

## **Substituent effects on the edge-to-face interaction\*\***

**Felix Raoul Fischer, W. Bernd Schweizer and François Diederich\***

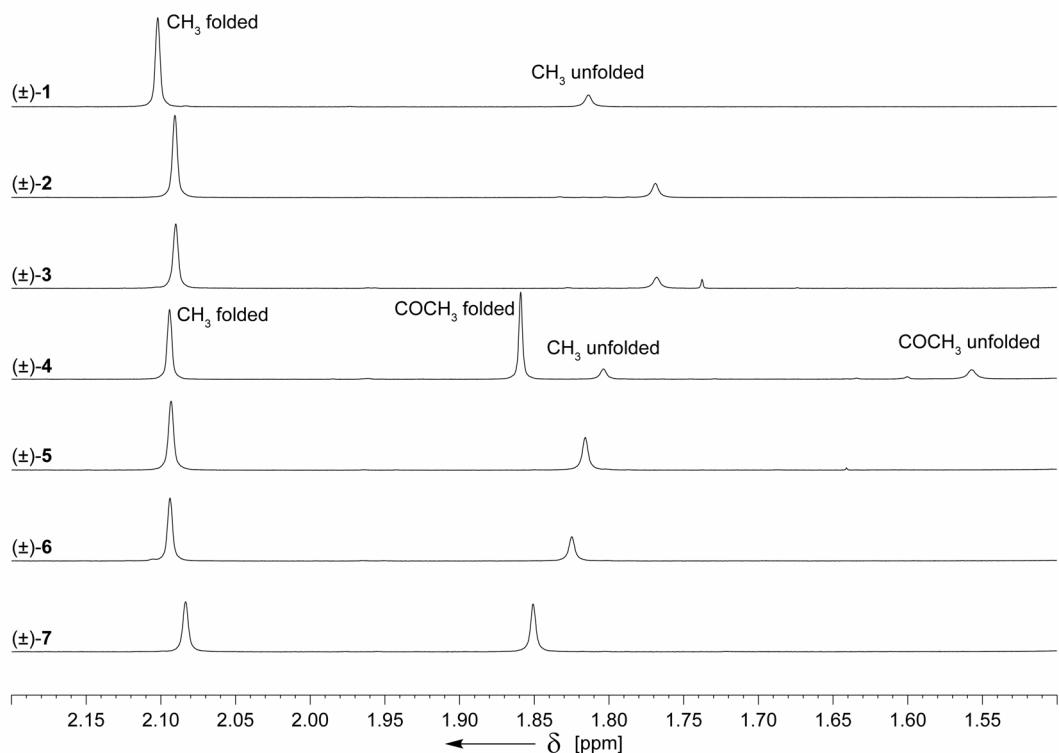
### **Electronic Supporting Information**

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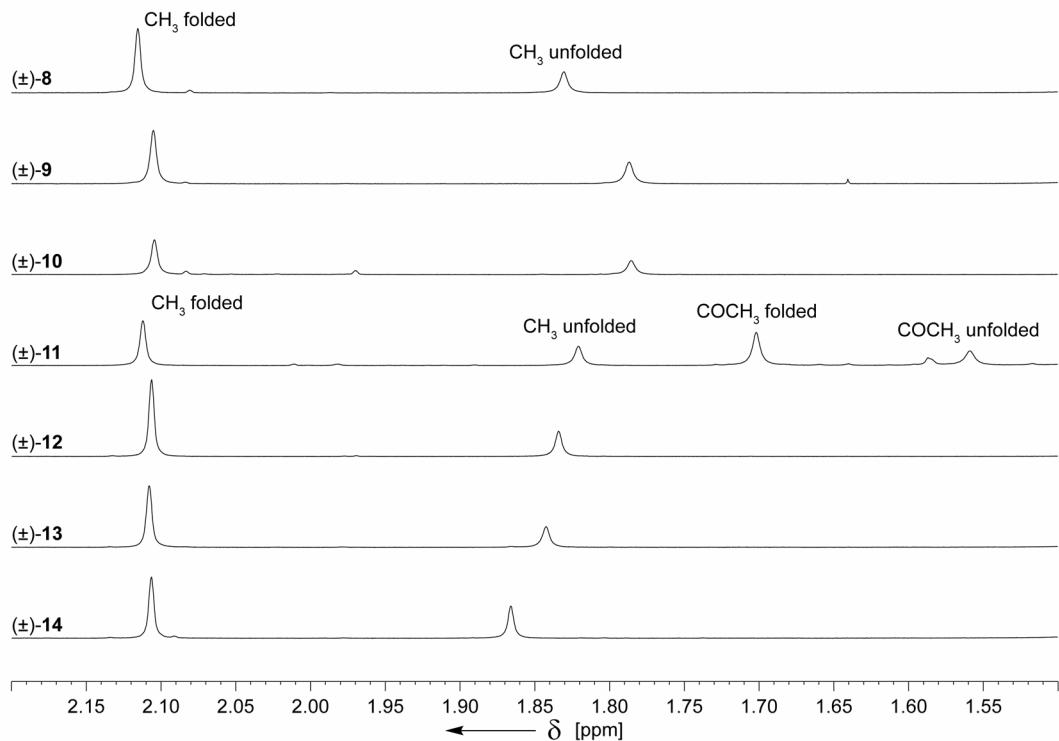
[\*\*] This work was supported by a grant from the ETH Research Council

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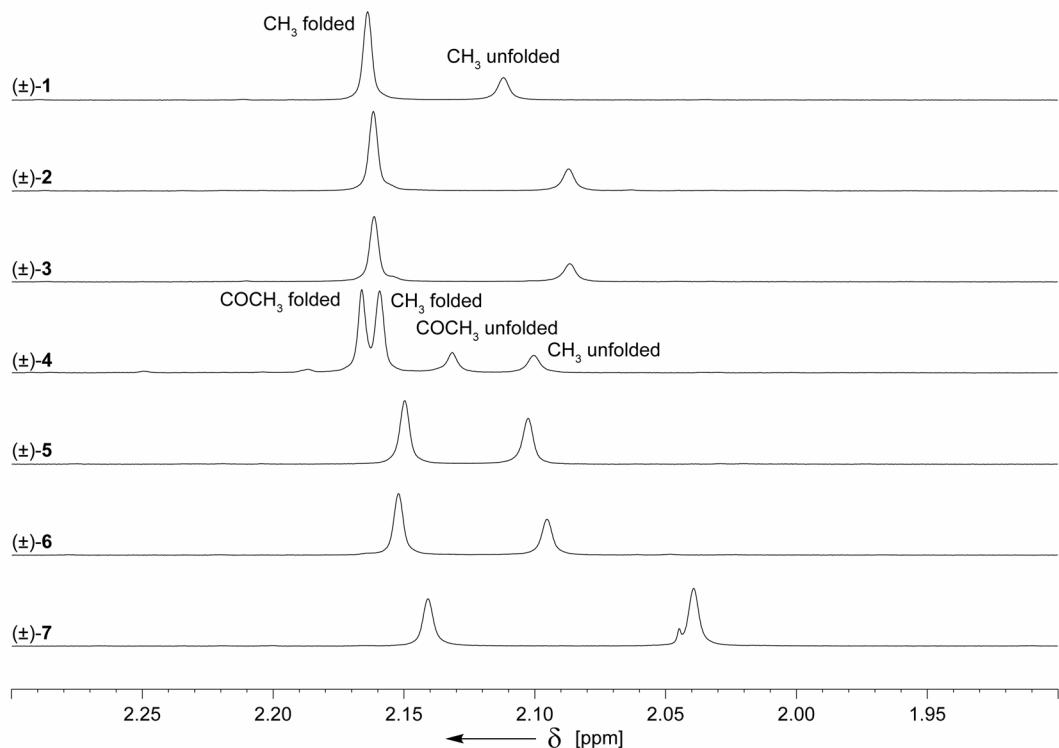
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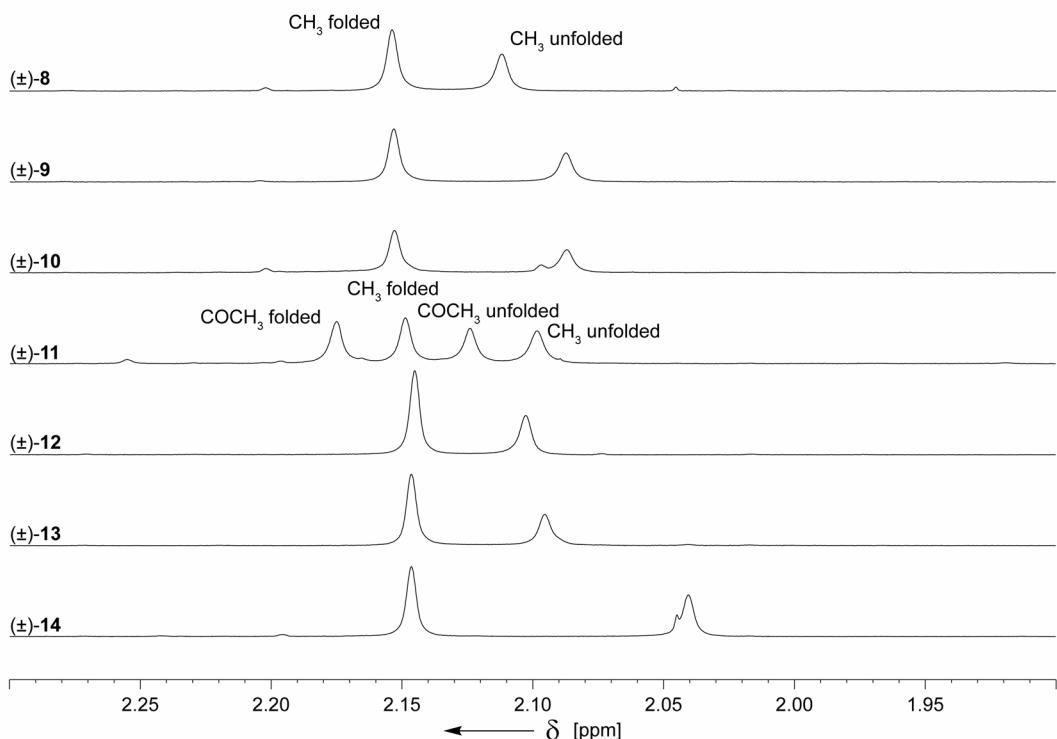
**Fig. S1** <sup>1</sup>H NMR spectra of (±)-1 to (±)-7 as 10 mM solutions in C<sub>6</sub>D<sub>6</sub> at 298 K.



**Fig. S2** <sup>1</sup>H NMR spectra of (±)-8 to (±)-14 as 10 mM solutions in C<sub>6</sub>D<sub>6</sub> at 298 K.



**Fig. S3** <sup>1</sup>H NMR spectra of (±)-1 to (±)-7 as 10 mM solutions in CDCl<sub>3</sub> at 298 K.



**Fig. S4** <sup>1</sup>H NMR spectra of (±)-8 to (±)-14 as 10 mM solutions in CDCl<sub>3</sub> at 298 K.

### Determination of the folding free enthalpy

The folding equilibrium of the torsion balances was determined by integration of the line-fitted (100% Lorentz functions)<sup>1</sup>H NMR (500 MHz) resonance signals of the CH<sub>3</sub> group on C3'. Equation (1) gives the folding free enthalpy from the relative population of both atropisomeric states.

$$\Delta G = RT \ln K = RT \ln \frac{c_{folded}}{c_{unfolded}} \quad (1)$$

### Error resulting from experimental deviation

Standard deviation of the equilibrium constant ( $K$ ) determined by multiple measurements and integration of the line-fitted (100% Lorentz functions)<sup>1</sup>H NMR (500MHz) spectra:  $\delta(K) \leq 5\%$ .

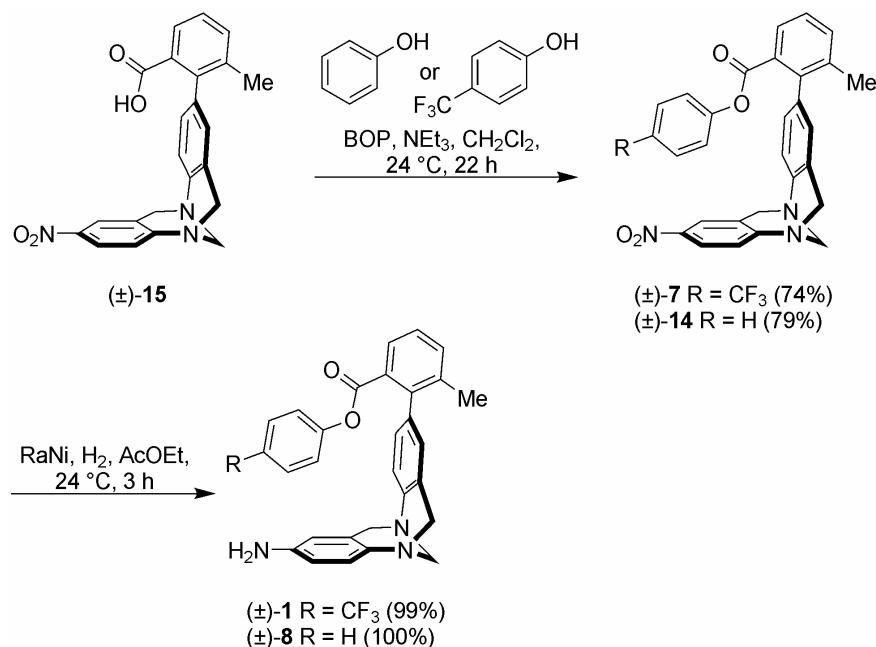
Only the error resulting from the experimental standard deviation is considered, since the error resulting from the integration method is smaller and of systematic nature therefore applies equally to all compared experiments.

$$\delta(\ln K) = \frac{\delta K}{K} = 0.05 \quad (2)$$

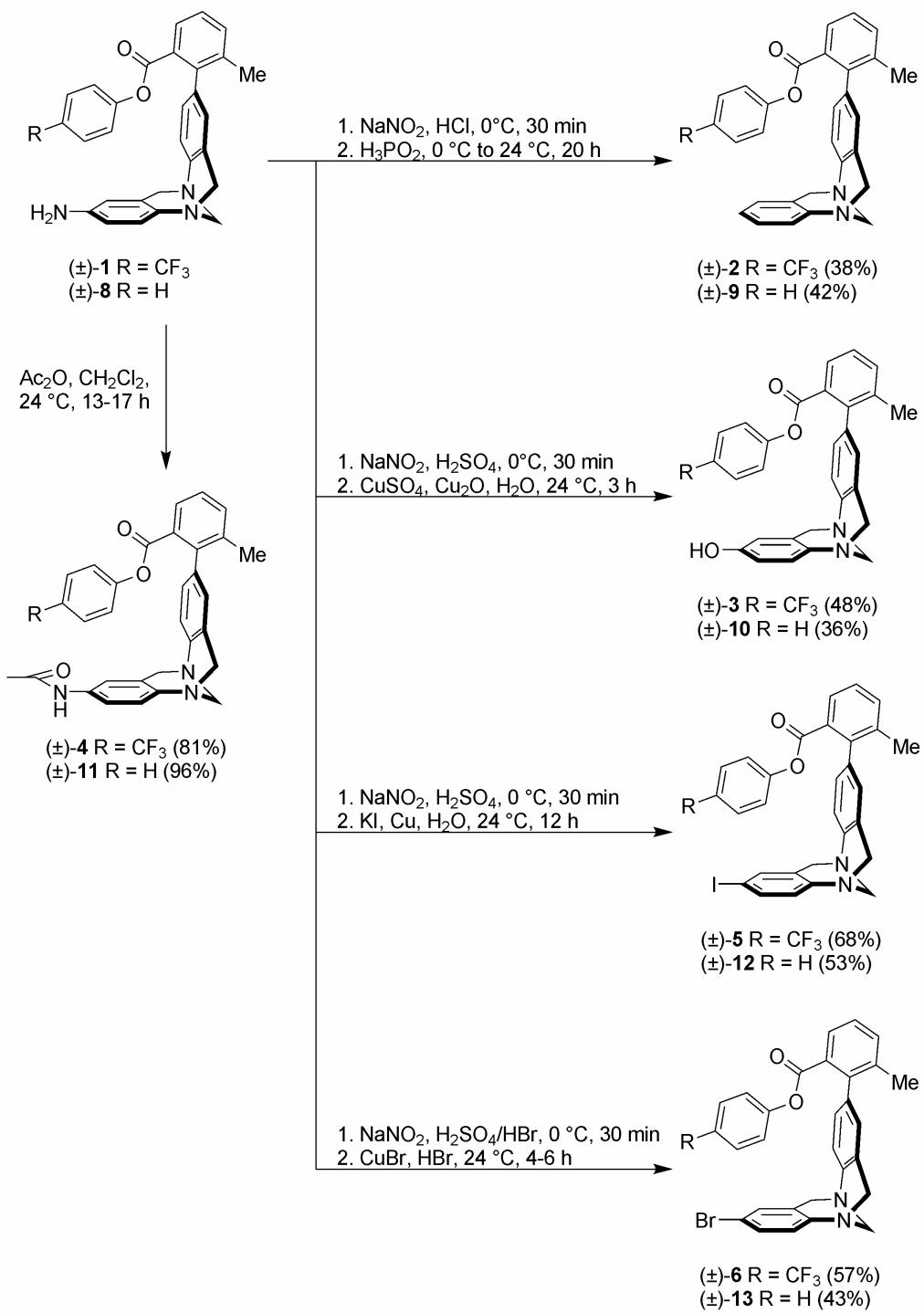
$$\delta(\Delta G) = RT [\delta(\ln K)] = 0.12 \text{ kJ mol}^{-1} \quad (3)$$

### Synthetic strategy

All molecules presented in this article were synthesized starting from the literature known carboxylic acid precursor ( $\pm$ )-**15**.<sup>1</sup>



**Scheme S1** Synthesis of the molecular torsion balances  $(\pm)$ -**7**,  $(\pm)$ -**14**,  $(\pm)$ -**1** and  $(\pm)$ -**8** from the common precursor  $(\pm)$ -**15**. BOP = (Benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate, RaNi = Raney nickel



**Scheme S2** Synthesis of the molecular torsion balances ( $\pm$ )-2 to ( $\pm$ )-6 and ( $\pm$ )-9 to ( $\pm$ )-13 from the common precursors ( $\pm$ )-1 and ( $\pm$ )-8.

## General Remarks

Thin-layer Chromatography (TLC) was conducted on aluminium sheets coated with SiO<sub>2</sub> F<sub>254</sub> obtained from Macherey-Nagel. Visualisation was performed with a UV lamp (254 or 366 nm) or by reaction with basic aqueous KMnO<sub>4</sub> solution. Column chromatography was carried out on Ultra Pure Silica Gel (230-400 mesh) purchased from Silicycle or Silica Gel 60 (230-400 mesh) purchased from Fluka using redistilled technical solvents and an overpressure of 0.2-0.6 bar. Melting Points (mp) were determined in an open capillary using a *Büchi Melting Point B540* apparatus and are uncorrected. <sup>1</sup>H NMR spectra were recorded on a *Varian Gemini 300*, *Varian Mercury 300*, *Varian Mercury-VX 300* and a *Bruker ARX 300* operating at 299.9 MHz for the <sup>1</sup>H nucleus. <sup>1</sup>H decoupled <sup>13</sup>C NMR spectra were recorded on a *Varian Gemini 300*, *Varian Mercury 300*, *Varian Mercury-VX 300* and a *Bruker ARX 300* operating at 75.4 MHz for the <sup>13</sup>C nucleus and decoupling at 299.9 MHz. <sup>19</sup>F NMR spectra were recorded on a *Varian Gemini 300*, *Varian Mercury 300* and a *Varian Mercury-VX 300* operating at 282.1 MHz for the <sup>19</sup>F nucleus. Chemical shifts are reported in  $\delta$  units (ppm) relative to the residual deuterated solvent signal of CDCl<sub>3</sub> (<sup>1</sup>H NMR:  $\delta$  7.26 ppm; <sup>13</sup>C NMR:  $\delta$  77.0 ppm); CD<sub>2</sub>Cl<sub>2</sub> (<sup>1</sup>H NMR:  $\delta$  5.30 ppm; <sup>13</sup>C NMR:  $\delta$  53.5 ppm); C<sub>2</sub>D<sub>2</sub>Cl<sub>4</sub> (<sup>1</sup>H NMR:  $\delta$  5.91 ppm; <sup>13</sup>C NMR:  $\delta$  74.2 ppm); CD<sub>3</sub>OD (<sup>1</sup>H NMR:  $\delta$  3.31 ppm; <sup>13</sup>C NMR:  $\delta$  49.0 ppm); C<sub>6</sub>D<sub>6</sub> (<sup>1</sup>H NMR:  $\delta$  7.16 ppm; <sup>13</sup>C NMR:  $\delta$  128.0 ppm) or relative to an external standard. The splitting patterns are designated as follows: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *m* (multiplet), *b* (broad signal). The coupling constant *J* is given in Hz. One dimensional <sup>1</sup>H NMR spectra were recorded using the acquisition parameters: 26.4° pulse, 3.138 s acquisition time, 5099.4 Hz spectral width, 32 K data size, number of transients 16, at 298 K. <sup>13</sup>C NMR spectra were recorded using the acquisition parameters: 45.0° pulse, 1.300 s acquisition time, 20000.0 Hz spectral width, 64 K data size, number of transients > 512, at 298 K. <sup>19</sup>F NMR spectra were recorded using the acquisition parameters: 45.0° pulse, 5.000 s acquisition time, 5643.3 Hz spectral width, 64 K data size, number of transients 32, at 298 K. <sup>1</sup>H NMR spectra for thermodynamic analysis were recorded on a *Bruker AMX-500* spectrometer operating at 500.1 MHz for the <sup>1</sup>H nucleus using the acquisition parameters: 30.0° pulse, 5.000 s acquisition time, 8012.8 Hz spectral width, 8.000 s D1 delay, 64 K data size, number of transients 64. The exact temperature was monitored by an external thermoelement. All data were processed using *Bruker TopSpin 2.1.0*. Deuterated solvents in the highest possible purity were used as purchased from ARMAR Chemicals. Infra Red Spectroscopy: IR spectra were recorded as neat samples on a *Perkin-Elmer Spectrum BX II* spectrometer. The absorption bands are referenced in wavenumbers (cm<sup>-1</sup>). Mass spectrometry was performed by the MS-Service of the Laboratory of Organic Chemistry ETH Zurich on a *Waters Micromass AutoSpec Ultima* (EI) spectrometer. High resolution (HR) EI-MS spectra were measured on a *Waters Micromass AutoSpec Ultima* spectrometer. The most important signals are reported in *m/z* units with M<sup>+</sup> as the molecular ion. X-ray crystal structure data was recorded on a *Bruker-Nonius*

*Kappa-CCD diffractometer* with Mo<sub>Kα</sub> ( $\lambda = 0.7107 \text{ \AA}$ ) radiation. Materials and general methods: Reagents and solvents were purchased at reagent grade from Acros, Aldrich, Fluka, Merck, ABCR, TCI, Strem and Apollo Scientific and used as received. Solvents were purified and dried by standard procedures and freshly distilled under an atmosphere of N<sub>2</sub>. Unless otherwise stated all reactions were performed in flame-dried glassware under an inert atmosphere of N<sub>2</sub> or Ar. The synthesis of torsion balances (±)-8, (±)-9, (±)-10, (±)-12, (±)-13, (±)-14, (±)-15<sup>1</sup> and (±)-1, (±)-2, (±)-4, (±)-7 and (±)-11 have been reported previously.<sup>2</sup>

## Synthetic Procedures

**(±)-4-(Trifluoromethyl)phenyl 2-(8-Nitro-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocin-2-yl)-3-methylcarboxylate (±)-7** A flame-dried *Schlenk* tube sealed with a septum was charged under Ar with (±)-**15** (1.50 g, 3.74 mmol), 4-(trifluoromethyl)phenol (1.82 g, 11.21 mmol) and BOP (3.31 g, 7.47 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (80 cm<sup>3</sup>). NEt<sub>3</sub> (3.03 g, 29.89 mmol) was added dropwise via syringe and the mixture stirred for 22 h at 24 °C. The solvents were evaporated and the residue was taken up in CH<sub>2</sub>Cl<sub>2</sub> (250 cm<sup>3</sup>). The organic phase was washed with saturated aqueous NaCl solution, dried (MgSO<sub>4</sub>) and concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 100:2) yielded (±)-**7** (1.51 g, 74%) as a yellow solid mp 226-228 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3068, 3008, 2944, 2914, 2855, 1738, 1608, 1579, 1505, 1433, 1322, 1279, 1214, 1161, 1119, 1060, 1016, 946, 913, 866, 832, 800, 760, 708 and 673;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>) 2.04/2.14 (3 H, s, ArCH<sub>3</sub>), 4.17-4.43 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.68-4.87 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.35-6.40 (1 H, m), 6.77-6.85 (1 H, m), 6.90-6.95 (1 H, m), 7.07-7.15 (2 H, m), 7.17-7.23 (1 H, m), 7.22-7.27 (1 H, m), 7.33-7.40 (1 H, m), 7.42-7.48 (1 H, m), 7.56-7.61 (1 H, m), 7.71-7.83 (1 H, m), 7.89-7.96 (1 H, m) and 8.02-8.09 (1 H, m);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 20.9, 58.3/58.4, 58.5/58.8, 66.5/66.7, 121.2, 121.7, 122.6/122.7, 122.7/123.0, 124.8, 125.5/125.7, 126.0/126.1, 126.5/126.6, 126.7, 126.7/126.8, 127.3/127.4, 128.3/128.5, 128.6/128.7, 130.5/130.6, 133.7/133.9, 136.0/136.3, 137.5/137.6, 140.6, 141.1, 143.5, 146.2/126.3, 152.4/152.9, 154.7/154.8 and 166.2/166.6;  $\delta_{\text{F}}$  (282 MHz; CDCl<sub>3</sub>) -62.0/-62.4 (CF<sub>3</sub>); *m/z* (EI) 545.1551 (M<sup>+</sup>, 26%. C<sub>30</sub>H<sub>22</sub>F<sub>3</sub>N<sub>3</sub>O<sub>4</sub><sup>+</sup> requires 545.1562) and 384.1 (M-C<sub>7</sub>H<sub>4</sub>F<sub>3</sub>O<sup>+</sup>, 100).

**(±)-Phenyl 2-(8-Nitro-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocin-2-yl)-3-methylcarboxylate (±)-14** A flame-dried *Schlenk* tube sealed with a septum was charged under Ar with (±)-**15** (1.50 g, 3.74 mmol), phenol (1.06 g, 11.21 mmol) and BOP (3.31 g, 7.47 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (80 cm<sup>3</sup>). NEt<sub>3</sub> (3.03 g, 29.89 mmol) was added dropwise via syringe and the mixture stirred for 22 h at 24 °C. The solvents were evaporated, and the residue was taken up in CH<sub>2</sub>Cl<sub>2</sub> (250 cm<sup>3</sup>). The organic phase was washed with saturated aqueous NaCl solution, dried (MgSO<sub>4</sub>) and concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 100:2) yielded (±)-**14** (1.41 g, 79%) as a yellow solid mp 189-191 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3024, 2959, 2906, 2846, 1750, 1607, 1579, 1488, 1432, 1330, 1282, 1210, 1184, 1119, 1096, 1003, 945, 895, 838, 799, 741, 709, 683 and 610;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>) 2.04/2.15 (3 H, s, ArCH<sub>3</sub>), 4.17-4.44 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.70-4.84 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 4.70-4.84 (1 H, m), 4.77-6.84 (2 H, m), 6.86-6.96 (2 H, m), 7.09-7.21 (3 H, m), 7.23-7.38 (2 H, m), 7.39-7.45 (1 H, m), 7.68-7.82 (1 H, m), 7.79-7.92 (1 H, m) and 7.95-8.08 (1 H, m);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 20.9, 58.4/58.5, 58.8, 66.6, 120.3, 121.1, 122.7/122.8, 123.0, 124.6/124.8, 125.4, 125.5/125.6, 126.6, 126.9, 127.2, 127.3, 128.3/128.4, 128.5, 128.7, 129.2, 131.3/131.4, 133.3/133.4, 136.1/136.4, 137.2/137.3, 140.4/140.8, 143.3/143.4, 146.0/146.1, 149.9/150.0, 154.6/154.9 and

166.9/167.3;  $m/z$  (EI) 477.1683 ( $M^+$ , 26%.  $C_{29}H_{23}N_3O_4^+$  requires 477.1683) and 384.1 ( $M-C_6H_5O^+$ , 100).

**( $\pm$ )-4-(Trifluoromethyl)phenyl 2-(8-Amino-6*H*,12*H*-5,11-methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate ( $\pm$ )-1** A round bottom flask was charged under Ar with RaNi (suspension in water) (0.5 cm<sup>3</sup>). The suspension was washed and rinsed with AcOEt (150 cm<sup>3</sup>) and resuspended in AcOEt (15 cm<sup>3</sup>). Compound ( $\pm$ )-7 (1.44 g, 2.64 mmol) in AcOEt (5 cm<sup>3</sup>) was added, the atmosphere saturated with H<sub>2</sub> and the mixture stirred for 3 h at 24 °C. The solution was filtered over a plug of celite and the solvent was concentrated on a rotary evaporator to yield ( $\pm$ )-1 (1.34 g, 99%) as a pale yellow solid mp 151-154 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3460, 3370, 3215, 3065, 2940, 2895, 2849, 1230, 1612, 1494, 1459, 1412, 1323, 1275, 1205, 1163, 1119, 1101, 1060, 1015, 949, 920, 862, 827, 760, 731 and 647;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>) 2.11/2.17 (3 H, s, ArCH<sub>3</sub>), 3.49/3.57 (2 H, s, NH<sub>2</sub>), 4.01-4.36 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.54-4.74 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.21-6.25 (1 H, m), 6.27-6.29 (1 H, m), 6.53-6.58 (1 H, m), 6.76-6.84 (1 H, m), 6.85-6.98 (1 H, m), 7.05-7.20 (2 H, m), 7.22-7.28 (2 H, m), 7.32-7.38 (1 H, m), 7.42-7.59 (2 H, m) and 7.74-7.77 (1 H, m);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 20.7/20.8, 58.3, 58.6, 67.0, 112.0/112.5, 115.0/115.1, 121.4/121.7, 124.8, 125.6/125.7, 126.0/126.2, 126.5, 126.6, 126.9, 127.1, 127.2, 127.3, 127.6, 127.8/127.9, 128.2/128.3, 128.6, 131.2/131.4, 133.5/133.7, 135.5/135.8, 137.6, 139.0/139.4, 140.7/141.2, 142.7/143.0, 147.5/147.6, 152.6/153.1 and 166.8/167.6;  $\delta_{\text{F}}$  (282 MHz; CDCl<sub>3</sub>) -61.7/-62.0 (CF<sub>3</sub>);  $m/z$  (EI) 515.1819 ( $M^+$ , 17%.  $C_{30}H_{24}F_3N_3O_2^+$  requires 515.1821).

**( $\pm$ )-Phenyl 2-(8-Amino-6*H*,12*H*-5,11-methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate ( $\pm$ )-8** A round bottom flask was charged under Ar with RaNi (suspension in water) (0.5 cm<sup>3</sup>). The suspension was washed and rinsed with AcOEt (150 cm<sup>3</sup>) and resuspended in AcOEt (15 cm<sup>3</sup>). Compound ( $\pm$ )-14 (1.26 g, 2.86 mmol) in AcOEt (5 cm<sup>3</sup>) was added, the atmosphere saturated with H<sub>2</sub> and the mixture stirred for 3 h at 24 °C. The solution was filtered over a plug of celite and the solvent was concentrated on a rotary evaporator to yield ( $\pm$ )-8 (1.28 g, 100%) as a pale yellow solid mp 167-171 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3414, 3344, 3235, 3001, 2934, 2890, 2846, 1722, 1633, 1589, 1492, 1456, 1334, 1280, 1189, 1162, 1123, 1088, 1007, 964, 921, 868, 834, 748, 686 and 644;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>) 2.12/2.16 (3 H, s, ArCH<sub>3</sub>), 3.49/3.53 (2 H, s, NH<sub>2</sub>), 4.02-4.35 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.56-4.75 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.21-6.17 (1 H, m), 6.25-6.29 (1 H, m), 6.52-6.57 (1 H, m), 6.73-6.77 (1 H, m), 6.77-6.83 (1 H, m), 6.93-7.19 (5 H, m), 2.59-2.36 (2 H, m), 7.39-7.44 (1 H, m) and 7.65-7.75 (1 H, m);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 20.8/20.9, 58.3/58.4, 58.6, 67.0, 112.3/112.4, 114.9/115.0, 120.8/121.1, 124.6, 125.2/125.6, 126.0, 126.8, 126.9 (2 C), 126.9/127.0, 127.1/127.5, 127.8/128.1, 128.2/128.6, 129.1 (2 C), 131.8/131.9, 133.0/133.2, 135.4/135.6, 137.3,

139.0/139.4, 140.5/140.8, 142.5/142.7, 147.2, 150.0/150.4 and 167.3/167.9;  $m/z$  (EI) 447.1943 ( $M^+$ , 67%.  $C_{29}H_{25}N_3O_2^+$  requires 447.1947).

**( $\pm$ )-4-(Trifluoromethyl)phenyl 2-(6*H*,12*H*-5,11-Methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate ( $\pm$ )-2** A round bottom flask was charged with ( $\pm$ )-1 (100 mg, 0.19 mmol) in 6N HCl (1 cm<sup>3</sup>) and cooled to 0 °C. NaNO<sub>2</sub> (15 mg, 0.21 mmol) in H<sub>2</sub>O (0.5 cm<sup>3</sup>) was added slowly and the mixture stirred for 30 min at 0 °C. H<sub>3</sub>PO<sub>2</sub> (50%) (0.2 cm<sup>3</sup>) was added dropwise and the mixture stirred for 6 h at 0 °C and for 14 h at 24°C. The solution was neutralised with saturated aqueous KHCO<sub>3</sub> solution and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic phase was washed with saturated aqueous NaCl solution, dried (MgSO<sub>4</sub>) and concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 500:1) yielded ( $\pm$ )-2 (37 mg, 38%) as a brown solid mp 145-148 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3071, 3010, 2921, 2851, 1751, 1609, 1485, 1460, 1411, 1324, 1277, 1206, 1162, 1119, 1060, 1014, 949, 864, 834, 801, 746, 709, 650 and 617;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>) 2.09/2.16 (3 H, s, ArCH<sub>3</sub>), 4.13-4.40 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.61-4.80 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.17-6.21 (1 H, m), 6.77-6.84 (1 H, m), 6.86-7.03 (2 H, m), 7.07-7.22 (6 H, m), 7.32-7.38 (1 H, m), 7.41-7.59 (2 H, m) and 7.64-7.78 (1 H, m);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 20.7/20.8, 58.4, 58.5, 66.7, 121.2/121.7/122.0 (2 C), 124.0/124.3, 124.9/125.4, 125.3/125.6, 126.5, 126.6, 126.8, 126.9, 127.0, 127.1, 127.2, 127.3, 127.5, 127.6, 127.9/128.0, 128.3, 131.1/131.3, 133.5/133.8, 135.6/135.9, 137.6, 140.6/141.2, 147.3/147.4, 148.0/148.1, 152.5/153.1 and 166.8/167.5;  $\delta_{\text{F}}$  (282 MHz; CDCl<sub>3</sub>) -62.0/-62.1 (CF<sub>3</sub>);  $m/z$  (EI) 500.1702 ( $M^+$ , 24%.  $C_{30}H_{23}F_3N_2O_2^+$  requires 500.1712).

**( $\pm$ )-Phenyl 2-(6*H*,12*H*-5,11-Methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate ( $\pm$ )-9** A round bottom flask was charged with ( $\pm$ )-8 (100 mg, 0.22 mmol) in 6N HCl (1 cm<sup>3</sup>) and cooled to 0 °C. NaNO<sub>2</sub> (17 mg, 0.25 mmol) in H<sub>2</sub>O (0.5 cm<sup>3</sup>) was added slowly and the mixture stirred for 30 min at 0 °C. H<sub>3</sub>PO<sub>2</sub> (50%) (0.2 cm<sup>3</sup>) was added dropwise and the mixture stirred for 6 h at 0 °C and for 14 h at 24°C. The solution was neutralised with saturated aqueous KHCO<sub>3</sub> solution and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic phase was washed with saturated aqueous NaCl solution, dried (MgSO<sub>4</sub>) and concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 250:1) yielded ( $\pm$ )-9 (41 mg, 42%) as a brown solid mp 72-75 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3063, 3018, 2945, 2895, 2848, 1730, 1592, 1485, 1455, 1335, 1274, 1190, 1161, 1086, 1001, 945, 907, 836, 806, 761, 722, 687, 694 and 606;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>) 2.10/2.17 (3 H, s, ArCH<sub>3</sub>), 4.14-4.42 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.63-4.81 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.13-6.18 (1 H, m), 6.75-6.93 (3 H, m), 7.19-7.24 (7 H, m), 7.23-7.37 (2 H, m), 7.39-7.45 (1 H, m) and 7.66-7.78 (1 H, m);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 20.8/20.9, 58.4 (2 C), 66.7, 120.7/121.1, 123.8/124.0, 124.7/125.1, 125.2/125.5, 126.8, 126.9, 127.0 (2 C), 127.1 (2 C), 127.3, 127.5, 127.8/127.9, 128.2, 129.0, 129.1, 131.8/131.9, 133.0/133.2, 135.5/135.7, 137.3, 140.4/140.8,

147.0, 147.9/148.0, 149.9/150.4 and 167.2/167.7;  $m/z$  (EI) 432.1836 ( $M^+$ , 30%).  $C_{29}H_{24}N_2O_2^+$  requires 432.1838) and 339.2 ( $M-C_6H_5O^+$ , 35).

**( $\pm$ )-4-(Trifluoromethyl)phenyl 2-(8-Hydroxy-6*H*,12*H*-5,11-methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate ( $\pm$ )-3** A round bottom flask was charged with ( $\pm$ )-1 (100 mg, 0.19 mmol) in  $H_2SO_4$  (20%) (1 cm<sup>3</sup>) and cooled to 0 °C.  $NaNO_2$  (15 mg, 0.22 mmol) in  $H_2O$  (0.5 cm<sup>3</sup>) was added slowly and the mixture stirred for 30 min at 0 °C. A round bottom flask was charged with  $CuSO_4$  (480 mg, 3.00 mmol) and  $Cu_2O$  (28 mg, 0.20 mmol) in  $H_2O$  (6 cm<sup>3</sup>). The above prepared diazonium solution was added dropwise and the mixture stirred for 3 h at 24 °C. The mixture was poured onto ice (50 cm<sup>3</sup>), extracted with  $CH_2Cl_2$ , washed with saturated aqueous  $NaHCO_3$  solution, saturated aqueous  $NaCl$  solution, dried ( $MgSO_4$ ) and concentrated on a rotary evaporator. Column chromatography ( $SiO_2$ ;  $CH_2Cl_2/MeOH$  200:1) yielded ( $\pm$ )-3 (48 mg, 48%) as a brown solid mp 74-76 °C;  $\tilde{\nu}_{max}$  (neat)/cm<sup>-1</sup> 3067, 2923, 2851, 1736, 1611, 1485, 1456, 1323, 1272, 1207, 1164, 1117, 1060, 1015, 946, 915, 862, 836, 805, 762, 725 and 651;  $\delta_H$  (300 MHz;  $CDCl_3$ ) 2.09/2.17 (3 H, s, Ar $CH_3$ ), 4.13-4.41 (4 H, m, - $NCH_2N$ -, - $CH_aH_bN$ -), 4.61-4.81 (2 H, m, - $CH_aH_bN$ -), 6.17-6.21 (1 H, m), 6.78-6.84 (1 H, m), 6.87-7.01 (1 H, m), 7.17-7.25 (6 H, m), 7.32-7.39 (1 H, m), 7.41-7.47 (1 H, m), 7.55-7.60 (1 H, m) and 7.65-7.78 (1 H, m);  $\delta_C$  (75 MHz;  $CDCl_3$ ) 20.8/20.9, 58.4, 58.5, 66.7/66.8, 121.1/121.6, 121.7/121.9, 123.9/124.2, 124.8/125.3, 125.2/125.5, 126.4, 126.5, 126.7, 126.8, 126.9, 127.1, 127.2, 127.4, 127.5, 127.8/127.9, 128.2, 131.0/131.2, 133.4/133.7, 135.5/135.8, 137.5, 140.5, 141.1, 147.2, 147.9, 152.4/153.0 and 166.6/167.3;  $\delta_F$  (282 MHz;  $CDCl_3$ ) -62.0/-62.1 ( $CF_3$ );  $m/z$  (EI) 516.1582 ( $M^+$ , 1%).  $C_{30}H_{23}F_3N_2O_3^+$  requires 516.1661) and 500.2 ( $M-OH^+$ , 32).

**( $\pm$ )-Phenyl 2-(8-Hydroxy-6*H*,12*H*-5,11-methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate ( $\pm$ )-10** A round bottom flask was charged with ( $\pm$ )-8 (100 mg, 0.22 mmol) in  $H_2SO_4$  (20%) (1 cm<sup>3</sup>) and cooled to 0 °C.  $NaNO_2$  (17 mg, 0.26 mmol) in  $H_2O$  (0.5 cm<sup>3</sup>) was added slowly and the mixture stirred for 30 min at 0 °C. A round bottom flask was charged with  $CuSO_4$  (553 mg, 3.46 mmol) and  $Cu_2O$  (32 mg, 0.20 mmol) in  $H_2O$  (6 cm<sup>3</sup>). The above prepared diazonium solution was added dropwise and the mixture stirred for 3 h at 24 °C. The mixture was poured onto ice (50 cm<sup>3</sup>), extracted with  $CH_2Cl_2$ , washed with saturated aqueous  $NaHCO_3$  solution, saturated aqueous  $NaCl$  solution, dried ( $MgSO_4$ ) and concentrated on a rotary evaporator. Column chromatography ( $SiO_2$ ;  $CH_2Cl_2/MeOH$  200:1) yielded ( $\pm$ )-10 (37 mg, 36%) as a brown solid mp 82-86 °C;  $\tilde{\nu}_{max}$  (neat)/cm<sup>-1</sup> 3063, 2958, 2899, 2849, 1730, 1591, 1485, 1454, 1335, 1273, 1190, 1161, 1086, 1023, 945, 871, 836, 805, 749, 721, 688, 650 and 606;  $\delta_H$  (300 MHz;  $CDCl_3$ ) 2.09/2.16 (3 H, s, Ar $CH_3$ ), 4.14-4.38 (4 H, m, - $NCH_2N$ -, - $CH_aH_bN$ -), 4.63-4.85 (2 H, m, - $CH_aH_bN$ -), 6.11-6.16 (1 H, m), 6.74-6.84 (2 H, m), 6.86-6.92 (1 H, m), 6.95-6.99 (1 H, m), 7.01-7.23 (6 H, m), 7.27-7.37 (2 H, m),

7.38-7.44 (1 H, m) and 7.64-7.76 (1 H, m);  $\delta_c$  (75 MHz; CDCl<sub>3</sub>) 20.8/20.9, 58.4, 58.5, 66.7, 120.7/121.1, 123.8/124.1, 124.7/125.1, 125.2/125.6, 126.8, 126.9, 127.0, 127.1, 127.2, 127.3, 127.4, 127.6, 127.9/128.0, 128.3, 129.0/129.1, 129.2/129.4, 131.8/131.9, 133.0/133.2, 135.6/135.8, 137.3, 140.4/140.8, 147.0, 147.9/148.0, 150.0/150.5 and 167.2/167.8; *m/z* (EI) 448.1793 (M<sup>+</sup>, 1%). C<sub>29</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub><sup>+</sup> requires 448.1787) and 432.2 (M-OH<sup>+</sup>, 30).

**(±)-4-(Trifluoromethyl)phenyl**

**2-(8-Acetamido-6*H,12H*-5,11-methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate (±)-4** A flame-dried round bottom flask was charged under Ar with (±)-1 (100 mg, 0.19 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (1.5 cm<sup>3</sup>). Ac<sub>2</sub>O (0.11 g, 1.06 mmol) was added and the mixture stirred for 13 h at 24 °C. The mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 cm<sup>3</sup>), washed with H<sub>2</sub>O, saturated aqueous NaHCO<sub>3</sub> solution, saturated aqueous NaCl solution and dried (MgSO<sub>4</sub>). The solvent was concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 100:1) yielded (±)-4 (88 mg, 81%) as a colourless foam mp 228-231 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3379, 3117, 3063, 2946, 2906, 2851, 2245, 1732, 1683, 1592, 1534, 1493, 1409, 1322, 1270, 1206, 1161, 1116, 1061, 1014, 964, 918, 863, 827, 760, 725, 658 and 614;  $\delta_h$  (300 MHz; CDCl<sub>3</sub>) 2.06/2.12 (3 H, s, ArCH<sub>3</sub>), 2.08/2.15 (3 H, s, COCH<sub>3</sub>), 4.06-4.37 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.56-4.76 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.14-6.19 (1 H, m), 6.75-6.81 (1 H, m), 6.85-7.12 (5 H, m), 7.14-7.24 (1 H, m), 7.31-7.37 (1 H, m), 7.40-7.46 (1 H, m) and 7.50-7.77 (3 H, m);  $\delta_c$  (75 MHz; CDCl<sub>3</sub>) 20.6/20.8, 24.2, 58.2/58.3, 58.4/58.6, 66.7, 117.6/118.5, 118.8/119.7, 121.4/121.7, 124.8/125.4, 125.5/125.6, 126.2, 126.3, 126.4, 126.5, 126.8, 126.9, 127.0, 127.1, 127.2, 127.3 (2 C), 131.0/131.1, 133.6/133.8/134.3 (2 C), 135.5/135.9, 137.6/137.7, 140.6/141.2, 143.9/144.3, 147.1/147.2, 152.5/153.1, 166.8/167.5 and 168.5;  $\delta_f$  (282 MHz; CDCl<sub>3</sub>) -61.8/-62.0 (CF<sub>3</sub>); *m/z* (EI) 557.1919 (M<sup>+</sup>, 100%). C<sub>32</sub>H<sub>26</sub>F<sub>3</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> requires 557.1926).

**(±)-Phenyl**

**2-(8-Acetamido-6*H,12H*-5,11-methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate (±)-11** A flame-dried round bottom flask was charged under Ar with (±)-8 (100 mg, 0.22 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (1.5 cm<sup>3</sup>). Ac<sub>2</sub>O (0.11 g, 1.06 mmol) was added and the mixture stirred for 17 h at 24 °C. The mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 cm<sup>3</sup>), washed with H<sub>2</sub>O, saturated aqueous NaHCO<sub>3</sub> solution, saturated aqueous NaCl solution and dried (MgSO<sub>4</sub>). The solvent was concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 100:1) yielded (±)-11 (104 mg, 96%) as a colourless foam mp 150-152 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3296, 3063, 2943, 2898, 2848, 1729, 1663, 1593, 1538, 1492, 1459, 1409, 1369, 1323, 1275, 1190, 1161, 1112, 1087, 1003, 963, 923, 871, 833, 748, 725, 687 and 605;  $\delta_h$  (300 MHz; CDCl<sub>3</sub>) 2.07/2.09 (3 H, s, ArCH<sub>3</sub>), 2.14/2.15 (3 H, s, COCH<sub>3</sub>), 4.07-4.38 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.59-4.79 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.19-6.24 (1 H, m), 6.73-6.83 (2 H, m), 6.92-6.96, (1 H, m), 7.01-7.23 (5 H, m), 7.26-7.38 (3 H, m),

7.38-7.44 (1 H, m) and 7.66-7.76 (1 H, m);  $\delta_c$  (75 MHz; CDCl<sub>3</sub>) 20.8/21.0, 24.4/24.5, 58.3/58.4, 58.5/58.6, 66.8, 117.8/118.4, 119.0/119.6, 120.7/121.1, 124.6/124.7, 125.1/125.3, 125.4/125.6, 126.8/126.9, 127.0, 127.1, 127.2, 128.0, 128.2, 128.4, 129.0, 129.1, 131.7, 133.1/133.2, 133.5/133.9, 125.6/135.7, 137.3, 140.6/140.8, 143.9/144.3, 146.8/146.9, 150.0/150.4, 167.3/167.7 and 167.8/168.1; *m/z* (EI) 489.2053 (M<sup>+</sup>, 41%). C<sub>31</sub>H<sub>27</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> requires 489.2052) and 396.2 (M-C<sub>6</sub>H<sub>5</sub>O<sup>+</sup>, 39).

**(±)-4-(Trifluoromethyl)phenyl 2-(8-Iodo-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocin-2-yl)-3-methylcarboxylate (±)-5** A round bottom flask was charged with (±)-1 (100 mg, 0.19 mmol) in H<sub>2</sub>SO<sub>4</sub> (20%) (1 cm<sup>3</sup>) and cooled to 0 °C. NaNO<sub>2</sub> (15 mg, 0.22 mmol) in H<sub>2</sub>O (0.5 cm<sup>3</sup>) was added slowly and the mixture stirred for 30 min at 0 °C. A round bottom flask was charged with KI (161 mg, 0.97 mmol) in H<sub>2</sub>O (6 cm<sup>3</sup>). The above prepared diazonium salt solution was added dropwise. Cu powder (5 mg, 0.08 mmol) was added and the mixture was stirred for 12 h at 24 °C. The mixture was poured onto ice (50 cm<sup>3</sup>), extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with saturated aqueous NaHCO<sub>3</sub> solution, saturated aqueous NaCl solution, dried (MgSO<sub>4</sub>) and concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 300:1) yielded (±)-5 (83 mg, 68%) as a yellow foam mp 104-106 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3062, 2947, 2899, 2848, 1735, 1612, 149, 1473, 1398, 1322, 1270, 1206, 1164, 1115, 1060, 1015, 940, 917, 862, 828, 761, 711 and 664;  $\delta_h$  (300 MHz; CDCl<sub>3</sub>) 2.10/2.15 (3 H, s, ArCH<sub>3</sub>), 4.06-4.38 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.59-4.78 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.29-6.34 (1 H, m), 6.76-6.83 (1 H, m), 6.87-6.94 (2 H, m), 7.06-7.12 (1 H, m), 7.14-7.20 (1 H, m), 7.26-7.31 (1 H, m), 7.33-7.39 (2 H, m), 7.42-7.47 (1 H, m), 7.48-7.54 (1 H, m), 7.55-7.59 (1 H, m) and 7.69-7.80 (1 H, m);  $\delta_c$  (75 MHz; CDCl<sub>3</sub>) 20.8/20.9, 57.9, 58.3/58.4, 66.5/66.6, 87.3/87.5, 121.4/121.7, 124.8, 126.6, 126.7, 126.9, 127.0, 127.1, 127.2, 127.3 (2 C), 127.8, 128.2, 128.5, 130.2/130.6, 130.9/131.1, 133.7/133.9, 135.6/135.7, 135.8/136.0, 136.3/136.4, 137.6/137.7, 140.6/141.2, 146.9, 147.9/148.1, 152.6/153.1 and 166.6/167.2;  $\delta_f$  (282 MHz; CDCl<sub>3</sub>) -61.3/-62.1 (CF<sub>3</sub>); *m/z* (EI) 626.0680 (M<sup>+</sup>, 58%). C<sub>30</sub>H<sub>22</sub>F<sub>3</sub>IN<sub>2</sub>O<sub>2</sub><sup>+</sup> requires 626.0678) and 465.0 (M-C<sub>7</sub>H<sub>4</sub>F<sub>3</sub>O<sup>+</sup>, 57).

**(±)-Phenyl 2-(8-Iodo-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocin-2-yl)-3-methylcarboxylate (±)-12** A round bottom flask was charged with (±)-8 (100 mg, 0.22 mmol) in H<sub>2</sub>SO<sub>4</sub> (20%) (1 cm<sup>3</sup>) and cooled to 0 °C. NaNO<sub>2</sub> (17 mg, 0.26 mmol) in H<sub>2</sub>O (0.5 cm<sup>3</sup>) was added slowly and the mixture stirred for 30 min at 0 °C. A round bottom flask was charged with KI (185 mg, 1.11 mmol) in H<sub>2</sub>O (6 cm<sup>3</sup>). The above prepared diazonium salt solution was added dropwise. Cu powder (5 mg, 0.08 mmol) was added and the mixture was stirred for 14 h at 24 °C. The mixture was poured onto ice (50 cm<sup>3</sup>), extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with saturated aqueous NaHCO<sub>3</sub> solution, saturated aqueous NaCl solution, dried (MgSO<sub>4</sub>) and concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 200:1) yielded (±)-12 (66 mg, 53%) as a yellow foam

mp 151-153 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3009, 2940, 2893, 2844, 1735, 1590, 1475, 1433, 1398, 1323, 1276, 1192, 1156, 1115, 1090, 1003, 964, 941, 905, 831, 750, 722, 687, 663 and 629;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>) 2.11/2.15 (3 H, s, ArCH<sub>3</sub>), 4.07-4.38 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.61-4.77 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.14-6.19 (1 H, m), 6.75-6.84 (2 H, m), 6.87-6.99 (2 H, m), 7.09-7.20 (3 H, m), 7.27-7.33 (2 H, m), 7.32-7.37 (1 H, m), 7.40-7.44 (1 H, m), 7.45-7.50 (1 H, m) and 7.66-7.78 (1 H, m);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 20.8/21.0, 57.9, 58.4/58.5, 66.5/66.6, 87.3/87.9, 120.5/121.1, 124.7, 125.5, 126.8, 126.9, 127.0, 127.1, 127.2, 128.1, 128.4, 129.1, 130.3/130.5, 131.6/131.9, 133.1/133.3, 135.5, 135.6/135.8, 136.0/136.1, 136.2, 137.2/137.3, 140.3/140.8, 146.6, 147.8/148.0, 149.9/150.5 and 167.1/167.7; *m/z* (EI) 558.0800 (M<sup>+</sup>, 47%). C<sub>29</sub>H<sub>23</sub>IN<sub>2</sub>O<sub>2</sub><sup>+</sup> requires 558.0804) and 465.0 (M-C<sub>6</sub>H<sub>5</sub>O<sup>+</sup>, 66).

**(±)-4-(Trifluoromethyl)phenyl 2-(8-Bromo-6H,12H-5,11-methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate (±)-6** A round bottom flask was charged with (±)-1 (100 mg, 0.19 mmol) in a mixture of H<sub>2</sub>SO<sub>4</sub> (20%) (1 cm<sup>3</sup>)/HBr (48%) (1 cm<sup>3</sup>) and cooled to 0 °C. NaNO<sub>2</sub> (15 mg, 0.22 mmol) in H<sub>2</sub>O (0.5 cm<sup>3</sup>) was added slowly and the mixture stirred for 30 min at 0 °C. A round bottom flask was charged with CuBr (83 mg, 0.58 mmol) in HBr (48%) (1.5 cm<sup>3</sup>). The above prepared diazonium salt solution was added dropwise and the mixture stirred for 6 h at 24 °C. The mixture was poured onto ice (50 cm<sup>3</sup>), extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with saturated aqueous NaHCO<sub>3</sub> solution, saturated aqueous NaCl solution, dried (MgSO<sub>4</sub>) and concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 500:1) yielded (±)-6 (64 mg, 57%) as a yellow solid mp 178-180 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3064, 3009, 2940, 2905, 2845, 1738, 1610, 1477, 1432, 1404, 1320, 1284, 1210, 1160, 1118, 1060, 1014, 943, 913, 867, 821, 800, 766, 726 and 668;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>) 2.10/2.16 (3 H, s, ArCH<sub>3</sub>), 4.07-4.39 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.59-4.79 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.27-6.30 (1 H, m), 6.77-6.83 (1 H, m), 6.88-6.92 (1 H, m), 7.17-7.20 (4 H, m), 7.48-7.39 (3 H, m), 7.42-7.47 (1 H, m), 7.55-7.60 (1 H, m) and 7.69-7.80 (1 H, m);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 20.8/20.9, 58.2, 58.4/58.5, 66.6/66.7, 116.4/116.7, 121.2/121.6, 124.7, 126.4, 126.5 (2 C), 126.8, 126.9, 127.0, 127.1, 127.2, 127.6, 128.0, 128.3, 129.4/129.6, 129.7/130.0, 130.3/130.5, 130.8/131.0, 133.5/133.7, 135.7/135.9, 137.4/137.5, 140.5/141.1, 146.8, 147.0/147.1, 152.4/153.0 and 166.4/167.1;  $\delta_{\text{F}}$  (282 MHz; CDCl<sub>3</sub>) -61.7/-62.1 (CF<sub>3</sub>); *m/z* (EI) 578.0806 (M<sup>+</sup>, 23%). C<sub>30</sub>H<sub>22</sub><sup>79</sup>BrF<sub>3</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> requires 578.0817) and 580.1 (M<sup>+</sup>, 24).

**(±)-Phenyl 2-(8-Bromo-6H,12H-5,11-methanodibenzo[*b,f*][1,5]diazocin-2-yl)-3-methylcarboxylate (±)-13** A round bottom flask was charged with (±)-8 (100 mg, 0.22 mmol) in a mixture of H<sub>2</sub>SO<sub>4</sub> (20%) (1 cm<sup>3</sup>)/HBr (48%) (1 cm<sup>3</sup>) and cooled to 0 °C. NaNO<sub>2</sub> (17 mg, 0.26 mmol) in H<sub>2</sub>O (0.5 cm<sup>3</sup>) was added slowly and the mixture stirred for 30 min at 0 °C. A round bottom flask was charged with CuBr (96 mg, 0.67 mmol) in HBr (48%) (1.5 cm<sup>3</sup>). The above prepared diazonium

salt solution was added dropwise and the mixture stirred for 4 h at 24 °C. The mixture was poured onto ice (50 cm<sup>3</sup>), extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with saturated aqueous NaHCO<sub>3</sub> solution, saturated aqueous NaCl solution, dried (MgSO<sub>4</sub>) and concentrated on a rotary evaporator. Column chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>/MeOH 200:1) yielded ( $\pm$ )-**13** (49 mg, 43%) as a yellow solid mp 153-156 °C;  $\tilde{\nu}_{\text{max}}$  (neat)/cm<sup>-1</sup> 3062, 2951, 2896, 2848, 2661, 1732, 1589, 1476, 1403, 1322, 1275, 1185, 1157, 1112, 1087, 999, 965, 940, 890, 829, 807, 748, 724, 687 and 606;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>) 2.10/2.15 (3 H, s, ArCH<sub>3</sub>), 4.07-4.39 (4 H, m, -NCH<sub>2</sub>N-, -CH<sub>a</sub>H<sub>b</sub>N-), 4.61-4.77 (2 H, m, -CH<sub>a</sub>H<sub>b</sub>N-), 6.14-6.19 (1 H, m), 6.75-6.84 (2 H, m), 6.93-7.20 (7 H, m), 7.27-7.31 (1 H, m), 7.32-7.37 (1 H, m), 7.40-7.44 (1 H, m) and 7.66-7.78 (1 H, m);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>) 20.7/20.8, 58.1, 58.4/58.5, 66.6/66.7, 116.4/116.8, 120.5/121.2, 124.7/124.8, 125.6/125.7, 126.9 (2 C), 127.0, 127.1 (2 C), 127.2, 127.3, 128.2/128.4, 129.1/129.2, 129.6/129.7, 129.8/130.1, 130.4/130.5, 131.7/132.0, 133.2/133.4, 135.9/136.2, 137.4, 140.5/140.9, 146.7, 147.2/147.3, 150.0/150.6 and 167.3/167.9; *m/z* (EI) 510.0941 (M<sup>+</sup>, 3%). C<sub>29</sub>H<sub>23</sub><sup>79</sup>BrN<sub>2</sub>O<sub>2</sub><sup>+</sup> requires 510.0943) and 510.0941 (M<sup>+</sup>, 3).

### X-ray crystal structure of (*R,R*)-4

Crystals of (*R,R*)-4 were grown by slow evaporation of a benzene solution of ( $\pm$ )-4: colourless plates,  $0.20 \times 0.18 \times 0.08$  mm; monoclinic, space group  $P2_1/n$ ;  $a = 10.3299(3)$ ,  $b = 12.4818(4)$ ,  $c = 20.5365(7)$  Å,  $V = 2625.27(14)$  Å<sup>3</sup>,  $\alpha = 90.00^\circ$ ,  $\beta = 97.4946(12)^\circ$ ,  $\gamma = 90.00^\circ$ ;  $\rho_{\text{calc}} = 1.411$  Mg m<sup>-3</sup>;  $2\theta_{\text{max}} = 54.90^\circ$ ; Mo<sub>Kα</sub> radiation,  $\lambda = 0.71073$  Å;  $T = 223$  K; 5891 independent of 9643 measured reflections, no absorption correction applied ( $\mu = 0.106$  mm<sup>-1</sup>); structure solution using SIR97;<sup>3</sup> 3839 reflections with  $I > 2\sigma(I)$  refined on |F<sup>2</sup>| using SHELLXL-97;<sup>4</sup>  $\Delta/\sigma_{\text{max}} = 0.005$ ,  $\Delta\rho_{\text{max}} = 0.196$  e Å<sup>3</sup>,  $\Delta\rho_{\text{min}} = -0.275$  e Å<sup>3</sup>; 474 parameters, H-atom parameters refined;  $R(\text{all}) = 0.0980$ ,  $R(\text{gt}) = 0.0568$ ,  $wR(\text{ref}) = 0.1730$ ,  $wR(\text{gt}) = 0.1440$ . CCDC-688 768 contains the supplementary crystallographic data for this paper and is available free of charge from the Cambridge Crystallographic Data Centre CCDC, 12 Union Road, Cambridge CB2 1EZ (UK); Tel.: (+44) 1223-336-408, E-mail: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk).

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