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Enantioselective Platinum-Catalyzed Tandem Hydroarylation–Cycloisomerization of 1,6-Enynes

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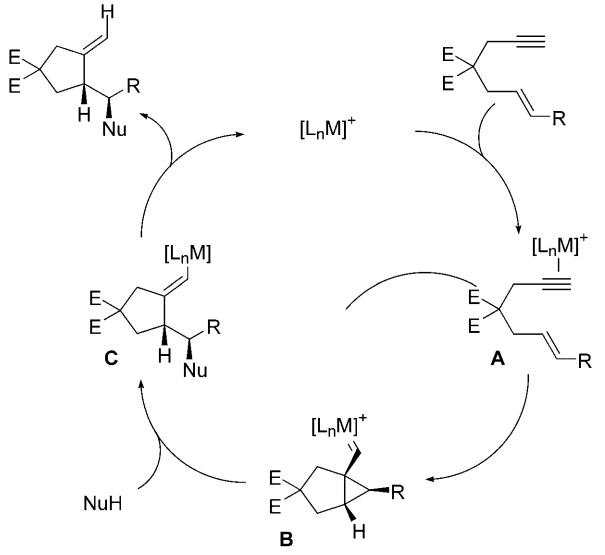
Abstract: The platinum(II) chloride/silver hexafluoroantimonate ($PtCl_2/AgSbF_6$) catalytic system associated with atropisomeric ligand Ph-BINEPINE promotes a stereoselective tandem hydroarylation (Friedel–Crafts-type addition) of electron-rich aromatic and heteroaromatic derivatives to unactivated alkenes followed by a C–C bond cyclization reaction (*ee* up to 96%). Some evidence shows that the catalytic species responsible for the highest enantiomeric excesses might reasonably be an L_3Pt^{2+} species, L being a monodentate ligand.

Keywords: asymmetric catalysis; atom economy; cycloisomerization; platinum; tandem reactions

Introduction

Recent years have witnessed a tremendous growth in the number of transition metal-catalyzed enyne cycloisomerization reactions.[1] Indeed, these transformations illustrate ideally the atom-economy concept allowing the synthesis of complex and functionalized cyclic structures with high efficiency under mild conditions.[2] Whereas a flurry of synthetic methodologies using a variety of transition metals have appeared during the last two decades, the ability of noble third row transition metals, such as gold and platinum, to act as catalytic carbophilic π-acids has resulted in a major change of perspective in this field.[3] The general mechanism of the reaction of 1,6-enynes involving these acids[4] proceeds through initial η^2-coordination of the metal to the alkyne (intermediate **A**) and subsequent intramolecular addition of the alkene leading to cyclopropylcarbene **B** (Scheme 1). In the presence of an external nucleophile, ring opening of the cyclopropylcarbene and rearrangement to cyclized vinylmetal complex **C** is observed. Protodemetalation completes the catalytic cycle. Whereas this synthetic methodology was first put on evidence with oxygen nucleophiles such as water or alcohols leading respectively to hydroxy- and alkoxycyclization reactions,[5] recent studies have demonstrated the possibility to extend the scope of this reaction to other classes of nucleophiles such as amines[6] and electron-rich aromatic systems.[7] In the latter case, the diastereoselective tandem hydroarylation/cyclization of 1,6-enynes catalyzed by cationic Au(I) species offers the opportunity to create two carbon-carbon bonds and introduce an aromatic ring[8] in a very selective manner related to the Friedel–Crafts reaction.[9] Considering the large occurrence of natural products containing five-membered rings found throughout the chemical literature



Scheme 1.

Scheme 2.

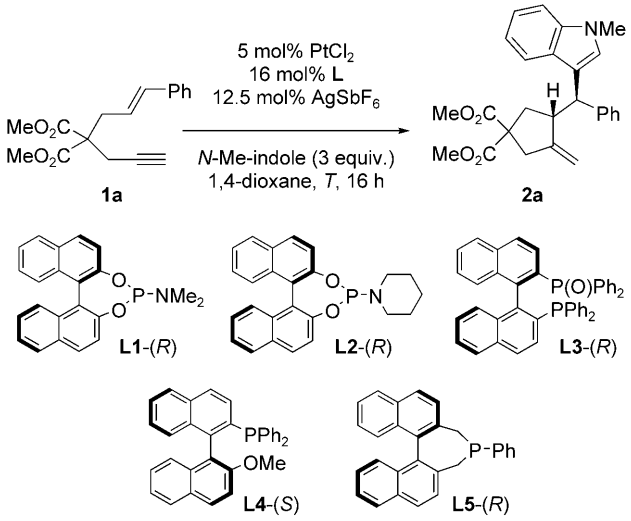
and our interest in the development of catalytic tandem and atom-economical reactions,[10] we envisioned that platinum chiral catalysts should offer a unique opportunity to develop an unprecedented enantioselective version of the tandem hydroarylation/cycloisomerization reaction.

Although impressive progress has been made in the development of enantioselective Au(I)-catalyzed transformations,[11] most catalytic systems described so far for alkyne electrophilic activation show either a moderate level of enantioselection or limited substrate scope.[12] We reasoned that this situation is the consequence of the linear geometry of the ligand-metal-alkyne intermediate **D** (Scheme 2), which is involved in the activation step of the alkyne function by Au(I) complexes.[3a,5n,13] As cationic platinum complexes have recently been shown to exhibit high catalytic activities for the hydroarylation of alkynes[14] and alkenes,[15] we speculated that square planar Pt-based complexes possessing a single empty coordination site (complex **E**) could provide the right combination for a high activity and a high degree of enantiocontrol to be met in the nucleophilic attack on the coordinated alkyne. Following our previous observations on enantioselective alkoxycyclization reactions,[5f] we also envisaged that an "optimum" chiral environment around the metal could be attained by the aid of axially chiral monodentate P donor ligands.

Results and Discussion

Initially, we examined the reaction of enyne **1a** with 1-methylindole (3 equiv.) in the presence of 5 mol% of $PtCl_2$, 12.5 mol% $AgSbF_6$ and 16 mol% of ligand (**L1**–**L5**) in dioxane at 90 °C (Table 1). We chose some monodentate phosphorus ligands such as phosphoramidite **L1** and **L2**,[16] BINAP monooxide[17] **L3**, MeO-MOP **L4**[18] and Ph-BINEPINE **L5**[19] ligands to build up *in situ* the catalytic species. We were pleased to find that all tested catalysts allowed complete conversions within 16 h to carbocyclic compound **2a**. While modest stereoselectivities of a similar range (20–37%) were promoted by ligands **L1–L4** (Table 1, entries 1–4), the catalyst formed from **L5** allowed the formation of product **2a** with 73% yield and 84% enantiomeric excess (Table 1, entry 5). Running the reaction at 60 °C with **L5** increased the *ee* to 95% (96% yield) (Table 1, entry 6). Lowering further the temperature to room temperature led to a lower yield (45%) and an equivalent level of enantioselectivity (96% *ee*) (Table 1, entry 7).

Table 1. Ligand screening on platinum-catalyzed asymmetric hydroarylation/cycloisomerization of **1a**.

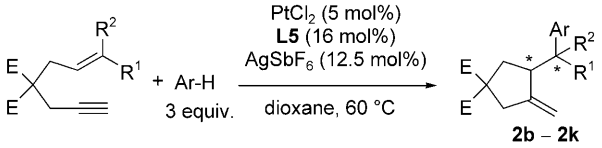


Entry	Ligand	T [°C]	Yield[a] [%]	*ee*[b] [%] (configuration)
1	(*R*)-**L1**	90	81	37 (−)
2	(*R*)-**L2**	90	75	33 (−)
3	(*R*)-**L3**	90	94	20 (+)
4	(*S*)-**L4**	90	51	21 (−)
5	(*R*)-**L5**	90	73	84 (−)
6	(*R*)-**L5**	60	96	95 (−)
7	(*R*)-**L5**	23	45	96 (−)

[a] Isolated yield.
[b] Determined by HPLC analysis.

Using the optimized catalytic conditions, we examined at first the scope of the 1,6-enyne partner (Table 2, Scheme 3). Changing the malonate substitution pattern from methyl to bulkier groups such as isopropyl, *tert*-butyl or benzyl groups led to lower *ee* (Table 2, entries 1–3). One may notice that there was no pronounced Thorpe–Ingold effect as the *ee*s were all in the same range. The reaction is tolerant towards a rather large variety of electron-rich aromatic and heteroaromatic nucleophile partners: 1,3-dimethoxybenzene, 1,3,5-trimethoxybenzene, 2- and 5-substituted indoles and pyrrole can be successfully introduced. The enantioselectivity depends on the structure of the aryl nucleophile and apparently it suffers from an increase in the steric hindrance as in the case of 2-substituted indoles (compare, entry 6 of Table 1 and entries 4–6 of Table 2). Similar enantiomeric excesses were obtained in the case of the introduction of dimethoxy- and trimethoxybenzene (Table 2, entries 7 and

Table 2. Substrate scope of platinum-catalyzed asymmetric hydroarylation/cycloisomerization reaction.[a]



1b E = CO_2*i*-Pr, R^1 = Ph, R^2 = H; **1c** E = CO_2Bn, R^1 = Ph, R^2 = H
1d E = CO_2*t*-Bu, R^1 = Ph, R^2 = H; **1e** E = CO_2Me, R^1 = 3,4-$(OCH_2O)C_6H_3$, R^2 = H

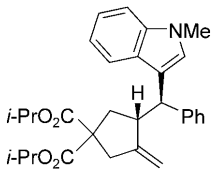
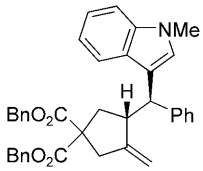
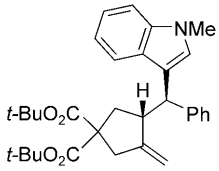
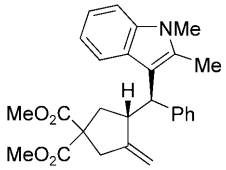
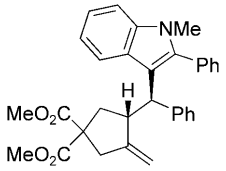
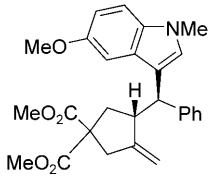
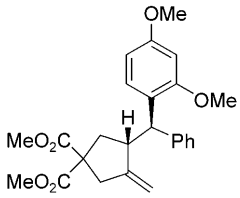
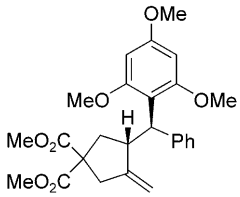
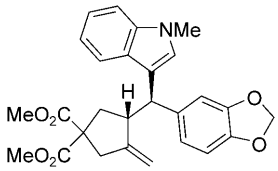
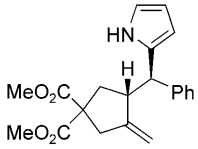
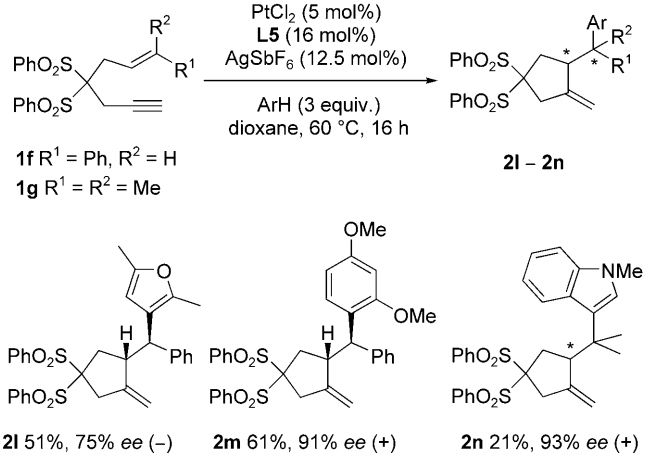
Entry	Enyne	Nucleophile	Product	Yield[b] [%]	*ee*[c] [%]
1	**1b**	1-methylindole	**2b** 	75	82 (−)
2	**1c**	1-methylindole	**2c** 	77	83 (−)
3	**1d**	1-methylindole	**2d** 	70	80 (−)
4	**1a**	1,2-dimethylindole	**2e** 	85	89 (−)
5	**1a**	1-methyl-2-phenylindole	**2f** 	58	74 (−)
6	**1a**	1-methyl-5-methoxyindole	**2g** 	95	87 (−)
7[d]	**1a**	1,3-dimethoxybenzene	**2h** 	53	80 (+)

Table 2. (Continued)

Entry	Enyne	Nucleophile	Product	Yield[b] [%]	*ee*[c] [%]
8[d]	**1a**	1,3,5-trimethoxybenzene	**2i** 	90	79 (+)
9	**1e**	1-methylindole	**2j** 	78	79 (−)
10	**1a**	pyrrole	**2k** 	46[e,f]	70 (+)

[a] $PtCl_2$ (5 mol%), **L5** (16 mol%), $AgSbF_6$ (12.5 mol%), nucleophile (3 equiv.), dioxane (0.5 M), 60 °C.
[b] Isolated yield.
[c] Determined by HPLC analysis.
[d] Reaction time: 4 h.
[e] Reaction run at 40 °C.
[f] 9% of the C-3 isomer was also obtained.

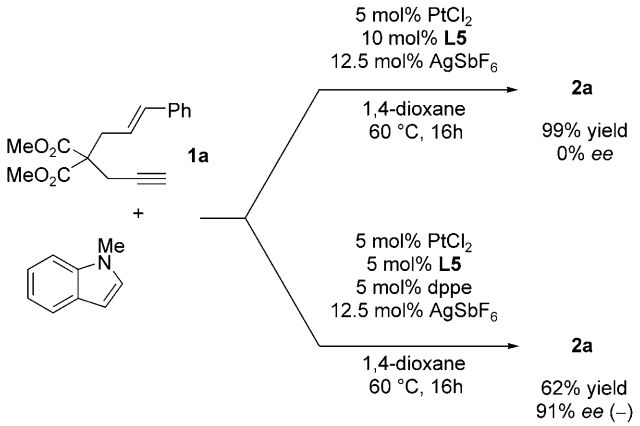
8). A benzodioxolane-substituted enyne was also engaged with success in the tandem process: the corresponding heterocyclic derivative **2j** was isolated in 78% yield and 79% enantiomeric excess (Table 2, entry 9). The introduction of pyrrole was possible and afforded the corresponding 2-substituted cyclic derivative **2k** in a modest yield and in 70% enantiomeric excess (Table 2, entry 10). For all substrates investigated, carbocyclic compounds **2a**–**2n** were formed in >19:1 *syn:anti* diastereoselectivity.



Scheme 3. Platinum-catalyzed asymmetric hydroarylation/cycloisomerization reaction of sulfonated enynes.

Other carbon tethered substrates, such as the sulfonated enynes **1f** and **g** were then engaged in the tandem process (Scheme 3). The corresponding arylated derivatives **2l–2n** resulting from the addition of 2,5-dimethylfuran, 1,3-dimethoxybenzene and 1-methylindole were isolated in moderate yields (21–61%). Nevertheless, a beneficial substrate effect was apparent in the case of **2m** as the observed enantiomeric excess (91%) was some ten points higher than in the case of **1a** (Table 2, entry 7). Furthermore, product **2n** containing a quaternary carbon center was obtained with 93% *ee*.

With the aim to get some clue into the exact nature of the active species, the enyne **1a** and 1-methylindole have been reacted at a Pt/**L5** ratio of 2 (Scheme 4). Product **2a** was obtained in 99% yield but in racemic form. Inspired by the work of Gagné's group on asymmetric Pt-catalyzed bicyclopropane synthesis,[20] we envisaged that a stereoselective tandem reaction might be accomplished even by a combination of a chiral and an achiral ligand. Indeed, a catalyst formed from $PtCl_2$ (5 mol%), dppe (diphenylphosphanoethane) (5 mol%), **L5** (5 mol%) and $AgSbF_6$ (12.5 mol%) lead to the formation of product **2a** in 62% yield and in 91% *ee*. Taken together, these last results are in keeping with the involvement of L_3Pt^{2+} species in the catalytic process.



Scheme 4. Pt-catalyzed arylation of enyne **1a**.

Conclusions

In summary, we have extended the methodology developed for Au to Pt allowing the enantioselective intermolecular tandem hydroarylation/cycloisomerization of 1,6-enynes with a variety of electron-rich aromatic and heteroaromatic nucleophiles under mild conditions. The corresponding functionalized cyclic derivatives were isolated in good to excellent yields and up to 96% enantiomeric excesses were obtained. We have also provided evidence that the catalytic species responsible for the highest enantiomeric excesses might reasonably be an L_3Pt^{2+} species, L being a monodentate ligand. This process paves the way for further applications in enantioselective tandem nucleophile addition/cycloisomerization reactions. Current efforts are focused on expanding the scope of this methodology to other classes of substrates such as 1,5-enynes and to develop an enantioselective intramolecular version of the transformation.

Experimental Section

General Remarks

$PtCl_2$ was obtained from Johnson–Matthey. $AgSbF_6$ was purchased from Acros. All manipulations were carried out under argon. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV 300 instrument. All signals are expressed as ppm (δ) and internally referenced to residual protio solvent signals. Coupling constants (J) are reported in Hz and refer to apparent peak multiplicities. Mass spectrometric analyses (direct introduction by chemical ionization with ammonia or electrospray) were performed at the Ecole Nationale Supérieure de Chimie de Paris. High resolution mass spectra were performed on a Varian MAT311 instrument at the Ecole Normale Supérieure (Paris). Enynes **1a**, **1f** and **1g** were prepared according to published procedures.[4b,5d] Enynes **1b**, **1c**, **1d** and **1e** were prepared in analogy with published procedures.[7a]

Diisopropyl 2-(3-phenylprop-2-enyl)-2-(prop-2-ynyl)malonate (1b): TLC (cyclohexane/ethyl acetate: 98/2): R_f=0.13; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.24 (d, J=6.3 Hz, 6H), 1.25 (d, J=6.3 Hz, 6H), 2.04 (t, J=2.5 Hz, 1H), 2.82 (d, J=2.6 Hz, 2H), 2.94 (dd, J=7.7, 0.9 Hz, 2H), 5.09 (hept, J=6.3 Hz, 2H), 6.03 (dt, J=15.7, 7.8 Hz, 1H), 6.51 (d, J=15.7 Hz, 1H), 7.20–7.34 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5, 21.6, 22.8, 35.6, 69.2, 71.4, 79.1, 123.4, 126.2, 127.4, 128.5, 134.4, 137.0, 169.2; CI-MS (NH_3): m/z= 360 $[M+NH_4]^+$, 343 $[M+H]^+$.

Dibenzyl 2-(3-phenylprop-2-enyl)-2-(prop-2-ynyl)malonate (1c): TLC (cyclohexane/ethyl acetate: 90/10): R_f=0.46; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.06 (t, J=2.7 Hz, 1H), 2.91 (d, J=2.7 Hz, 2H), 3.02 (d, J=7.8 Hz, 2H), 5.16 (d, J=12.3 Hz, 2H), 5.19 (d, J=12.3 Hz, 2H), 5.92 (dt, J=15.6, 7.8 Hz, 1H), 6.46 (d, J=15.6 Hz, 1H), 7.21–7.35 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=22.9, 35.8, 57.3, 67.4, 71.8, 78.8, 122.9, 126.3, 127.5, 128.3, 128.4, 128.4, 128.5, 134.7, 135.2, 136.9, 169.4; CI-MS (NH_3): m/z=456 $[M+NH_4]^+$, 439 $[M+H]^+$.

Di(*tert*-butyl) 2-(3-phenylprop-2-enyl)-2-(prop-2-ynyl)-malonate (1d): TLC (cyclohexane/ethyl acetate: 98/2): R_f= 0.21; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.46 (s, 18H), 2.04 (t, J=2.7 Hz, 1H), 2.74 (d, J=2.7 Hz, 2H), 2.87 (dd, J=7.6, 1.2 Hz, 2H), 6.04 (dt, J=15.7, 7.6 Hz, 1H), 6.51 (d, J= 15.7 Hz, 1H), 7.20–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=22.8, 27.9, 35.6, 57.7, 71.2, 79.4, 81.8, 123.8, 126.2, 127.3, 128.5, 134.1, 137.2, 168.9; ESI-MS (NH_3): m/z= 393 $[M+Na]^+$.

Dimethyl 2-[3-(3′,4′-methylenedioxy)phenylprop-2-enyl]-2-(prop-2-ynyl)malonate (1e): TLC (cyclohexane/ethyl acetate: 80/20): R_f=0.41; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.06 (t, J=2.7 Hz, 1H), 2.69 (d, J=2.6 Hz, 2H), 2.91 (dd, J=7.7, 1.0 Hz, 2H), 3.73 (s, 6H), 5.81 (dt, J=15.5, 7.7 Hz, 1H), 5.90 (m, 2H), 6.40 (d, J=15.5 Hz, 1H), 6.68–6.79 (m, 2H), 6.84 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=22.9, 35.8, 52.8, 57.2, 71.6, 78.8, 101.0, 105.6, 108.2, 120.8, 121.2, 131.5, 134.2, 147.2, 148.0, 170.1; ESI-MS (Na): m/z=353 $[M+Na]^+$.

Standard Catalytic Procedure

A mixture of $PtCl_2$ (5 mol%) and (*R*)-BINEPINE[19a] (16 mol%) in degassed dioxane (0.5 M) was stirred under an argon atmosphere at 60 °C for 30 min. The formation of a white precipitate was observed. The reaction mixture was cooled down to room temperature and $AgSbF_6$ (12.5 mol%) was added. The reaction was stirred at room temperature for 15 min. The aromatic nucleophile (3 equiv.) was then added and the mixture was stirred for 3 min. The enyne (1 equiv.) was finally added and the mixture was warmed to 60 °C and stirred until completion of the reaction monitored by TLC. The mixture was filtered through a short pad of silica (cyclohexane/EtOAc, 50/50) and the solvents were evaporated under reduced pressure. The crude product was purified by silica gel flash chromatography using eluent conditions reported for TLC.

Dimethyl 3-[1-(1-methyl-1*H*-indol-3-yl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2a): ^{1}H, ^{13}C NMR and mass spectroscopic data for compound **2a** were identical to literature values.[2] The product ratio was determined by HPLC using a Chiralcel OD-H (hexane/2-propanol: 98/2, 1 mL min^{-1}). The retention times for the two enantiomers

were 21.7 and 24.9 min; $[\alpha]_D$ −7.3 ($CHCl_3$, *c* 0.45) at 95% *ee*.

Diisopropyl 3-[1-(1-methyl-1*H*-indol-3-yl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2b): TLC (petroleum ether/ethyl acetate: 95/5): $R_f = 0.13$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.21$ (d, $J = 6.3$ Hz, 3H), 1.17–1.23 (m, 9H), 1.94 (dd, $J = 13.6$, 8.6 Hz, 1H), 2.73 (dd, $J = 13.6$, 7.8 Hz, 1H), 2.87 (d, $J = 16.0$ Hz, 1H), 3.11 (dq, $J = 15.9$, 1.9 Hz, 1H), 3.50–3.58 (m, 1H), 3.76 (s, 3H), 4.12 (s, 1H), 4.16 (d, $J = 10.5$ Hz, 1H), 4.78 (s, 1H), 4.97 (hept, $J = 6.3$ Hz, 1H), 5.06 (hept, $J = 6.3$ Hz, 1H), 7.00–7.35 (m, 8H), 7.56 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.5$, 32.7, 39.7, 41.7, 46.9, 48.0, 58.5, 68.7, 68.9, 109.1, 109.6, 117.3, 118.8, 119.5, 121.5, 125.9, 126.2, 127.6, 128.0, 128.4, 136.9, 144.7, 149.4, 171.2, 171.4; CI-MS (NH_3): $m/z = 474$ $[M+H]^+$; HR-MS (CI-CH_4): $m/z = 474.2633$, calcd. for $C_{30}H_{36}O_4N$: 474.2644. The product ratio was determined by HPLC using a Chiralcel AD-H (hexane/2-propanol: 98/2, 1 mL min^{-1}). The retention times for the two enantiomers were 10.6 and 11.2 min; $[\alpha]_D$: −9.7 ($CHCl_3$, *c* 0.48) at 82% *ee*.

Dibenzyl 3-[1-(1-methyl-1*H*-indol-3-yl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2c): TLC (petroleum ether/ethyl acetate: 95/5): $R_f = 0.08$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.03$ (dd, $J = 13.2$, 8.0 Hz, 1H), 2.78 (dd, $J = 13.6$, 7.9 Hz, 1H), 2.95 (d, $J = 15.8$ Hz, 1H), 3.16 (dd, $J = 16.0$, 1.9 Hz, 1H), 3.48–3.57 (m, 1H), 3.72 (s, 3H), 4.14–4.17 (m, 2H), 4.78 (s, 1H), 4.99 (d, $J = 12.3$ Hz, 1H), 5.10 (d, $J = 12.3$ Hz, 1H), 5.12 (s, 2H), 6.94 (s, 1H), 7.01–7.32 (m, 13H), 7.53 (d, $J = 7.9$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 32.7$, 39.8, 41.8, 47.9, 58.6, 67.2, 109.1, 110.0, 117.1, 118.9, 119.4, 121.5, 126.0, 126.1, 127.6, 127.9, 128.0, 128.1, 128.2, 128.4, 135.4, 135.5, 136.9, 144.6, 148.9, 171.4, 171.5; CI-MS (NH_3): $m/z = 587$ $[M+NH_4]^+$, 570 $[M+H]^+$; HR-MS (CI-CH_4): $m/z = 570.2645$, calcd. for $C_{38}H_{36}O_4N$: 570.2644. The product ratio was determined by HPLC using a Chiralcel OD-H (hexane/2-propanol: 98/2, 1 mL min^{-1}). The retention times for the two enantiomers were 36.4 and 53.9 min; $[\alpha]_D$: −3.2 ($CHCl_3$, *c* 0.50) at 83% *ee*.

Di-*tert*-butyl 3-[1-(1-methyl-1H-indol-3-yl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2d): TLC (petroleum ether/ethyl acetate: 95/5): $R_f = 0.25$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.29$ (s, 9H), 1.35 (s, 9H), 1.76 (dd, $J = 13.6$, 8.7 Hz, 1H), 2.55 (ddd, $J = 13.6$, 7.9, 1.5 Hz, 1H), 2.68 (dd, $J = 15.6$, 1.3 Hz, 1H), 2.92 (dq, $J = 15.8$, 2.5 Hz, 1H), 3.37–3.46 (m, 1H), 3.65 (s, 3H), 3.98 (s, 1H), 4.04 (d, $J = 10.4$ Hz, 1H), 4.66 (s, 1H), 6.89–7.15 (m, 7H), 7.21–7.25 (m, 2H), 7.44 (d, $J = 7.9$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 27.9$, 32.7, 39.7, 41.8, 46.7, 48.2, 59.7, 81.0, 81.3, 109.0, 109.4, 117.3, 118.7, 119.6, 121.4, 125.9, 126.2, 127.7, 128.0, 128.5, 137.0, 144.8, 149.6, 171.0, 171.2; CI-MS (NH_3): $m/z = 502$ $[M+H]^+$, 446 $[M-C_4H_8+H]^+$: HR-MS (CI-CH_4): $m/z = 501.2871$, calcd. for $C_{32}H_{39}O_4N$: 501.2879. The product ratio was determined by HPLC using a Chiralcel OD-H (hexane/2-propanol: 99/1, 1 mL min^{-1}). The retention times for the two enantiomers were 10.0 and 11.7 min; $[\alpha]_D$: −14.8 ($CHCl_3$, *c* 0.54) at 80% *ee*.

Dimethyl 3-[1-(1-methyl-2-methyl-1*H*-indol-3-yl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2e): TLC (cyclohexane/ethyl acetate: 80/20): $R_f = 0.50$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.70$–1.90 (m, 1H), 2.45 (s, 3H), 2.50–2.60 (m, 1H), 3.62 (s, 3H), 3.65 (s, 3H), 3.75 (s, 3H), 3.80–4.20 (m, 2H), 4.30 (br s, 1H), 4.70 (br s, 1H), 6.90–7.80 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 10.8$, 29.5, 39.6, 41.8, 45.1, 48.2, 52.6, 52.7, 57.9, 108.7, 109.4, 113.7, 119.0, 119.4, 120.3, 125.7, 126.6, 128.1, 128.2, 133.1, 136.7, 145.0, 150.2, 172.2, 172.3; CI-MS (NH_3): $m/z = 432$ $[M+H]^+$; HR-MS: $m/z = 432.2177$, calcd. for $C_{27}H_{30}O_4N$: 432.2175. The product ratio was determined by HPLC using a Chiralcel AS-H (hexane/2-propanol: 98/2, 1 mL min^{-1}). The retention times for the two enantiomers were 12.3 and 14.7 min; $[\alpha]_D$: −8.9 ($CHCl_3$, *c* 1.02) at 89% *ee*.

Dimethyl 3-[1-(1-methyl-2-phenyl-1*H*-indol-3-yl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2f): TLC (cyclohexane/ethyl acetate: 80/20): $R_f = 0.45$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.90$ (dd, $J = 13.8$, 9.3 Hz, 1H), 2.57 (dd, $J = 13.8$, 9.3 Hz, 1H), 2.99 (s, 2H), 3.49 (s, 3H), 3.68 (s, 3H), 3.76 (s, 3H), 3.90–4.00 (m, 1H), 4.12 (s, 1H), 4.72 (s, 1H), 7.05–7.97 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 30.7, 40.0, 41.7, 45.0, 48.1, 52.6, 52.7, 57.9, 109.3, 109.4, 115.4, 119.5, 120.5, 121.4, 125.7, 126.3, 127.9, 128.2, 128.4, 131.2, 132.2, 137.2, 138.5, 144.9, 149.8, 172.2, 172.3; CI-MS (NH_3): $m/z = 494$ $[M+H]^+$; HR-MS: $m/z = 494.2327$, calcd. for $C_{32}H_{32}O_4N$: 494.2331. The product ratio was determined by HPLC using a Chiralcel OD-H (hexane/2-propanol: 99/1, 1 mL min^{-1}). The retention times for the two enantiomers were 10.4 and 11.7 min; $[\alpha]_D$: +35.0 ($CHCl_3$, *c* 0.68) at 74% *ee*.

Dimethyl 3-[1-(1-methyl-5-methoxy-1*H*-indol-3-yl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2g): TLC (cyclohexane/ethyl acetate: 80/20): $R_f = 0.27$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.88$ (dd, $J = 13.6$, 8.5 Hz, 1H), 2.68 (ddd, $J = 13.6$, 7.9, 1.5 Hz, 1H), 2.80 (dd, $J = 15.8$, 1.0 Hz, 1H), 3.03 (dq, $J = 15.8$, 2.5 Hz, 1H), 3.36–3.43 (m, 1H), 3.56 (s, 3H), 3.64 (s, 6H), 3.72 (s, 3H), 3.99 (d, $J = 10.3$ Hz, 1H), 4.03 (s, 1H), 4.71 (s, 1H), 6.75 (dd, $J = 8.9$, 2.3 Hz, 1H), 6.87–6.89 (m, 2H), 7.00–7.25 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 32.9$, 39.9, 41.8, 46.8, 48.1, 52.6, 52.7, 55.9, 58.4, 101.6, 109.8, 109.9, 111.6, 116.6, 126.0, 126.8, 127.9, 128.1, 128.4, 132.3, 144.6, 149.0, 153.6, 172.1, 172.3; CI-MS (NH_3): $m/z = 448$ $[M+H]^+$; HR-MS (CI-NH_3): $m/z = 448.2133$, calcd. for $C_{27}H_{30}O_5N$ $[M+H]^+$: 448.2124. The product ratio was determined by HPLC using a Chiralcel AD-H (hexane/2-propanol: 90/10, 1 mL min^{-1}). The retention times for the two enantiomers were 12.5 and 14.6 min; $[\alpha]_D$: −19.5 ($CHCl_3$, *c* 0.48) at 87% *ee*.

Dimethyl 3-[1-(2,4-dimethoxyphenyl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2h): ^{1}H, ^{13}C NMR and mass spectroscopy data for compound **2h** were identical to literature values.[2] The product ratio was determined by HPLC using a Chiralcel AS-H (hexane/2-propanol: 98/2, 1 mL min^{-1}). The retention times for the two enantiomers were 11.1 and 12.6 min; $[\alpha]_D$: +26.6 ($CHCl_3$, *c* 1.58) at 80% *ee*.

Dimethyl 3-[1-(2,4,6-trimethoxyphenyl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2i): ^{1}H, ^{13}C NMR and mass spectroscopy data for compound **2i** were identical to literature values.[2] Product ratio was determined by HPLC using a Chiralcel AS-H (hexane/2-propanol: 98/2, 1 mL min^{-1}). The retention times for the two enantiomers were 11.8 and 12.8 min; $[\alpha]_D$: + 92.1 ($CHCl_3$, *c* 2.9) at 77% *ee*.

Dimethyl 3-[1-(1-methyl-1*H*-indol-3-yl)-(3,4-methylenedioxy)phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2j): TLC (cyclohexane/ethyl acetate: 80/20): $R_f = 0.35$;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.92 (dd, J = 13.6, 8.4 Hz, 1H), 2.75 (dd, J = 13.7, 7.9 Hz, 1H), 2.88 (d, J = 14.9 Hz, 1H), 3.12 (d, J = 15.9 Hz, 1H), 3.39–3.47 (m, 1H), 3.63 (s, 3H), 3.70 (s, 3H), 3.73 (s, 3H), 4.05 (d, J = 10.5 Hz, 1H), 4.21 (s, 1H), 4.83 (s, 1H), 5.86 (d, J = 5.9 Hz, 1H), 6.67 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 6.4 Hz, 1H), 6.99 (s, 1H), 7.04 (t, J = 7.8 Hz, 1H), 7.18 (t, J = 8.0 Hz, 1H), 7.25 (d, J = 5.8 Hz, 1H), 7.52 (d, J = 7.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.8, 40.0, 41.7, 47.0, 47.8, 52.6, 52.7, 58.4, 100.7, 107.7, 108.7, 109.1, 110.1, 117.2, 118.9, 119.4, 120.9, 121.5, 121.6, 126.0, 127.5, 136.9, 138.7, 145.6, 147.4, 148.8, 172.1, 172.3. CI-MS (NH_3): m/z = 462 $[M+H]^+$; HR-MS (CI-NH_3): m/z = 462.1932, calcd. for $C_{27}H_{28}O_6N$: 462.1917. The product ratio was determined by HPLC using a Chiralcel OD-H (hexane/2-propanol: 90/10, 1 mL min^{-1}). The retention times for the two enantiomers were 14.6 and 18.1 min; $[\alpha]_D$: −7.6 ($CHCl_3$, c 1.44) at 79% *ee*.

Dimethyl 3-[1-pyrrol-2-yl)-phenylmethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2k): ^{1}H, ^{13}C NMR and mass spectroscopy data for compound **2k** were identical to literature values.[2] The product ratio was determined by HPLC using a Chiralcel OD-H (hexane/2-propanol: 99/1, 1 mL min^{-1}). The retention times for the two enantiomers were 10.4 and 11.7 min; $[\alpha]_D$: +20.3 ($CHCl_3$, c 1.085) at 70% *ee*.

1,1-Bis(phenylsulfonyl)-3-[1-(2,5-dimethylfuran-3-yl)-phenylmethyl]-4-methylenecyclopentane (2l): TLC (cyclohexane/ethyl acetate: 80/20): R_f = 0.30; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (s, 3H), 2.25 (s, 3H), 2.40 (dd, J = 15.7, 8.7 Hz, 1H), 2.63 (dd, J = 15.7, 8.7 Hz, 1H), 3.07 (d, J = 17.7 Hz, 1H), 3.20–3.50 (m, 2H), 3.63 (d, J = 10.7 Hz, 1H), 4.09–4.16 (m, 1H), 4.61 (br s, 1H), 5.84 (br s, 1H), 7.16–8.08 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.6, 13.6, 36.8, 39.1, 46.2, 46.8, 90.9, 105.3, 110.2, 121.6, 126.4, 127.7, 128.5, 128.7, 128.8, 131.1, 131.2, 134.6, 134.7, 136.0, 136.8, 143.3, 145.4, 146.8, 150.1; CI-MS (NH_3): m/z = 564 $[M+NH_4]^+$, 546 $[M]^+$; HR-MS: m/z = 564.1885, calcd. for $C_{31}H_{34}O_5NS_2$: 564.1878. The product ratio was determined by HPLC using a Chiralcel OD-H (hexane/2-propanol: 90/10, 1 mL min^{-1}). The retention times for the two enantiomers were 18.9 and 23.7 min; $[\alpha]_D$: −1.9 ($CHCl_3$, c 0.50) at 75% *ee*.

1,1-Bis(phenylsulfonyl)-3-[1-(2,4,6-trimethoxyphenyl)-phenylmethyl]-4-methylenecyclopentane (2m): ^{1}H, ^{13}C NMR and mass spectroscopy data for compound **2m** were identical to literature values.[2] The product ratio was determined by HPLC using a Chiralcel OD-H (hexane/2-propanol: 90/10, 1 mL min^{-1}). The retention times for the two enantiomers were 41.7 and 49.1 min; $[\alpha]_D$: +75.0 ($CHCl_3$, c 0.42) at 91% *ee*.

1,1-Bis(phenylsulfonyl)-3-[1-(1-methyl-1*H*-indol-3-yl)-methylethyl]-4-methylenecyclopentane (2n): ^{1}H, ^{13}C NMR and mass spectroscopy data for compound **2n** were identical to literature values.[2] The product ratio was determined by HPLC using a Chiralcel AD (hexane/2-propanol: 90/10, 1 mL min^{-1}). The retention times for the two enantiomers were 30.6 and 36.6 min; $[\alpha]_D$: +6.9 ($CHCl_3$, c 0.89) at 49% *ee*.

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