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A Recyclable Chiral 2-(Triphenylmethyl)pyrrolidine Organocatalyst Anchored to [60]Fullerene

Cristian Rosso,[a] Marco G. Emma,[b] Ada Martinelli,[b] Marco Lombardo,[b,*] Arianna Quintavalla,[b] Claudio Trombini,[b,e] Zois Syrgiannis,[a] Maurizio Prato[a,c,d,*]

[a] Department of Chemical and Pharmaceutical Sciences, University of Trieste, Trieste, Italy; e-mail: prato@units.it
[b] Department of Chemistry "G. Ciamician", University of Bologna, Bologna, Italy. Phone: +39 051 2099544; e-mail: marco.lombardo@unibo.it
[c] Nanobiotechnology Laboratory, CIC biomaGUNE, San Sebastiàn, Spain
[d] Ikerbasque, Basque Foundation for Science, Bilbao, Spain
[e] CINMPIS (Consorzio Interuniversitario Nazionale di ricerca in Metodologie e Processi Innovativi di Sintesi), University of Bari, Bari, Italy

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Abstract. Hybridization of a chiral 3-hydroxy-2-trityl-pyrrolidine deriving from (*R*)-pyrrolidinol with [60]fullerene via click chemistry provides a highly efficient supported enantioselective organocatalyst, which was successfully exploited in a Michael addition of malonates to cinnamaldehydes, via iminium ion activation. The supported organocatalyst was recycled up to six times with only a moderate decrease in terms of activity and with no loss in enantioselectivity.

Keywords: Enantioselective organocatalysis; [60]Fullerene; Supported trityl-pyrrolidine; Michael addition; Catalyst recycling.

Introduction

Carbon nanoforms such as fullerenes, nanotubes and graphene have attracted the interest of the scientific community, owing to their potential use in a wide range of applications.[1] Fullerenes, the oldest members of this family, was initially investigated in terms of reactivity and different procedures to synthesize more soluble and processable derivatives were examined. After this first 25 years' momentum, nowadays fullerenes chemistry focuses mostly on new applications.[2] Fullerenes have also been employed as supports for metal catalysts, either nanoparticles and organometallic complexes.[3] However, only few examples have appeared in the literature dealing with fullerene as support for organocatalysts.[4]

The Hayashi-Jørgensen catalysts **1** (Figure 1) are nowadays among the most reliable organocatalysts, particularly for iminium-based transformations such as cycloaddition reactions (*e.g.* Diels-Alder and 1,3-dipolar cycloadditions, *etc.*) and conjugate addition reactions (*e.g.* Michael additions, 1,4-additions of C, S, N or O nucleophiles and epoxidation of α,β-unsaturated carbonyl compounds, carboxylic acid derivatives, α-aminations *etc.*).[5] Contrary to the MacMillan catalysts that are almost exclusively used in iminium-mediated reactions,[6] the Hayashi-Jørgensen catalysts **1** are also effectively used in enamine-based processes.[5] The privileged catalysts **1**, however, are not drawback-free and are indeed object of investigations and modifications in order to overcome their intrinsic limitations. The major one is the relative hydrolytic stability of the silyl ether group, which in many cases prevents an efficient catalyst recycling. A general way to increase the lifetime of **1** is to bind them to a proper scaffold that confers the desired stability. There are studies in which Hayashi-Jørgensen catalysts are supported on a solid matrix to optimize both the catalyst-product separation and the catalyst recycling. Among solid supports for the Hayashi-Jørgensen catalysts, oligomeric silsesquioxane (POSS) or Wang resins,[7] super-paramagnetic nanoparticles[8] and porous polymers[9] are worth mentioning.

A different approach involves the replacement of the water sensitive diarylmethyl silyloxy group present

in **1** with an isosteric bulky and more stable group. Maruoka recently proposed the use of trityl pyrrolidines **2** (Figure 1) as a surrogate of **1**, where the bulky trityl group shields one diastereotopic face of the reactive intermediate.[10] Trityl pyrrolidines have been used in enamine-type organocatalysis for asymmetric α-functionalizations of aldehydes, such as the α-benzoyloxylation with dibenzoyl peroxide in combination with hydroquinone,[10a,c] the α-hydroxyamination in combination with MnO_2[10b,11] or more recently in the asymmetric conjugate addition of aldehydes to α–selenoenones.[10d] In these studies **2** was found more reactive and stereoselective than **1**.

Results and Discussion

Inspired by trityl-pyrrolidines **2**, virtually unexplored in organocatalytic applications other than the previously mentioned papers,[10,11] we decided to bind a similar derivative to [60]fullerene (C_{60}) through a flexible acyclic linker and to investigate reactivity, reaction rates, enantioselectivity and recyclability of the newly obtained species **3** (Figure 1).

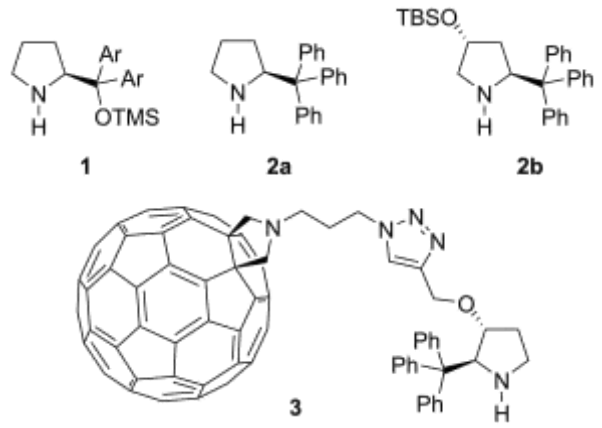
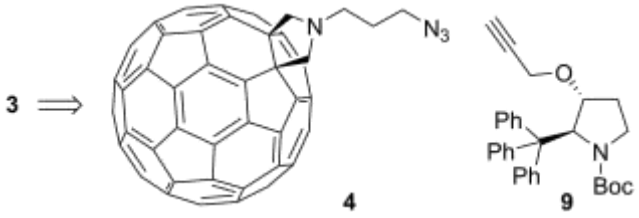


Figure 1. Hayashi-Jørgensen catalysts **1**, Maruoka catalysts **2** and C_{60}-supported catalyst **3**.

Some examples of [60]fullerene-organocatalyst hybrids were recently reported. Thus, fullerothioureas were claimed as recyclable and stereoselective catalysts for the nitro-Michael reaction.[4b] Fullerene anchoring two, four or twelve TEMPO moieties have been also reported by Gruttadauria *et al*. as efficient oxidizing agents for alcohols.[4c,d] Kokotos *et al*. conjugated both fullerene[4e] and multi-walled carbon nanotubes[4f,g] with proline getting new catalysts for the asymmetric aldol reaction.

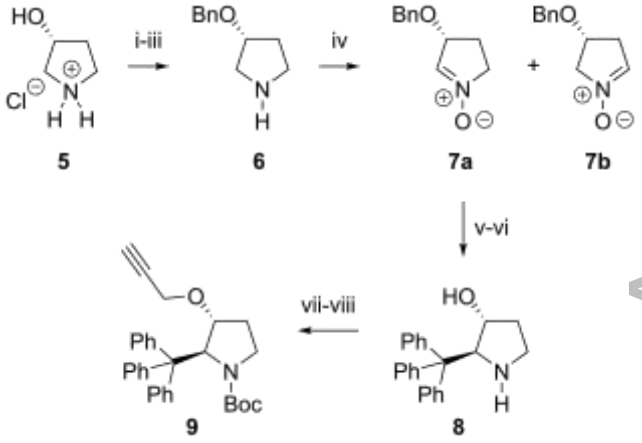
Besides acting as a platform covalently binding a catalytically active species, fullerene, as well as carbon-nanotubes (CNTs) and graphene, exert their own effects as catalysts, which we refer to with the term carbocatalysis.[12] In particular, we are interested in investigating the possible participation of intrinsic redox properties of C_{60} as well as the effect of π-stacking interaction between C_{60} and conjugate planar substrates.[4a]

At a first glance, the convergent synthesis of [60]fullerene−tritylpyrrolidine hybrid **3**, starting from a pyrrolidine cycloadduct functionalized with a 3-azidopropyl chain on nitrogen (**4**) and *N*-Boc-3-propargyloxy-2-trityl-pyrrolidine (**9**) respectively, clicked together in the final step, seemed the most obvious strategy (Scheme 1). However, the 1,3-dipolar cycloaddition took place in very poor yield under all reaction conditions tested, most probably due to the presence of the reactive azido group, able to participate in undesired C_{60} functionalizations.



Scheme 1. Initial retrosynthetic strategy to C_{60}-supported catalyst **3**.

The key-intermediate **9** was prepared starting from the chiral cyclic 5-membered ring nitrone **7a**, in turn derived from commercial (*R*)-3-hydroxypyrrolidine hydrochloride **5**. Addition of trityl lithium to **7a** and reductive cleavage of both the Bn-O and the N-O bonds, afforded **8**, which led in a few steps to the protected trityl-pyrrolidine **9** (Scheme 2).



Scheme 2. i) K_2CO_3, EtOCOCl, MeOH, 0 °C, 78 %; ii) BnBr, NaH, TBAI, THF, 0 °C, 91 %; iii) KOH, EtOH/H_2O 4:1, reflux, 88 %; iv) Oxone®, Na_2EDTA, $NaHCO_3$, CH_3CN/THF 4:1, 0 °C, 88 % (**7a**:**7b** = 85:15); v) Ph_3CLi, THF, 0 °C to RT, 74%; vi) H_2, Pd/C, AcOH, 76 %; vii)

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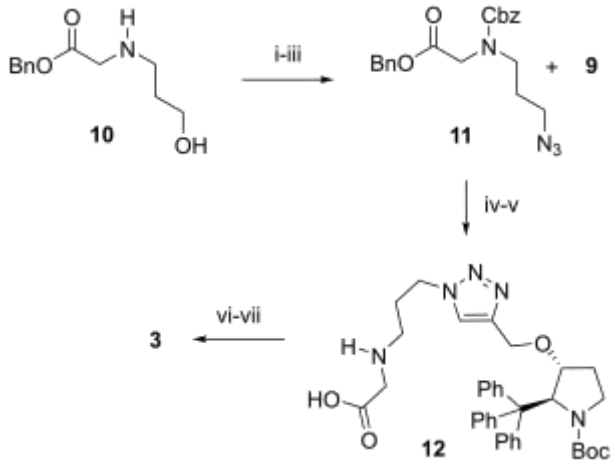
Boc_2O, Et_3N, DCM, 96 %; viii) propargyl bromide, TBAI, NaH, 0 °C, 90 %.

Using the key intermediate **9**, we eventually succeeded in the synthesis of **3** by carrying out the cycloaddition reaction in the late stage, according to Scheme 3.



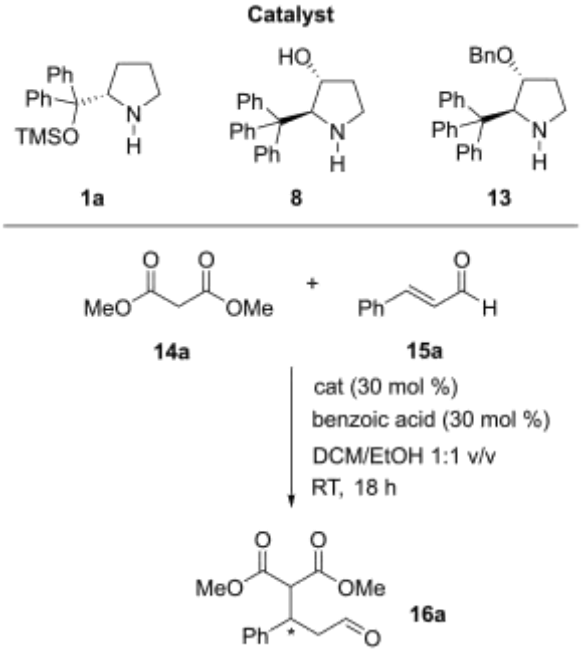
Scheme 3. i) CbzCl, Et_3N, DCM, 95 %; ii) MsCl, Et_3N, DCM, 99 %; iii) NaN_3, DMF, 71%; iv) $CuSO_4 \cdot 5H_2O$, sodium ascorbate, H_2O/*t*-BuOH, 93 %; v) H_2, Pd/C, MeOH, 99%; vi) C_{60}, $(CH_2O)_n$, toluene, reflux, 53 %; vii) TFA, DCM, 0 °C, 99 %.

Click-chemistry offered the tool to bind **9** and **11**, in turn easily accessible from the glycine derivative **10**. Hydrogenolytic cleavage of the protective groups on the glycine moiety and the cycloaddition reaction were the final transformations that allowed us to get **3**, after removal of the Boc group, in an overall 50 % yield over the last two steps. We found that **3** can be preserved intact for a few months stored under an inert atmosphere. Air contact under light generates in the medium term (1 week) some amount of oxidation products of fullerene.

As the benchmark reaction, we chose the Michael addition of dimethyl malonate **14a** to cinnamaldehyde **15a**, a reaction that involves the formation of an intermediate iminium ion (Table 1). It is interesting to note that the few applications of trityl pyrrolidines in organocatalysis have been essentially limited to enamine-based chemistry.[10,11] In an elegant kinetic study, Mayr confirmed that the trityl group as well as the $CPh_2(OSiMe_3)$ group increase the electrophilicity of iminium ions derived from **2** and **1**, respectively, compared to simple pyrrolidine iminium ions.[13]

Before testing the catalytic performance of **3**, we checked as catalysts **1a** and two intermediates in the synthesis of **3**, namely **8** and **13**, in order to have a reference material on which to compare the reactivity of **3**. The results obtained in these preliminary runs are collected in Table 1.

Table 1. Michael additions of methyl malonate (**14a**) to cinnamaldehyde (**15a**) catalyzed by unsupported organocatalysts **1a**, **8** and**13**.



Catalyst[a]	Conversion [%][b]	**16a**, *ee* [%][c]
1a	99	(*R*)-**16a**, 74
8	85	(*S*)-**16a**, 92
13	79	(*S*)-**16a**, 90

[a] The reactions were carried out on a 0.1 mmol scale of **14a** in DCM/EtOH (1:1 v/v) using a catalyst loading of 30 mol % in the presence of benzoic acid (30 mol %) and **15a** (1.5 equiv). [b] Determined by ^{1}H-NMR analysis of the crude reaction mixture after 18 h. [c] Determined by CSP-HPLC analysis of the Horner-Wadsworth-Emmons ester derivative (see Experimental Section).

Under the selected reaction conditions, both **8** and **13** revealed less reactive than the Hayashi catalyst **1a**, but more enantioselective. These preliminary promising results prompted us to investigate the reactivity of **3**, but the extension to the supported organocatalyst had to cope with solubility problems. Indeed, the Michael reaction that exploits benzoic acid as co-catalyst needs methanol or ethanol as co-solvent, but the solubility of **3** in the presence of relevant amounts of alcohols is quite poor. The best solvent for **3** is DCM alone and a solution was found by moving from benzoic acid to a basic additive.

Pericàs, for instance, successfully proposed the use of solid lithium acetate in DCM for Michael reactions catalyzed by α,α-diphenylmethylprolinol methyl- and trimethylsilyl ethers, anchored onto a polystyrene resin.[14] Under the same conditions, we got highly promising results, as summarized in Table 2.

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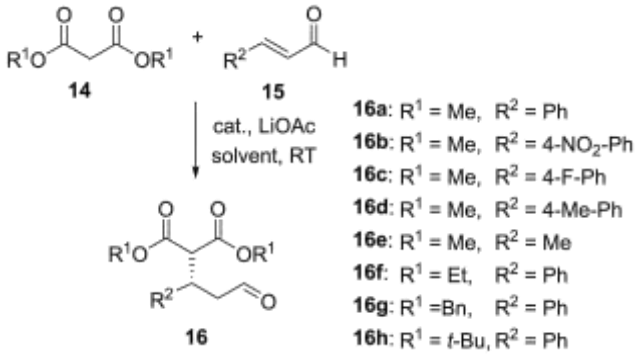
Table 2. Michael additions of malonates **14** to cinnamaldehydes **15**, catalyzed by **3** or **13**, in the presence of LiOAc.



Entry[a]	Solvent	cat. [mol %]	t [h]	**16**, conv. [%][b]	*ee* [%][c]
1	DCM	**3**, 10	8	**a**, 85	94
2	DCM/MeOH (9:1 v/v)	**3**, 10	5	**a**, 97	80
3	DCM/MeOH (95:5 v/v)	**3**, 10	5	**a**, 96	84
4	DCM	**3**, 5	16	**a**, 91	91
5	DCM	**13**, 5	16	**a**, 80	88
6[d]	DCM	**13**, 5	16	**a**, 76	77
7	DCM	**3**, 5	24	**b**, 83	85
8	DCM	**3**, 5	24	**c**, 89	85
9	DCM	**3**, 5	24	**d**, 88	84
10	DCM	**3**, 5	24	**e**, 0	-
11	DCM	**3**, 5	24	**f**, 74	nd[e]
			48	**f**, 82	93
12	DCM	**3**, 5	24	**g**, 79	nd[e]
			48	**g**, 80	92
13	DCM	**3**, 5	24	**h**, 0	-
14[f]	DCM	**3**, 5	16	**a**, 89[g]	94
15[f]	DCM	**3**, 5	24	**c**, 83[g]	85
16[h]	DCM	**3**, 5	16	**a**, 90	94

[a] Reaction conditions: Aldehyde **15** (0.1 mmol), malonate **14** (3 equiv), catalyst, dry LiOAc (3 equiv. with respect to catalyst amount) and solvent with a concentration of the limiting aldehyde = 0.5 M. [b] Conversion determined by ^{1}H-NMR analysis of the crude reaction mixture. [c] Determined by CSP-HPLC analysis of the Horner-Wadsworth-Emmons ester derivative (see Experimental Section). [d] LiOAc·2H_2O was used. [e] nd = not determined. [f] Reaction run on 0.5 mmol of limiting aldehyde **15**. [g] Isolated yield after purification by flash chromatography on silica. [h] Reaction run on 2 mmol of limiting aldehyde **15**.

Entries 2 and 3 show that the presence of 5-10 % of MeOH in DCM does not significantly affect the solubility of **3**. Indeed, compared to pure DCM (entry 1), the presence of methanol speeds up the reactions (Figure 2), but at the expenses of enantioselectivity.

The catalyst loading may be lowered to 5 mol %, but in this case a 2-fold increase of the reaction time is required (entry 4). When the unsupported catalyst **13** was used in these conditions (entry 5), the enantioselectivity was almost the same, but a notable drop in reactivity was observed. It is worth noticing also that if LiOAc·2H_2O is used as the co-catalyst instead of dry LiOAc (entry 6), the enantioselectivity obtained is considerably lower.

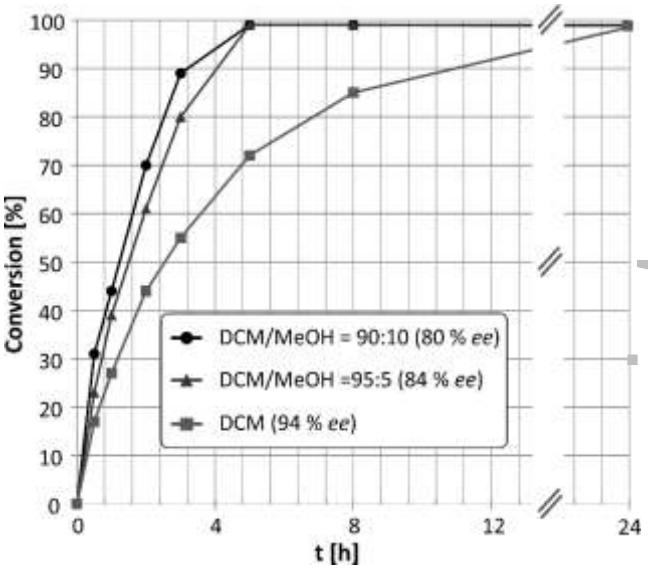


Figure 2. Michael additions of malonate **14a** to cinnamaldehyde **15a** catalyzed by **3** and dry LiOAc in different solvents.

Substituents on the phenyl ring of cinnamaldehydes provide slightly reduced enantioselectivities (entries 7-9), while primary alkyl groups on the ester moiety of malonates (Et and Bn) do not impact on the final *ee* values (entries 11 and 12), although an expected reactions slowdown was observed. The two substrates that do not work are crotonaldehyde (entry 10) and *t*-butyl malonate (entry 13). Crotonaldehyde-derived iminium ion can rearrange into a dienamine, which can be responsible of the several observed side-products,[15] while the bulkiness of the two *t*-butoxy groups of *t*-butyl malonate could hinder the approach of malonate anion to the iminium ion.

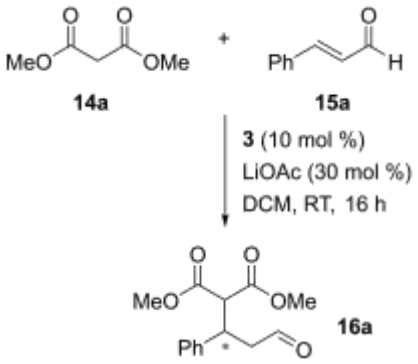
The reactions with aldehydes **15a** and **15c** were scaled up to 0.5 mmol (entries 14 and 15) and the final yield was determined after purification by flash-chromatography on silica. Finally, the reaction with cinnamaldehyde **15a** was run on the 2 mmol scale (entry 16), confirming the excellent performances of the catalytic system.

The robustness of a catalyst and the reliability of a catalytic process find an important hint in the recyclability of the catalytically active species. To recycle the organocatalyst **3**, the reaction mixture corresponding to Table 2, entry 1, was stirred in a microcentrifuge tube (2 mL) and purged with inert gas. After 16 h, the mixture was diluted with MTBE (1 mL) and centrifuged (5 min, 8000 rpm). The organic layer

containing the product was removed and the extraction procedure was repeated three times. The catalyst containing solid residue was dried under vacuum and directly reused for the next run by adding the appropriate amount of solvent, cinnamaldehyde and dimethylmalonate.

As shown in Table 3, conversion slightly decreased after the second cycle, probably due to a limited catalyst leaching during the extraction phase. The catalytic activity was almost completely restored in the sixth cycle, by simply doubling up the reaction time to 32 h. Noteworthy, the enantioselectivity was preserved virtually unchanged over the six runs.

Table 3. Recycling experiments of catalyst **3** in the asymmetric addition of dimethyl malonate **14a** to cinnamaldehyde **15a**.



Cycle[a]	Conversion [%][b]	*ee* [%][c]
1	99	94
2	95	92
3	85	94
4	86	94
5	85	92
6[d]	95	92

[a)] The reactions are carried out on a 0.1 mmol scale of the limiting aldehyde **15a** in DCM (aldehyde concentration = 0.5 M) in the presence of catalyst **3** (10 mol %), dry lithium acetate (30 mol %) and **14a** (3 equiv). [b)] Determined by ^{1}H-NMR analysis of the crude reaction mixture after 16 h. [c)] Determined by CSP-HPLC analysis of the Horner-Wadsworth-Emmons ester derivative (see Experimental Section). [d)] reaction time = 32 h.

Conclusions

Optically active 2-tritylpyrrolidine, accessible via nucleophilic addition of trityl lithium to 1pyrroline 1oxide followed by reductive N-O bond cleavage of the intermediate hydroxylamine, has been recently proposed by Maruoka as a potential proxy of the family of the Hayashi-Jørgensen catalysts **1**. However, 2-trityl pyrrolidines have not been sufficiently explored yet, especially in iminium ion-based organocatalytic applications. We applied the tritylation protocol of cyclic nitrones to (*S*)-3-hydroxy-3,4-dihydro-2H-pyrrole 1-oxide with the aim to exploit the OH group on C3 as anchoring position for a fullerene containing framework. The goal was to test the optically active fullerene-trityl pyrroline hybrid **3** in the Michael addition of malonates to cinnamaldehydes, a reaction that involves the formation of an intermediate 3-aryl-2-propen-1-iminium ion. Results were very good, even though in the case of enals carrying an enolizable C-H bond in the γ position, complex mixtures for the equilibration of the intermediate iminium ion into a dienamine were obtained. The catalyst robustness was also proved by the recycling experiments that allowed us to reuse the same catalyst for six runs with only a moderate decrease in terms of activity and with identical enantioselectivity. Currently, our efforts are focused on increasing the catalytic performances by varying: i) the flexible spacer between C_{60} and the pyrrolidine ring, ii) the trityl group with bulkier groups, and iii) the spacer attachment point on the pyrrolidine ring, namely C4 instead of C3. This exploration of fullerene–trityl pyrrolidine hybrid properties in organocatalysis can be also considered as a benchmark for other nanosized carbon allotropes such as carbon nanotubes and graphene, with the aim to open new routes in this area.

Experimental Section

^{1}H NMR spectra were recorded on Varian Inova 400 NMR instrument with a 5 mm probe. Chemical shifts (δ) are reported in ppm, relative to the residual peaks of deuterated solvent signals. HPLC-MS analyses were performed on an Agilent Technologies HP1100 instrument coupled with an Agilent Technologies MSD1100 single-quadrupole mass spectrometer. A Phenomenex Gemini C18, 3 μm (100 × 3mm) column was employed for the chromatographic separation: mobile phase H_2O/CH_3CN, gradient from 30% to 80% of CH_3CN in 8 min, 80% of CH_3CN until 22 min, then up to 90% of CH_3CN in 2 min, flow rate 0.4 mL·min^{-1}. CSP-HPLC analyses were performed on an Agilent Technologies Series 1200 instrument using chiral columns and *n*-hexane/2-propanol (*n*-Hex/IPA) mixtures. The enantiomeric compositions were checked against the corresponding racemic products, obtained under the same reaction conditions using pyrrolidine as the catalyst. Flash chromatography purifications were carried out using Merck Geduran® Si 60 silica gel (40-63 μm particle size). Thin layer chromatography was performed on Merck 60 F254 plates. Commercial reagents were used as received without additional purification.

(*R*)-3-(benzyloxy)pyrrolidine (6). ***Step i (Scheme 2)***: Ethyl chloroformate (4.02 mL, 42 mmol) was added dropwise to a stirred suspension of (*R*)-3-pyrrolidinol hydrochloride **5** (4.94 g, 40 mmol) and K_2CO_3 (5.80 g, 42 mmol) in MeOH (80 mL) at 0 °C. The reaction was stirred at RT overnight

and then diluted with water. MeOH was removed under reduced pressure and the aqueous layer was extracted with DCM (3 × 25 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated under vacuum. Purification by flash-chromatography on silica (AcOEt) afforded 4.98 g of (*R*)-ethyl-3-hydroxypyrrolidine-1-carboxylate (31.3 mmol, 78 %) as a pale yellow oil. Analytical data are comparable to the ones reported in literature.[16] $[\alpha]_D^{25}$ = −15.6 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.47 (tt, *J* = 4.5, 2.5 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.56 – 3.47 (m, 3H), 3.41 (d, *J* = 11.9 Hz, 1H), 2.04 – 1.88 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 155.0, 70.0 and 69.2, 60.6, 53.9 and 53.5, 43.6 and 43.3, 33.4 and 32.8, 14.3. ***Step ii (Scheme 2)***: A solution of (*R*)-ethyl-3-hydroxypyrrolidine-1-carboxylate (4.78 g, 30 mmol) in THF (10 mL) was added dropwise at 0 °C to a stirred suspension of NaH (1.26 g, 60 % w/w, 31.5 mmol) in THF (20 mL) and the reaction was stirred at 0 °C for 30 minutes. When the gas evolution ceased, a solution of benzyl bromide (3.75 mL, 31.5 mmol) in THF (10 mL) was added dropwise, followed by TBAI (0.55 g, 1.5 mmol) and the reaction was allowed to reach RT and stirred overnight. The reaction mixture was quenched with saturated aqueous NH_4Cl (20 mL) and water (20 mL). The aqueous phase was extracted with Et_2O (3 × 20 mL), dried (Na_2SO_4), filtered and concentrated under vacuum. Purification by flash-chromatography on silica (cyclohexane/AcOEt 75:25) afforded 6.79 g (27.2 mmol, 91 %) of (*R*)-ethyl-3-benzyloxypyrrolidine-1-carboxylate as a colorless oil. $[\alpha]_D^{25}$ = −10.6 (c = 0.86, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of rotamers) = 7.41 – 7.26 (m, 5H), 4.63 – 4.46 (m, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.72 – 3.38 (m, 2H), 2.15 – 2.03 (m, 1H), 2.04 – 1.88 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 154.7, 137.7, 128.0, 127.2, 127.1, 76.5, 70.4, 60.5, 50.8, 43.6 and 43.5, 31.0 and 30.1, 14.4; HPLC-MS (ESI): 250 [M + H^+], 272 [M + Na^+], 288 [M + K^+]. $C_{14}H_{19}NO_3$ (249.31): calcd C 67.45, H 7.68; N 5.62; found C 67.27, H 7.64, N 5.62. ***Step iii (Scheme 2)***: KOH (5.05 g, 90 mmol) was added to a stirred solution of (*R*)-ethyl-3-benzyloxypyrrolidine-1-carboxylate (2.24 g, 9.0 mmol) in EtOH/H_2O 4:1 (20 mL) and the reaction was refluxed for 8 h. Ethanol was removed under vacuum and the aqueous phase was extracted with DCM (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated under vacuum. Purification by flash-chromatography on silica (DCM/MeOH/NH_4OH 90:10:2) afforded 1.4 g of **6** (7.9 mmol, 88 %) as a yellow oil. Analytical data are comparable to the ones reported in literature.[17] $[\alpha]_D^{25}$ = +10.8 (c = 1.6, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.26 (m, 5H), 4.50 (s, 2H), 4.22 – 4.10 (m, 1H), 3.24 – 3.09 (m, 2H), 3.05 – 2.89 (m, 2H), 1.98 – 1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9, 127.9, 127.1, 127.1, 79.3, 77.3, 77.0, 76.7, 70.4, 52.4, 45.1, 32.2; HPLC-MS (ESI): 178 [M + H^+], 355 [2M + H^+]. $C_{11}H_{15}NO$ (177.25): calcd C 74.54, H 8.53; N 7.90; found C 74.83, H 8.46, N 7.88.

(*R*)-4-(Benzyloxy)-3,4-dihydro-2H-pyrrole 1-oxide (7a). ***Step iv (Scheme 2)***. Oxone® (4.84 g, 7.88 mmol) was added portionwise over 1 hour at 0 °C to a stirred suspension of (*R*)-3-(benzyloxy)pyrrolidine **6** (1.33 g, 7.5 mmol) and $NaHCO_3$ (3.15 g, 37.5 mmol) in a mixture of CH_3CN/THF 4:1 (15 mL) and aqueous Na_2EDTA (0.01 M, 12 mL, 0.12 mmol). After the final addition, the reaction mixture was stirred at 0 °C for 1 hour and finally diluted with EtOAc (30 mL). The organic phase was separated and the aqueous layer was extracted with DCM (2 × 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated under vacuum. Purification by flash-chromatography on silica (DCM/MeOH 98:2) afforded 1.08 g of **7a** (5.65 mmol, 75 %, R_f >) and 0.19 g of the isomer **7b** (1 mmol, 13 %, R_f <) as light orange oils.**7a**: $[\alpha]_D^{25}$ = +96.5 (c = 1.5, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.29 (m, 5H), 7.01 (broad s, 1H), 4.86 – 4.74 (m, 1H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 4.28 – 4.08 (m, 1H), 3.98 – 3.76 (m, 1H), 2.56 (dddd, *J* = 13.9, 9.3, 7.7, 6.3 Hz, 1H), 2.26 (dddd, *J* = 13.9, 9.0, 5.0, 3.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.9, 133.1, 128.0, 127.5, 127.3, 77.8, 70.9, 60.8, 27.0; HPLC-MS (ESI): 192 [M + H^+], 214 [M + Na^+], 383 [2M + H^+], 405 [2M + Na^+]. $C_{11}H_{13}NO_2$ (191.23): calcd C 69.09, H 6.85; N 7.32; found C 68.87, H 6.80, N 7.34.

(2*S*,3*R*)-2-Tritylpyrrolidin-3-ol (8). ***Steps v-vi (Scheme 2)***. BuLi (1.6 M in hexane, 3.2 mL, 5.12 mmol) was added dropwise at 0 °C to a solution of triphenylmethane (1.23 g, 5.02 mmol) in THF (10 mL). The solution became deeply red and the mixture was stirred at 0 °C for 1 h. A solution of nitrone **7a** (0.48 g, 2.51 mmol) in THF (5 mL) was added dropwise at 0 °C and the reaction was stirred at room temperature for 2 h. Finally, the reaction was quenched with saturated aqueous NH_4Cl (5 mL) and THF was removed under reduced pressure. The aqueous phase was extracted with DCM (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4), filtered and concentrated under vacuum. The crude product was purified by flash-cromatography on silica (cyclohexane/AcOEt 95:5) to afford the corresponding hydroxylamine (0.809 g, 1.86 mmol, 74 %). The hydroxylamine was immediately dissolved in AcOH (35 mL), Pd/C (10 % w/w, 0.278 g, 0.26 mmol) was added to the solution and the reaction mixture was kept stirring under H_2 (1 atm) overnight. The catalyst was removed by filtration on Celite®, the filter cake was washed with MeOH and the solvent was removed under reduced pressure. The solution was made basic (pH ~ 9) with a 5 % aqueous solution of NaOH and it was extracted with DCM (3 x 15 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under vacuum. The crude product was purified with flash-cromatography on silica (cyclohexane/AcOEt 1:1) to give **8** (0.468 g, 1.42 mmol, 76 %) as a white solid. m. p. = 168-170 °C; $[\alpha]_D^{25}$ = − 62.4 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$) δ = 7.41 (d, *J* = 7.8 Hz, 6H), 7.32 – 7.23 (m, 6H), 7.23 – 7.17 (m, 3H), 4.87 (d, *J* = 1.5 Hz, 1H), 4.20 (d, *J* = 5.4 Hz, 1H), 3.07 (ddd, *J* = 11.6, 9.6, 6.0 Hz, 1H), 2.76 (ddd, *J* = 9.5, 7.9, 1.4 Hz, 1H), 1.40 (dd, *J* = 13.3, 5.9 Hz, 1H), 0.58 (dddd, *J* = 13.3, 11.6, 8.0, 5.4 Hz, 1H).^{13}C NMR (100MHz, $CDCl_3$) δ = 130.0, 127.8, 126.2, 75.2, 72.4, 60.6, 44.7, 35.4; HPLC-MS (ESI): 330 [M + H^+]. $C_{23}H_{23}NO$ (329.44): calcd C 83.85, H 7.04; N 4.25; found C 84.08, H 6.99, N 4.21.

(2*S*,3*R*)-*N*-Boc-3-(prop-2-yn-1-yloxy)-2-tritylpyrrolidine (9). ***Steps vii (Scheme 2)***. Boc_2O (0.348 g,

1.60 mmol) was added at 0 °C to a solution of (2*S*,3*R*)-2-tritylpyrrolidin-3-ol **8** (0.438 g, 1.33 mmol) in DCM (3.3 mL) and Et_3N (0.56 mL, 3.99 mmol) and the reaction mixture was allowed to reach RT and stirred overnight. The reaction mixture was diluted with water (5 mL), the organic phase was collected and the aqueous phase was extracted with DCM (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under vacuum. The crude product was purified with flash-cromatography on silica (cyclohexane/AcOEt 1:1) to afford the N-Boc protected pyrrolidine (0.541 g, 1.26 mmol, 95 %) as a white solid. m. p.= 87-90 °C; $[\alpha]_D^{25}$ = −65.3 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.50 – 7.40 (m, 6H), 7.26 – 7.20 (m, 6H), 7.19 – 7.14 (m, 3H), 5.77 (s, 1H), 4.37 (d, *J* = 5.2 Hz, 1H), 3.54 (q, *J* = 9.7 Hz, 1H), 2.97 (td, *J* = 10.8, 2.5 Hz, 1H), 1.35 (s, 9H), 1.26 (ddd, *J* = 14.2, 9.2, 2.5 Hz, 1H), 0.01 (dtd, *J* = 14.8, 9.9, 5.2 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.5, 144.6, 130.7, 127.3, 125.9, 79.9, 77.3, 77.0, 76.7, 76.1, 72.3, 60.7, 49.3, 32.1, 28.2; HPLC-MS (ESI): 430 [M + H$^+$], 374 [(M – *t*-Bu) + H$^+$], 330 [(M – Boc) + H$^+$]. $C_{28}H_{31}NO_3$ (429.56): calcd C 78.29, H 7.27; N 3.26; found C 78.53, H 7.29, N3.28. ***Steps viii (Scheme 2)***. A solution of Boc-protected pyrrolidine (0.856 g, 2 mmol) in THF (5 mL) was added dropwise to a stirred suspension of NaH (0.088 g, 60 % w/w, 2.2 mmol) in THF (5 mL) at 0 °C and the reaction mixture was stirred at 0 °C for 1 h. A solution of propargyl bromide (80 wt. % in toluene, 0.26 mL, 2.4 mmol) in THF (5 mL) was added dropwise at 0 °C, followed by TBAI (0.037 g, 0.1 mmol) and the reaction was stirred at RT overnight. The reaction mixture was quenched with saturated NH_4Cl (5 mL) and water (5 mL). THF was removed under vacuum and the aqueous phase was extracted with AcOEt (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under vacuum. The crude product was purified by flash-cromatography on silica (cyclohexane/AcOEt 80:20) to afford **9** (0.848 g, 1.81 mmol, 90 %) as a white solid. m. p. = 77-80 °C; $[\alpha]_D^{25}$ = −58.4 (*c* = 0.88, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.49 – 7.41 (m, 6H), 7.25 – 7.20 (m, 6H), 7.19 – 7.12 (m, 3H), 5.81 (s, 1H), 4.27 – 4.17 (m, 2H), 3.97 (dd, *J* = 16.2, 2.3 Hz, 1H), 3.44 (q, *J* = 9.6 Hz, 1H), 2.95 (td, *J* = 10.6, 2.5 Hz, 1H), 2.36 (t, *J* = 2.4 Hz, 1H), 1.53 – 1.40 (m, 1H), 1.33 (s, 9H), -0.22 (dtd, J = 14.7, 9.8, 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ =157.1, 144.6, 130.8, 127.3, 125.9, 82.3, 74.3, 71.1, 61.0, 54.8, 49.3, 28.2; HPLC-MS (ESI): 368 [(M – Boc) + H$^+$], 412 [(M – *t*-Bu) + H$^+$], 468 [M + H$^+$], 490 [M + Na$^+$], 957 [2M + Na$^+$]. $C_{31}H_{33}NO_3$ (467.61): calcd C 79.79, H 7.11, N 3.00; found C 79.63, H 7.17, N 3.03.

Benzyl (3-hydroxypropyl)glycinate (10). Benzyl bromoacetate (1.58 mL, 10 mmol) was added at 0 °C to a solution of 3-amino-1-propanol (1.9 mL, 25 mmol) in THF (20 mL) and the mixture was stirred at 0 °C for 1 h. The reaction was quenched with water (10 mL), the organic layer was separated and the aqueous phase was extracted with AcOEt (2 × 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated under reduced pressure. Purification by flash-chromatography on silica (AcOEt/MeOH 9:1) afforded 1.46 g of **10** (6.54 mmol, 65 %) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.30 (m, 5H), 5.18 (s, 2H), 3.81 (t, *J* = 5.6 Hz, 2H), 3.48 (s, 2H), 2.88 (t, *J* = 5.9 Hz, 2H), 1.73 (tt, J = 5.6/5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 135.3, 128.4, 128.2, 128.1, 66.4, 62.5, 50.4, 48.2, 31.1; HPLC-MS (ESI): 224 [M + H$^+$]. $C_{12}H_{17}NO_3$ (223.27): calcd C 64.55, H 7.67; N 6.27; found C 64.75, H 7.61, N 6.31.

Benzyl *N*-(3-azidopropyl)-*N*-((benzyloxy)carbonyl) glycinate (11). ***Step i (Scheme 3)***: CbzCl (1.57 mL, 11 mmol) was added at 0 °C to a solution of **10** (2.23 g, 10 mmol) and Et_3N (1.67 mL, 12 mmol) in DCM (20 mL) and the mixture was allowed to reach RT and stirred overnight. The reaction was quenched with water (10 mL), the organic layer was separated and the aqueous phase was extracted with DCM (2 × 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated under reduced pressure. Purification by flash-chromatography on silica (AcOEt) afforded 3.4 g of the *N*-protected intermediate (9.51 mmol, 95 %) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (3:1 mixture of rotamers) = 7.43 – 7.21 (m, 10H, major + minor), 5.19 (s, 2H, minor), 5.18 (s, 2H, minor), 5.12 (s, 2H, major), 5.11 (s, 2H, major), 4.09 (s, 2H, minor), 4.00 (s, 2H, major), 3.63 (t, *J* = 5.7 Hz, 2H, major + minor), 3.53 (t, *J* = 6.2 Hz, 2H, major), 3.48 (t, *J* = 6.8 Hz, 2H, minor), 1.86 – 1.62 (m, 2H, major + minor); ^{13}C NMR (100 MHz, $CDCl_3$): δ (3:1 mixture of rotamers) = 169.6 and 169.4, 156.8 and 156.4, 136.0 and 135.1, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.8, 127.7, 67.63 and 67.57, 66.9, 59.4 and 58.4, 49.6 and 49.4, 45.4 and 45.2, 31.1 and 30.4; HPLC-MS (ESI): 358 [M + H$^+$], 380 [M + Na$^+$], 737 [2M + Na$^+$]. $C_{20}H_{23}NO_5$ (357.41): calcd C 67.21, H 6.49; N 3.92; found C 67.18, H 6.48, N 3.90. ***Step ii (Scheme 3)***: MsCl (0.85 mL, 11 mmol) was added at 0 °C to a solution of the *N*-protected intermediate (3.57 g, 10 mmol) and Et_3N (1.67 mL, 12 mmol) in DCM (20 mL) and the mixture was allowed to reach RT and stirred overnight. The reaction was quenched with water (10 mL), the organic layer was separated and the aqueous phase was extracted with DCM (2 × 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated under reduced pressure. The so-obtained crude mesylated alcohol (4.33 g, 9.94 mmol, 99 %) is unstable and was used immediately in the next step without further purifications. ^{1}H NMR (400 MHz, $CDCl_3$): δ (1.5:1 mixture of rotamers) = 7.45 – 7.25 (m, 10H, major + minor), 5.19 (s, 2H, minor), 5.18 (s, 2H, minor), 5.11 (s, 2H, major), 5.09 (s, 2H, major), 4.29 (t, *J* = 6.1 Hz, 2H, major), 4.23 (t, *J* = 6.1 Hz, 2H, minor), 4.09 (s, 2H, minor), 4.03 (s, 2H, major), 3.58 – 3.44 (m, 4H, major + minor), 2.98 (s, 3H, major), 2.87 (s, 3H, minor), 2.09 – 1.90 (m, 4H, major + minor); ***Step iii (Scheme 3)***: Sodium azide (0.62 g, 9.6 mmol) was added at 0 °C to a solution of the mesylated intermediate (3.48 g, 8 mmol) in DMF (30 mL) and the mixture was allowed to reach RT and stirred overnight. The reaction was diluted with AcOEt (30 mL) and washed with 5 % aqueous LiCl solution (6 × 10 mL) to remove most of the DMF. The organic phase was dried (Na_2SO_4), filtered and evaporated under reduced pressure. Purification by flash-chromatography on silica (cyclohexane/AcOEt 8:2) afforded 2.18 g of the product **11** (5.7 mmol, 71 %) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (1:1 mixture of rotamers A and B) = 7.41 – 7.27 (m, 10H, A + B), 5.19 (broad s, 4H, A + B), 5.11 (s, 2H, A), 5.10 (s, 2H, B), 4.08

(s, 2H, A), 4.02 (s, 2H, B), 3.50 – 3.39 (m, 2H, A + B), 3.37 (t, *J* = 6.7 Hz, 2H, A), 3.30 (t, *J* = 6.6 Hz, 2H, B), 1.93 – 1.74 (m, 2H, A + B); ^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 169.3 and 169.2, 156.1 and 155.6, 136.1, 135.1 and 135.0, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 67.4 and 67.2, 66.72and 66.69, 49.5 and 49.4, 48.6 and 48.4, 46.4, 45.6, 27.6 and 27.3; HPLC-MS (ESI): 355 [M + H$^+$− N_2], 383 [M + H$^+$], 405 [M + Na$^+$]. $C_{20}H_{22}N_4O_4$ (382.42): calcd C 62.82, H 5.80; N 14.65; found C 63.02, H 5.76, N 14.50.

(3-(4-((((2*S*,3*R*)-N-Boc-2-tritylpyrrolidin-3-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl) propyl) glycine (12). ***Step iv (Scheme 3)*.** A solution of $CuSO_4 \cdot 5H_2O$ (0.011 g, 0.043 mmol) in H_2O (0.5 mL) and a solution of sodium ascorbate (0.017 g, 0.086 mmol) in H_2O (0.5 mL) were slowly added to a stirred solution of **11** (0.164 g, 0.43 mmol) and **9** (0.201 g, 0.43 mmol) in *t*-butanol (1 mL) and the resulting suspension was stirred at RT overnight. The reaction mixture was diluted with AcOEt (5 mL), the organic phase was collected and the aqueous phase was extracted with AcOEt (3 × 5 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated under reduced pressure. Purification by flash-chromatography on silica (cyclohexane/AcOEt 8:2) afforded 0.34 g of the corresponding triazole (0.4 mmol, 93 %). $[\alpha]_D^{25}$ = −50.4 (c = 0.78, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.71 (s, 1H), 7.47 – 7.36 (m, 6H), 7.37 – 7.30 (m, 6H), 7.30 – 7.27 (m, 2H), 7.19 (t, J = 7.2 Hz, 6H), 7.16 – 7.10 (m, 3H), 5.83 (s, 1H), 5.19 (s, 1H), 5.12 (d, *J* = 2.7 Hz, 2H), 4.61 (dd, *J* = 26.0, 12.3 Hz, 1H), 4.49 – 4.30 (m, 3H), 4.14 – 4.01 (m, 3H), 3.58 – 3.38 (m, 3H), 2.91 (td, *J* = 10.6, 2.7 Hz, 1H), 2.16 (dq, *J* = 11.7, 6.1 Hz, 2H), 1.63 – 1.49 (m, 1H), 1.32 (s, 9H), -0.12 (dtd, *J* = 14.8, 9.6, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of rotamers) =169.7, 157.1, 156.2, 144.9, 144.7, 136.1, 135.2, 135.1, 130.7, 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.1, 127.8, 127.3, 125.9, 125.9, 123.3, 122.5, 83.2, 83.1, 79.7, 71.1, 67.9, 67.7, 67.1, 61.4, 61.0, 50.0, 49.7, 49.4, 47.6, 46.4, 45.9, 29.7, 29.4, 29.2, 28.2, 26.7; HPLC-MS (ESI): 850 [M + H$^+$]. $C_{51}H_{55}N_5O_7$ (850.03): calcd C 72.06, H 6.52, N 8.24; found C 72.19 H 6.47, N 8.16. ***Step v (Scheme 3)***: Pd/C (10 % w/w, 0.03 g, 0.028 mmol) was added to a solution of the protected triazole (0.239 g, 0.28 mmol) in MeOH (3 mL) and the reaction mixture was kept stirring under H_2 (1 atm) overnight. The catalyst was removed by filtration on Celite®, the filter cake was washed with MeOH and the solvent was removed under reduced pressure to afford pure **12** (0.175 g, 0.28 mmol, 99 %) as a white solid. m. p. = 127-130 °C; $[\alpha]_D^{25}$ = − 62.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.72 (s, 1H), 7.38 (d, *J* = 7.8 Hz, 6H), 7.21 – 7.06 (m, 10H), 5.80 (s, 1H), 4.67 – 4.46 (m, 4H), 4.36 (d, *J* = 12.2 Hz, 1H), 4.06 (d, *J* = 5.2 Hz, 1H), 3.54 (s, 2H), 3.49 – 3.34 (m, 1H), 3.13 (broad t, *J* = 7.7 Hz, 2H), 2.88 (dt, *J* = 10.7, 5.6 Hz, 1H), 2.45 (dt, *J* = 13.9, 6.5 Hz, 2H), 1.63 – 1.45 (m, 1H), 1.28 (s, 9H), 0.04 – -0.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ(mixture of rotamers) = 171.0, 156.9, 144.9, 144.5, 130.5, 127.2, 125.9, 125.8, 123.5, 83.3, 79.5, 70.9, 61.3, 60.9, 53.3, 50.2, 49.3, 47.3, 44.5, 28.1, 26.8; HPLC-MS (ESI): 626 [M + H$^+$], 1251 [2M + H$^+$]. $C_{36}H_{43}N_5O_5$ (625.77): calcd C 69.10, H 6.93, N 11.19; found C 69.06, H 6.88, N 11.27.

Supported catalyst 3. ***Step vi (Scheme 3)***. Pristine C_{60} (0.168 g, 0.23 mmol) was dissolved in toluene (60 mL) and was sonicated for 20 min under inert atmosphere. **12** (0.117 g, 0.19 mmol) and paraformaldehyde (0.014 g, 0.47 mmol) were added to the solution and the reaction mixture was refluxed for 1 h. The solution was cooled to RT and directly purified by flash-chromatography on SiO_2 (first only toluene to remove unreacted C_{60}, then toluene/AcOEt 7:3) affording the *N*-Boc protected supported catalyst (0.131 g, 0.099 mmol, 53 %) as a brown powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.80 (s, 1H), 7.47 – 7.38 (m, 6H), 7.24 – 7.18 (m, 6H), 7.17 – 7.10 (m, 3H), 5.86 (s, 1H), 4.82 (t, *J* = 6.9 Hz, 2H), 4.70 (d, *J* = 12.3 Hz, 1H), 4.51 (d, *J* = 12.4 Hz, 1H), 4.47 – 4.43 (m, 4H), 4.12 (d, *J* = 5.2 Hz, 1H), 3.48 (q, *J* = 9.5 Hz, 1H), 3.16 (broad t, *J* = 6.6 Hz, 2H), 2.92 (td, *J* = 10.7, 2.6 Hz, 1H), 2.58 (broad dt, *J* = 13.0, 5.6 Hz, 2H), 1.63 – 1.52 (m, 1H), 1.32 (s, 9H), -0.10 (ddt, *J* = 19.4, 9.5, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ= 157.2, 147.3, 146.3, 146.1, 145.9, 145.7, 145.5, 145.3, 144.7, 144.6, 143.1, 142.7, 142.2, 142.1, 141.9, 140.2, 136.2, 130.7, 129.0, 128.6, 127.3, 126.0, 123.1, 83.3, 71.1, 70.5, 67.6, 61.6, 61.0, 51.1, 49.4, 48.3, 29.7, 28.3, 26.8. ***Step vii (Scheme 3)***. The *N*-Boc protected catalyst (0.140 g, 0.106 mmol) was dissolved in CH_2Cl_2 (20 mL) and was sonicated for 20 min. TFA (1 mL, 13.3 mmol) was added dropwise at 0 °C to the solution and the reaction mixture was stirred at RT overnight. The organic solvent was removed under vacuum and the crude solid was re-dissolved in CH_2Cl_2/H_2O (10 mL + 10 mL). The organic phase was collected and the aqueous phase was extracted with CH_2Cl (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated under reduced pressure. Purification by flash-chromatography on silica (CH_2Cl_2/MeOH 99:1) afforded **3** (0.128 g, 0.105 mmol, 99 %) as a brown powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.78 (s, 1H), 7.46 – 7.31 (m, 6H), 7.28 – 7.19 (m, 6H), 7.20 –.11 (m, 3H), 4.91 (s, 1H), 4.81 (t, *J* = 6.8 Hz, 2H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.46 (d, *J* = 12.2 Hz, 1H), 4.44 – 4.39 (m, 4H), 3.90 (d, *J* = 4.8 Hz, 1H), 3.13 (t, *J* = 6.6 Hz, 2H), 2.97 (td, J = 10.4, 5.3 Hz, 1H), 2.77 (t, *J* = 8.4 Hz, 1H), 2.55 (p, *J* = 6.8 Hz, 2H), 1.67 (dd, *J* = 13.4, 5.5 Hz, 1H), 0.55 – 0.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.7, 147.3, 146.3, 146.1, 145.9, 145.6, 145.5, 145.4, 145.3, 144.6, 136.1, 130.0, 127.6, 126.0, 123.1, 83.3, 70.9, 70.6, 67.7, 62.7, 61.0, 50.7, 48.1, 44.9, 30.5, 29.1; MS (ESI): 1214 (100 %), 1215 (98 %), 1216 (35 %), 1217 (14 %) [M + H$^+$]. $C_{91}H_{35}N_5O$ (1213.28); isotopic pattern prediction: 1213.28 (100 %), 1214.28 (98 %), 1215.96 (43 %), 1216.29 (12 %).

Michael addition of malonates to unsaturated aldehydes (Table 2, Entry 16). Catalyst **3** (0.121 g, 0.05 mmol, 5 mol %) was dissolved in CH_2Cl_2 (4 mL) and sonicated for 5 min. (*E*)-cynnamaldehyde **15a** (0.252 mL, 2 mmol), dry LiOAc (0.0198 g, 0.15 mmol, 15 mol%) and dimethylmalonate **14a** (0.686 mL, 6 mmol) were added to the solution and the reaction was stirred at RT for the 16 h. The reaction mixture was directly charged on the top of a silica-gel column and the product **16a** (0.478 g, 1.81 mmol, 90%) was isolated eluting with cyclohexane/AcOEt 8:2. The product **16a** was converted into the unsaturated Horner-Wadsworth-Emmons ester derivative using commercial ethyl (triphenylphosphoranylidene) acetate in CH_2Cl_2. The corresponding derivative was purified by flash-

chromatography on silica (cyclohexane/AcOEt 8:2) and analyzed by CSP-HPLC to determine the enantiomeric excess (see Supporting Info).

Recycling of the catalyst 3. (Table 3). Catalyst **3** (0.012 g, 0.01 mmol, 10 mol %) was dissolved in CH_2Cl_2 (0.2 mL) and sonicated for 5 min in a microcentrifuge tube (2 mL). (*E*)-cinnamaldehyde **15a** (0.013 mL, 0.1 mmol), dry LiOAc (0.0198 g, 0.03 mmol, 30 mol %) and dimethylmalonate **14a** (0.034 mL, 0.3 mmol) were added to the solution, the tube was purged with inert gas and the reaction was stirred at RT for 16 h. The reaction mixture was diluted with MTBE (1 mL), centrifuged (8000 rpm, 5 min) and the organic layer was collected (4 times). The combined organic layers were evaporated under vacuum and the crude product was analyzed as reported in the previous procedure. The solid residue after the centrifugation step, containing the supported catalyst and LiOAc, was dried under vacuum and directly used in the next cycle.

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FULL PAPER

A Recyclable Chiral 2-(Triphenylmethyl)pyrrolidine Organocatalyst Anchored to [60]Fullerene

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Cristian Rosso, Marco G. Emma, Ada Martinelli, Marco Lombardo,* Arianna Quintavalla, Claudio Trombini, Zois Syrgiannis, Maurizio Prato*