DOI: 10.1002/adsc.200606125

New Recoverable Poly(ethylene glycol)-Supported C_1-Diamino-oligothiophene Ligands for Palladium-Promoted Asymmetric Allylic Alkylation (AAA) Reactions

Marco Bandini,[a,*] Maurizio Benaglia,[b,*] Tommaso Quinto,[a] Simona Tommasi,[a] and Achille Umani-Ronchi[a]

[a] Dipartimento di Chimica "G. Ciamician", Università di Bologna, via Selmi 2, 40126, Bologna, Italy
Fax: (+39)-051-209-9456; e-mail: marco.bandini@unibo.it
[b] Dipartimento di Chimica Organica e Industriale, Università degli Studi di Milano, via Golgi 19, 20133 Milano, Italy
Fax: (+39)-02-5031-4159; e-mail: maurizio.benaglia@unimi.it

Received: March 22, 2006; Accepted: June 2, 2006

Dedicated to Professor Mauro Cinquini on occasion of his 65th birthday.

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: A new class of chiral C_1-symmetrical diamino-oligothiophene ligands easy-grafted on a soluble polymeric support ($MeOPEG_{5000}$) is described. The diamines were found to be effective promoting agents for the [Pd(0)]-catalysed asymmetric allylic alkylation (AAA) of dimethyl malonate in high yields and excellent enantioselectivity (*ee* up to 99%). The supported chiral ligand was readily recovered by precipitation and filtration was recycled up to three times without an appreciable loss in activity. The recycle of the organometallic catalytic system was also investigated.

Keywords: asymmetric synthesis; palladium; PEG; supported catalysts; thiophene

The design and application of new chiral catalysts for the synthesis of enantiomerically enriched molecules have gained an ever-growing attention in the field of the chemical research over the last three decades.[1,2]

In this context, although the major developments in this field have mainly concerned processes in which a catalytic stereoselective system is solubilised in the reaction media, homogeneous catalysis suffers from a limited use on an industrial scale, because of the lack of easy separation and recycling of the undesired components of the final product and environmental concerns.[3] The grafting of chiral ligands as well as organometallic complexes onto solid insoluble supports (heterogeneous catalysis)[4] is commonly accepted as a promising route for the diffusion of asymmetric catalytic transformations at the industry level.

In many instances, the main goal of the immobilisation was the simplification of the reaction work-up, the separation of the product being simpler in the case of a supported rather than a non-supported catalyst. However, with the continuing discovery of more and more sophisticated chiral catalytic species, also recovery and recycling will surely become an important issue in justifying catalyst immobilisation. Immobilisation is obviously convenient if the catalyst is expensive, or has been obtained after a complex synthesis, or is employed in a relatively large amount. A catalyst's instability can be another reason for immobilisation. Chiral catalysts do exist that slowly decompose under the reaction conditions and release trace amounts of by-products that must be separated from the products. If decomposition is slow and the catalyst is very chemically active, this phenomenon does not markedly affect the efficiency of the catalyst and its recycling, but product purification remains a problem. Last but definitely not least, immobilisation of a chiral catalyst can be used in a combinatorial approach to facilitate the process of catalyst discovery and/or optimisation.

Despite this interest, the use of chiral catalysts immobilised on heterogeneous supports is often characterised by some problems; for example, they commonly promote the reaction with a chemical and stereochemical efficiency lower than those of the non-supported catalytic systems. The immobilisation of an organometallic catalyst, generally obtained by anchoring an organic ligand on the support followed by metal addition, may also suffer from the serious drawback of metal leaching.

To overcome these limitations, soluble organic polymers were introduced as a valuable alternative;

thus a reaction promoted by soluble polymer-supported catalysts can be run under homogeneous (and likely best performing) conditions while the catalyst itself can be easily precipitated and then recovered by filtration as if it was bound to an insoluble polymer. Among the different polymeric matrixes, poly(ethylene glycols) (PEGs) occupy a prominent position because of their easy functionalisation, inexpensiveness and unique property of being soluble in most organic solvents but insoluble in a few common ones, like Et_2O or hexanes.[5]

Recently, we reported on the effectiveness of diamino-oligothiophene compounds (DATs, **1**, Figure 1) as valuable ligands for Pd-catalysed nucleophilic allylic alkylations.[6] Although the synthesis of unsubstituted ligands (i.e., DAT2, **1a**) can be readily accomplished starting from commercially available precursors,[7a] the isolation of variously functionalised analogous (i.e., **1b**) required a multi-step sequence[7b] and the possibility to recover them at the end of each reaction is strongly desirable.

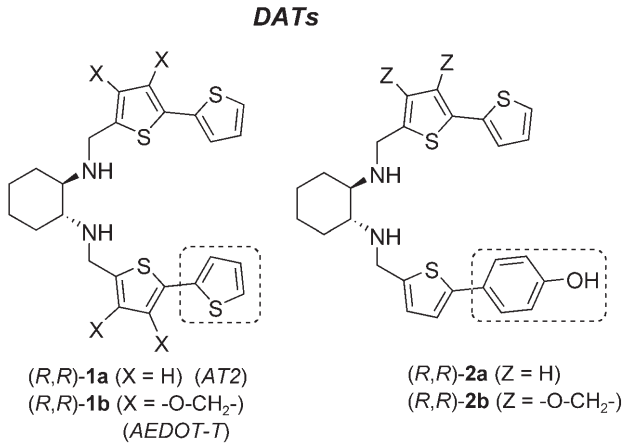
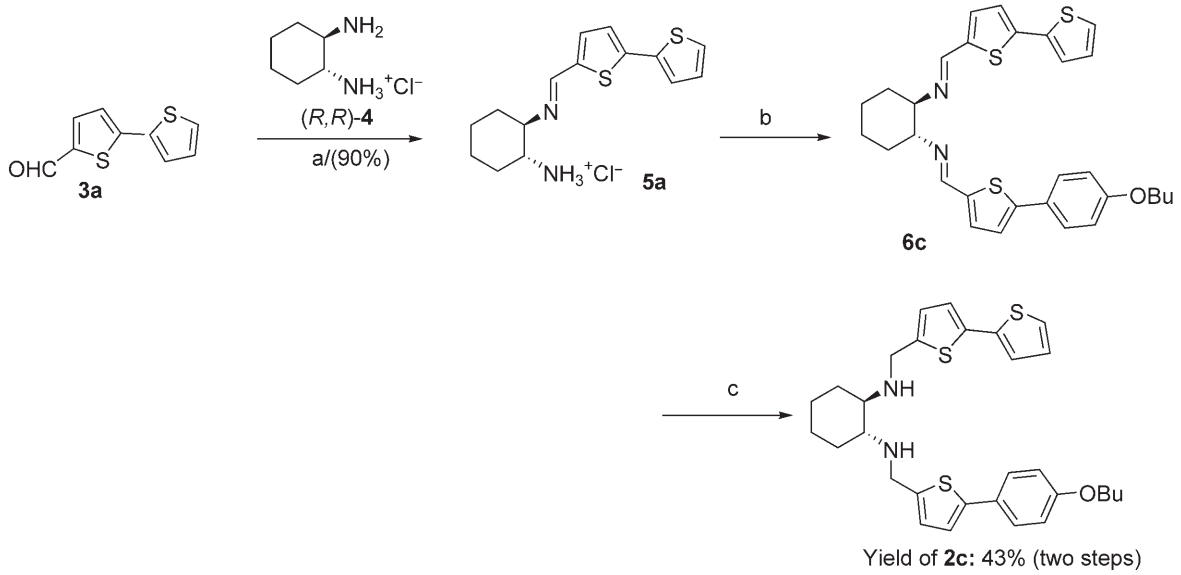


Figure 1. Damino-oligothiophene compounds (DATs).

In this paper, we describe a novel synthetic route for the grafting of **1** to the monomethyl ether of PEG_{5000} (MeOPEG) and applications of the products in [Pd(0)]-catalysed asymmetric allylic alkylation (AAA). Triggered by the physical properties of PEG, it was possible to accomplish the asymmetric transformations both under homogeneous and heterogeneous conditions simply by choosing the proper reaction media (CH_2Cl_2 where the ligands are completely soluble or THF for the heterogeneous version). It is worthy of note that, to the best of our knowledge, a PEG-supported catalyst has never been used under heterogeneous phase conditions.

The synthetic plan involved the replacement of one outer thiophene by a 4′-phenol ring suitable for the anchoring to the organic polymer (**2**, Figure 1). Here, to evaluate the effect of the thienyl/phenol substitution on the catalytic performances of the ligands we prepared the C_1-symmetrical **2c** bearing a butoxy group mimicking the pattern introduced by the linkage of the PEG. Firstly we performed the desymmetrisation of the enantiopure scaffold by transforming (*R,R*)-1,2-cyclohexandiamine (DACH) into the corresponding monochlorohydrate salt (**4**, Scheme 1).[8] Subsequently, the condensation of **4** with commercially available 2,2′-bithiophene-5-carbaldehyde (**3a**) furnished the corresponding mono-imine **5a** in high purity (judged $>95\,\%$ by ^1H NMR).

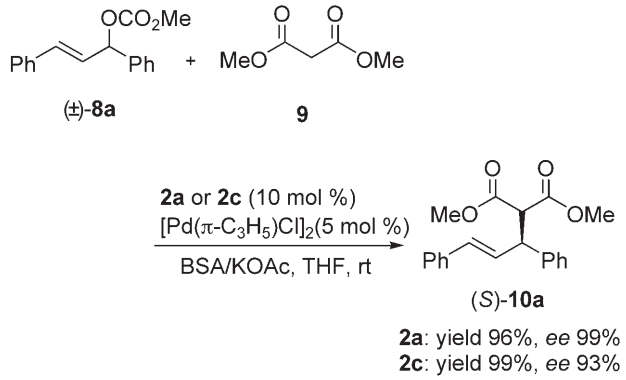


Scheme 1. Multistep synthesis of **1c**. *Reagents and conditions:* a) (*R,R*)-**4**/MeOH/EtOH 1/1, room temperature; b) **3c**/TEA/$MgSO_4$/DCM; c) $NaBH_4$/MeOH, 0 °C → room temperature, 16 h.

The introduction of the 4-*n*-BuO-phenyl ring facilitates the final reductive amination with aldehyde **3c**, easily obtainable through Suzuki cross-coupling (yield 89%, see Experimental Section). The present synthetic approach gave rise to **2c** in 43% yield (2 steps).

The catalytic performance of **2c** was tested by using the [Pd(0)]-catalysed AAA of dimethyl malonate **9** with 1,3-diphenylallyl carbonate (**8**) as the probe reaction (Scheme 2). Under optimal conditions, comparable results for **1a** in terms of isolated yield and enantiomeric excess (yield 99%, *ee* 93%) were obtained, proving the reliability of our approach.

Recent investigations addressed toward the possibility of fine-tuning the features of these chiral Pd-complexes by *molecular remote control* (MRC)[7b] pointed out that the introduction of electron-donating groups both on the outer and inner thienyl unit markedly increases the catalytic properties of the whole catalyst. In the light of these findings we decided to evaluate this peculiar electronic effect also in the analogous supported catalysis by synthesizing the C_1 precursor **2b**.

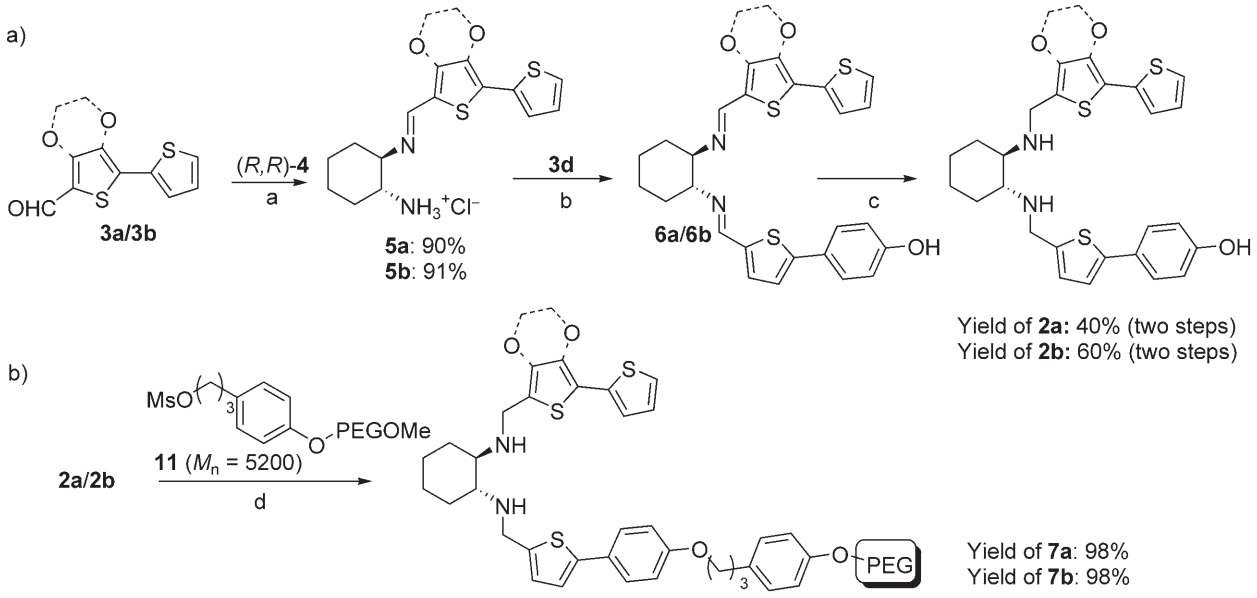


Scheme 2. Asymmetric allylic alkylation: model reaction.

The syntheses of **2a** and **2b** were carried out following the synthetic plan highlighted in Scheme 1 for **2c**. Here, the chemoselective condensation of (*R*,*R*)-**4** to commercially available 2,2′-bithiophene-5-carbaldehyde **3a** or (2-EDOT-2′-thienyl)-5-carbaldehyde **3b**[7b] furnished the corresponding mono-imines **5a**, **5b** (90% and >90%, respectively) that were subsequently transformed to the bis-imines **6a**/**6b** in the presence of the phenol-thienylaldehyde **3d** (see Supporting Information for details). The final ligands were easily obtained by reduction of **6a**/**6b** with $NaBH_4$ in 40% and 60% yield, respectively (Scheme 3, reaction a).

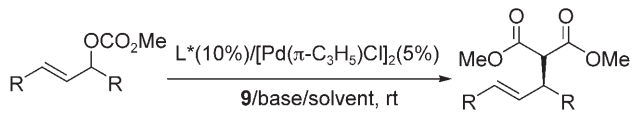
Following the well-developed methodology employed in the synthesis of poly(ethylene glycol)-supported chiral organic[9] as well as organometallic catalysts[10], C_1 DAT ligands were anchored to a properly modified PEG derivative. The reaction of 1.1 mol equivs. of ligands **2a/2b** with 1 mol equiv. of the readily available mesylate **11**[11] in the presence of Cs_2CO_3 (DMF, 55°C, 48 h) afforded the PEG-supported ligands **7a** and **7b** in quantitative yield (Scheme 3, reaction b).

In analogy with the homogeneous *DATs* applications,[7] we chose to test the new PEG-C_1-*DATs* **7a** and **7b** in the model reaction depicted in Scheme 2, and we examined the generality of the protocol by applying the supported catalysts to different linear hindered and unhindered allyl carbonates (**8a–c**).



Scheme 3. Synthesis of **2a,b** and their grafting to $MeOPEG_{5000}$. *Reagents and conditions:* a) (*R,R*)-**4**/$MgSO_4$/EtOH:MeOH, room temperature, 48 h; b) **3c**/TEA/$MgSO_4$/DCM; c) $NaBH_4$/MeOH, 0°C → room temperature, 16 h; d) Cs_2CO_3, DMF, 55°C, 48 h.

Table 1. Optimization of reaction conditions for allylic substitution with supported Pd(II)-**7a** and **7b**.[a]



(±)-**8a** R = C_6H_5
(±)-**8b** R = *p*-ClC_6H_4
(±)-**8c** R = Me

(*S*)-**10a, 10b,** (*S*)-**10c**

Entry	L*	Solvent	Base	**10**	Yield [%][b]	*ee* [%][c]
1[d]	**1a**	THF	BSA/ KOAc	**10a**	96	99
2	**7a**	CH_2Cl_2	K_2CO_3	**10a**	80	86
3	**7a**	CH_2Cl_2	Cs_2CO_3	**10a**	90	95
4	**7a**	CH_2Cl_2[e]	NaH	**10a**	99	97
5	**7b**	CH_2Cl_2	Cs_2CO_3	**10a**	58	82
6	**7a**	THF	Cs_2CO_3	**10a**	98	99
7	**7a**	THF	NaH	**10a**	99	97
8	**7a**	CH_2Cl_2	Cs_2CO_3	**10b**	80	99
9	**7a**	CH_2Cl_2	Cs_2CO_3	**10c**	50	78
10	**7b**	CH_2Cl_2	Cs_2CO_3	**10c**	41	38

[a] All the reactions were carried out at room temperature by using a 1:1 L:Pd ratio (24 h).
[b] Isolated yields after flash chromatography.
[c] Determined by chiral HPLC (**10a**, **10b**) and by chiral GC for **10c**. The absolute configuration was assigned by comparison with the known optical rotation value.
[d] $[Pd_2(dba)_3]\cdot CHCl_3$ was used as the palladium source.
[e] Sodium malonate was prepared in THF and then added to the CH_2Cl_2 reaction mixture (CH_2Cl_2:THF, 3:1).

In Table 1 we summarise a collection of results obtained during the survey of reaction conditions. To ensure truly homogeneous conditions we initially tested the *in situ* formed catalyst[12] [Pd(II)-**7a**] CH_2Cl_2 with a range of base systems (entries 2–4). To our delight, no loss of activity was recorded with the structurally modified **7a** (10 mol%) respect to the non-supported ligand **1a** (entry 1). In particular, the employment of Cs_2CO_3 and NaH furnished **10a** in > 90% yield with enantiomeric excesses up to 97% (entries 3 and 4). Noteworthy, these values are among the highest reported to date for AAA in the presence of PEG-supported catalysts.[13]

Due to the fact that THF resulted to be the solvent of choice for the protocol with ligand **1a/b**, we investigated the possibility to employ [Pd(II)]-**7a** in such a reaction medium (heterogeneous catalysis). Remarkably, the reaction was successful giving **10a** with yield (98%) and stereoselectivity (*ee* 99%) comparable to that obtained in homogeneous conditions (entry 6 *vs.* 3). To our knowledge, this is the first case in which a catalytic system can be employed in the same transformation with comparably high efficiency both under homogeneous and heterogeneous conditions.

Moreover, the supported catalyst displayed the generality in scope of homogeneous *DATs* with particular regard to acyclic allyl carbonates. Here, hindered aromatic substrate **8b** underwent smoothly the allylic alkylation in 80% yield and 99% *ee* (entry 8), and also in the case of the more challenging aliphatic carbonate **8c** comparable enantioselectivity with respect to **1a** was recorded (*ee* 78% *vs.* 77%).[7a]

Finally, inferior results in terms of chemical and optical outcomes were obtained with **7b** that proved to be less effective than **7a** for both aromatic as well as aliphatic substrates (entries 5 and 10). We tentatively ascribed the drop in catalytic performace to deleterious interactions involving the EDOT pendage and the bulk of the PEG structure that significantly limits the necessary conformational flexibility of the anchored chiral unit.

Next, attempts to recover and reuse the ligand were carried out and the results over three consecutive runs are summarised in Table 2. An optimised reaction work-up that involves removal of the insolubles (Cs_2CO_3 and [Pd(0)] species) by filtration on celite, allowed **7a** to be recovered (65–70%) after each run and effectively reused in the AAA of **8a** with **9** without appreciable loss of activity.

Table 2. Recycling of (*R,R*)-**7a** in the Pd-catalysed allylic substitution with carbonate **8a.**[a]

Entry	Time [h]	Yield [%][b]	*ee* [%][c]
1	24	90	95 (*S*)
2	24	91	92 (*S*)
3	24	84	92 (*S*)

[a] All the reactions were carried out in CH_2Cl_2 at room temperature, [Pd(II)]:**7a** = 1:1 and Cs_2CO_3 as the base. [Pd(η^3-C_3H_5)Cl]$_2$ (5 mol%) was added for each consecutive run.
[b] Isolated yields after flash chromatography.
[c] Determined by HPLC analysis with chiral column (Chiralcel AD). The absolute configuration was assigned by comparison with the known optical rotation value.

Then, the coordination mode of **7a** was investigated by comparing the ^{1}H NMR spectrum (CD_3CN, room temperature) of the isolated cationic [Pd(η^3-$Ph_2C_3H_3$)]-**7a** complex (see Experimental Section) with that of [Pd(η^3-$Ph_2C_3H_3$)]-**1a**. The comparable chemical shifts of the diagnostic allyl unit {supported complex: δ = 4.68 (d, J = 9.2 Hz, 1H), 5.48 (d, J = 9.2 Hz, 1H), 6.60–6.72 (m, 1H) to be compared with [Pd(η^3-$Ph_2C_3H_3$)]-**1a**: δ = 4.64 (d, J = 9.2 Hz, 1H), 5.46 (d, J = 9.2 Hz, 1H), 6.64–6.71 (m, 1H)}, led us to suppose an *N,N*-binding mode also for the supported ligand.

The possibility of recovering and successively recycling the supported organometallic catalytic species

was then examined. To this purpouse, when the reaction under the model homogeneous conditions (**8a**/**9**/Cs_2CO_3/CH_2Cl_2) was judged complete by TLC, anhydrous Et_2O was added to the reaction crude under an inert atmosphere with the consequent precipitation of the supported Pd catalyst. The slurry was then kept at 0 °C (ice bath) for 10 min and the liquid removed by syringe.

The solid residue was then dried under vacuum and reused without the addition of Pd salt. This procedure allowed us to perform up to three consecutive runs (Table 3) although losses in activity (from 98 % to 30 % yield) and enantioselectivity (from 95 % to 66 % *ee*) were observed over the three cycles. These results are comparable to those previously reported for AAA reactions promoted by chiral phosphine-based ligands linked to soluble organic polymers.[13g,h] The formation of black insoluble, poorly stereoselective [Pd(0)] clusters that are retained by the PEG matrix could be responsible for the drop in catalytic performaces.[14]

Table 3. Recycling of **7a** in the Pd-catalysed allylic substitution with carbonate **8a** without any addition of Pd after the first run.[a]

Entry	Time [h]	Yield [%][b]	*ee* [%][c]
1	24	90	95 (*S*)
2	36	46	86(*S*)
3	48	30	66 (*S*)

[a] All the reactions were carried out in CH_2Cl_2 at room temperature, by using 5 mol % of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ as the Pd source, **7a** as ligand, a 1:1 L:Pd ratio and Cs_2CO_3 as the base.

[b] Isolated yields after flash chromatography.

[c] Determined by HPLC analysis with chiral column (Chiralcel AD). The absolute configuration was assigned by comparison with the known optical rotation value.

In summary, we have presented our preliminary results toward the recovery and the recycle of a "young" class of chiral ligands (*DATs*), obtained by grafting two phenolic-modified derivatives to $MeOPEG_{5000}$. The anchored ligands proved to be efficient in Pd-catalysed AAA under homogeneous as well as heterogeneous conditions on various substrates affording yields and enantioselectivities comparable to those obtained with the non-immobilised catalytic species. The present strategy allowed the almost complete recovery of the ligand (up to three times), that was reused without appreciable loss of chemical and stereochemical efficiency. Then, a properly optimised reaction work-up rendered possibile also the recycling of the whole organometallic species even if a significant erosion in chemical and stereochemical yields was observed over three consecutive runs. We are currently examining the scope of this class of supported ligands in different environmentally friendly metallo-catalysed stereoselective transformations and the results will be reported in due course.

Experimental Section

Suzuki Cross-Coupling for the Synthesis of 3b and 3c

In a 100 mL, two-necked flask 5-bromo-2-thiophenecarbaldehyde (2 mmol) and $PdCl_2(PPh_3)_2$ (0.1 mmol) were dissolved in 8 mL of DME. Then, 4 mL of EtOH were added followed by the corresponding boronic acid (2.6 mmol) and 6 mL of Na_2CO_3 (2 M). The reaction mixture was refluxed overnight, then the solution was cooled at room temperature and 10 mL of H_2O were added. After elimination of the volatiles under vacuum, the aqueous phase was extracted with AcOEt, dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel.

Synthesis of 2a,b and 2c

In a 50 mL two-necked flask, mono-ammonium salt (*R,R*)-**4**[8] (1 equiv.) and aldehyde **3** (1 equiv.) were dissolved in 20 mL of a mixture of EtOH/MeOH (1/1). After the reaction mixture had been stirred at room temperature for 24 h, the solvent was removed under reduced pressure leaving the mono-imine compound **5**.

Imine-mono salt intermediate **5** (1 equiv.) was dissolved under a N_2 atmosphere in 15 mL of CH_2Cl_2. Then, TEA (2.0. equivs.), aldehyde **3c**/**d** (1 equiv.) and $MgSO_4$ (2.5 equivs.) were successively added and the mixture stirred at room temperature for 32 h. After evaporation of CH_2Cl_2, the crude was washed with Et_2O to separate the insoluble ammonium salts from the desired product and the solvent evaporated under reduced pressure. Finally, **6** (1 equiv.) was dissolved in 5 mL of MeOH and $NaBH_4$ (5.0 equivs.) was added portionwise. The mixture was stirred overnight at room temperature then, 8 mL of water were added and the product was extracted with CH_2Cl_2 (3 × 4 mL). Evaporation of the volatiles afforded a crude **2** product that was purified by washing with 10 mL of *c*-hexane.

Synthesis of PEG-C_1-*DATs* (7a,b)

To a solution of mesylate **11** (0.9 g, 0.17 mmol) in dry DMF (3 mL) stirred under nitrogen at 55 °C, caesium carbonate (0.180 g, 0.55 mmol), and ligand **2a** or **2b** (0.19 mmol) were added. The mixture was stirred for 48 h at 55 °C. After filtration, the reaction mixture was cooled to room temperature to eliminate Cs_2CO_3, then dichloromethane (1 mL) was added and the solution was poured into Et_2O (70 mL); the precipitated PEG-supported ligands were recovered by filtration and washed with Et_2O (20 mL).

Representative Procedure for Pd-Catalysed AAA under Homogeneous Conditions (CH_2Cl_2)

A flamed-dried, 25 mL, two-necked flask was charged, under a nitrogen atmosphere with $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.8 mg, $5\cdot10^{-3}$ mmol), supported diamine **7a** (55 mg, 0.01 mmol) and 1.5 mL of anhydrous CH_2Cl_2. The mixture was stirred at room temperature for 5 min, then **8** (0.1 mmol), dimethyl malonate **9** (57 μL, 0.5 mmol), and Cs_2CO_3 (65 mg, 0.2 mmol) were added sequentially. The mixture was stirred overnight at room temperature until the reaction was judged complete by TLC analysis. The ligand was recovered by solvent evaporation followed by addition of Et_2O (5 mL). The solid was recovered by filtration on a sintered glass funnel and washed with Et_2O. The filtrate was evaporated under vacuum to give a crude product that was purified by flash chromatography.

Representative Procedure for the Synthesis of the 7a-$[Pd(\eta^3\text{-}Ph_2C_3H_3)]\cdot[BF_4]$ Complex

A flamed-dried, 25 mL flask was charged with 3 mL of anhydrous DCM followed by 85 mg ($\approx$ 0.015 mmol) of **7a** and 6.6 mg ($7.5\cdot10^{-3}$ mmol) of $[Pd(\eta^3\text{-}Ph_2C_3H_3)Cl]_2$. The yellow-orange mixture was stirred for 1 h after which 4 mg of $AgBF_4$ (0.015 mmol) were added at once. The mixture was then placed in the dark and stirred overnight at room temperature. The insolubles were then filtered and the filtrate reduced to 1/3 of its original volume. Cold anhydrous Et_2O (2 mL) was then added causing precipitation of the supported complex as a pale-yellow solid. The slurry was kept at 0 °C for 30 min then filtered to recover the complex. Yield: 62 mg (*ca.* 71 %). ^{1}H NMR (CD_3CN, 300 MHz, diagnostic signals): $\delta = 4.68$ (d, $J = 9.2$ Hz, 1 H), 5.48 (d, $J = 9.2$ Hz, 1 H), 6.60–6.72 (m, 1 H).

Recovery of the Ligand 7a (Table 2)

The crude reaction mixture was passed through a pad of celite and washed with a mixture DCM:MeOH (95:5) in order to remove the excess of Cs_2CO_3 and the black [Pd(0)] particles. The pale yellow filtrate was concentrated under reduced pressure and the PEG-**7a** was finally recovered by precipitation with an excess of Et_2O. After filtration 70 % of the supported ligand was recovered and reused in the next run without further purification.

Recovery of the Whole Pd-7a under Homogeneous Conditions (Table 3)

To isolate the reaction adduct and recover the organometallic system, anhydrous diethyl ether was added to the reaction mixture under an inert atmosphere to precipitate the supported catalyst. After holding the mixture at 0 °C for 10 min, the solution was removed under an N_2 atmosphere by syringe. The solid residue was dried and reused in the same flask without any further Pd addition.

Representative Procedure for Pd-Catalysed AAA under Heterogeneous Conditions (THF)

A flame-dried, 25 mL two-necked flask was charged, under a nitrogen atmosphere, with $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.8 mg, $5\cdot10^{-3}$ mmol), supported diamine **7** (0.01 mmol) and 1.5 mL of anhydrous THF. The mixture was stirred at room temperature for 5 min, then **8** (0.1 mmol), dimethyl malonate **9** (57 μL, 0.25 mmol), and Cs_2CO_3 (65 mg, 0.2 mmol) were added sequentially. The reaction mixture was stirred overnight at room temperature and the liquid removed by a syringe, collected and evaporated to give the crude product which was then purified by flash cromatography.

Acknowledgements

This work was supported by M.I.U.R. (Rome), National project "Sintesi e stereocontrollo di molecole organiche per lo sviluppo di metodologie innovative di interesse applicativo", FIRB Project (Progettazione, preparazione e valutazione biologica e farmacologica di nuove molecole organiche quali potenziali farmaci innovativi) and from University of Bologna.

References

[1] E. N. Jacobsen, A. Pfaltz, H. Yamamoto, (Eds.), *Comprehensive Asymmetric Catalysis*, Springer, Berlin, **1999**.
[2] B. M. Trost, *Proc. Nat. Acad. Sci.* **2004**, *101*, 5348–5353.
[3] a) R. A. Sheldon, H. van Bekkum, *Fine Chemicals Through Heterogeneous Catalysis*, Wiley-VCH, Weinheim, **2001**; b) B. H. Lipshutz, B. A. Frieman, A. E. Tomaso, Jr., *Angew. Chem. Int. Ed.* **2006**, *45*, 1259–1264.
[4] a) N. E. Leadbeater, M. Marco, *Chem. Rev.* **2002**, *102*, 3217–3274; b) D. E. Bergbreiter, *Chem. Rev.* **2002**, *102*, 3345–3384; c) Q.-H. Fan, Y.-M. Li, A. S. C. Chan, *Chem. Rev.* **2002**, *102*, 3385–3466.
[5] a) T. J. Dickerson, N. N. Reed, K. D. Janda, *Chem. Rev.* **2002**, *102*, 3325–3344; b) D. E. Bergbreiter, *Chem. Rev.* **2002**, *102*, 3345–3384. For a recent review on polymer-supported organic catalysts, see: M. Benaglia, A. Puglisi, F. Cozzi, *Chem. Rev.* **2003**, *103*, 3401–3429.
[6] a) B. M. Trost, D. L. Van Vraken, *Chem. Rev.* **1996**, *96*, 395–422; b) G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336–345; c) B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921–2943.
[7] a) V. G. Albano, M. Bandini, M. Melucci, M. Monari, F. Piccinelli, S. Tommasi, A. Umani-Ronchi, *Adv. Synth. Catal.* **2005**, *347*, 1507–1512; b) V. G. Albano, M. Bandini, G. Barbarella, M. Melucci, M. Monari, F. Piccinelli, S. Tommasi, A. Umani-Ronchi, *Chem. Eur. J.* **2006**, *12*, 667–675.

[8] E. J. Campbell, S. T. Nguyen, *Tetrahedron Lett.* **2001**, *42*, 1221–1225.
[9] For selected references, see: a) M. Benaglia, G. Celentano, F. Cozzi, *Adv. Synth. Catal.* **2001**, *343*, 171–173; b) M. Benaglia, M. Cinquini, G. Celentano, F. Cozzi, A. Puglisi, *Adv. Synth. Catal.* **2002**, *344*, 533–542; c) M. Benaglia, M. Cinquini, G. Celentano, F. Cozzi, *Eur. J. Org. Chem.* **2004**, 567–573 and references cited therein.
[10] a) R. Annunziata, M. Benaglia, M. Cinquini, F. Cozzi, M. Pitillo, *J. Org. Chem.* **2001**, *66*, 3160–3166; b) M. Benaglia, M. Cinquini, G. Celentano, F. Cozzi, *Org. Biomol. Chem.* **2004**, *2*, 3401–3407.
[11] M. Benaglia, S. Guizzetti, C. Rigamonti, A. Puglisi, *Tetrahedron* **2005**, *61,* 12100–12106.
[12] $Pd(\pi\text{-}C_3H_3)Cl]_2$ proved to be superior to [Pd(0)] species in the present supported catalytic asymmetric transformation.
[13] a) Y. Uozumi, H. Danjo, T. Hayashi, *Tetrahedron Lett.* **1998**, *39*, 8303–8306; b) M. Glos, O. Reiser, *Org. Lett.* **2000**, *2*, 2045–2048; c) C. Saluzzo, R. ter Halle, F. Touchard, F. Fache, E. Schulz, M. Lemaire, *J. Organomet. Chem.* **2000**, *603*, 30–39; d) Y. Uozumi, K. Shibatomi, *J. Am. Chem. Soc.* **2001**, *123*, 2919–2920; e) O. Belda, S. Lundgren, C. Moberg, *Org. Lett.* **2003**, *5*, 2275–2278; f) D. Zhao, J. Sun, K. Ding, *Chem. Eur. J.* **2004**, *10*, 5952–5963; g) H. Nakano, K. Takahashi, Y. Suzuki, R. Fujita, *Tetrahedron: Asymmetry* **2005**, *16*, 609–614; h) H. Nakano, K. Takahashi, R. Fujita, *Tetrahedron: Asymmetry* **2005**, *16*, 2133–2140.
[14] Indications for the presence of [Pd(0)] species embedded into the organic polymer came from the dark grey colour of the recovered PEG-supported catalyst.

