Novel Recyclable Chiral Bifunctional Thioureas derived from [60]Fullerene and their use as Highly Efficient Organocatalysts for Asymmetric nitro-Michael Reaction.

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Abstract.

Three novel fullerothioureas derived from natural valine, phenylalanine and *tert*-leucine have been prepared by Prato´s reaction of [60]fullerene and the corresponding aldehydes. These hybrids have been used as organocatalysts in a typical stereoselective nitro-Michael addition in homogenous and neat conditions. The catalysts are easily recoverable by filtration, and they are recyclable for at least five times. The addition products were obtained with excellent yields and stereoselectivities by using loading of catalyst as low as 0.5 mol%.

Keywords: Asymmetric synthesis, fullerene, fullerothiuoreas, Michael addition, organocatalysis.

Introduction

Chiral bifunctional thioureas are privileged structures acting as catalysts for different stereoselective transformations,[1] but their use is sometimes related with problems associated with the recovering of the organocatalyst from the reaction mixtures. That process normally requires tedious chromatographic separations.

The anchorage of the active molecule onto different solid supports facilitates the recovering of the catalysts.[2] In that way, chiral bifunctional thioureas have been supported on different materials, such as polysiloxanes,[3] PEG (polyethylene glycol),[4] polystyrene,[5] and inorganic nanoparticles,[6] including those obtained by co-polymerization.[7] As a part of a project directed to the synthesis of recoverable and reusable organocatalysts we have recently prepared thioureas supported onto different commercially available polystyrene derivatives which are able to efficiently promote stereoselective transformations.[8]

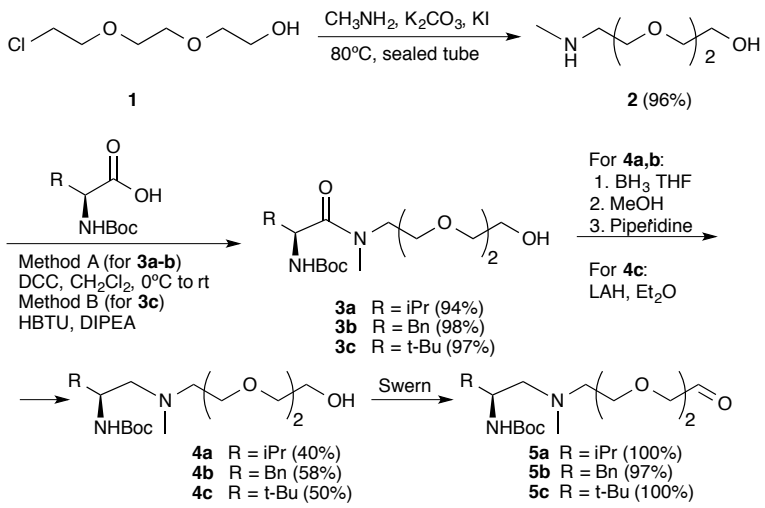
The synthesis of these materials is simple and efficient, but the catalytic activity of these polymers is dependent on parameters such as leaching, swelling, and accessibility of the reactants to the active site.[2] A plausible solution for these problems could be the synthesis of well-defined molecular organocatalysts taking into account that the starting compounds would be commercially available, the synthetic method would be versatile, allowing variations in the thiourea structure, and the catalysts could be robust and easily recoverable. That condition led us to consider [60]fullerene as a support of chiral bifunctional thioureas because the low solubility of the fullerene derivatives in organic solvents[9] facilitates the recovering and reusing of the catalysts.

Because the Prato´s reaction is a well-established methodology for the synthesis of chemically stable pyrrolidino fullerenes, we decided to apply that reaction to support the thiourea moiety onto [60]fullerene. Pyrrolidino fullerenes have been prepared by organocatalytic[10] and metal-catalyzed[11] cycloadditions, but the use of chiral derivatives of C_{60} as catalysts has been scarcely studied. Only a few [60]fullerene derivatives complexed with metals have been employed as catalysts,[12] and recently, octahedrally substituted TEMPO-fullerenes,[13] and fullerene-proline hybrids[14] have been used as organocatalysts in oxidation of alcohols and aldol reactions, respectively.

Results and Discusion

Fullerothioureas **8a-c** were prepared by 1,3-dipolar cycloaddition of azomethine ylides following the Prato´s methodology. To this end, enantiopure functionalized aldehydes **5a-c** were synthesized from commercially available triethyleneglycol monochlorohydrin (**1**), and N-Boc-protected *L*-valine, *L*-phenylalanine, and *L-tert*-leucine, respectively (Scheme 1).

Starting chloro alcohol (**1**) was transformed into N-methylamino alcohol **2** by heating with methylamine in a sealed tube. After extensive experimentation,[15] we found that the best yields for the condensation of **2** with the corresponding protected amino acids were obtained by using DCC as activating reagent for N-Boc-L-valine, and N-Boc-L-phenylalanine, but HBTU in the presence of DIPEA for N-Boc-L-tert-Leucine. The transformation of amides **3a-c** into diamino alcohols **4a-c** was also tried in different conditions,[15] but the best results were observed by using LAH as reductive reagent for **3c**, or BH_3-THF complex for the reduction of **3a-b**. Swern oxidation of **4a-c** lead to chiral diamino aldehydes **5a-c**, maintaining the stereochemical integrity.[16]

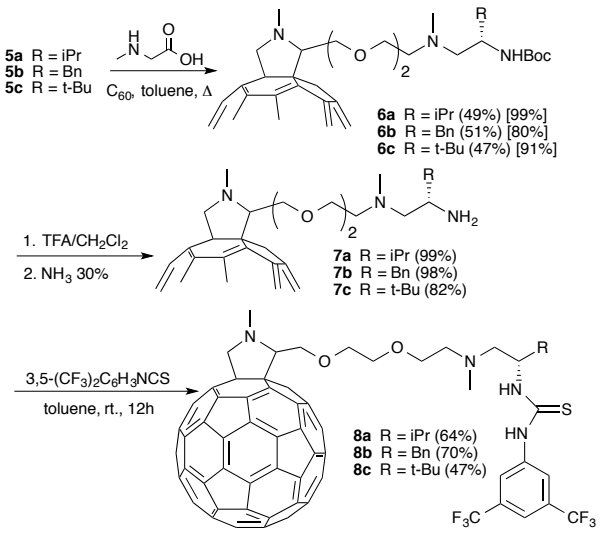


Scheme 1. Synthesis of chiral diamino aldehydes. Numbers in parenthesis indicate the yields of isolated compounds.

The synthesis of fullerothioureas was carried out, in three steps, as summarized in Scheme 2. Fullerene derivatives **6a-c** was obtained by refluxing in toluene a mixture of C_{60} (1 equiv), sarcosine (5 equiv) and the corresponding aldehyde **5a-c** (1.2

equiv).[17] In this process, a mixture of diastereoisomers that differ in the configuration of the pyrrolidine C-2 stereocenter could be formed, but we were not able to detect or separate the two possible diastereoisomers. In any way, we thought that the stereochemistry of C-2 stereocenter could not affect the stereo-effectiveness of the catalysts because the bifunctional thiourea, which is the active site of the catalyst, is located far away from that stereogenic center. Additionally, the polyether nature of the tether connecting the fullerene structure and the active thiourea terminus increases the solubility of the fulleropyrrolidine derivatives in organic solvents.[18]

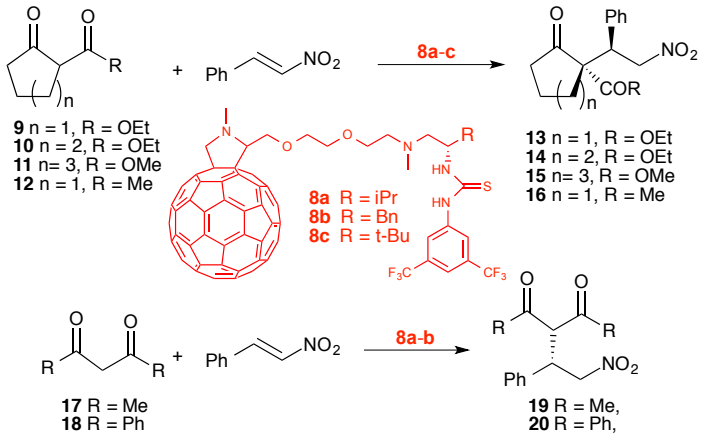
Compounds **6a-c** were deprotected, in excellent yields, to amines **7a-c** by treatment with TFA, followed by neutralization with a solution of ammonia. These amines are only moderately stable, and they were transformed into the final thioureas **8a-c** by reaction with 3,5-bis(triflurometyl) phenyl isothiocyanate in toluene at rt.



Scheme 2. Synthesis of fullerothioureas used as catalysts. Numbers in parenthesis indicate the yields of isolated compounds. Numbers in square brackets indicate the yields on the basis of the recovered C_{60}.

The stereoselective Michael addition is one of the most studied organocatalyzed reaction,[1] and we select the conjugate addition of ethyl 2-oxocyclopentane carboxylate (**9**) and ethyl 2-oxocyclohexane carboxylate (**10**) to *trans*-nitrostyrene to study the ability of the novel fullerothioureas as stereoselective organocatalysts. This process has been selected for comparative purposes because it allows for the construction of two contiguous quaternary and tertiary stereocenters, and it has been previously described[19] (Scheme 3 and Table 1).

We first searched for the best reaction conditions by using fullerothiourea **8a** as catalyst for the addition of ethyl 2-oxo-cyclopentyl carboxylate (**9**) to *trans*-nitrostyrene. The first attempts were done under homogenous reaction conditions in solvents (DCM, Toluene, or THF) that are able to solubilize catalyst **8a**. To this end, a 0.25 M solution of nitrostyrene and 2 equiv of **9** was stirred at rt in the presence of only 2 mol% of catalyst **8a** in the corresponding solvent until the reactions were finished (TLC). In all cases the addition product **13** was isolated with excellent yields and stereoselectivities (entries 1-3 in Table 1). Very similar results were obtained under heterogeneous conditions by using solvents such as diethyl ether or acetonitrile where the catalyst **8a** is not soluble (entries 4, 5 in Table 1), and this fact lead us to consider to test the reaction under solvent-free conditions.



Scheme 3. Stereoselective nitro-Michael addition catalyzed by **8a-c**.

The reaction of *trans*-nitrostyrene with 2-oxo-cyclopentyl carboxylate (2 equiv) in the presence of 10 mol% of **8a** at rt was very quickly, leading to the addition product **13** in near quantitative yield, and excellent diastereoselection (97:3 dr) and enantioselectivity (95:5 er) after 1 h of stirring (entry 6 in Table 1). Similar results were obtained when only 5 mol% of **8a** was used (entry 7 in Table 1), and in these conditions we test the ability of catalysts **8b** and **8c**. Phenylalanine-derived fullerothiourea **8b** promoted the reaction also in quantitative yield, but on longer reaction time, and lower enantioselectivity, although maintaining the level of diastereoselection (entry 8). On the contrary, the thiourea derived from *tert*-leucine

(**8c**) showed less active, because the addition product was formed in only 50% yield after 4 h of reaction (entry 9 in Table 1).

The best catalyst **8a** was used for studying the effect of the catalyst loading in the reaction. When the reaction was carried out under neat conditions by using 2 mol% of catalyst, we obtain excellent results in terms of yield and stereocontrol (entry 10). These results were much better than those observed for the reaction catalyzed by the same thiourea supported on sulfonylpolystyrene.[8b] Similar stereochemical discrimination and good yields were obtained when 1 mol%, or even 0.5 mol% of catalyst were used, although at expenses of increase the reaction time to 7 h or 14 h, respectively (entries 11, 12 in Table 1). The reaction also worked well by using 0.1 mol% of **8a**, but the reaction time increased to 56 h, and the stereoselection was only moderate (entry 13). No improvement in the diastereo- and enantioselectivities was observed when the reaction temperature was decreased to 0 ^{o}C (entry 14).

The reaction was extended to the use of ethyl 2-oxo-cyclohexane carboxylate (**10**) and methyl 2-oxo-cycloheptane carboxylate (**11**) as nucleophiles, and the data summarized in entries 15 and 16 show that cyclohexanone derivative **10** is much less reactive than its homolog **9**. The addition product **14** was obtained as a near single isomer (er = 98:2) by using 2 mol% of **8a** (entry 16) or as a pure enantiomer in the presence of 5 mol% of catalyst (entry 15), with excellent diastereoselection and good yields, but in much longer reaction time (144 h). On the contrary, the reaction of cycloheptanone derivative (**11**), catalyzed by **8b**, lead to the addition product **15** in excellent yield and good enantioselectivity, but moderate diastereoselectivity (entry 17 in Table 1).

It is noteworthy that the addition of 2-acetyl cyclopentanone (**12**) to nitrostyrene was less stereoselective than that of its homolog β-keto ester **9** in the same reaction conditions (compare entry 18 versus 10 in Table 1). Acyclic symmetrical β-diketones can also be used as nucleophile in the enantioselective addition to nitrostyrene. In that way, both fullerothioureas **8a** and **8b** were able to catalyze the addition of acetylacetone (**17**) to nitrostyrene, in neat conditions, leading to **19** in high yield and moderate to good enantioselectivity (entries 20, 21 in Table 1). Additionally, dibenzoylmethane (**18**) reacted with the same nitroolefin yielding the addition product

(**20**) in moderate yield, but excellent enantioselection (entries 22, 23 in Table). The last reactions were done in DCM as solvent because the solid nature of both reactants.

Table 1. Michael additions of **9-12** and **17**, **18** to *trans*-nitrostyrene catalyzed by fullerothioureas **8a-c**.[a]

Entry	Catalyst (mol%)	Solvent	Time (h)	Product yield (%)[b]	Dr (anti:syn)[c]	Er (anti)[c]
1	**8a** (2)	DCM[d]	3.5	**13** (95)	95:5	95:5
2	**8a** (2)	Toluene[d]	3.5	**13** (95)	93:7	96:4
3	**8a** (2)	THF[d]	3.5	**13** (95)	96:4	96:4
4	**8a** (2)	Et_2O[d]	3.5	**13** (95)	96:4	96:4
5	**8a** (2)	MeCN[d]	3.5	**13** (95)	92:8	93:7
6	**8a** (10)	neat	1	**13** (99)	97:3	95:5
7	**8a** (5)	neat	1	**13** (99)	96:4	95:5
8	**8b** (5)	neat	3.5	**13** (99)	93:7	90:10
9	**8c** (5)	neat	4	**13** (50)	97:3	96:4
10	**8a** (2)	neat	3	**13** (99)	96:4 [88:12][e]	96:4 [94:6][e]
11	**8a** (1)	neat	7	**13** (87)	96:4	96:4
12	**8a** (0.5)	neat	14	**13** (88)	93:7	96:4
13	**8a** (0.1)	neat	56	**13** (93)	83:17	73:27
14	**8a** (2)	Neat[f]	3	**13** (95)	93:7	96:4
15	**8a** (5)	neat	144	**14** (86)	98:2	>99:<1[g]
16	**8a** (2)	neat	144	**14** (76)	97:3	98:2
17	**8b** (5)	neat	7	**15** (91)	76:24	91:9
18	**8a** (2)	neat	7	**16** (94)	97:3	92:8
19	**8b** (2)	neat	9	**16** (80)	89:11	90:10
20	**8a** (2)	neat	4	**19** (87)	---	92:8
21	**8b** (2)	neat	6	**19** (85)	---	86:14
22	**8a** (2)	DCM[d]	6	**20** (58)	---	>99:<1[g]

23	**8b** (2)	DCM[c]	10	**20** (65)	---	96:4
24	**8a** (2)[h]	neat	3	**13** (99)	96:4	95:5
25	**8a** (2)[h]	neat	3	**13** (99)	96:4	95:5
26	**8a** (2)[h]	neat	3	**13** (97)	96:4	93:7
27	**8a** (2)[h]	neat	3	**13** (87)	90:10	97:3

[a] All the reaction were done at 0.1 mmol scale. The recyclability study started with 0.6 mmol. [b] Yields refer to pure isolated compound. [c] Determined by chiral HPLC. [d] The reactions were carried out with 0.25M solution of nitrostyrene in the corresponding solvent. [e] Numbers in brackets correspond to the best results previously described in the same reaction conditions by using the same thiourea supported on sulfonylpolystyrene resin (see Ref. 8b). [f] The reaction was carried out at 0 ^{o}C. [g] >99:<1 means that only one enantiomer was detected by chiral HPLC. [h] Entries 24-27 correspond to the 2nd, 3th, 4th and 5th cycles, respectively, of entry 10.

Finally, we test the recyclability of the catalyst in the addition of ethyl 2-oxo-cylopentane carboxylate (**9**) to *trans*-nitrostyrene under solvent-free conditions at rt, and 2 mol% loading. The reaction time (3 h) was maintained constant in each cycle, and the catalyst was recovered by filtration, washed with acetonitrile, dried, and reused in the next cycle. Fullerothiourea **8a** was used five times affording the addition product **13** without loss of activity and stereocontrol in the first four cycles, and only slight decreasing of the yield and diastereoselection, but increasing the enantioselection in the fifth cycle (entries 10, and 24-27 in Table 1).

Conclusion

In summary, we have prepared three different C_{60}-bifunctional chiral thioureas from easily commercially available starting materials, and demonstrated that they are excellent organocatalysts in stereoselective nitro-Michael additions. These thioureas can be used in homogeneous, or better in neat conditions, and the best results in terms of yield, reactivity, and stereoselection were obtained with fullerothiourea **8a**, derived from natural L-valine. The catalyst works very well with a loading as low as 0.5 mol%, and it was easily recoverable, and used for five cycles without loss of activity.

Experimental section

General information

^{1}H–NMR (400 MHz or 500 MHz) and ^{13}C–NMR (100 MHz) spectra were recorded in $CDCl_3$. Chemical shifts for protons are reported in ppm from TMS as internal

standard. Chemical shifts for carbons are reported in ppm from TMS and are referenced to the carbon resonance of the solvent. TLC analysis was performed on glass-backed plates coated with silica gel 60 and an F_{254} indicator, and visualized by either UV irradiation or by staining with phosphomolybdic acid solution. Flash chromatography was carried out using silica gel (230-240 mesh). Chiral HPLC analysis was performed using different chiral columns. IR spectra were recorded on a FT-IR instrument. Specific rotations were measured using a 5-mL cell with a 1-dm path length, and concentration is given in g per 100 mL.

*2-(2-(2-(Methylamino)ethoxy)ethoxy)ethan-1-ol (**2**)*. A solution of methylamine, 33% wt in EtOH (12.45 mL, 100.0 mmol, 5 equiv), 2-(2-(2-(methylamino)ethoxy)ethoxy)ethan-1-ol, **1** (2.91 mL, 20.0 mmol, 1 equiv), potassium carbonate (5.53 g, 40.0 mmol, 2 equiv) and potassium iodide (332 mg, 2.0 mmol, 0.1 equiv) were charged in a sealed tube and the mixture was stirred at 80°C for 6h. The mixture was filtrated and the filtrate was washed with dichloromethane. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (methanol/dichloromethane 1:20 to methanol/ammonia solution 30% 5:1) yielding 3.13 g of **2** (19.2 mmol, 96%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.72-3.68 (m, 2H, C<u>H</u>$_2$OH), 3.66-3.63 (m, 2H, C<u>H</u>$_2$O), 3.63-3.60 (m, 4H, C<u>H</u>$_2$O), 3.59-3.57 (m, 2H, C<u>H</u>$_2$O), 2.74 (t, J = 5.1 Hz, 2H, C<u>H</u>$_2$NH), 2.70 (br, 1H, N<u>H</u>), 2.42 (s, 3H, NC<u>H</u>$_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 72.7 (CH_2), 70.2 (CH_2), 70.1 (CH_2), 69.9 (CH_2), 61.1 (CH_2), 50.9 (CH_2), 35.9 (CH_3); IR 3311, 2862, 1562, 1452, 1352, 1297, 1249, 1102, 1069, 929, 888, 829, 730 cm^{-1}; HRMS (UPLC-ESI-MS) m/z: calcd for $[C_7H_{17}NO_3+H]^+$ 164.1281, found: 164.1281.

*tert-Butyl (S)-(1-((2-(2-(2-hydroxyethoxy)ethoxy)ethyl)(methyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (**3a**)*. A mixture of Boc-L-valine (2.73 g, 12.6 mmol, 0.9 equiv) and *N*,*N*′-dicyclohexylcarbodiimide (2.88 g, 14.0 mmol, 1.0 equiv) in anhydrous dichloromethane (40 mL) was stirred for 30 min under nitrogen atmosphere at 0°C. After that time, a solution of aminoalcohol **2** (2.28 g, 14.0 mmol, 1 equiv) in anhydrous dichloromethane (40 mL) was added dropwise and the reaction mixture was stirred at room temperature for 15h. The solids were filtered and washed with dichloromethane and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (methanol/dichloromethane 1:30 to 1:15) yielding 4.77 g of compound **3a** (13.2

mmol, 94%) as a pale yellow oil. $[\alpha]_D^{23}$ = +8.2 (c= 1.0 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 2 rotamers) δ 5.38 (d, *J*= 9.2 Hz, 0.7H, NH), 5.34 (d, *J*= 9.2 Hz, 0.3H, NH), 4.48 (dd, *J*= 9.5, 6.2 Hz, 0.3H, CHCO), 4.44 (d, *J*= 9.5, 6.2 Hz, 0.7H, CHCO), 3.75-3.73 (m, 2H, CH_2O), 3.71-3.54 (m, 9H, CH_2O), 3.50-3.46 (m, 1H, CH_2O), 3.15 (s, 2.1H, CH_3N), 2.97 (s, 0.9H, CH_3N), 2.49 (br, 1H, OH), 1.97-1.91 (m, 1H, $CH(CH_3)_2$), 1.44 (s, 7H, Boc), 1.43 (s, 2H, Boc), 0.94 (2d, *J*= 6.9 Hz, 3H, $CH(CH_3)_2$), 0.89 (2d, *J*= 6.9 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (126 MHz, $CDCl_3$, 2 rotamers) δ 173.0 (CON), 172.8 (CON), 155.9 (OCON), 155.8 (OCON), 79.5 (C), 72.3 and 72.1 (CH_2), 70.8 (CH_2), 70.2 and 69.9 (CH_2), 68.6 (CH_2), 61.5 and 61.3 (CH_2), 55.2 and 54.9 (CH), 47.9 (CH_2), 36.5 and 34.2 (CH_3), 31.2 (CH), 28.3 ($3CH_3$), 19.4 and 19.3 (CH_3), 17.4 and 17.3 (CH_3); IR 3418, 2969, 2877, 1702, 1632, 1495, 1393, 1168, 1109, 840, 557 cm^{-1}; HRMS (UPLC-ESI-MS) m/z: calcd for $[C_{17}H_{34}N_2O_6+H]^+$ 363.2490, found: 363.2490.

*tert-Butyl (S)-(1-((2-(2-(2-hydroxyethoxy)ethoxy)ethyl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (**3b**)*. Obtained according to the described method used for **3a**, using Boc-L-phenylalanine (3.70 g, 14.0 mmol, 0.9 equiv), *N*,*N*′-dicyclohexylcarbodiimide (3.20 g, 15.5 mmol, 1.0 equiv) and aminoalcohol **2** (2.53 g, 15.5 mmol, 1 equiv). The residue was purified by column chromatography on silica gel (ethyl acetate/hexane 2:1, to methanol/dichloromethane 1:30 and methanol/dichloromethane 1:20) to yield 6.30 g of compound **3b** (15.4 mmol, 98%) as pale yellow oil. $[\alpha]_D^{23}$ = +46.0 (c= 1.0 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 2 rotamers) δ 7.25-7.16 (m, 5H, H_{ar}), 5.43 (d, *J*= 8.4 Hz, 0.6H, NH), 5.39 (d, *J*= 8.4 Hz, 0.4H, NH), 4.85-4.76 (m, 1H, CHCO), 3.69-3.65 (m, 2H, CH_2OH), 3.60-3.52 (m, 5H, CH_2O and CHHN), 3.50-3.44 (m, 3H, CH_2O), 3.38-3.34 (m, 1H, CH_2O), 3.28-3.13 (m, 1H, CHHN), 3.01-2.91 (m, 2H, CH_2Ph), 2.88 (s, 1H, CH_3N), 2.76 (s, 2H, CH_3N), 2.70 (br, 1H, OH), 1.37 (s, 5H, Boc), 1.36 (s, 4H, Boc); ^{13}C NMR (126 MHz, $CDCl_3$, 2 rotamers) δ 172.2 and 171.7 (CON), 155.1 and 155.0 (OCON), 136.8 and 136.4 (C), 129.4 (2CH), 128.3 (2CH), 126.8 and 126.7 (CH), 79.5 (CH_2), 72.5 (CH_2), 70.7 and 70.4 (CH_2), 70.3 and 70.2 (CH_2), 68.9 and 68.6 (CH_2), 61.6 (CH_2), 51.5 and 51.3 (CH), 49.2 and 48.1 (CH_2), 40.1 and 39.9 (CH_2), 36.6 and 34.5 (CH_3), 28.3 ($3CH_3$); IR 3429, 3308, 2932, 2870, 1702, 1636, 1492, 1363, 1168, 1117, 730, 700, 645 cm^{-1}; HRMS (UPLC-ESI-MS) m/z: calcd for $[C_{21}H_{34}N_2O_6+H]^+$ 411.2490, found: 411.2492.

*tert-Butyl (S)-(1-((2-(2-(2-hydroxyethoxy)ethoxy)ethyl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (**3c**)*. A mixture of Boc-L-*tert*-leucine (2.3 g, 10.0 mmol), DIPEA (5.2 mL, 30.0 mmol, 3.0 equiv) and HBTU (3.8 g, 10.0 mmol, 1 equiv) in anhydrous dichloromethane (40 mL) was stirred for 30 min under nitrogen atmosphere at 0°C. After that time, a solution of aminoalcohol **2** (1.6 g, 10.0 mmol, 1 equiv) in anhydrous dichloromethane (40 mL) was added drop wise and the reaction mixture was stirred at room temperature for 15h. Then the mixture was hydrolyzed by addition of H_2O (50 mL) and the organic layer washed with 1 M aqueous HCl (50 mL), dried over anhydrous magnesium sulfate, filtered and the solvent was removed under reduced pressure. The obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane 2:1, to methanol/dichloromethane 1:30 and methanol/dichloromethane 1:20) to yield 3.65 g of compound **3c** (9.7 mmol, 97%) as pale yellow oil. $[\alpha]_D^{23}$ = +8.4 (c= 1.0 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 2 rotamers) δ 5.42 (d, *J*= 9.9 Hz, 0.4H, NH), 5.35 (d, *J*= 9.9 Hz, 0.6H, NH), 4.51 (2d, *J*= 9.5 Hz, 1H, CHCO), 4.11-4.05 (m, 0.5H, CH_2O), 3.81-3.72 (m, 3H, CH_2O and CHHN), 3.69-3.54 (m, 7.5H, CH_2O), 3.42 (dt, *J*= 4.8 Hz, 0.5H, CHHN), 3.26 (dt, *J*= 4.4 Hz, 0.5H, CHHN), 3.19 (s, 2H, CH_3N), 2.97 (s, 1H, CH_3N), 2.35 (br, 1H, OH), 1.43 and 1.42 (2s, 9H, Boc), 0.97 and 0.96 (2s, 9H, $(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$, 2 rotamers) δ 172.7 and 172.2 (CON), 155.7 and 155.6 (OCON), 79.6 and 79.5 (C), 72.1 and 72.0 (CH_2), 69.9 and 69.7 (CH_2), 68.5 and 68.4 (CH_2), 61.3 and 61.1 (CH_2), 56.0 and 55.9 (CH), 50.2 (CH_2), 47.8 (CH_2), 37.4 and 34.2 (CH_3), 35.6 (C), 28.3 and 28.2 ($3CH_3N$), 26.3 and 26.2 ($3CH_3$);IR 3437, 2958, 2881, 1706, 1628, 1496, 1367, 1164, 1058, 840, 557 cm^{-1}; HRMS (UPLC-ESI-MS) m/z: calcd for $[C_{18}H_{36}N_2O_6+H]^+$ 377.2646, found: 377.2648.

*tert-Butyl (S)-(1-((2-(2-(2-hydroxyethoxy)ethoxy)ethyl)(methyl)amino)-3-methylbutan-2-yl)carbamate (**4a**)*. To a solution of **3a** (1.60 g, 4.90 mmol) in dry THF (6 mL) was added a 1 M solution of BH_3·THF in THF (14.7 mL, 3 equiv) at 0°C. The mixture of reaction was stirred at 50°C for 5h. Then MeOH (1 mL) was added at 0°C and the stirring maintained at this temperature for 0.5h. After that, HCl 12M (3 mL) was added and the mixture was stirred at room temperature for another 0.5h. The mixture was neutralized by addition of a 6 M aqueous solution of NaOH (6 mL) while cooling in an ice bath. The mixture was extracted with dichloromethane (3 × 10 mL), and the organic solution was dried over anhydrous magnesium sulfate, filtered and the solvent

was removed under reduced pressure. The residue was purified by column chromatography on silica gel (methanol/dichloromethane 1:40 to 1:20) yielding 0.69 g of compound **4a** (2.0 mmol, 40%) as a colorless oil. $[\alpha]_D^{23}$= -2.7 (c= 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.89 (br, 1H, NH), 3.76-3.72 (m, 2H, CHHO and CHN), 3.71-3.57 (m, 9H, CH_2O), 2.65-2.57 (m, 2H, CH_2O), 2.45 (br, 1H, CHHN), 2.37-2.28 (m, 1H, CHHN), 2.24 (s, 3H, CH_3N), 1.90 (br, 1H, $CH(CH_3)_2$), 1.44 (s, 9H, Boc), 0.90 (d, *J*= 6.8 Hz, 3H, $CH(CH_3)_2$), 0.86 (d, *J*= 6.9 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2 (OCON), 78.8 (C), 72.6 (CH_2), 70.4 ($3CH_2$), 61.7 (CH_2), 58.8 (CH_2), 57.1 (CH_2), 53.2 (CH), 43.1 (CH_3), 30.1 (CH), 28.4 ($3CH_3$), 18.9 (CH_3), 17.4 (CH_3); IR 3348, 2961, 2871, 1693, 1522, 1457, 1387, 1367, 1245, 1167, 1118, 1061, 866 cm^{-1}. HRMS (UPLC-ESI-MS) m/z: calcd for $[C_{17}H_{37}N_2O_5]^+$ 349.2699, found: 349.2697.

*tert-Butyl (S)-(1-((2-(2-(2-hydroxyethoxy)ethoxy)ethyl)(methyl)amino)-3-phenylpropan-2-yl)carbamate (**4b**)*. Obtained according to the described method used for **4a**, starting from compound **3b** (2.00 g, 4.90 mmol). The obtained residue was purified by column chromatography on silica gel (methanol/ethyl acetate 1:20) yielding 1.10 g of compound **4b** (2.80 mmol, 58%) as colorless oil. $[\alpha]_D^{23}$ = +22.0 (c= 1.0 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.23 (m, 2H, H_{ar}), 7.23-7.16 (m, 3H, H_{ar}), 5.12 (br, 1H, NH), 3.86 (br, 1H, CHNH), 3.72-3.70 (m, 2H, CH_2OH), 3.67-3.64 (m, 2H, CH_2O), 3.62-3.59 (m, 4H, CH_2O), 3.57-3.55 (m, 2H, CH_2O), 2.95-2.91 (m, 1H, CHHPh), 2.80-2.76 (m, 1H, CHHPh), 2.66-2.53 (m, 2H, CH_2N), 2.46 (br, 1H, CHHN), 2.35-2.32 (m, 1H, CHHN), 2.26 (s, 3H, CH_3N), 1.42 (s, 9H, Boc); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8 (OCON), 138.3 (C), 129.5 (2CH), 128.2 (2CH), 126.1 (CH), 79.0 (C), 72.6 (CH_2), 70.3 ($2CH_2$), 69.2 (CH_2), 61.6 (CH_2), 60.2 (CH_2), 57.1 (CH_2), 49.8 (CH), 43.0 (CH_3), 39.2 (CH_2), 28.4 ($3CH_3$); IR 3348, 2925, 2862, 1695, 1455, 1363, 1168, 1058, 745, 700 cm^{-1}; HRMS (UPLC-ESI-MS) m/z: calcd for $[C_{21}H_{36}N_2O_5+H]^+$ 397.2697, found: 397.2695.

*tert-Butyl-(S)-(1-((2-(2-(2-hydroxyethoxy)ethoxy)ethyl)(methyl)amino)-3,3-dimethylbutan-2-yl)carbamate (**4c**)*. To a suspension of lithium aluminium hydride (0.22 g, 5.87 mmol, 2 equiv) in anhydrous diethyl ether (25 mL) under nitrogen atmosphere at 0°C was added drop wise a solution of carbamate **3c** (1.11 g, 2.94 mmol) in anhydrous diethyl ether (15 mL) and left stirring at room temperature for 1

h. After that, the mixture was hydrolyzed at 0°C by sequential addition of water (0.4 mL), 15% NaOH (0.4 mL) and water (1 mL). Hydroxides were removed by filtration, washed with diethyl ether. Then the filtrate was dried over anhydrous magnesium sulfate, filtered and the solvent was removed under reduced pressure. The obtained residue was purified by column chromatography on silica gel (methanol/ethyl acetate 1:20) yielding 0.53 g of **4c** (1.46 mmol, 50%) as a pale yellow oil.. $[\alpha]_D^{23}$ = +6.4 (c= 1.0 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.88 (d, *J*= 9.9 Hz, 1H, NH), 3.76-3.71 (m, 2H, CH_2O), 3.65-3.58 (m, 8H, CH_2O), 3.52 (br, 1H, CHN), 2.72-2.66 (m, 1H, CHHN), 2.58-2.54 (m, 1H, CHHN), 2.52-2.44 (m, 2H, CH_2N), 2.29 (s, 3H, CH_3N), 1.43 (s, 9H, Boc), 0.87 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.4 (OCON), 78.5 (C), 72.6 (CH_2), 70.2 ($2CH_2$), 69.6 (CH_2), 61.3 (CH_2), 57.6 (CH_2), 56.4 (CH_2), 55.9 (CH_2), 50.0 (CH), 42.7 (CH_3), 34.3 (C), 28.3 ($3CH_3N$), 26.3 ($3CH_3$); IR 3356, 2958, 2870, 1698, 1455, 1363, 1245, 1172, 1058, 921, 844, 557 cm^{-1}; HRMS (UPLC-ESI-MS) m/z: calcd for $[C_{18}H_{38}N_2O_5+H]^+$ 363.2853, found: 363.2850.

*tert-Butyl-(S)-(3-methyl-1-(methyl(2-(2-(2-oxoethoxy)ethoxy)ethyl)amino)butan-2-yl)carbamate (**5a**)*. To a solution of freshly distilled oxalyl chloride (0.24 mL, 2.77 mmol, 1.35 equiv) in anhydrous dichloromethane (6 mL) under nitrogen atmosphere at -78°C was added dropwise a solution of anhydrous dimethyl sulfoxide (0.41 mL, 5.80 mmol, 2.82 equiv) in anhydrous dichloromethane (0.5 mL) under nitrogen atmosphere. The reaction mixture was stirred at -78°C for 30 min. Then, a solution of the alcohol **4a** (0.72 g, 2.06 mmol, 1 equiv) in anhydrous dichloromethane (6 mL) was added dropwise and stirred at -78°C for other 30 min more before adding triethylamine (0.82 mL, 5.90 mmol, 2.87 equiv). After 1h of reaction, water (12 mL) was added. The organic layer was separated and the aqueous phase was extracted with dichloromethane (6 mL). Both organic layers were combined and washed with a saturated solution of sodium bicarbonate and water. Then the organic solution was dried over anhydrous magnesium sulfate, filtered and the solvent was removed under reduced pressure to give 0.71 g of amino aldehyde **5a** (2.06 mmol, quantitative) as a pale yellow oil, which was further used without additional purification. $[\alpha]_D^{23}$= -3.1 (c= 1.0 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H, CHO), 4.68 (br, 1H, NH), 4.15 (s, 1H, CHHO), 3.72-3.55 (m, 8H, CH_2O and CHN), 2.63-2.56 (m, 2H, CH_2N), 2.39-2.37 (m, 2H, CH_2N), 2.27 (s, 3H, CH_3N), 1.90 (br, 1H, $CH(CH_3)_2$), 1.44 (s, 9H, Boc), 0.90 (d, *J*= 6.9 Hz, 3H, $CH(CH_3)_2$), 0.84 (d, *J*= 6.9 Hz, 3H, $CH(CH_3)_2$); ^{13}C

NMR (126 MHz, $CDCl_3$) δ 200.9 (CHO), 156.2 (OCON), 78.7 (C), 76.8 (CH_2), 71.3 (CH_2), 70.4 (CH_2), 68.7 (CH_2), 58.8 (CH_2), 57.0 (CH_2), 53.4 (CH), 43.1 (CH_3), 29.9 (CH), 28.4 ($3CH_3$), 18.9 (CH_3), 17.2 (CH_3); IR 3353, 2959, 2931, 2874, 1698, 1515, 1459, 1389, 1365, 1247, 1170, 1113, 922, 861, 731 cm^{-1}; HRMS (UPLC-ESI-MS) m/z: calcd for $[C_{17}H_{35}N_2O_5]^+$ 347.2540, found: 347.2540.

*tert-Butyl (S)-(1-(methyl(2-(2-(2-oxoethoxy)ethoxy)ethyl)amino)-3-phenylpropan-2-yl)carbamate (**5b**)*. Obtained according to the described method used for **5a**, staring from compound **4b** (3.8 g, 9.6 mmol) to give 3.7 g of compound **5b** (9.31 mmol, 97%) as a pale yellow oil, which was used without additional purification. $[\alpha]_D^{23}$ = +10.0 (c= 1.0 $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 9.70 (s, 1H, C<u>H</u>O), 7.29-7.24 (m, 2H, <u>H</u>$_{ar}$), 7.22-7.17 (m, 3H, <u>H</u>$_{ar}$), 4.85 (br, 1H, N<u>H</u>), 4.12 (s, 1H, C<u>H</u>HO), 3.85 (br, 1H, C<u>H</u>N), 3.72-3.50 (m, 7H, C<u>H</u>$_2$O), 2.96-2.88 (m, 1H, C<u>H</u>HN), 2.85-2.77 (m, 1H, CH<u>H</u>N), 2.66-2.53 (m, 2H, C<u>H</u>$_2$N), 2.40 (dd, *J*= 12.7, 8.2 Hz, 1H, C<u>H</u>HN), 2.33 (dd, *J*= 12.7, 5.9 Hz, 1H, CH<u>H</u>N), 2.26 (s, 3H, C<u>H</u>$_3$N), 1.42 (s, 9H, Boc); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.8 (CHO), 155.7 (OCON), 138.2 (C), 129.6 (2CH), 128.2 (2CH), 126.2 (CH), 79.0 (C), 76.8 (CH_2), 73.5 (CH_2), 71.2 (CH_2), 70.4 (CH_2), 69.5 (CH_2), 60.1 (CH_2), 57.0 (CH_2), 49.8 (CH), 43.1 (CH_3), 39.0 (CH), 28.4 ($3CH_3$); IR 3347, 2924, 2857, 1702, 1497, 1455, 1388, 1250, 1166, 1049, 739, 701 cm^{-1}; HRMS (UPLC-ESI-MS) m/z: calcd for $[C_{21}H_{34}N_2O_5+H]^+$ 395.2540, found: 395.2536.

*tert-Butyl-(S)-(3,3-dimethyl-1-(methyl(2-(2-(2-oxoethoxy)ethoxy)ethyl)amino) butan-2-yl)carbamate (**5c**)*. Obtained according to the described method used for **5a**, starting from compound **4c** (1.13 g, 3.13 mmol) to give 1.13 g of compound **5c** (3.13 mmol, quantitative) as pale yellow oil, which was f used without additional purification. $[\alpha]_D^{23}$ = +7.3 (c= 1.0 $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 9.74 (s, 1H, C<u>H</u>O), 4.67 (br, 1H, N<u>H</u>), 4.15 (s, 1H, C<u>H</u>HO), 3.75-3.50 (m, 8H, C<u>H</u>$_2$O and C<u>H</u>N), 2.71 (br, 1H, C<u>H</u>HN), 2.63-2.50 (m, 2H, CH<u>H</u>N and C<u>H</u>$_2$N), 2.43 (br, 1H, CH<u>H</u>N), 2.31 (s, 3H, C<u>H</u>$_3$N), 1.43 (s, 9H, Boc), 0.89 (s, 9H, C(C<u>H</u>$_3$)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.9 (CHO), 156.4 (OCON), 78.7 (C), 76.8 (CH_2), 71.2 (CH_2), 70.4 (CH_2), 69.7 (CH_2), 57.8 (CH_2), 56.4 (CH_2), 56.0 (CH), 42.8 (CH_3), 34.4 (C), 28.4 ($3CH_3N$), 26.4 ($3CH_3$); IR 3356, 2962, 2866, 1702, 1518, 1363, 1245, 1172, 1113, 1050, 775 cm^{-1}; HRMS (UPLC-ESI-MS) m/z: calcd for $[C_{18}H_{36}N_2O_5+H]^+$ 361.2697, found: 361.2699.

*N-Methyl-2-[(S)-10-tert-butoxycarbonylamino-8,11-dimethyl-8-aza-2,5-dioxadodecyl]pyrrolidino[3,4:1,2][60]fullerene (**6a**)*. To a suspension of C_{60} (607 mg, 0.84 mmol, 1 equiv) in anhydrous toluene (820 mL), aldehyde **5a** (350 mg, 1.01 mmol, 1.2 equiv) and sarcosine (375 mg, 4.21 mmol, 5 equiv) were added and refluxed for 6 hours. The solvent was removed under reduced pressure and the residue obtained was purified by column chromatography on silica gel using toluene to recover the unreacted C_{60} and toluene/isopropanol 40:1 to recover the product yielding 456 mg of **6a** (0.42 mmol, 49%) as a brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.77 (d, *J*= 9.4 Hz, 1H, C<u>H</u>HPyrr), 4.63 (br, 1H, N<u>H</u>), 4.56-4.52 (m, 1H, CH<u>H</u>-CHPyrr), 4.37-4.33 (m, 1H, CH<u>H</u>-CHPyrr), 4.12 (d, *J*= 9.4 Hz, 1H, CH<u>H</u>Pyrr), 4.11-4.09 (m, 1H, C<u>H</u>Pyrr), 3.72-3.70 (m, 2H, C<u>H</u>$_2$O), 3.62-3.55 (m, 2H, C<u>H</u>$_2$O), 3.50-3.44 (m, 3H, C<u>H</u>$_2$O and C<u>H</u>N), 2.98 (s, 3H, C<u>H</u>$_3$NPyrr), 2.58-2.53 (m, 2H, C<u>H</u>$_2$N), 2.36-2.33 (m, 2H, C<u>H</u>$_2$N), 2.25 (s, 3H, C<u>H</u>$_3$N), 1.91 (br, 1H, C<u>H</u>(CH$_3$)$_2$), 1.42 (s, 9H, Boc), 0.87 (d, *J*= 6.9 Hz, 3H, CH(C<u>H</u>$_3$)$_2$), 0.83 (d, *J*= 6.9 Hz, 3H, CH(C<u>H</u>$_3$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2 (OCON), 155.8 (C), 154.3 (C), 153.8 (C), 152.6 (C), 147.3 (C), 147.2 (C), 146.4 (C), 146.3 (C), 146.3 (C), 146.3 (C), 146.2 (C), 146.2 (C), 146.1 (C), 146.0 (C), 146.0 (C), 145.9 (C), 145.8 (C), 145.6 (C), 145.6 (C), 145.5 (C), 145.4 (C), 145.3 (C), 145.3 (C), 145.2 (C), 145.2 (C), 144.7 (C), 144.6 (C), 144.4 (C), 144.4 (C), 143.2 (C), 143.0 (C), 142.7(C), 142.6 (C), 142.6 (C), 142.3 (C), 142.2 (C), 142.1 (C), 142.1 (C), 142.1 (C), 142.1 (C), 142.0 (C), 141.8 (C), 141.7 (C), 141.7 (C), 140.3 (C), 140.2 (C), 139.6 (C), 139.6 (C), 139.4 (C), 137.3 (C), 136.4 (C), 135.9 (C), 135.6 (C), 78.8 (C), 76.2 (CH), 74.1 (C), 71.9 (CH$_2$), 71.0 (CH$_2$), 70.5 (CH$_2$), 70.4 (CH$_2$), 69.7 (CH$_2$), 69.6 (C), 58.8 (CH$_2$), 57.0 (CH$_2$), 53.2 (CH), 43.3 (CH$_3$), 43.2 (CH$_3$), 40.7 (CH$_2$), 29.9 (CH), 28.5 (3CH$_3$), 19.0 (CH$_3$), 17.3 (CH$_3$); IR 2954, 2870, 2782, 1694, 1513, 1458, 1362, 1244, 1164, 1110, 765, 572, 526 cm^{-1}; HRMS (MALDI/Matrix DCTB) m/z: calcd for $C_{79}H_{40}N_3O_4$ 1094.3013, found: 1094.3079.

*N-Methyl-2-[(S)-10-tert-butoxycarbonylamino-8-methyl-11-phenyl-8-aza-2,5-dioxaundecyl]pyrrolidino[3,4:1,2][60]fullerene (**6b**)*. Obtained according to the described method used for **6a**, but starting from compound **5b** (465 mg, 1.18 mmol). The compound was purified by column chromatography on silica gel using toluene to recover the unreacted C_{60} and toluene/isopropanol 20:1 to recover the product yielding 577 mg of **6b** (0.50 mmol, 51%) as a brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.24 (m, 2H, <u>H</u>$_{ar}$), 7.19-7.16 (m, 3H, <u>H</u>$_{ar}$), 4.82 (br, 1H, N<u>H</u>), 4.77 (d,

J= 9.5 Hz, 1H, CHHPyrr), 4.55-4.51 (m, 1H, CHH-CHPyrr), 4.37-4.33 (m, 1H, CHH-CHPyrr), 4.11 (d, *J*= 9.5, 1H, CHHPyrr), 4.10-4.09 (m, 1H, CHPyrr), 3.83 (br, 1H, CHN), 3.71-3.69 (m, 2H, CH_2O), 3.61-3.52 (m, 2H, CH_2O), 3.49 (t, *J*= 5.8 Hz, 2H, CH_2O), 2.99 (s, 3H, CH_3NPyrr), 2.93-2.89 (m, 1H, CHHPh), 2.84-2.80 (m, 1H, CHHPh), 2.60-2.51 (m, 2H, CH_2N), 2.40-2.27 (m, 2H, CH_2N), 2.23 (s, 3H, CH_3N), 1.41 (s, 9H, Boc); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8 (OCON), 155.7 (C), 155.7 (C), 154.3 (C), 153.8 (2C), 152.6 (2C), 147.3 (C), 147.2 (C), 146.4 (C), 146.3 (2C), 146.2 (2C), 146.1 (C), 146.0 (2C), 145.9 (C), 145.8 (C), 145.6 (2C), 145.50 (C), 145.4 (C), 145.3 (2C), 145.2 (2C), 144.7 (C), 144.6 (C), 144.4 (2C), 143.2 (C), 143.0 (C), 142.7 (C), 142.6 (2C), 142.2 (C), 142.1 (3C), 142.0 (3C), 141.8 (C), 141.6 (C), 140.3 (C), 140.2 (C), 139.6 (2C), 139.4 (C), 138.2 (C), 137.3 (2C), 136.4 (C), 136.0 (2C), 129.6 (2CH), 128.3 (2CH) 126.2 (CH), 79.0 (C), 76.1 (CH), 74.1 (C), 71.9 (CH_2), 71.0 (CH_2), 70.4 (CH_2), 70.3 (CH_2), 69.6 (CH_2), 69.5 (C), 60.1 (CH_2), 57.1 (CH_2), 49.8 (CH), 43.2 (CH_3), 40.7 (CH_3), 39.0 (CH_2), 28.5 ($3CH_3$); IR 3343, 2853, 2782, 1702, 1492, 1455, 1245, 1166, 1111, 730, 701, 525 cm^{-1}; HRMS (MALDI/Matrix DCTB) m/z: calcd for $C_{83}H_{40}N_3O_4$ 1142.3013, found: 1142.3146.

*N-Methyl-2-[(S)-10-tert-butoxycarbonylamino-8,11,11-trimethyl-8-aza-2,5-dioxadodecyl]pyrrolidino[3,4:1,2][60]fullerene (**6c**)*. Obtained according to the described method used for **6a**, starting from compound **5c** (540 mg, 1.5 mmol). The compound was purified by column chromatography on silica gel using toluene to recover the unreacted C_{60} and toluene/isopropanol 20:1 to recover the product yielding 651 mg of **6c** (0.59 mmol, 47%) as a brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.81 (d, *J*= 9.4 Hz, 1H, CHHPyrr), 4.59-4,56 (m, 1H, CHH-CHPyrr), 4.40-4.36 (m, 1H, CHH-CHPyrr), 4.14 (d, *J*= 9.4 Hz, 1H, CHHPyrr), 4.11-4.09 (m, 1H, CHPyrr), 3.73 (t, *J*= 4.7 Hz, 2H, CH_2O), 3.66-3.58 (m, 2H, CH_2O), 3.53 (t, *J*= 5.9 Hz, 2H, CH_2O), 3.50 (br, 1H, CHN), 3.01 (s, 3H, CH_3NPyrr), 2.66-2.59 (m, 1H, CHHN), 2.52-2.49 (m, 2H, CH_2N), 2.36-2.29 (m, 1H, CHHN), 2.27 (s, 3H, CH_3N), 1.44 (s, 9H, Boc), 0.89 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.5 (OCON), 155.8 (C), 154.3 (C), 153.8 (C), 152.6 (C), 147.3 (C), 147.2 (2C), 146.4 (C), 146.3 (2C), 146.2 (C), 146.1 (2C), 146.0 (2C), 145.9 (C), 145.8 (C), 145.6 (2C), 145.5 (C), 145.4 (C), 145.3 (2C), 145.2 (2C), 144.7 (C), 144.6 (C), 144.4 (2C), 143.2 (C), 143.0 (C), 142.7 (C), 142.6 (C), 142.6 (C), 142.2 (C), 142.1 (2C), 142.1 (2C), 142.0 (2C), 141.8 (C), 141.7 (2C), 140.3 (C), 140.2 (C), 139.7 (2C), 139.4 (C), 137.3 (2C), 136.4

(C), 136.4 (C), 136.0 (C), 135.6 (C), 78.6 (C), 76.1 (C), 74.0 (C), 72.0 (CH_2), 71.0 (CH_2), 70.5 (CH_2), 70.3 (CH_2), 70.1 (CH_2), 69.6 (C), 58.2 (CH_2), 56.6 (CH_2), 56.2 (CH), 43.1 (CH_3), 40.7 (CH_3), 34.4 (C), 28.5 ($3CH_3N$), 26.5 ($3CH_3$); IR 2950, 2855, 2781, 1698, 1500, 1456, 1361, 1241, 1167, 1050, 728, 523 cm^{-1}; HRMS (MALDI/Matrix DCTB) m/z: calcd for $C_{80}H_{42}N_3O_4$ 1108.3170, found: 1108.3396.

*N-Methyl-2-[(S)-10-amino-8,11-dimethyl-8-aza-2,5-dioxadodecyl]pyrrolidino [3,4:1,2][60]fullerene (**7a**).* A suspension of compound **6a** (516 mg, 0.47 mmol) in 18 mL chloroform/trifluoroacetic acid mixture (5/1 v/v) was stirred at room temperature for 2h and then the solvent was removed under reduced pressure. The crude product was dissolved in dichloromethane and 30% solution of ammonia was added until basic pH. The organic layer was separated and the water solution was extracted with dichloromethane (4 x 10 mL). Both organic layers were combined and the solvent was removed under reduced pressure yielding 469 mg of **7a** (0.47 mmol, quantitative) as a brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.78 (d, *J*= 9.4 Hz, 1H, C<u>H</u>HPyrr), 4.56-4.52 (m, 1H, C<u>H</u>H-CHPyrr), 4.38-4.36 (m, 1H, CH<u>H</u>-CHPyrr), 4.12 (d, *J*= 9.4 Hz, 1H, CH<u>H</u>Pyrr), 4.09-4.06 (m, 1H, C<u>H</u>Pyrr), 3.72-3.69 (m, 2H, C<u>H</u>$_2$O), 3.64-3.46 (m, 4H, C<u>H</u>$_2$O), 3.00 and 2.99 (2s, 3H, C<u>H</u>$_3$NPyrr), 2.65-2.60 (m, 2H, C<u>H</u>HN and C<u>H</u>N), 2.48-2.42 (m, 1H, CH<u>H</u>N), 2.41-2.16 (m, 2H, C<u>H</u>$_2$N), 2.24 and 2.23 (2s, 3H, C<u>H</u>$_3$N), 1.61-1.48 (m, 1H, C<u>H</u>$(CH_3)_2$), 0.91 (d, *J* = 6.6 Hz, 3H, CH(C<u>H</u>$_3$)$_2$), 0.89 (d, *J* = 6.6 Hz, 3H, CH(C<u>H</u>$_3$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8 (C), 154.3 (C), 153.8 (C), 152.8 (C), 147.3 (C), 147.2 (2C), 147.1 (C), 146.4 (C), 146.3 (3C), 146.2 (2C), 146.1 (2C), 146.0 (2C), 145.9 (C), 145.8 (C), 145.6 (C), 145.6 (2C), 145.5 (C), 145.4 (C), 145.3 (2C), 145.2 (2C), 145.2 (2C), 144.7 (C), 144.6 (C), 144.4 (2C), 143.2 (C), 143.0, 142.7 (C), 142.6 (C), 142.6 (C), 142.6 (2C), 142.2 (C), 142.1 (3C), 142.1 (C), 142.0 (2C), 141.8 (C), 141.7 (C), 140.3 (C), 140.2 (C), 139.7 (C), 139.5 (C), 137.3 (C), 137.0 (C), 136.4 (C), 135.9 (C), 135.6 (C), 76.4 (CH), 74.1 (C), 71.8 (CH_2), 71.0 (CH_2), 70.5 (CH_2), 70.3 (CH_2), 69.6 (CH_2), 69.4 (C), 62.7 (CH_2), 57.3 (CH_2), 54.4 (CH), 43.6 (CH_3), 40.6 (CH_3), 32.0 (CH), 19.5 (CH_3), 18.1 (CH_3); IR 2922, 2853, 2780, 1459, 1345, 1182, 1109, 767, 735, 523 cm^{-1}; HRMS (MALDI/Matrix DCTB) m/z: calcd for $C_{74}H_{32}N_3O_2$ 994.2489, found: 994.2513.

*N-Methyl-2-[(S)-10-amino-8-methyl-11-phenyl-8-aza-2,5-dioxaundecyl] pyrrolidino [3,4:1,2][60]fullerene (**7b**).* Obtained according to the described method used for **7a**, starting from compound **6b** (470 mg, 0.41 mmol), yielding 412 mg of **7b** (0.40 mmol,

98%) as a brown solid. The obtained compound was further used without additional purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.14 (m, 5H, H_{ar}), 4.82 (br, 1H, CHHPyrr), 4.79-4.69 (m, 1H, CHH-CHPyrr), 4.54-4.43 (m, 1H, CHH-CHPyrr), 4.38-4.30 (m, 1H, CHHPyrr), 4.12-4.02 (m, 1H, CHPyrr), 3.91-3.79 (m, 1H, CHN), 3.76-3.32 (m, 6H, CH_2O), 3.20-2.32 (m, 12H, CH_3Pyrr, CH_2N, CH_3N, CH_2Ph); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8 (C), 154.3 (C), 153.8 (C), 152.6 (C), 147.3 (C), 147.2 (C), 146.4 (C), 146.3 (2C), 146.2 (5C), 146.1 (5C), 146.0 (3C), 145.9 (4C), 145.8 (2C), 145.6 (3C), 145.6 (2C), 145.5 (2C), 145.4 (C), 145.3 (2C), 145.2 (4C), 144.7 (C), 144.6 (C), 144.4 (2C), 143.2 (C), 143.0, 142.7 (C), 142.6 (2C), 142.6 (C), 142.2 (C), 142.1 (3C), 142.0 (3C), 141.8 (C), 141.7 (C), 140.3 (C), 140.2 (C), 139.6 (C), 139.4 (C), 139.3 (C), 138.2 (C), 136.4 (C), 136.1 (C), 135.9 (2C), 129.2 (2CH), 128.4 (2CH), 126.2 (CH), 76.2 (CH), 74.1 (C), 71.7 (CH_2), 71.0 (CH_2), 70.4 (CH_2), 70.3 (CH_2), 69.6 (CH_2), 69.5 (C), 64.7 (CH_2), 57.2 (CH_2), 50.3 (CH), 43.5 (CH_3), 40.6 (CH_3), 40.1 (CH_2); IR 2921, 2853, 2783, 1671, 1456, 1179, 1125, 727, 523 cm^{-1}; HRMS (MALDI/Matrix Ditranol) m/z: calcd for $C_{78}H_{32}N_3O_2$ 1042.2489, found: 1042.2549.

*N-Methyl-2-[(S)-10-amino-8,11,11-trimethyl-8-aza-2,5-dioxadodecyl]pyrrolidino [3,4:1,2][60]fullerene (**7c**)*. Obtained according to the described method used for **7a**, but starting from compound **6c** (400 mg, 0.36 mmol), yielding 298 mg of **7c** (0.30 mmol, 82%) as a brown solid. The obtained compound was used without additional purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.76 (d, *J*= 9.4 Hz, 1H, CHHPyrr), 4.54-4.51 (m, 1H, CHH-CHPyrr), 4.36-4.33 (m, 1H, CHH-CHPyrr), 4.10 (d, *J*= 9.4 Hz, 1H, CHHPyrr), 4.08-4.06 (m, 1H, CHPyrr), 3.70 (t, *J*= 4.5 Hz, 2H, CH_2O), 3.63-3.54 (m, 2H, CH_2O), 3.53-3.46 (m, 2H, CH_2O), 2.97 (s, 3H, CH_3NPyrr), 2.65-2.60 (m, 1H, CHHN), 2.56-2.52 (m, 1H, CHN), 2.45-2.38 (m, 1H, CHHN), 2.30-2.27 (m, 1H, CHHN), 2.22 (s, 3H, CH_3N), 2.19-2.11 (m, 1H, CHHN), 0.86 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8 (C), 154.3 (C), 153.8 (C), 152.7 (C), 147.2 (2C), 146.4 (2C), 146.3 (2C), 146.2 (2C), 146.1 (C), 146.0 (2C), 145.8 (C), 145.6 (2C), 145.5 (C), 145.4 (C), 145.3 (3C), 145.2 (3C), 144.7 (C), 144.6 (C), 144.4 (2C), 143.2 (C), 143.0 (C), 142.7 (C), 142.6 (2C), 142.2 (C), 142.1 (4C), 142.11 (C), 142.0 (2C), 141.8 (C), 141.7 (C), 141.6 (C), 140.3 (C), 140.2 (C), 139.7 (C), 139.4 (2C), 139.2 (C), 137.3 (C), 137.2 (C), 136.4 (C), 135.9 (C), 135.6 (C), 76.2 (CH), 74.0 (C), 71.8 (CH_2), 71.0 (CH_2), 70.4 ($2CH_2$), 69.7 (C), 69.6 (CH_2), 60.3 (CH_2), 57.3 (CH_2), 57.0

(CH), 43.5 (CH_3), 40.7 (CH_3), 33.0 (C), 26.4 ($3CH_3$); IR 2953, 2855, 2781, 1460, 1182, 1109, 966, 951, 765, 523 cm^{-1}; HRMS (MALDI/Matrix DCTB) m/z: calcd for $C_{75}H_{34}N_3O_2$ 1008.2646, found: 1008.2660.

*1-(3,5-bis(Trifluoromethyl)phenyl)-3-[N-methyl-2-((S)-10-amino-8,11-dimethyl-8-aza-2,5-dioxadodecyl)pyrrolidino[3,4:1,2][60]fullerenyl]thiourea (**8a**)*. To a suspension of compound **7a** (469 mg, 0.47 mmol, 1 equiv) in anhydrous toluene (40 mL), 1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (0.21 mL, 1.42 mmol, 3 equiv) was added. The mixture was stirred for 12h and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (CS_2/isopropanol 40:1) yielding 381 mg of thiourea **8a** (0.301 mmol, 64%) as a brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.71 (s, 1H, NHCSNH), 8.12 (s, 2H, H_{ar}), 7.56 (s, 1H, H_{ar}), 6.19 (s, 1H, NHCSNH), 4.77 (d, *J*= 9.4 Hz, 1H, CHHPyrr), 4.41-4.32 (m, 1H, CHH-CHPyrr), 4.24-4.18 (m, 1H, CHH-CHPyrr), 4.09 (d, *J*= 9.4 Hz, 1H, CHHPyrr), 3.99 (t, *J*= 5.1 Hz, 1H), 3.74-3.70 (m, 1H, CH_2O), 3.60-3.46 (m, 4H, CH_2O and CHN), 3.43-3.33 (m, 2H, CH_2O), 2.92 (s, 3H, CH_3NPyrr), 2.82-2.75 (m, 1H, CHHN), 2.72-2.75 (m, 1H, CHHN), 2.63-2.53 (m, 2H, CH_2N), 2.43 (s, 3H, CH_3N), 1.90 (br, 1H, $CH(CH_3)_2$), 1.01 (t, *J*= 6.7 Hz, 6H, $CH(CH_3)_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.0 (CS), 155.8 (C), 154.3 (C), 153.8 (C), 152.6 (C), 147.3 (C), 147.2 (C), 146.3 (2C), 146.2 (2C), 146.1 (C), 146.0 (2C), 145.8 (C), 145.6 (2C), 145.4 (2C), 145.3 (2C), 145.2 (3C), 144.7 (C), 144.5 (C), 144.4 (C), 144.3 (2C), 143.2 (C), 143.0 (C), 142.7 (C), 142.6 (C), 142.2 (C), 142.1 (3C), 142.0 (2C), 141.8 (C), 141.7 (2C), 141.6 (2C), 140.3 (C), 140.2 (C), 139.5 (2), 139.3 (2C), 137.2 (C), 136.4 (C), 136.3 (C), 136.0 (C), 135.6 (C), 131.4 (q, *J*= 34.7 Hz, C), 123.3 ($2CF_3$, q, *J*= 272.5 Hz), 123.0 (2CH), 117.2 (CH), 76.1 (CH), 74.0 (C), 71.6 (CH_2), 70.7 (CH_2), 70.6 (CH_2), 70.4 ($2CH_2$), 69.5 (C), 68.1 (CH_2), 62.4 (CH_2), 60.2 (CH), 57.9 (CH_2), 43.4 (CH_3), 40.5 (CH_3), 31.6 (CH), 18.6 (CH_3), 18.5 (CH_3); ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.72, -62.74; IR 2954, 2853, 2782, 1463, 1383, 1273, 1168, 1126, 879, 727, 698, 677, 576, 526 cm^{-1}; HRMS (MALDI/Matrix DCTB) m/z: calcd. for $C_{83}H_{35}F_6N_4O_2S$ 1265.2379, found: 1265.2333.

*1-(3,5-bis(Trifluoromethyl)phenyl)-3-[N-methyl-2-((S)-10-amino-8-methyl-11-phenyl-8-aza-2,5-dioxaundecyl]pyrrolidinio [3,4:1,2][60]fullerenyl]thiourea (**8b**)*. Obtained according to the described method used for **8a**, but starting from compound **7b** (405 mg, 0.35 mmol). The obtained residue was purified by column chromatography on

silica gel (CS_2/isopropanol 40:1) yielding 322 mg of compound **8b** (0.25 mmol, 70%) as a brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.78 (s, 1H, NHCSNH), 8.20-8.12 (m, 2H, H_{ar}), 7.54 (s, 1H, H_{ar}), 7.35-7.22 (m, 5H, H_{ar}), 6.63 (s, 1H, NHCSNH), 4.73-4.66 (m, 1H, CHHPyrr), 4.36-4.21 (m, 2H, CH_2-CHPyrr), 4.12-3.98 (m, 2H, CHHPyrr and CHPyrr), 3.70-3.36 (m, 7H, CH_2O and CHN), 2.89 (s, 3H, CH_3NPyrr), 2.81-2.59 (m, 6H, CH_2N and CH_2Ph), 2.34-2.32 (m, 3H, CH_3N); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.5 (CS), 155.8 (C), 154.2 (C), 153.6 (C), 152.6 (C), 147.2 (2C), 146.3 (C), 146.2 (2C), 146.1 (C), 146.0 (2C), 145.9 (C), 145.6 (2C), 145.8 (C), 145.6 (C), 145.4 (3C), 145.3 (2C), 145.2 (3C), 144.7 (C), 144.5 (C), 144.4 (C), 144.3 (2C), 143.2 (C), 143.0 (C), 142.6 (C), 142.1 (3C), 142.0 (C), 141.7 (2C), 141.6 (C), 141.6 (C), 140.3 (C), 140.2 (C), 139.5 (C), 139.3 (C), 137.6 (C), 137.3 (C), 136.4 (C), 136.0 (C), 135.6 (C), 132.4 (q, *J*= 33.6 Hz, C), 128.2 (CH), 128.7 (2CH), 129.2 (2CH), 123.2 ($2CF_3$, q, *J*= 272.7 Hz), 123.0 (2CH), 117.2 (CH), 76.0 (CH), 74.0 (C), 71.6 (CH_2), 70.7 (CH_2), 70.6 (CH_2), 70.3 (CH_2), 69.6 (CH_2), 69.5 (C), 65.0 (CH_2), 64.6 (CH), 60.6 (CH_2), 43.5 (CH_3), 40.4 (CH_3), 36.1 (CH_2); ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.6, -63.0; IR 2925, 2856, 2786, 1456, 1378, 1276, 1167, 1126, 682, 527 cm^{-1}; HRMS (QTOF-electrospray) m/z: calcd. for $C_{87}H_{34}F_6N_4O_2S$ 1313.2379, found: 1313.2377.

*1-(3,5-bis(Trifluoromethyl)phenyl)-3-[N-methyl-2-((S)-10-amino-8,11,11-trimethyl-8-aza-2,5-dioxadodecyl]pyrrolidinio [3,4:1,2][60]fullerenyl]thiourea (**8c**).* Obtained according to the described method used for **8a**, starting from compound **7c** (252 mg, 0.22 mmol). The obtained residue was purified by column chromatography on silica gel (CS_2/isopropanol 40:1) yielding 132 mg of compound **8c** (0.10 mmol, 47%) as a brown solid. ^{1}H NMR (500 MHz, $CDCl_3$), as a mixture of rotamers, δ 12.59 (s, 1H, NHCSNH), 8.10 (s, 2H, H_{ar}), 7.50 (s, 1H, H_{ar}), 6.26 (s, 1H, NHCSNH), 4.76 (d, *J*= 9.4 Hz, 1H, CHHPyrr), 4.39-4.31 (m, 1H, CHH-CHPyrr), 4.21 (br, 1H, CHH-CHPyrr), 4.10-4.08 (m, 1H, CHHPyrr), 4.00 (br, 1H, CHPyrr), 3.59-3.26 (m, 7H, CH_2O and CHN), 2.92 (s, 3H, CH_3NPyrr), 2.82-2.75 (m, 1H, CHHN), 2.84-2.81 (m, 1H, CHHN), 2.73-2.71 (m, 1H, CHHN), 2.64-2.59 (m, 1H, CHHN), 2.44 (s, 3H, CH_3N), 1.03 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.1 (CS), 155.8 (C), 154.3 (C), 153.8 (C), 152.5 (C), 147.3 (C), 147.2 (C), 146.4 (2C), 146.3 (2C), 146.2 (C), 146.1 (C), 146.0 (2C), 145.8 (C), 145.6 (C), 145.5 (2C), 145.4 (C), 145.3 (2C), 145.2 (2C), 144.7 (C), 144.5 (C), 144.4 (C), 144.3 (C), 143.2 (C), 143.0 (C), 142.7

(C), 142.6 (C), 142.2 (C), 142.1 (4C), 142.0 (2C), 141.8 (C), 141.7 (C), 141.6 (2C), 140.8 (C), 140.3 (C), 140.2 (C), 139.5 (2C), 139.3 (C), 137.8 (C), 137.3 (C), 136.3 (C), 136.0 (C), 135.5 (C), 131.4 (q, *J*= 34.0 Hz, C), 123.2 ($2CF_3$, q, *J*= 273.1 Hz), 122.9 (2CH), 117.1 (CH), 76.1 (CH), 74.0 (C), 71.5 (CH_2), 70.7 (CH_2), 70.4 ($2CH_2$), 69.5 (C), 68.2 (CH_2), 64.3 (CH_2), 61.2 (CH_2), 57.8 (CH_2), 43.3 (CH_3), 40.5 (CH_3), 26.7 ($3CH_3$); ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.63, -63.02; IR 2925, 2856, 1464, 1378, 1276, 1126, 727, 682, 527 cm^{-1}; HRMS (MALDI/Matrix DCTB) m/z: calcd. for $C_{84}H_{37}F_6N_4O_2S$ 1279.2536, found: 1279.2500.

General procedure for the nitro-Michael reaction using fullerothioureas 8a-c.

A mixture of β-nitrostyrene (0.1 mmol), 1,3-dicarbonyl compound (0.2 mmol, 2 equiv), and the corresponding catalyst (0.002 mmol), was stirred at rt in a Wheaton vial until consumption of the starting material (monitored by TLC). Acetonitrile (1 mL) was added and the catalyst was filtered off and washed with acetonitrile. The solvent was removed under reduced pressure, and the residue was purified by column chromatography. The diastereo- and enantiomeric ratios were determined by chiral HPLC of the purified product.

(S)-Ethyl 1-((R)-2-nitro-1-phenylethyl)-2-oxocyclopentanecarboxylate ***(13)***.[20] Colorless solid. ^1H NMR (500 MHz, $CDCl_3$) δ 1.27 (t, *J* = 7.2 Hz, 3H, $C\underline{H}_3$), 1.80–2.09 (m, 4H, $C\underline{H}_2$), 2.36 (m, 2H, $C\underline{H}_2CO$), 4.07 (dd, *J* = 10.9, 3.8 Hz, 1H, C<u>H</u>Ph), 4.21 (q, *J* = 7.1 Hz, 1H, C<u>H</u>HCH_3), 4.22 (q, *J* = 7.1 Hz, 1H, CH<u>H</u>CH_3), 5.01 (dd, *J* = 13.5, 11.0 Hz, 1H, C<u>H</u>HNO_2), 5.17 (dd, *J* = 13.5, 3.7 Hz, 1H, CH<u>H</u>NO_2), 7.20–7.35 (m, 5H, Har); HPLC (Chiralcel OD, *n*-hexane/2-propanol = 80/20, 1.0 mL/min, λ = 220 nm); tR (major diastereoisomer) = 9.2 min (major), 12.4 min (minor).

(S)-Ethyl 1-((R)-2-nitro-1-phenylethyl)-2-oxocyclohexanecarboxylate ***(14)***.[20] Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.26 (t, *J* = 7.1 Hz, 3H), 1.44–1.74 (m, 4H), 2.00–2.12 (m, 2H), 2.42–2.54 (m, 2H), 4.00 (dd, *J* = 11.3, 3.2 Hz, 1H), 4.20 (m, 2H), 4.79 (dd, *J* = 13.5, 11.4 Hz, 1H), 5.06 (dd, *J* = 13.5, 3.3 Hz, 1H), 7.14–7.17 (m, 2H), 7.25–7.30 (m, 3H); HPLC (Chiralcel OD, n-hexane/2-propanol = 95/5, 1.0 mL/min, λ = 220 nm); tR (major diastereoisomer) = 14.5 min (major), 18.8 min (minor).

(S)-Methyl 1-((R)-2-nitro-1-phenylethyl)-2-oxocycloheptanecarboxylate ***(15)***.[19k] Colorless solid. Major diastereoisomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40–1.94 (m, 8H, C$\underline{H}_2$), 2.50–2.63 (m, 2H, C$\underline{H}_2$CO), 3.77 (s, 3H, C$\underline{H}_3$O), 4.06 (dd, *J*= 10.0, 4.2 Hz, 1H, C$\underline{H}$), 4.92 (dd, *J*= 13.6, 10.0 Hz, 1H, CH$\underline{H}$NO$_2$), 4.96 (dd, *J*= 13.6, 4.2 Hz, 1H, C$\underline{H}$HNO$_2$), 7.14–7.21 (m, 2H, $\underline{H}_{ar}$), 7.28–7.34 (m, 3H, $\underline{H}_{ar}$). HPLC (Chiralcel OD, n-hexane/2-propanol = 95/5, 1.0 mL/min, λ= 220 nm); tR (major diastereoisomer) = 12.9 min (major), 29.5 min (minor).

(R)-2-Acetyl-2-((R)-2-nitro-1-phenylethyl)cyclopentanone ***(16)***.[20] Colorless solid. Major diastereoisomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.66–1.74 (m, 3H), 1.86–1.93 (m, 1H), 2.16–2.21 (m, 1H), 2.30 (s, 3H, C$\underline{H}_3$), 2.54–2.57 (m, 1H, C$\underline{H}$), 4.37 (dd, *J*= 11.5, 3.9 Hz, 1H, C$\underline{H}$Ph), 4.51 (dd, *J*= 13.6, 3.9 Hz, 1H, C$\underline{H}$HNO$_2$), 4.86 (dd, *J*= 13.6, 11.5 Hz, 1H, CH$\underline{H}$NO$_2$), 7.24–7.33 (m, 5H, $\underline{H}_{ar}$). HPLC (Chiralcel OD, n-hexane/2-propanol = 70/30, 1.0 mL/min, λ = 220 nm); tR (major diastereoisomer) = 10.8 min (major), 42.5 min (minor).

(S)-3-(2-Nitro-1-phenylethyl)pentane-2,4-dione ***(19)***.[21] Colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.94 (s, 3H, C$\underline{H}_3$), 2.29 (s, 3H, C$\underline{H}_3$), 4.22–4.27 (m, 1H, C$\underline{H}$), 4.37 (d, *J*= 10.8 Hz, 1H, C$\underline{H}$COMe), 4.61 (dd, *J*= 11.3, 3.9 Hz, 1H, CH$\underline{H}$NO$_2$), 4.65 (dd, *J*= 11.3, 6.8 Hz, 1H, C$\underline{H}$HNO$_2$), 7.15–7.17 (m, 2H, $\underline{H}_{ar}$), 7.24–7.33 (m, 3H, $\underline{H}_{ar}$). HPLC (Lux-amylose-1, n-hexane/2-propanol = 90/10, 1.0 mL/min, λ= 220 nm); tR = 12.4 min (major, *S*), 16.6 min (minor, *R*).

(S)-2-(2-Nitro-1-phenylethyl)-1,3-diphenylpropane-1,3-dione ***(20)***.[21] Colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.61–4.66 (m, 1H, C$\underline{H}$Ph), 4.99 (d, *J*= 6.8 Hz, 2H, C$\underline{H}_2$NO$_2$), 5.85 (d, *J*= 7.9 Hz, 1H, C$\underline{H}$(COPh)$_2$), 7.16–7.24 (m, 5H, $\underline{H}_{ar}$), 7.34–7.41 (m, 4H, $\underline{H}_{ar}$), 7.49–7.56 (m, 2H, $\underline{H}_{ar}$), 7.77–7.79 (m, 2H, $\underline{H}_{ar}$), 7.85–7.87 (m, 2H, $\underline{H}_{ar}$). HPLC (Lux-amylose-1, n-hexane/2-propanol = 75/25, 1.0 mL/min, λ= 220 nm); tR = 11.5 min (major, *S*).

Recyclability of the fullerothioureas in nitro-Michael reaction.

The catalyst was recovered from the reaction mixtures by filtration with a membrane filter, thoroughly washed with acetonitrile, dried and reused in the next cycle.

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Supporting Information Available: Copies of ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR, and IR spectra for all new compounds and copies of the HPLC chromatograms are available as supporting information. This material is available on the WWW under http://dx.doi.org/10.1002/ejoc.201601640.

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