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Supporting Information

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New Molecular Torsion Balances: Evidence for Favorable Orthogonal Dipolar Interactions Between Organic Fluorine and Amide Groups[**]

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Dedicated to Prof. Dr. David Reinhoudt on the occasion of his 65. birthday

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References

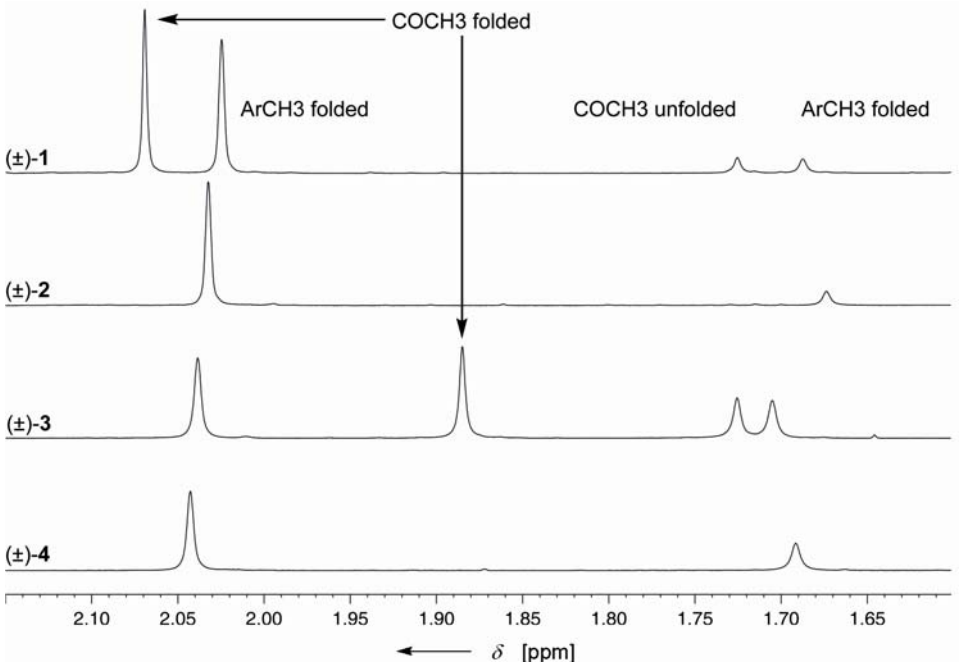


Figure 1SI. ^{1}H NMR spectra of (±)-**1**, (±)-**2**, (±)-**3**, and (±)-**4** in C_6D_6 as 10mM solutions at 298 K.[1]

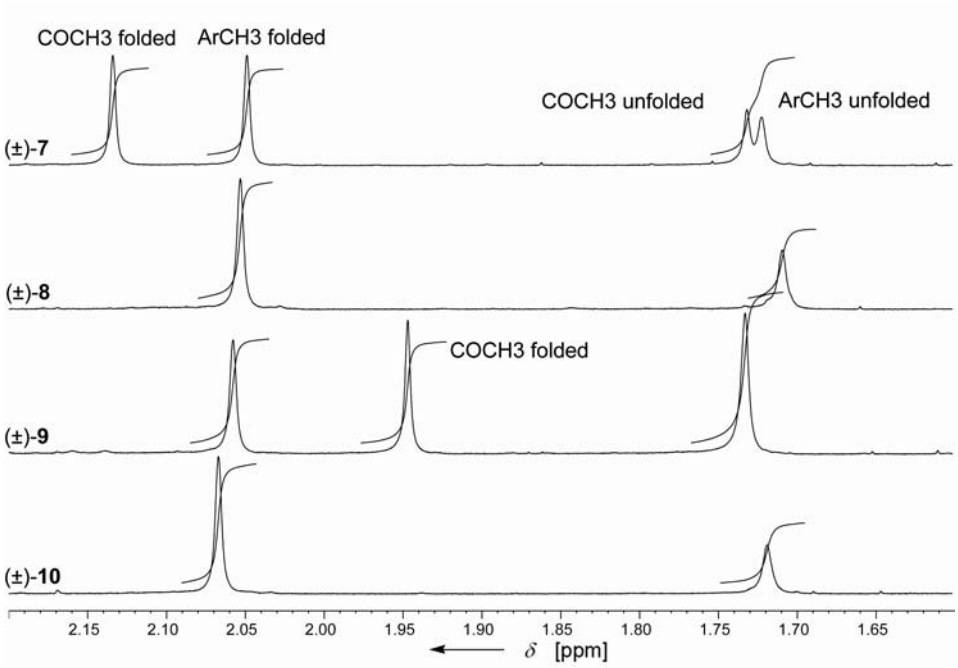


Figure 2SI. ^{1}H NMR spectra of (±)-**7**, (±)-**8**, (±)-**9**, and (±)-**10** in C_6D_6 as 10mM solutions at 298 K.[1] In the spectrum of (±)-**9**, the signals for the unfolded $COCH_3$ and unfolded $ArCH_3$ group overlap.

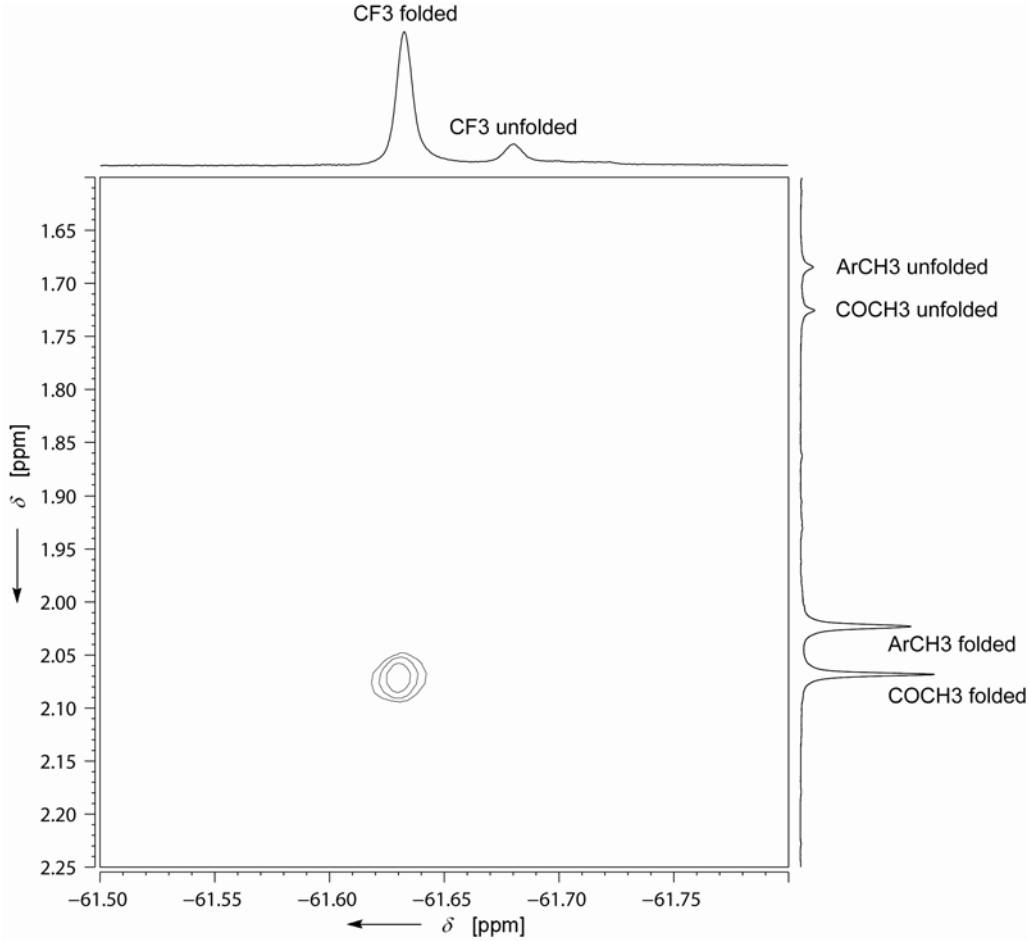


Figure 3SI. ^{1}H-^{19}F NOESY spectra of (±)-**1** in C_6D_6 at 298 K showing the proximity between the CF_3 group and the CH_3 group of the acetamide in the folded conformation.

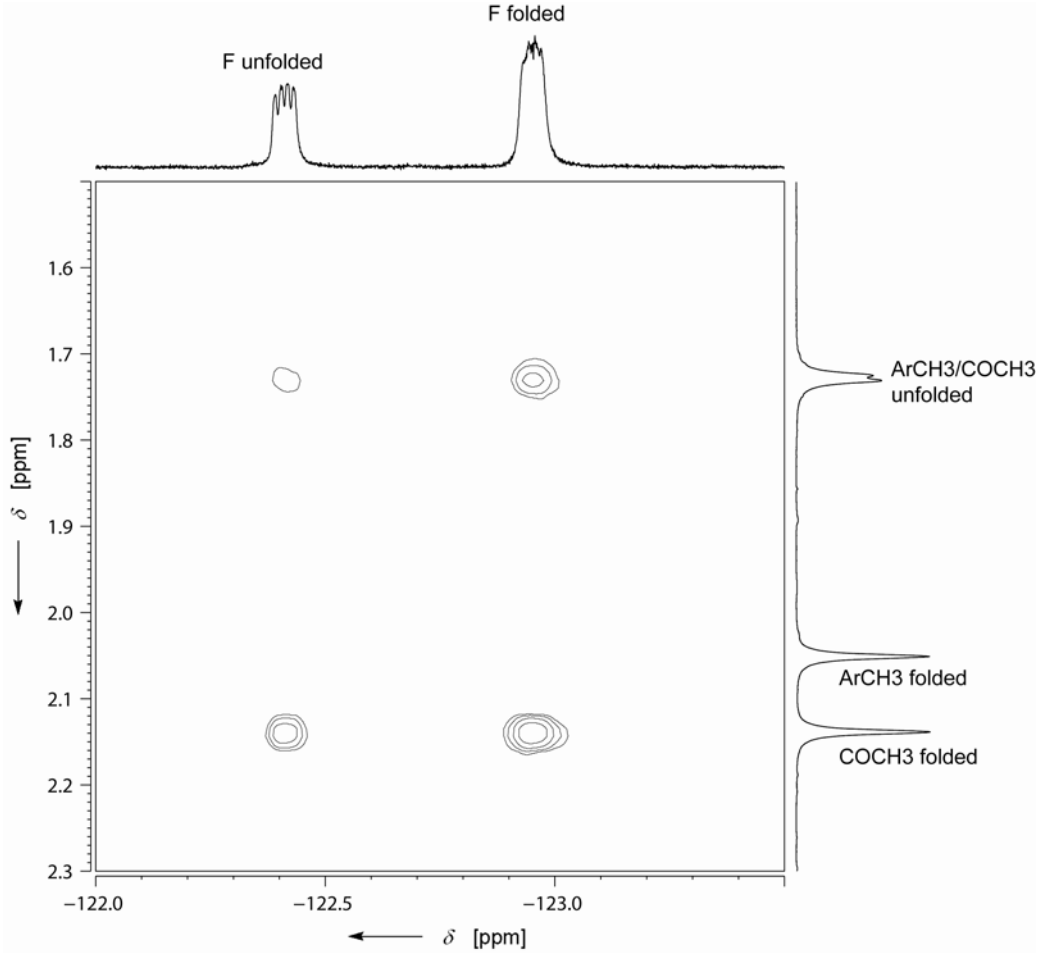


Figure 4SI. ^{1}H-^{19}F NOESY spectra of (±)-**7** in C_6D_6 at 298 K showing the proximity between the fluorine atom and the CH_3 group of the acetamide in the folded conformation. Additional signals can be observed resulting from spin relaxation in the unfolded conformer. The kinetics of the atropisomer equilibrium lie in the range of the relaxation.

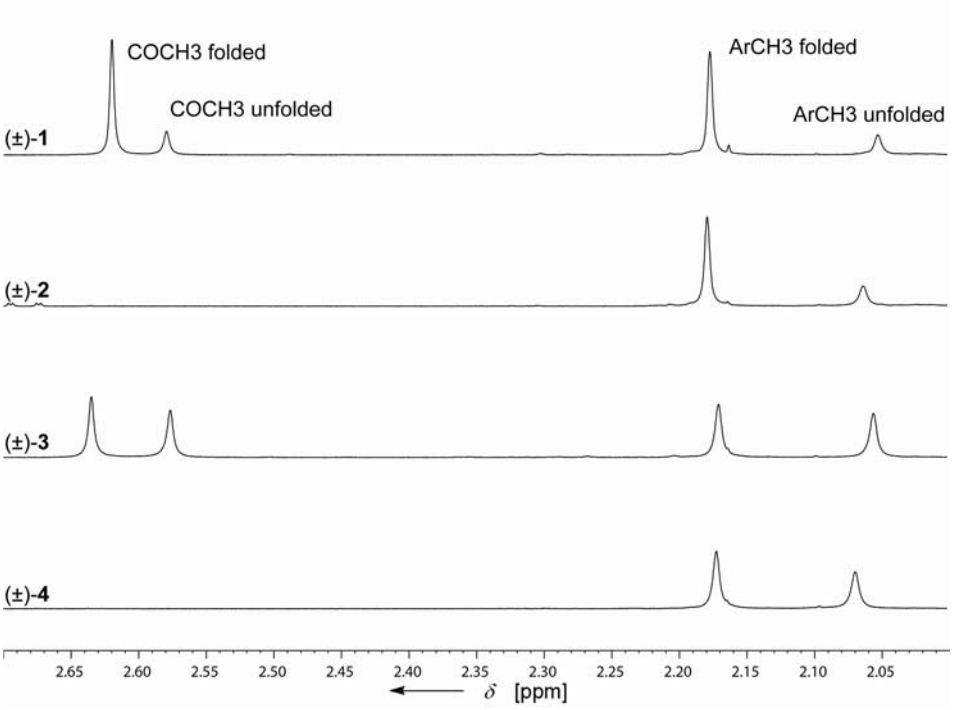


Figure 5SI: ^{1}H NMR spectra of (±)-**1**, (±)-**2**, (±)-**3**, and (±)-**4** in $C_2D_2Cl_4$ as 10mM solutions at 298 K.

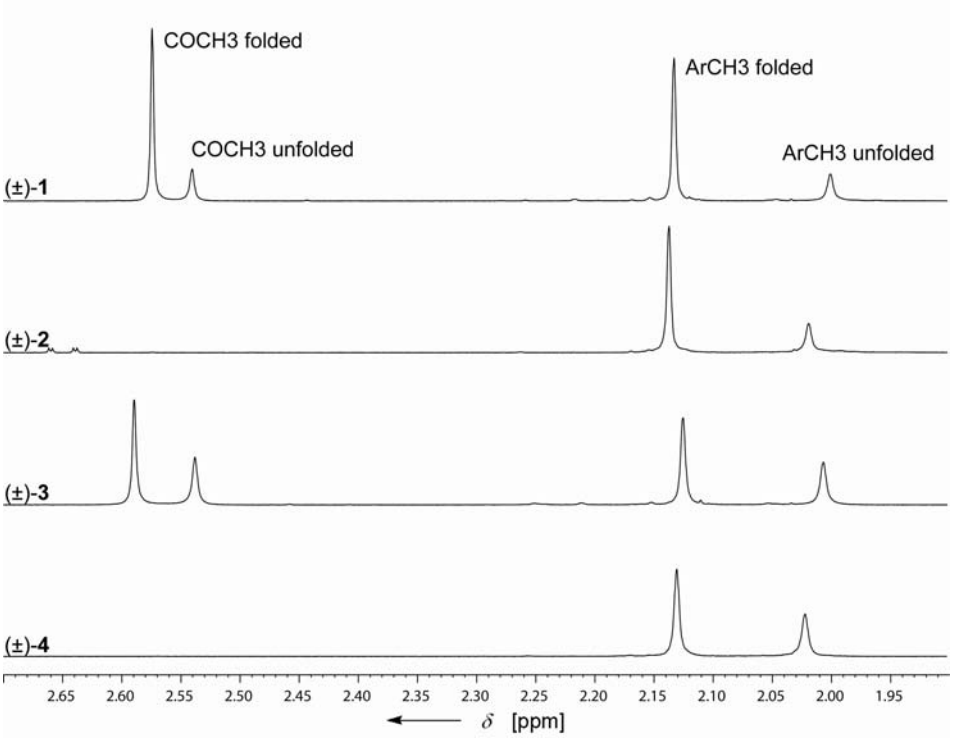


Figure 6SI: ^{1}H NMR spectra of (±)-**1**, (±)-**2**, (±)-**3**, and (±)-**4** in CD_2Cl_2 as 10mM solutions at 298 K.

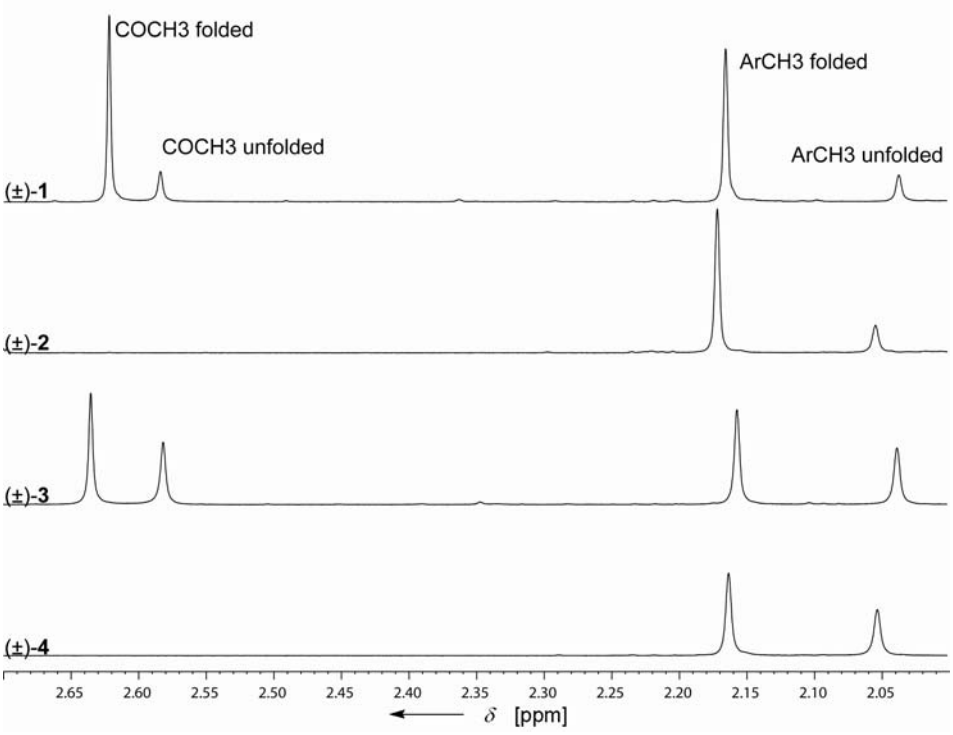


Figure 7SI: ^{1}H NMR spectra of (±)-**1**, (±)-**2**, (±)-**3**, and (±)-**4** in $CDCl_3$ as 10mM solutions at 298 K.

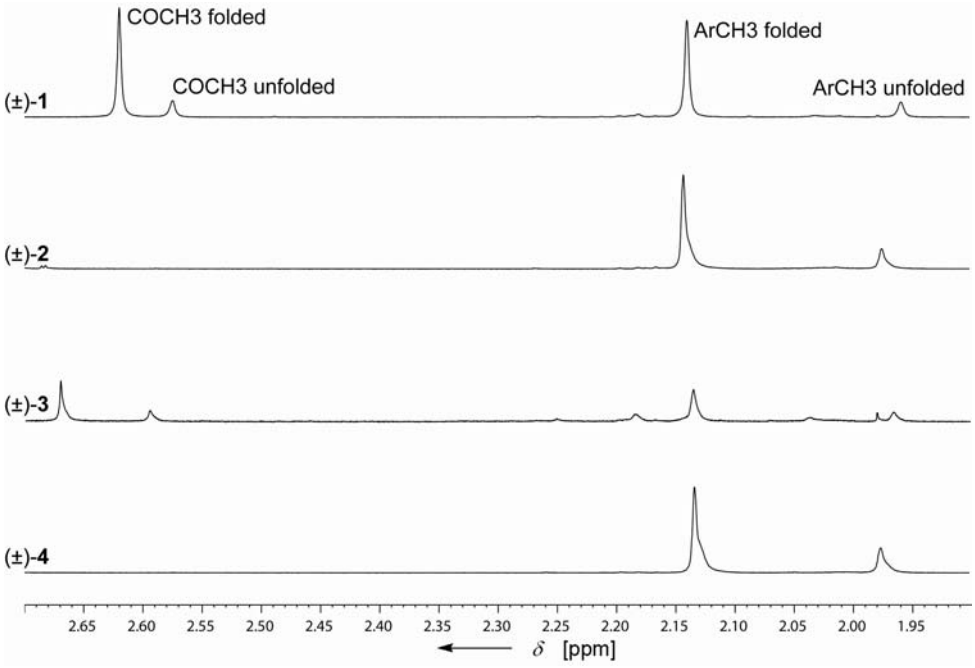


Figure 8SI: ^{1}H NMR spectra of (±)-**1**, (±)-**2**, (±)-**3**, and (±)-**4** in CD_3OD as 10mM solutions at 298 K.

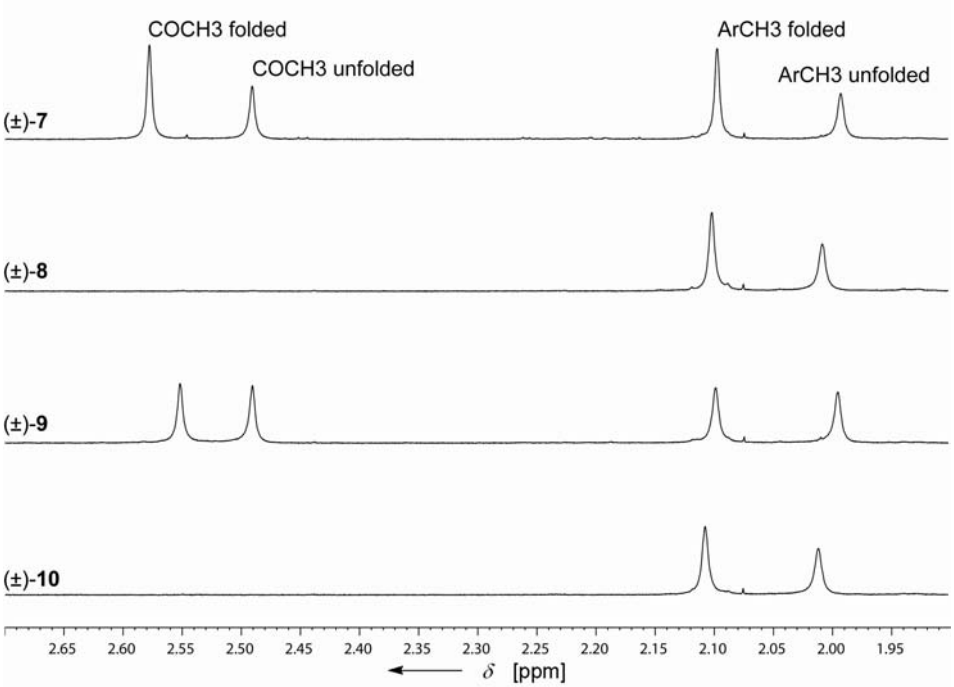


Figure 9SI. ^{1}H NMR spectra of (±)-**7**, (±)-**8**, (±)-**9**, and (±)-**10** in $C_2D_2Cl_4$ as 10mM solutions at 298 K.[1]

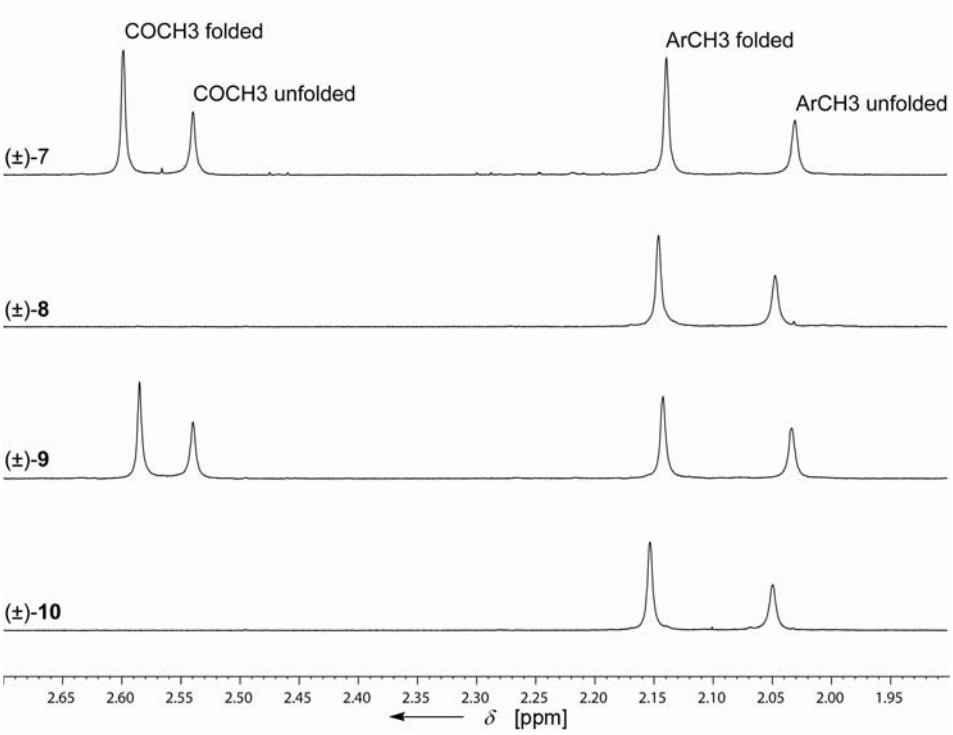


Figure 10SI. ^{1}H NMR spectra of (±)-**7**, (±)-**8**, (±)-**9**, and (±)-**10** in CD_2Cl_2 as 10mM solutions at 298 K.[1]

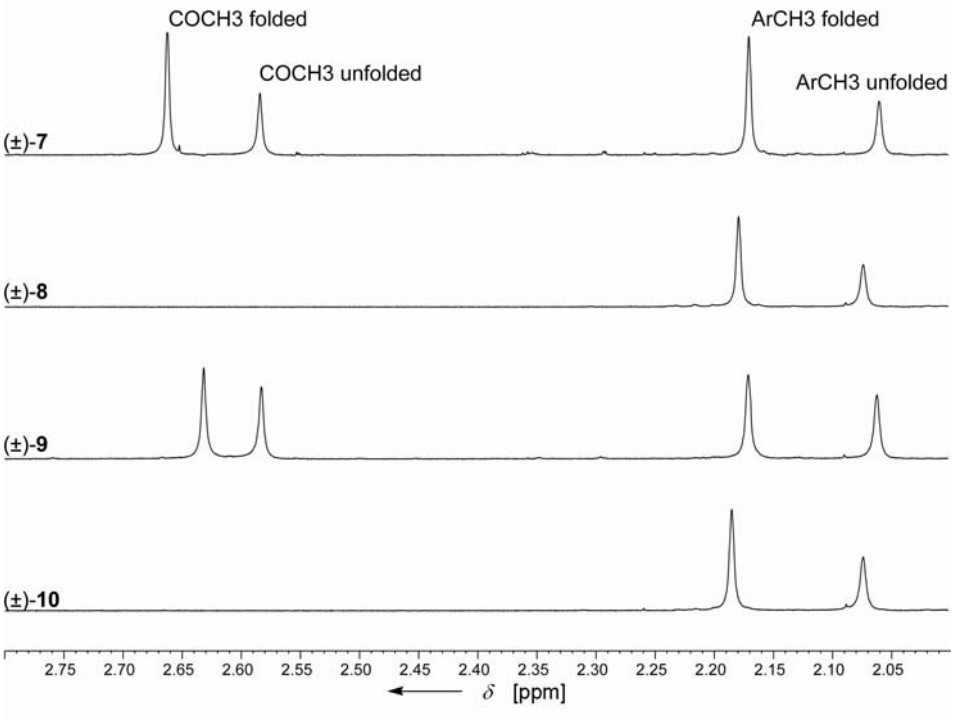


Figure 10SI. ^{1}H NMR spectra of (±)-**7**, (±)-**8**, (±)-**9**, and (±)-**10** in $CDCl_3$ as 10mM solutions at 298 K.[1]

Error analysis:

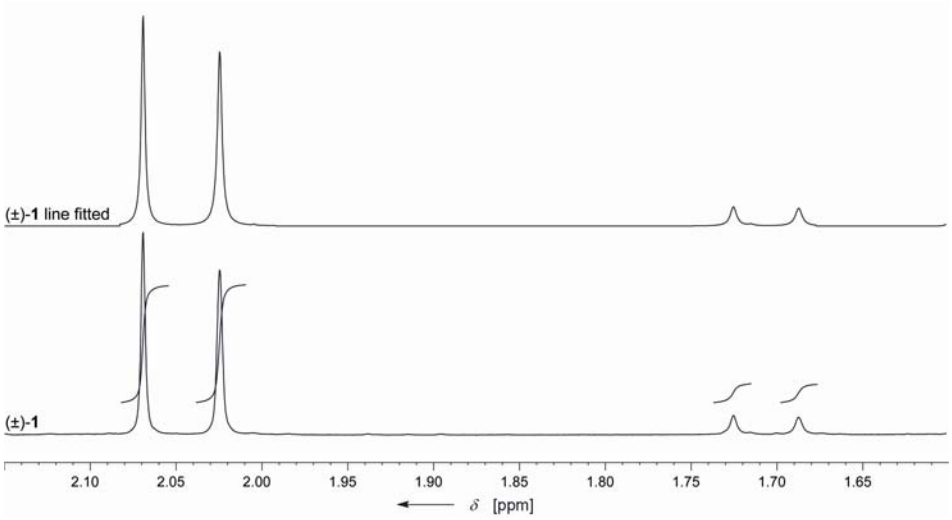


Figure 12SI. ^{1}H NMR spectrum of (±)-**1**, and line-fitted ^{1}H NMR spectrum of (±)-**1** in C_6D_6 as 10mM solutions at 298 K.[1]

Error resulting from integration method:

Equilibrium constant ***K*** by integration:

K_{int} = 6.451

Equilibrium constant ***K*** by integration of the line-fitted spectra:

$K_{line\ fitted}$ = 6.298

Error of the equilibrium constant $\delta(K_{line\ fitted}) \leq 2.5\%$

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) ^{1}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.

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

$$\delta(\Delta G) = RT[\delta(\ln K)] = \underline{0.12 kJmol^{-1}}$$

$$\delta(\Delta G_{CF_3 \bullet\bullet\bullet CO}) = \sqrt{\delta(\Delta G_{(\pm)-1})^2 + \delta(\Delta G_{(\pm)-2})^2 + \delta(\Delta G_{(\pm)-3})^2 + \delta(\Delta G_{(\pm)-4})^2} =$$

$$= \sqrt{\delta(\Delta G_{(\pm)-7})^2 + \delta(\Delta G_{(\pm)-8})^2 + \delta(\Delta G_{(\pm)-9})^2 + \delta(\Delta G_{(\pm)-10})^2} = \underline{\underline{0.25 kJmol^{-1}}}$$

Structural analysis of 1-acetylindoles

The 1-acetylindole moiety in torsion balances (±)-**1**, (±)-**3**, (±)-**7**, and (±)-**9** adopts a conformation in which the O-Atom of the carbonyl points towards the phenyl ring as depicted in **B** (Figure 13SI).

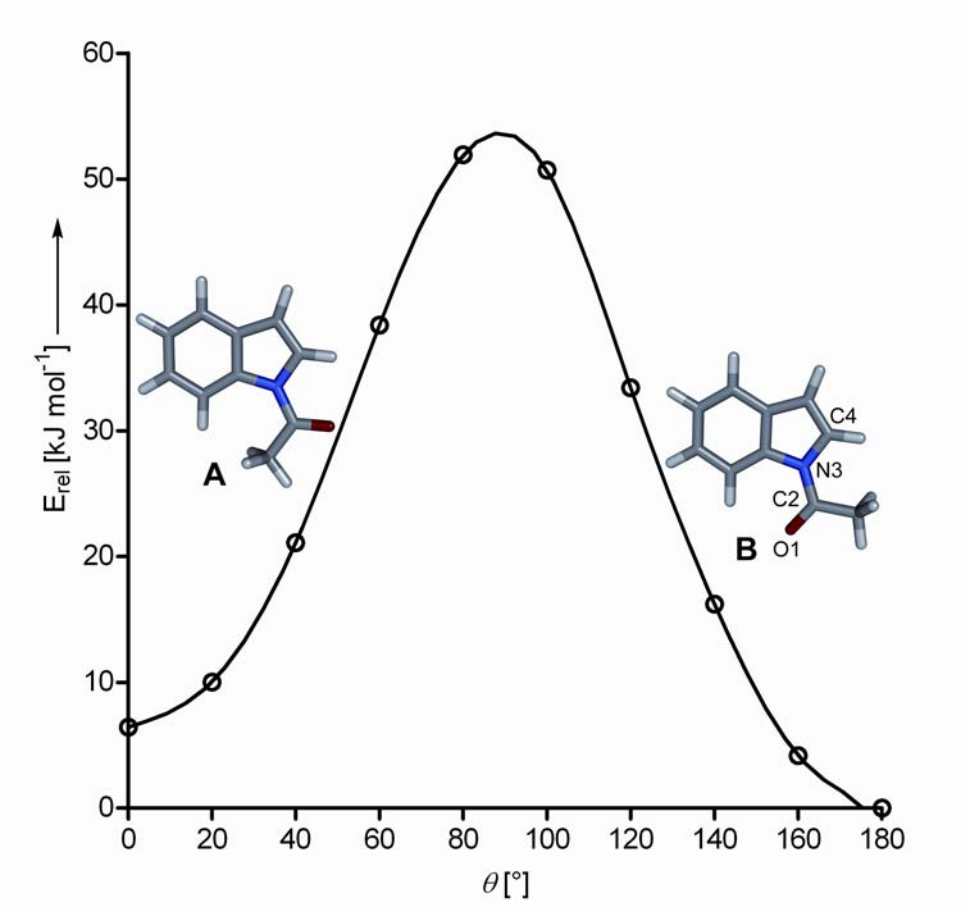


Figure 13SI. Energy profile of the torsion angle θ (O1-C2-N3-C4) calculated on DFT B3LYP (6-31G*) level of theory.[2] The conformer **B** is 6.5 kJ mol^{-1} lower in energy than the conformer **A.** Both conformations are separated by a barrier of 54.7 kJ mol^{-1}.

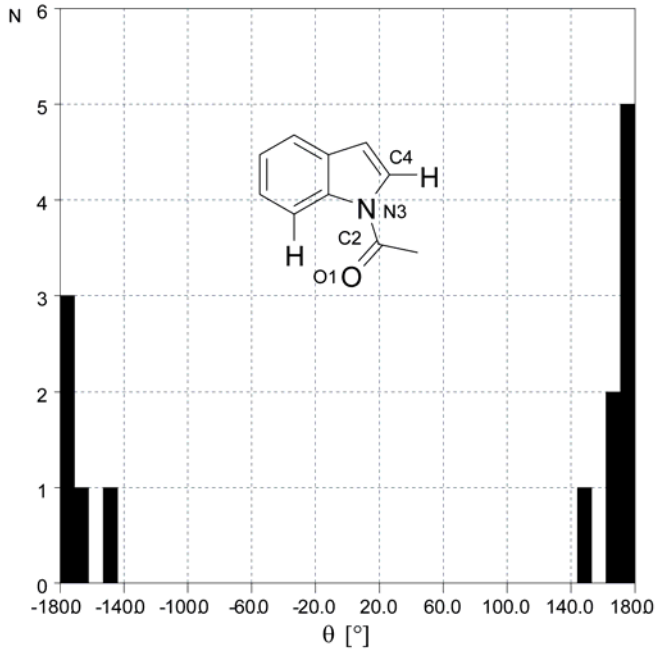
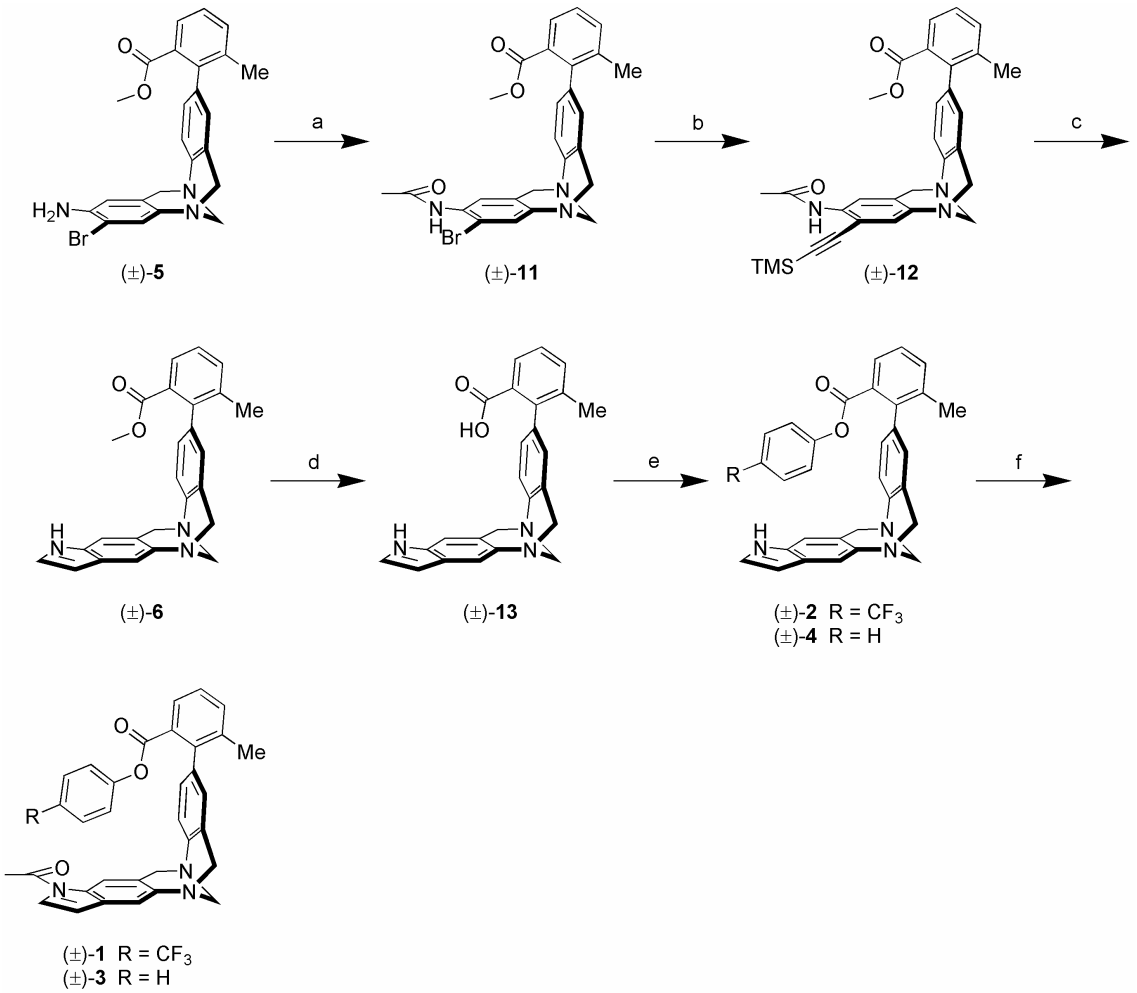


Figure 14SI. Histogram of a CSD search for the torsion angle θ (O1-C2-N3-C4) showing a clear preference for the **B** conformer. The search was performed for 2,7-unsubstituted N-acetylindoles.

Experimental Section:

Materials and general methods: Reagents and solvents were purchased at reagent grade from Acros, Aldrich, ABCR, and Fluka, and used as received. Tetrahydrofuran (THF) was freshly distilled from Na/Benzophenone, CH_2Cl_2 from CaH_2 and NET_3 from $LiAlH_4$ under N_2. All reactions were performed in flame dried glassware under an inert atmosphere of N_2 or Ar. Column chromatography was carried out using Ultra Pure Silica Gel (230-400 mesh) purchased from Silicycle. Thin-layer chromatography (TLC) was conducted on aluminium sheets coated with SiO_2 F_{254} obtained from Macherey-Nagel; visualization with a UV lamp (254 or 366 nm). Melting points (M.p.) were determined in an open capillary using a ***Büchi Melting Point B540*** apparatus and are uncorrected. IR spectra were recorded neat on a ***Perkin-Elmer Spectrum BX II*** spectrometer. The absorption bands are referenced in wavenumbers (cm^{-1}). Analytical ^{1}H NMR (300 MHz), ^{13}C NMR (151 MHz), and ^{19}F NMR (282 MHz) spectra were recorded at 293 K on a ***Varian Mercury-VX 300*** spectrometer. Chemical shifts (δ) are reported in ppm relative to the signal of tetramethylsilane (TMS). Residual solvent signals in the ^{1}H and ^{13}C NMR spectra were used as internal reference. Coupling constants (*J*) are given in Hz. The resonance multiplicity is described as *s* (singlet), *d* (doublet), *t*

(triplet), *q* (quartet), and *m* (multiplet). ^{1}H NMR (500 MHz) spectra for thermodynamic analysis were recorded on a ***Bruker AMX-500*** spectrometer. The exact temperature (298 K) was monitored with an external thermoelement. ^{1}H–^{19}F NOESY experiments were recorded on a ***Bruker AMX-400*** spectrometer. Deuterated solvents in the highest possible purity were used as purchased from ARMAR Chemicals. High resolution (HR) EI-MS spectra were measured on a ***Hitachi-Perkin-Elmer VG-Tribid*** spectrometer. The most important signals are reported in *m*/*z* units with M^{+} as the molecular ion. X-ray crystal structure data was recorded on a ***Bruker-Nonius Kappa-CCD diffractometer*** with $Mo_{K\alpha}$ (λ = 0.7107 Å) radiation.



Scheme 1SI. Synthesis of (±)-**1** – (±)-**4**. a) Ac_2O, CH_2Cl_2, 0 °C-24 °C, 98%. b) $Me_3SiC{\equiv}CH$, CuI, $[Pd(PPh_3)_4]$, Et_3N, 75 °C, 99%. c) *n*-Bu_4NF, THF, 70 °C, 92%. d) LiOH, MeOH/H_2O, 50 °C, 91%. e) Phenol or 4-(trifluoromethyl)phenol, BOP, Et_3N, CH_2Cl_2, 24 °C, 72-83%. f) Ac_2O, DMAP, Et_3N, CH_2Cl_2, 24 °C, 57-72%.

Synthetic protocols:

(±)-Methyl 2-(8-Acetamido-9-bromo-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocin-2-yl)3-methylbenzoate ((±)-**11**). A 100 mL round bottom flask sealed with a septum was charged with (±)-**5** (1.99 g, 4.28 mmol) in dry CH_2Cl_2 (50 mL) and cooled to 0 °C. Ac_2O (0.81 mL, 8.58 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise via syringe and the mixture stirred for 16 h at 24 °C. The mixture is washed with saturated aqueous $NaHCO_3$ solution, saturated aqueous NaCl solution, dried ($MgSO_4$), and concentrated on a rotary evaporator to yield (±)-**11** (2.12 g, 98 %) as a yellow solid. M.p. 215-217 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.04/2.14 (*s*, 3 H, ArC**H**$_3$), 2.19 (*s*, 3 H, COC**H**$_3$), 3.00/3.57 (*s*, 3 H, OC**H**$_3$), 4.02-4.41 (*m*, 4 H, -NC**H**$_2$N-, -CH$_a$**H**$_b$N-), 4.60-4.74 (*m*, 2 H, -C**H**$_a$H$_b$N-), 6.69 (*s*, 1 H), 6.98 (*d*, *J* = 8.3, 1 H), 7.13 (*d*, *J* = 8.2, 1 H), 7.21-7.27 (*m*, 1 H), 7.31-7.38 (*m*, 2 H), 7.40-7.48 (*m*, 1 H), 7.52-7.62 (*m*, 1 H), 7.91 (*s*, 1 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8/21.0 (Ar**C**H$_3$), 24.7 (CO**C**H$_3$), 51.1/51.8 (O**C**H$_3$), 58.2/58.5 (-**C**H$_2$N-), 58.8/59.0 (-**C**H$_2$N-), 66.6/67.0 (-N**C**H$_2$N-), 111.4/111.8, 119.7/120.0, 124.2/124.5, 126.6 (2 C), 126.8/126.9, 127.0, 127.9/128.0, 128.1, 128.2/128.3, 131.3, 131.7/132.1, 132.8, 135.8/135.9, 136.7/137.2, 140.4/140.7, 144.8/145.3, 146.1/146.2, 167.8/168.0, 168.7/169.1 ppm; IR (neat): $\tilde{\nu}$ =

3391, 2909, 2853, 1689, 1570, 1503, 1466, 1432, 1397, 1367, 1323, 1289, 1240, 1200, 1142, 1099, 1067, 1023, 965, 927, 887, 841, 817, 788, 763, 672 cm^{-1}; EI-MS: ***m/z***: 507.1 (78, M^+), 505.1 (73, M^+); EI-HR-MS: ***m/z***: 505.1025 (M^+, $C_{26}H_{24}BrN_3O_3^+$, calc. 505.0996).

(±)-Methyl 2-(8-Acetamido-9-{2-[trimethylsilyl]ethin-1-yl}-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocin-2-yl)-3-methylbenzoate ((±)-**12**) A resealable 25 mL ***Schlenk*** tube was charged with (±)-**11** (2.00 g, 3.95 mmol), $[Pd(Ph_3)_4]$ (183 mg, 0.16 mmol), CuI (45 mg, 0.24 mmol), and $Me_3SiC{\equiv}CH$ (1.12 mL, 7.90 mmol) in degassed NEt_3 (16 mL). The tube was sealed and heated for 21 h to 75 °C. The solvent was concentrated on a rotary evaporator. The residue was taken up in CH_2Cl_2, washed with saturated aqueous NaCl, dried ($MgSO_4$) and concentrated on a rotary evaporator. Column chromatography (SiO_2; CH_2Cl_2/CH_3OH 100:1) yielded (±)-**12** (2.06 g, 99%) as a yellow solid. M.p. 123-128 °C; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.29 (***s***, 9 H, $Si(C\mathbf{H}_3)_3$), 2.00/2.14 (***s***, 3 H, $ArC\mathbf{H}_3$), 2.15 (***s***, 3 H, $COC\mathbf{H}_3$), 2.94/3.57 (***s***, 3 H, $OC\mathbf{H}_3$), 4.02-4.42 (***m***, 4 H, $-NC\mathbf{H}_2N-$, $-CH_a\mathbf{H}_bN-$), 4.60-4.74 (***m***, 2 H, $-C\mathbf{H}_aH_bN-$), 6.65 (***s***, 1 H), 6.93/7.01 (***m***, 1 H), 7.12 (***dd***, ***J*** = 1.9, 8.2, 1 H), 7.20 (***s***, 1 H), 7.22-7.28 (***m***, 1 H), 7.30-7.38 (***m***, 1 H), 7.52-7.62 (***m***, 1 H), 7.81/7.83 (***s***, 1 H), 7.98

(*s*, 1 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.01 (3 C, Si(**C**H_3)$_3$), 20.8/20.9 (Ar**C**H_3), 24.7 (CO**C**H_3), 51.1/51.8 (O**C**H_3), 58.5/58.8 (-**C**H_2N-), 58.9/59.3 (-**C**H_2N-), 66.8/67.1 (-N**C**H_2N-), 99.7/99.9 (ArC≡**C**), 101.7/101.9 (Ar**C**≡C), 110.9/110.9, 116.8/117.1, 124.1/124.4, 126.4-127.0 (3 C), 127.4/127.7, 127.8/128.0, 128.2/128.4, 130.1/130.4, 131.7/131.9, 132.7/132.8, 134.9, 135.7/135.9, 136.7/137.2, 140.5/140.8, 143.0/143.3, 146.2/146.3, 167.5/167.6, 168.7/169.2 ppm; IR (neat): $\tilde{\nu}$ = 3388, 2951, 2899, 2147, 1694, 1571, 1512, 1460, 1414, 1325, 1288, 1245, 1206, 1137, 1097, 964, 930, 838, 760, 625 cm^{-1}; EI-MS: *m*/*z*: 523.2 (100, M$^+$); EI-HR-MS: *m*/*z*: 523.2285 (M$^+$, $C_{31}H_{33}N_3O_3Si^+$, calc. 523.2286).

(±)-Methyl 2-(1,12-Dihydro-6H-5,11-methanoindolo[6,5-c][1,5]benzodiazocin-8-yl)-3-methylbenzoate ((±)-**6**) A 20 mL *Schlenk* tube with reflux condenser was charged with (±)-**12** (956.1 mg, 1.84 mmol) in THF (5 mL). Dry *n*-Bu_4NF (1M in THF) (5.53 mL, 5.53 mmol) was added via syringe and the mixture heated to reflux for 16 h. The solvent was concentrated on a rotary evaporator. The oily residue was taken up in saturated aqueous NaCl solution and extracted with CH_2Cl_2. The combined organic phases were washed with H_2O, 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/CH_3OH 100:2) yielded (±)-**6** (697.3 mg, 92%) as a yellow solid. M.p. 193-199 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.98/2.16 (*s*, 3 H, ArC**H**$_3$), 2.67/3.57 (*s*, 3 H, OC**H**$_3$), 4.17-4.51 (*m*, 4 H, -NC**H**$_2$N-, -CH$_a$**H**$_b$N-), 4.63-4.96 (*m*, 2 H, -C**H**$_a$H$_b$N-), 6.45 (*d*, *J* = 10.9, 1 H), 6.66 (*d*, *J* = 6.7, 1 H), 6.87-6.99 (*m*, 2 H), 7.08-7.15 (*m*, 1 H), 7.14 (*d*, *J* = 8.2, 1 H), 7.21-7.27 (*m*, 1 H), 7.28-7.38 (*m*, 1 H), 7.43 (*d*, *J* = 5.6, 1 H), 7.47-7.60 (*m*, 1 H), 7.92-8.07 (*m*, 1 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8/20.9 (Ar**C**H$_3$), 50.9/51.9 (O**C**H$_3$), 59.3/59.6 (-**C**H$_2$N-), 60.0/60.2 (-**C**H$_2$N-), 67.1/67.7 (-N**C**H$_2$N-), 101.8, 107.9/108.1, 115.7/116.0, 122.1/122.3, 124.0/124.3, 125.0, 126.5/125.7, 126.8/127.1, 127.3/127.4, 127.6/127.8, 128.3/128.5, 131.8/132.0, 131.9/132.3, 132.7, 133.4/133.5, 135.4/135.5, 136.8/137.1, 140.5/140.6, 140.8/141.0, 146.7/146.8, 169.0/169.3 ppm; IR (neat): $\tilde{\nu}$ = 3376, 2946, 2894, 2847, 1712, 1499, 1459, 1433, 1343, 1288, 1192, 1138, 1097, 963, 933, 871, 840, 761, 724, 624 cm^{-1}; EI-MS: *m*/*z*: 409.2 (59, M$^+$); EI-HR-MS: *m*/*z*: 409.1789 (M$^+$, $C_{26}H_{23}N_3O_2^+$, calc. 409.1785).

(±)-2-(1,12-Dihydro-6H-5,11-methanoindolo[6,5-c][1,5]benzodiazocin-8-yl)-3-methylbenzoic acid ((±)-**13**) A

10 mL round bottom flask was charged with $LiOH \cdot H_2O$ (384.0 mg, 8.29 mmol) in CH_3OH/H_2O (5 mL, 4:1). A solution of (±)-**6** (200.0 mg, 0.49 mmol) in CH_3OH (2.5 mL) was added dropwise over 30 min. The flask was sealed with a septum and stirred for 14 h at 50 °C. The mixture was concentrated on a rotary evaporator, and the residue was taken up in H_2O (25 mL). The pH was adjusted to 5.5 with 2N hydrochloric acid, and the white precipitate was extracted with AcOEt. The combined organic phases were dried ($MgSO_4$) and concentrated on a rotary evaporator to yield (±)-**13** (176.2 mg, 91%) as a colorless solid. M.p. 235 °C (decomp.); ^{1}H NMR (300 MHz, CD_3OD): δ = 1.86/2.05 (*s*, 3 H, ArC**H**$_3$), 4.18-4.50 (*m*, 4 H, -NC**H**$_2$N-, -CH$_a$**H**$_b$N-), 4.64-4.90 (*m*, 2 H, -C**H**$_a$H$_b$N-), 6.35 (*d*, *J* = 3.0, 1 H), 6.76 (*s*, 1 H), 6.97 (*s*, 1 H), 6.99 (*dd*, *J* = 2.0, 8.3, 1 H), 7.15 (*d*, *J* = 3.0, 1 H), 7.17-7.29 (*m*, 2 H), 7.30-7.41 (*m*, 2 H), 7.42-7.57 (*m*, 1 H) ppm; ^{13}C NMR (75 MHz, CD_3OD): δ = 21.0 (Ar**C**H$_3$), 60.0/60.1 (-**C**H$_2$N-), 60.5 (-**C**H$_2$N-), 67.9 (-N**C**H$_2$N-), 101.9, 109.4, 116.4, 122.0, 125.3, 126.7, 127.0/127.2, 127.9, 128.1, 128.2, 129.1, 129.3, 133.3, 134.8/134.9, 135.9, 137.7, 138.2, 139.4/139.6, 141.4/141.5, 147.0, 172.8 ppm; IR (neat): $\tilde{\nu}$ = 3281, 3055, 2949, 2917, 2852, 1701, 1571, 1500, 1461, 1346, 1287, 1238, 1177, 1151, 1097, 963, 931, 871, 842, 763, 729, 702, 622 cm^{-1}; EI-MS: *m*/*z*: 395.2

(100, M^+); EI-HR-MS: *m/z*: 395.1638 (M^+, $C_{25}H_{21}N_3O_2^+$, calc. 395.1628).

(±)-Phenyl 2-(1,12-Dihydro-6H-5,11-methanoindolo[6,5-c][1,5]benzodiazocin-8-yl)-3-methylbenzoate ((±)-**4**) A 20 mL *Schlenk* tube sealed with a septum was charged with (±)-**13** (200.0 mg, 0.51 mmol), phenol (142.8 mg, 1.52 mmol), and BOP (447.3 mg, 1.01 mmol) in CH_2Cl_2 (12 mL). NEt_3 (409.4 mg, 4.05 mmol) was added dropwise via syringe and the mixture stirred for 14 h at 24 °C. The solvents were evaporated, and the residue was taken up in Et_2O (50 mL). The organic phase was washed with saturated aqueous NaCl solution, dried ($MgSO_4$), and concentrated on a rotary evaporator. Column chromatography (SiO_2; CH_2Cl_2/CH_3OH 100:1) yielded (±)-**4** (171.6 mg, 72%) as a colorless foam. M.p. 132-133 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.05/2.18 (*s*, 3 H, ArC**H**$_3$), 4.18-4.48 (*m*, 4 H, -NC**H**$_2$N-, -CH$_a$**H**$_b$N-), 4.69-4.95 (*m*, 2 H, -C**H**$_a$H$_b$N-), 6.05 (*d*, *J* = 7.6, 1 H), 6.36 (*t*, *J* = 8.0, 1 H), 6.45-6.49 (*m*, 1 H), 6.66-6.94 (*m*, 3 H), 7.05-7.47 (*m*, 7 H), 7.63-7.77 (*m*, 1 H), 8.16-8.24 (*m*, 1 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6/20.7 (Ar**C**H$_3$), 59.1 (-**C**H$_2$N-), 59.6 (-**C**H$_2$N-), 67.1 (-N**C**H$_2$N-), 101.8/102.1, 108.2, 116.0, 120.6, 121.2, 121.8/122.2, 124.5/124.6, 124.9/125.0, 125.1, 125.7, 126.8, 126.9/127.0, 127.1, 127.4/127.6,

127.9/128.1, 128.7, 129.2, 131.9, 133.1/133.3, 133.6/133.7, 135.4/135.5, 137.4, 140.5/140.7, 140.9, 147.1/147.2, 150.0/150.5, 167.5/168.1 ppm; IR (neat): $\tilde{\nu}$ = 3406, 2946, 2896, 2849, 2359, 2325, 1731, 1591, 1490, 1461, 1344, 1280, 1192, 1160, 1119, 1088, 964, 934, 791, 763, 689, 629 cm^{-1}; EI-MS: *m*/*z*: 471.2 (53, M^+); EI-HR-MS: *m*/*z*: 471.1938 (M^+, $C_{31}H_{25}N_3O_2^+$, calc. 471.1941).

(±)-4-(Trifluoromethyl)phenyl 2-(1,12-dihydro-6H-5,11-methanoindolo[6,5-c][1,5]benzodiazocin-8-yl)-3-methylbenzoate ((±)-**2**) A 20 mL *Schlenk* tube sealed with a septum was charged with (±)-**13** (162.2 mg, 0.41 mmol), 4-(trifluoromethyl)phenol (200.0 mg, 1.23 mmol), and BOP (362.8 mg, 0.82 mmol) in CH_2Cl_2 (12 mL). NEt_3 (332.0 mg, 3.28 mmol) was added dropwise via syringe and the reaction mixture stirred for 14 h at 24 °C. The solvents were evaporated, and the residue was taken up in Et_2O (50 mL). The organic phase was washed with saturated aqueous NaCl solution, dried ($MgSO_4$), and concentrated on a rotary evaporator. Column chromatography (SiO_2; CH_2Cl_2/MeOH 100:1) yielded (±)-**2** (183.1 mg, 83%) as a colorless foam. M.p. 128-129 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06/2.20 (*s*, 3 H, ArC**H**$_3$), 4.21-4.51 (*m*, 4 H, -NC**H**$_2$N-, -CH_a**H**$_b$N-), 4.69-4.97 (*m*, 2 H, -C**H**$_a$H$_b$N-), 6.08 (*d*, *J* = 8.3, 2 H), 6.45-6.50 (*m*, 1

H), 6.64 (*d*, *J* = 8.5, 2 H), 6.76–6.94 (*m*, 2 H), 7.12 (*dd*, *J* = 1.9, 8.2, 1 H), 7.17–7.20 (*m*, 1 H), 7.24 (*d*, J = 8.3, 1 H), 7.32–7.38 (*m*, 1 H), 7.45 (*d*, *J* = 6.23, 1 H), 7.50 (*s*, 1 H), 7.55–7.79 (*m*, 1 H), 8.41 (*s*, 1 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (Ar**C**H_3), 59.3 (-**C**H_2N-), 59.7 (-**C**H_2N-), 67.1 (-N**C**H_2N-), 101.9, 107.9, 116.0, 121.2, 121.6, 121.8/122.1, 124.5, 125.0, 125.4, 126.0/126.1, 126.4/126.5, 126.6, 126.8/126.9, 127.0/127.1, 127.3, 127.5, 127.7, 127.8/127.9, 131.1, 133.3/133.4, 133.5/133.6, 135.2, 135.5, 137.4, 140.5, 147.2, 152.3, 167.4 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -61.7/-62.0 (ArC**F**$_3$) ppm; IR (neat): $\tilde{\nu}$ = 3407, 2947, 2899, 2852, 2360, 2326, 1732, 1611, 1501, 1461, 1412, 1323, 1270, 1204, 1164, 1117, 1061, 1015, 964, 934, 865, 843, 797, 763, 732, 619 cm^{-1}; EI-MS: *m*/*z*: 539.2 (100, M^+); EI-HR-MS: *m*/*z*: 539.1818 (M^+, $C_{32}H_{24}F_3N_3O_2^+$, calc. 539.1815).

(±)-Phenyl 2-(1-acetyl-6H,12H-5,11-methanoindolo[6,5-c][1,5]benzodiazocin-8-yl)-3-methylbenzoate ((±)-**3**) A 10 mL *Schlenk* tube sealed with a septum was charged with (±)-**4** (75.0 mg, 0.16 mmol), DMAP (1.9 mg, 0.02 mmol), and Et_3N (1.0 mL, 7.17 mmol) in CH_2Cl_2 (1 mL). Ac_2O (0.2 mL, 2.12 mmol) was added via syringe, and the mixture was stirred for 24 h at 24 °C. The solvent was evaporated on a rotary evaporator. Column chromatography (SiO_2; CH_2Cl_2/MeOH 100:2)

yielded (±)-**3** (30.8 mg, 57%) as a colorless foam. M.p. 242-243 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.04/2.16 (*s*, 3 H, ArC**H**$_3$), 2.58/2.64 (*s*, 3 H, COC**H**$_3$), 4.16-4.48 (*m*, 4 H, -NC**H**$_2$N-, -CH$_a$**H**$_b$N-), 4.67-4.94 (*m*, 2 H, -C**H**$_a$H$_b$N-), 6.07 (*d*, *J* = 7.7, 1 H), 6.53-6.64 (*m*, 2 H), 6.68-6.81 (*m*, 2 H), 7.06-7.44 (*m*, 8 H), 7.62-7.75 (*m*, 1 H), 8.08 (*s*, 1 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9 (Ar**C**H$_3$), 23.8 (CO**C**H$_3$), 59.4 (2 C, -**C**H$_2$N-), 67.0 (-N**C**H$_2$N-), 108.9, 109.1, 109.8, 114.5, 116.5, 120.5, 121.1, 124.7, 124.8, 125.0, 125.4, 125.5, 125.6, 126.8, 126.9, 127.0, 127.1, 127.2, 128.1, 128.3, 128.7, 129.1, 130.0, 133.1, 133.2, 137.3, 168.0, 168.2 ppm; IR (neat): $\tilde{\nu}$ = 3059, 2947, 2901, 2849, 2324, 1733, 1700, 1591, 1573, 1536, 1491, 1446, 1380, 1331, 1275, 1191, 1159, 1109, 1086, 1003, 964, 928, 884, 839, 794, 733, 689, 629 cm^{-1}; EI-MS: *m*/*z*: 513.2 (74, M$^+$); EI-HR-MS: *m*/*z*: 513.2026 (M$^+$, $C_{33}H_{27}N_3O_3^+$, calc. 513.2047).

(±)-4-(Trifluoromethyl)phenyl 2-(1-acetyl-6H,12H-5,11-methanoindolo[6,5-c][1,5]benzodiazocin-8-yl)-3-methylbenzoate ((±)-**1**) A 10 mL *Schlenk* tube sealed with a septum was charged with (±)-**2** (100.0 mg, 0.19 mmol), DMAP (2.3 mg, 0.02 mmol), and Et_3N (1.0 mL, 7.17 mmol) in CH_2Cl_2 (1 mL). Ac_2O (0.2 mL, 2.12 mmol) was added via syringe and the mixture stirred for 32 h at 24 °C. The solvent was

evaporated on a rotary evaporator. Column chromatography (SiO_2; CH_2Cl_2/MeOH 100:2) yielded (±)-**1** (77.5 mg, 72%) as a colorless foam. M.p. 123-125 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.04/2.17 (*s*, 3 H, ArC**H**$_3$), 2.58/2.62 (*s*, 3 H, COC**H**$_3$), 4.16-4.53 (*m*, 4 H, -NC**H**$_2$N-, -CH$_a$**H**$_b$N-), 4.66-4.99 (*m*, 2 H, -C**H**$_a$H$_b$N-), 6.02 (*d*, *J* = 8.3, 2 H), 6.56 (*dd*, *J* = 0.6, 3.8, 1 H), 6.68 (*d*, *J* = 8.4, 2 H), 6.75/6.80 (*d*, *J* = 1.8, 1 H), 7.12 (*dd*, *J* = 2.0, 8.2, 1 H), 7.20/7.24 (*s*, 1 H), 7.31-7.46 (*m*, 4 H), 7.65/7.75 (*dd*, *J* = 0.9, 7.6, 1 H), 8.08/8.21 (*s*, 1 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7/20.8 (Ar**C**H$_3$), 23.4/23.7 (CO**C**H$_3$), 59.2 (-**C**H$_2$N-), 59.3 (-**C**H$_2$N-), 67.0 (-N**C**H$_2$N-), 108.6, 114.5, 116.6, 121.4, 121.7, 124.8, 124.9, 126.1 (3 C), 126.1, 127.2, 127.3, 128.3, 130.0, 131.3, 132.7, 133.6, 133.7, 136.0, 137.6, 140.6, 144.3, 147.3, 152.4, 167.6, 168.6 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -61.9/-62.0 (ArC**F**$_3$) ppm; IR (neat): $\tilde{\nu}$ = 2925, 2852, 2325, 1739, 1704, 1612, 1573, 1537, 1500 1447, 1381, 1327, 1273, 1207, 1167, 1122, 1062, 1016, 964, 929, 865, 840, 764, 732 686, 631 cm^{-1}; EI-MS: *m*/*z*: 581.6 (100, M$^+$); EI-HR-MS: *m*/*z*: 581.1918 (M$^+$, $C_{34}H_{26}F_3N_3O_3^+$, calc. 581.1921).

X-ray crystal structure of (±)-3: Crystals of (±)-**3** were grown by vapor diffusion of pentane into a solution of (±)-**3** in $CHCl_3$/AcOEt (1:3): colorless cube, 0.3×0.1×0.08 mm; orthorhombic, space group $P2_1P2_1P2_1$; a = 8.1838(2) Å, b = 10.0312(2) Å, c = 31.1403(7) Å, V = 2556.41(10) Å^3, $\alpha = \beta = \gamma = 90°$; ρ_{calc} = 1.334 Mg m^{-3}; $2\theta_{max}$ = 54.96°; $Mo_{K\alpha}$ radiation, λ = 0.71073 Å; T = 203 K; 5761 independent of 5789 measured reflections, R_{int} = 0.035, no absorption correction applied (μ = 0.086 mm^{-1}); structure solution using SIR97;[3] 4224 reflections with $I > 2\sigma(I)$ refined on $|F^2|$ using *SHELXL*-97;[4] Δ/σ_{max} = 0.036, $\Delta\rho_{max}$ = 0.288 e Å^3, $\Delta\rho_{min}$ = −0.260 e Å^3; 424 parameters, all hydrogen atom parameters refined; R(all) = 0.0956, R(gt) = 0.0612, wR(ref) = 0.1758, wR(gt) = 0.1469. CCDC-649861 contains the supplementary crystallographic data for this paper and is available free of charge from the Cambridge Crystallographic Data Centre.[5]

X-ray crystal structure of (±)-8: Crystals of (±)-**8** were grown by vapor diffusion of pentane into a solution of (±)-**3** in AcOEt: colorless plate, 0.16×0.1×0.01 mm; monoclinic, space group $P2_1$; a = 10.6614(7) Å, b = 10.3936(7) Å, c = 12.2535(11) Å, V = 1325.0(2) Å^3, α = 90.00°, β = 102.63°, γ = 90.00°; ρ_{calc} = 1.353 Mg m^{-3}; $2\theta_{max}$ = 48.34°; $Mo_{K\alpha}$

radiation, λ = 0.71073 Å; *T* = 233 K; 4083 independent of 7001 measured reflections, R_{int} = 0.061, no absorption correction applied (μ = 0.090 mm^{-1}); structure solution using SIR97;[3] 2716 reflections with $I > 2\sigma(I)$refined on $|F^2|$ using *SHELXL*-97;[4] Δ/σ_{max} = 0.016, $\Delta\rho_{max}$ = 0.127 e $Å^3$, $\Delta\rho_{min}$ = −0.151 e $Å^3$; 370 parameters, H-atom positions based on stereochemical considerations; *R*(all) = 0.0984, *R*(gt) = 0.0577, *wR*(ref) = 0.1729, *wR*(gt) = 0.1420. CCDC-649862 contains the supplementary crystallographic data for this paper and is available free of charge from the Cambridge Crystallographic Data Centre.[5]

X-ray crystal structure of (±)-10: Crystals of (±)-**10** were grown by vapor diffusion of pentane into a solution of (±)-**10** in $CHCl_3$/AcOEt (1:1): colorless plate, 0.36×0.2×0.06 mm; monoclinic, space group $P2_1$; *a* = 10.3816(5), *b* = 10.2734(5), *c* = 12.6059(6) Å, V = 1317.85(11) $Å^3$, α = 90.00°, β = 101.422°, γ = 90.00°; ρ_{calc} = 1.351 Mg m^{-3}; $2\theta_{max}$ = 50.06°; $Mo_{K\alpha}$ radiation, λ = 0.71073 Å; *T* = 298 K; 4298 independent of 4302 measured reflections, no absorption correction applied (μ = 0.082 mm^{-1}); structure solution using SIR97;[3] 3246 reflections with $I > 2\sigma(I)$refined on $|F^2|$ using *SHELXL*-97;[4] Δ/σ_{max} = 0.000, $\Delta\rho_{max}$ = 0.173 e $Å^3$,

$\Delta\rho_{min}$ = −0.183 e Å^3; 361 parameters, H-atom positions based on stereochemical considerations; ***R***(all) = 0.0823, ***R***(gt) = 0.0566, ***wR***(ref) = 0.1653, ***wR***(gt) = 0.1426. CCDC-649863 contains the supplementary crystallographic data for this paper and is available free of charge from the Cambridge Crystallographic Data Centre.[5]

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[1] Spectra were processed with the program: TOPSPIN, Version 1.3 (February, 16, 2005), © Bruker BioSpin 2005.

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