(3-bromophenyl)-2-(diphenylmethyleneamino)propanoate* (7bf):** IR (film): ν = 3063, 1731, 1660, 1107 cm^{-1}; ^1H NMR: δ = 1.22, 1.24 (6H, 2d, *J* = 6.2 Hz), 3.14 (1H, dd, *J* = 13.3, 9.1 Hz), 3.22 (1H, dd, *J* = 13.3, 4.5 Hz), 4.17 (1H, dd, *J* = 9.1, 4.5 Hz), 5.05 (1H, hept, *J* = 6.2 Hz), 6.68 (1H, d, *J* = 6.1 Hz), 7.02–7.57 (12H, m), 7.80 (1H, d, *J* = 7.9 Hz); ^{13}C NMR: δ = 21.8, 39.2, 66.9, 68.6, 122.1, 127.6, 128.0, 128.2, 128.4, 128.6, 128.7, 129.3, 129.6, 130.0, 130.3, 131.5, 132.4, 132.7, 136.1, 139.3, 140.5, 170.9, 171.0; MS: *m/z* = 449 (M^+, 0.1), 364 (29), 362 (29), 281 (18), 280 (85), 238 (41), 194 (18), 193 (83), 180 (20), 179 (11), 166 (28), 165 (100), 102 (10), 77 (15); HRMS: calcd. for $C_{21}H_{17}NBr$ ($M^+ - CO_2Pr$-*i*): 362.0544; found: 362.0540; GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 50.23 min, t_R (*S*) 51.61 min.

***Isopropyl 3-(4-bromophenyl)-2-(diphenylmethyleneamino)propanoate* (7bg):** mp 97–98 °C; IR (KBr): ν = 3065, 1731, 1623, 1110 cm^{-1}; ^1H NMR: δ = 1.22, 1.24 (6H, 2d, *J* = 6.1 Hz), 3.23 (1H, dd, *J* = 13.4, 9.8 Hz), 3.48 (1H, dd, *J* = 13.4, 4.0 Hz), 4.14 (1H, dd, *J* = 9.8, 4.0 Hz), 5.04 (1H, hept, *J* = 6.1 Hz), 6.60 (1H, d, *J* = 6.1 Hz), 7.01–7.59 (12H, m), 7.81 (1H, d, *J* = 7.9 Hz); ^{13}C NMR δ = 21.8, 39.5, 64.6, 68.5, 125.2, 126.9, 127.6, 127.9, 128.0, 128.1, 128.24, 128.3, 128.8, 130.0, 130.2, 132.4, 132.5, 132.7, 133.3, 136.0, 137.3, 139.3, 171.0; MS: *m/z* = 406 (M^+ – *i*-Pr, 0.05), 364 (17), 363 (18), 281 (18), 280 (92), 238 (50), 194 (18), 193 (78), 192 (40), 166 (29), 165 (100), 90 (10), 77 (16); HRMS: calcd. for $C_{21}H_{17}NBr$ ($M^+ - CO_2Pr$-*i*): 362.0544; found: 362.0593; GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 41.11 min, t_R (*S*) 42.10 min.

***Isopropyl 2-(diphenylmethyleneamino)-3-(4-iodophenyl)propanoate* (7bh):** mp 106–107 °C; IR (KBr); ν = 3068, 3022, 1742, 1624 cm^{-1}; ^1H NMR: δ = 1.21, 1.23 (6H, 2d, *J* = 6.3 Hz), 3.10 (1H, dd, *J* = 13.4, 8.9 Hz) 3.18 (1H, dd, *J* = 13.4, 4.3 Hz), 4.15 (1H, dd, *J* = 8.9, 4.3 Hz), 5.03 (1H, hept, *J* = 6.3 Hz), 6.67 (1H, d, *J* = 6.3 Hz), 6.80 (1H, d, *J* = 7.9 Hz), 7.09–7.40 (6H, m), 7.45–7.59 (4H, m), 7.66 (1H, d, *J* = 7.9 Hz), 7.80 (1H, d, *J* = 7.9 Hz); ^{13}C NMR: δ = 21.7, 39.0, 67.0, 68.5, 91.4, 125.2, 127.5, 128.0, 128.2, 128.2, 128.4, 128.7, 129.0, 130.0, 130.3, 130.8, 131.9, 132.4, 136.0, 137.1, 137.8, 137.9, 139.2, 170.8, 170.9; MS: *m/z* = 410 ($M^+ - CO_2Pr$-*i*, 25), 281 (20), 280 (100), 238 (46), 194 (17), 193 (71), 192 (37), 180 (14), 179 (12), 166 (26), 165 (88), 90 (14), 77 (14); HRMS: calcd. for $C_{21}H_{17}NI$ ($M^+ - CO_2Pr$-*i*): 410.0406; found: 410.0370; GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 45.19 min, t_R (*S*) 46.09 min.

***Isopropyl 2-(diphenylmethyleneamino)-3-(4-nitrophenyl)propanoate* (7bi):** mp 140–141 °C; IR (KBr): ν = 3083, 1732, 1628 cm^{-1}; ^1H NMR: δ = 1.22, 1.24 (6H, 2d, *J* = 6.2 Hz), 3.29 (1H, dd, *J* = 13.3, 8.5 Hz), 3.34 (1H, dd, *J* = 13.3, 4.9 Hz), 4.24 (1H, dd, *J* = 8.5, 4.9 Hz), 5.05 (1H, hept, *J* = 6.2 Hz), 6.71 (1H, d, *J* = 6.9 Hz), 7.23–7.39 (4H, m), 7.46–7.62 (4H, m), 7.81 (2H, m), 8.06 (1H, m), 8.26 (2H, m); ^{13}C NMR: δ = 21.8, 39.4, 66.5, 68.9, 126.4, 127.5, 127.5, 128.1, 128.3, 128.7, 130.0, 130.6, 130.7, 132.4, 135.9, 137.6, 139.0, 146.2, 170.5, 171.3; MS: *m/z* = 329 ($M^+ - CO_2Pr$-*i*, 63), 281 (11), 280 (53), 238 (32), 194 (15), 193 (66), 192 (37), 180 (17), 179 (17), 178 (12), 166 (26), 165 (100), 104 (12), 77 (18); HRMS: calcd. for $C_{21}H_{17}N_2O_2$ ($M^+ - CO_2Pr$-*i*): 329.1290; found: 329.1290; GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 53.02 min, t_R (*S*) 54.07 min.

***Isopropyl 3-(4-cyanophenyl)-2-(diphenylmethyleneamino)propanoate* (7bj):**[9b] ^1H NMR: δ = 1.21, 1.23 (6H, 2d, *J* = 6.3 Hz), 3.24 (1H, dd, *J* = 13.3, 8.6 Hz), 3.31 (1H, dd, *J* = 13.3, 4.8 Hz), 4.20 (1H, dd, *J* = 8.6, 4.8 Hz), 5.04 (1H, hept, *J* = 6.3 Hz), 6.70 (1H, d, *J* = 6.7 Hz), 7.18 (2H, d, *J* = 8.3 Hz), 7.26–7.62 (10H, m), 7.66 (1H, d, *J* = 8.4 Hz), 7.80 (1H, d, *J* = 8.4 Hz); GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 53.43 min, t_R (*S*) 54.20 min.

***Isopropyl 2-(diphenylmethyleneamino)-3-(4-methoxyphenyl)propanoate* (7bk):** IR (film): ν = 3059, 3029, 1732, 1660, 1278, 1248 cm^{-1}; ^1H NMR: δ = 1.21, 1.23 (6H, 2d, *J* = 6.3 Hz), 3.11 (1H, dd, *J* = 13.5, 9.1 Hz), 3.21 (1H, dd, *J* = 13.5, 4.5 Hz), 3.75 (3H, s), 4.15 (1H, dd, *J* = 9.1, 4.5 Hz), 5.03 (1H, hept, *J* = 6.3 Hz), 6.67 (1H, d, *J* = 6.9 Hz), 6.73 (2H, d, *J* = 8.8 Hz), 6.97 (2H, d, *J* = 8.7 Hz), 7.25–7.37 (3H, m), 7.46 (2H, m), 7.55 (2H, m), 7.79 (2H, m); ^{13}C NMR: δ = 21.8, 38.7, 55.2, 67.6, 68.3, 113.5, 127.6, 127.9, 128.1, 128.3, 128.4, 128.7, 130.0, 130.0, 130.7, 132.4, 136.4, 137.7, 139.5, 158.1, 170.5, 171.3; MS: *m/z* = 401 (M^+, 2), 314 (16), 281 (20), 280 (100), 238 (67), 194 (16), 193 (53), 192 (50), 166 (22), 165 (75), 121 (86), 91 (12), 77 (17); HRMS: calcd. for $C_{26}H_{27}NO_3$: 401.1991; found: 401.1991; GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 37.34 min, t_R (*S*) 38.28 min.

***Isopropyl 2-(diphenylmethyleneamino)-3-(naphthalen-2-yl)propanoate* (7bl):**[9b] ^1H NMR: δ = 1.21, 1.23 (6H, 2d, *J* = 6.3 Hz), 3.33 (1H, dd, *J* = 13.3, 9.2 Hz), 3.47 (1H, dd, *J* = 13.3, 4.4 Hz), 4.31 (1H, dd, *J* = 9.2, 4.4 Hz), 5.04 (1H, hept, *J* = 6.3 Hz), 6.54 (2H, d, *J* = 7.0 Hz), 7.14–7.81 (15H, m); GLC (*N*-trifluoroacetamide ester): *Conditions A*, t_R (*R*) 50.31 min, t_R (*S*) 51.08 min.

***Isopropyl 2-(diphenylmethyleneamino)pent-4-enoate* (7bm):** IR (film): ν = 3063, 1747, 1660 cm^{-1}; ^1H NMR: δ = 1.22, 1.24 (6H, d, *J* = 6.2 Hz), 2.58–2.74 (2H, m), 4.08 (2H, dd, *J* = 7.6, 5.5 Hz), 4.99–5.10 (3H, m), 5.64–5.78 (1H, m), 7.17 (1H, m), 7.29–7.50 (6H, m), 7.60 (2H, m); ^{13}C NMR: δ = 21.7, 38.1, 65.3, 68.2, 117.4, 127.8, 127.9, 128.2, 128.4, 128.5, 128.8, 130.0, 130.2, 132.4, 134.4, 136.5, 137.5, 139.6, 170.4, 171.2; MS: *m/z* = 321 (M^+, 22), 280 (51), 238 (51), 235 (21), 234 (96), 194 (15), 193 (50), 192 (67), 166 (25), 165 (100), 131 (25), 129 (15), 116 (12), 104 (13), 91 (27), 77 (13); HRMS: calcd. for $C_{21}H_{23}NO_2$: 321.1729; found: 321.1755; GLC (*N*-trifluoroacetamide ester): *Conditions B*, t_R (*R*) 7.50 min, t_R (*S*) 8.54 min.

***Isopropyl 2-(diphenylmethyleneamino)pent-4-ynoate* (7bn):** IR (film): ν = 3296, 3065, 3031, 1734, 1623 cm^{-1}; ^1H NMR: δ = 1.21, 1.23 (6H, 2d, *J* = 6.2 Hz), 2.72–2.88 (3H, m), 4.24 (1H, dd, *J* = 7.5, 6.5 Hz), 5.05 (1H, hept, *J* = 6.2 Hz), 7.25–7.56 (5H, m), 7.59 (1H, d, *J* = 7.2 Hz), 7.65 (2H, d, *J* = 7.3 Hz), 7.80 (2H, d, *J* = 7.5 Hz); ^{13}C NMR: δ = 21.7, 23.3, 64.2, 68.8, 70.1, 81.0, 128.0, 128.2, 128.4, 128.6, 128.9, 130.0, 130.4, 132.4, 136.1, 137.6, 139.9, 169.9, 171.7; MS: *m/z* = 319 (M^+, 18), 318 (70), 280 (26), 276 (15), 238 (29), 233 (16), 232 (82), 205 (12), 194 (13), 193 (49), 192 (77), 166 (23), 165 (100), 129 (19), 128 (37), 127 (24), 77 (14); HRMS: calcd. for $C_{21}H_{21}NO_2$: 319.1572; found: 319.1571; GLC (*N*-trifluoroacetamide ester): *Conditions B*, t_R (*R*) 7.84 min, t_r (*S*) 8.26 min.

Preparation of SynPhase™ Lantern-Supported Ammonium Salts 9 and 10

To a suspension of cinchonidine or cinchonine (0.5 mmol, 148 mg) in CH_2Cl_2 (8 mL) was added A-Series chloromethylat-

ed SynPhase™ Lantern (see General Remarks). The Lantern was shaken into this mixture for 7 d at room temperature under an inert atmosphere, removed, rinsed with CH_2Cl_2 (10 mL) and dried under vacuum (15 Torr). The alkaloid incorporation was estimated as quantitative according to weight difference.

Enantioselective Benzylation of Iminic Glycine ester 6b using SynPhase™ Lantern-Supported Ammonium Salts 9 or 10 under PTC Conditions

To a solution of **6b** (0.35 mmol, 98 mg) in toluene (4 mL) was added the Lantern-supported ammonium salt **9** or **10** from above, 25% aqueous NaOH (3 mL) and benzyl bromide (0.42 mmol, 72 μL). The mixture was shaken at the appropriate temperature (see Table 2) and when the reaction was finished (GLC), the Lantern was removed and rinsed with toluene (2 mL) which was poured on the reaction mixture. The combined organics were washed with water (3×15 mL), dried ($MgSO_4$), filtered off and evaporated (15 Torr) to give compound **7ba**. The separated Lantern was rinsed with CH_2Cl_2 (10 mL) and dried under vacuum (15 Torr) for further reuse.

Acknowledgements

We thank the Ministerio de Educación y Cultura (MEC) of Spain (DGICYT, research project BQU2001–0724-C02–01), the Generalitat Valenciana (GV99-33-1-02) and the Universidad de Alicante for financial support.

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