Controlling Regioselectivity in Palladium-Catalyzed C–H Activation/Aryl–Aryl Coupling of 4-Phenylamino[2.2]paracyclophane

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2 Materials and Methods

Nuclear Magnetic Resonance Spectroscopy (NMR)

The NMR spectra of the compounds described herein were recorded on a Bruker Avance 300 NMR instrument at 300 MHz for $^1$H NMR and 75 MHz for $^{13}$C NMR, a Bruker Avance 400 NMR instrument at 400 MHz for $^1$H NMR and 101 MHz for $^{13}$C NMR or a Bruker Avance 500 NMR instrument at 500 MHz for $^1$H NMR and 125 MHz for $^{13}$C NMR. The NMR spectra were recorded at room temperature in deuterated solvents acquired from Eurisotop. The chemical shift $\delta$ is displayed in parts per million [ppm] and the references used were the $^1$H and $^{13}$C peaks of the solvents themselves: $d_1$-chloroform (CDCl$_3$): 7.26 ppm for $^1$H and 77.0 ppm for $^{13}$C, $d_6$-dimethyl sulfoxide (DMSO-$d_6$): 2.50 ppm for $^1$H and 39.4 ppm for $^{13}$C and $d_6$-benzene (C$_6$D$_6$): 7.16 ppm for $^1$H and 128.06 ppm for $^{13}$C. For the characterization of centrosymmetric signals, the signal’s median point was chosen, for multiplets the signal range. The following abbreviations were used to describe the proton splitting pattern: d = doublet, t = triplet, m = multiplet, dd = doublet of doublet, ddd = doublet of doublet of doublet, dt = doublet of triplet. Absolute values of the coupling constants “$J$” are given in Hertz [Hz] in absolute value and decreasing order. Signals of the $^{13}$C spectrum were assigned with the help of distortionless enhancement by polarization transfer spectra DEPT90 and DEPT135 and were specified in the following way: DEPT: + = primary or tertiary carbon atoms (positive DEPT signal), – = secondary carbon atoms (negative DEPT signal), C$_q$ = quaternary carbon atoms (no DEPT signal).

Infrared Spectroscopy (IR)

The infrared spectra were recorded with a Bruker, IFS 88 instrument. Solids were measured by attenuated total reflection (ATR) method. The positions of the respective transmittance bands are given in wavenumbers $\tilde{\nu}$ [cm$^{-1}$] and were measured in the range from 3600 cm$^{-1}$ to 500 cm$^{-1}$. Characterization of the transmittance bands was done in a sequence of transmission strength $T$ with following abbreviations: vs (very strong, 0–9% T), s (strong, 10–39% T), m (medium, 40–69% T), w (weak, 70–89% T), vw (very weak, 90–100% T) and br (broad).

Mass Spectrometry (MS)

Electron ionization (EI) and fast atom bombardment (FAB) experiments were conducted using a Finnigan, MAT 90 (70 eV) instrument, with 3-nitrobenzyl alcohol (3-NBA) as matrix and reference for high resolution. For the interpretation of the spectra, molecular peaks [M]+, peaks of protonated molecules [M+H]$^+$ and characteristic fragment peaks are indicated with their mass-to-charge ratio ($m/z$) and in case of EI their intensity in percent, relative to the base peak (100%) is given. In the case of high-resolution measurements, the tolerated error is 0.0005 m/z. APCI and ESI experiments were recorded on a Q-Exactive (Orbitrap) mass spectrometer (Thermo Fisher Scientific, San Jose, CA, USA) equipped with a HESI II probe to record high resolution. The tolerated error is 5 ppm of the molecular mass.
Again, the spectra were interpreted by molecular peaks [M]+, peaks of protonated molecules [M+H]+ and characteristic fragment peaks and indicated with their mass-to-charge ratio (m/z).

**Thin Layer Chromatography (TLC)**

For the analytical thin layer chromatography, TLC silica plates coated with a fluorescence indicator, from Merck (silica gel 60 F254, thickness 0.2 mm) were used. UV-active compounds were detected at 254 nm and 366 nm excitation wavelength with a Heraeus UV-lamp, model Fluotest.

**Solvents and Chemicals**

Solvents of p.a. quality (per analysis) were commercially acquired from Sigma Aldrich, Carl Roth, or Acros Fisher Scientific and, unless otherwise stated, used without further purification. Dry solvents were either purchased from Carl Roth, Acros, or Sigma Aldrich (< 50 ppm H2O over molecular sieves). All reagents were commercially acquired from abcr, Acros, Alfa Aesar, Sigma Aldrich, TCI, Chempbur, Carbolution or Synchemie, or were available in the group. Unless otherwise stated, all chemicals were used without further purification.

**Gas Chromatography (GC)**

To determine the degree of conversion, gas chromatograms were recorded on a Bruker 430 GC device equipped with a FactorFourTM VF-5ms (30 m × 0.25 mm × 0.25 mm) capillary column and a flame ionization detector (FID).

**Reaction Monitoring**

The progress of the reaction in the liquid phase was monitored by TLC. UV active compounds were detected with a UV-lamp at 254 nm and 366 nm excitation wavelength. When required, vanillin solution, potassium permanganate solution, or methanolic bromocresol green solution was used as TLC-stain, followed by heating. Additionally, APCI-MS (atmospheric pressure chemical ionization mass spectrometry) was recorded on an Advion expression CMS in positive ion mode with a single quadrupole mass analyzer. The observed molecule ion is interpreted as [M+H]+.

**Product Purification**

Unless otherwise stated, the crude compounds were purified by column chromatography. For the stationary phase of the column, silica gel, produced by Merck (silica gel 60, 0.040 × 0.063 mm, 260 – 400 mesh ASTM), and sea sand by Riedel de-Haën (baked out and washed with hydrochloric acid) were used. Solvents used were commercially acquired in HPLC-grade and individually measured volumetrically before mixing.
Crystallography

Crystal Structure Determinations of 3a, 3c, 3d, 4 and 6

The single-crystal X-ray diffraction study was carried out on a Bruker D8 Venture diffractometer with Photon100 detector or PhotonII detector at 123(2) K or 298(2) K using Cu-Kα radiation (α = 1.54178 Å). Dual space methods (SHELXT for 5a) [G. M. Sheldrick, Acta Crystallogr. 2015, A71, 3-8] were used for structure solution and refinement was carried out using SHELXL-2014 (full-matrix least-squares on F2) [G. M. Sheldrick, Acta Crystallogr. 2015, C71, 3-8]. Hydrogen atoms were localized by difference electron density determination and refined using a riding model (H(N)) free, except 3d. Semi-empirical absorption corrections were applied.
3 Synthetic Protocols and NMRs

(rac)-4-Bromo[2.2]paracyclophane

A solution of bromine (3.77 mL, 11.8 g, 73.7 mmol, 1.02 equiv.) in 80 mL of dichloromethane was prepared in a dropping funnel. Of this solution, 5 mL was added to iron filings (10.0 mg, 2 mol%, 1.44 mmol) in a 500 mL three-necked flask and stirred for 1 h at room temperature. Then, 250 mL of dichloromethane and [2.2]paracyclophane (15.0 g, 72.0 mmol, 1.00 equiv.) was added and stirred for further 30 min. The remaining bromine solution was added dropwise for 5 h and the mixture was stirred for 16 h. The reaction was quenched with a saturated Na₂SO₃ solution (200 mL) and stirred for 30 min until the full discoloration of the mixture. The organic phase was separated, washed with brine (200 mL), and dried over Na₂SO₄. The solvent was removed under reduced pressure to yield the title compound (20.2 g, 70.3 mmol, 98%) as a white solid.

R_f = 0.63 (cyclohexane/ethyl acetate; 50:1).

¹H NMR (400 MHz, CDCl₃) δ = 7.19 (dd, J = 7.9, 2.0 Hz, 1H), 6.58 (dd, J = 7.8, 2.0 Hz, 1H), 6.56 – 6.52 (m, 2H), 6.52 – 6.45 (m, 3H), 3.48 (ddd, J = 13.0, 10.1, 2.2 Hz, 1H), 3.22 (ddd, J = 13.1, 10.1, 6.1 Hz, 1H), 3.17 – 3.02 (m, 4H), 2.98 – 2.78 (m, 2H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 141.73 (C₈), 139.43 (C₈), 139.22 (C₂, 2C), 137.37 (+, C₆ArH), 135.17 (+, C₆ArH), 133.43 (+, C₆ArH), 133.03 (+, C₆ArH), 132.37 (+, C₆ArH), 131.59 (+, C₆ArH), 128.81 (+, C₆ArH), 127.09 (C₈), 35.98 (–, CH₂), 35.61 (–, CH₂), 34.95 (–, CH₂), 33.61 (–, CH₂) ppm.

IR (ATR) ν = 2924 (w), 2849 (w), 1585 (w), 1541 (w), 1497 (w), 1475 (w), 1431 (w), 1408 (w), 1390 (w), 1186 (w), 1092 (vw), 1034 (m), 941 (w), 869 (w), 839 (m), 793 (w), 708 (m), 668 (w), 640 (m), 576 (w), 514 (m), 473 (w), 404 (vw), 382 (w) cm⁻¹.

MS (EI, 70 eV) m/z (%) = 288 (27) [M⁺(Br)]⁺, 286 (28) [M⁻(Br)]⁻, 184 (17) [C₆H₈⁺(Br)]⁺, 182 (17) [C₆H₇⁻(Br)], 104 (100) [C₆H₈⁺].

HRMS (EI, C₁₆H₁₅⁺Br) calcd. 286.0352; found 286.0350.

The analytical data is consistent with literature.[1]
Figure S1. $^1$H NMR of (rac)-4-bromo[2.2]paracyclophane.

Figure S2. $^{13}$C NMR of (rac)-4-bromo[2.2]paracyclophane.
(rac)-4-N-(Phenyl)amino[2.2]paracyclophane (1)

A sealable vial was charged with (rac)-4-bromo[2.2]paracyclophane (1.15 g, 4.00 mmol, 1.00 equiv.), potassium tert-butoxide (630 mg, 5.60 mmol, 1.40 equiv.), Pd2dba3 (70.0 mg, 0.08 mmol, 2.0 mol%) and SPhos (100 mg, 0.240 µmol, 6.0 mol%) and evacuated and purged with argon three times. Through the septum, 10 mL of dry toluene and aniline (440 µL, 450 mg, 4.80 mmol, 1.20 equiv.) were added. The mixture was stirred at 115 °C for 16 h. The mixture was diluted with water (100 mL) and extracted with ethyl acetate (3 × 200 mL), then washed with saturated NaHCO3 solution (100 mL) and brine (100 mL). The combined organic layers were dried over Na2SO4 and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica, cyclohexane/ethyl acetate; 50:1) to yield the title compound (988 mg, 3.30 mmol, 82%) as a white solid.

Rf = 0.35 (cyclohexane/ethyl acetate; 50:1).

1H NMR (500 MHz, CDCl3) δ = 7.23 (t, J = 7.9 Hz, 2H, HA), 7.01 (dd, J = 7.8, 1.9 Hz, 1H), 6.93 (d, J = 8.5 Hz, 2H), 6.87 (t, J = 7.3 Hz, 1H), 6.59 (dd, J = 7.8, 1.9 Hz, 1H), 6.51 – 6.41 (m, 3H), 6.37 (dd, J = 7.8, 1.8 Hz, 1H), 5.55 (bs, 1H), 3.12 – 2.86 (m, 7H), 2.69 (ddd, J = 13.7, 10.1, 6.8 Hz, 1H) ppm.

13C NMR (126 MHz, CDCl3) δ = 143.74 (Cq.), 141.35 (Cq.), 140.21 (Cq.), 139.64 (Cq.), 139.13 (Cq.), 135.99 (+, CAH), 133.64 (+, CAH), 132.85 (+, CAH), 131.48 (Cq.), 131.34 (+, CAH), 129.28 (+, CAH), 127.55 (+, CAH), 127.04 (+, CAH), 125.99 (+, CAH), 120.17 (+, CAH), 116.09 (+, CAH), 35.35 (–, CH2), 35.01 (–, CH2), 33.95 (–, CH2), 33.93 (–, CH2) ppm.

IR (ATR) ν = 3372 (w, ν(NH)), 3005 (vw), 2922 (0.85), 2851 (vw), 1591 (w), 1563 (w), 1492 (m), 1433 (w), 1305 (w), 1280 (w), 1239 (w), 1173 (w), 1151 (w), 1108 (w), 1091 (w), 1027 (vw), 996 (vw), 977 (vw), 938 (vw), 886 (w), 800 (w), 780 (vw), 741 (m), 716 (w), 693 (m), 659 (w), 642 (w), 615 (vw), 588 (vw) cm–1.

MS (El, 70 eV) m/z (%) = 300 (17) [M+H]+, 299 (73) [M]+, 298 (34) [M–H]+, 195 (78) [M–C8H8]+, 194 (84) [M–C8H9]+, 193 (24) [M–C8H10]+, 104 (100) [C8H5]+.

HRMS (El, C22H21N) calcd. 299.1669; found 299.1670.

The analytical data is consistent with the literature.[2]
Figure S3. $^1$H NMR of 1.

Figure S4. $^{13}$C NMR of 1.
General Procedure of Controlling regioselective C–H Activation using liquid bromoarenes (GP1)

In a sealable vial, (rac)-4-phenylamino[2.2]paracyclophane (150 mg, 500 µmol, 1.00 equiv.), potassium tert-butoxide (70.1 mg, 625 µmol, 1.25 equiv.) and Pd(PPh₃)₄ (28.9 mg, 25 µmol, 5.0 mol%) were added. The vial was evacuated and purged with argon three times. Then, 3 mL of dry toluene and the respective liquid bromoarene (625 µmol, 1.25 equiv.) was added via syringe. The reaction mixture was stirred at 120 °C for 16 h. It was quenched with sat. NH₄Cl solution (5 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified by column chromatography.

General Procedure of Controlling regioselective C–H Activation protocol using solid bromoarenes (GP2)

In a sealable vial, (rac)-4-phenylamino[2.2]paracyclophane (150 mg, 500 µmol, 1.00 equiv.), potassium tert-butoxide (70.1 mg, 625 µmol, 1.25 equiv.), Pd(PPh₃)₄ (28.9 mg, 25.0 µmol, 5.0 mol%), and the respective solid bromoarene (625 µmol, 1.25 equiv.) were added. The vial was evacuated and purged with argon three times. Then, 3 mL of dry toluene was added via syringe. The reaction mixture was stirred at 120 °C for 16 h. It was quenched with sat. NH₄Cl solution (5 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified by column chromatography.
(rac)-4-Phenylamino-7-phenyl[2.2]paracyclophane (3a)

In a sealable vial, (rac)-4-phenylamino[2.2]paracyclophane (150 mg, 500 µmol, 1.00 equiv.), potassium tert-butoxide (112 mg, 1.00 mmol, 2.00 equiv.) and Pd(PPh₃)₄ (28.9 mg, 25.0 µmol, 5.0 mol%) were added. The vial was evacuated and purged with argon three times. Then, 3 mL of dry toluene and bromobenzene (160 µL, 236 mg, 1.50 mmol, 3.00 equiv.) were added via syringe. The reaction mixture was stirred at 120 °C for 16 h. It was quenched with sat. NH₄Cl solution (5 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica, n-hexane/ethyl acetate; 10:1) to yield the title compound (96.0 mg, 2.57 mmol, 51%) as a white solid.

Rᶠ = 0.41 (n-hexane/ethyl acetate; 10:1).

¹H NMR (500 MHz, DMSO-d₆) δ = 7.80 (s, 1H), 7.54 – 7.44 (m, 4H), 7.33 (dt, J = 6.0, 3.2 Hz, 1H), 7.18 (t, J = 7.6 Hz, 2H), 7.07 (d, J = 7.7 Hz, 1H), 6.93 (d, J = 8.0 Hz, 2H), 6.76 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 7.9 Hz, 1H), 6.55 – 6.50 (m, 2H), 6.48 (d, J = 7.8 Hz, 1H), 6.03 (s, 1H). 3.28 (ddd, J = 12.9, 9.8, 2.4 Hz, 1H), 3.05 – 2.93 (m, 2H), 2.90 – 2.74 (m, 2H), 2.73 – 2.59 (m, 2H), 2.40 (ddd, J = 12.6, 10.0, 5.9 Hz, 1H) ppm.

¹³C NMR (126 MHz, DMSO-d₆) δ = 143.78 (C₂q.), 140.91 (C₂q.), 140.11 (C₂q.), 138.98 (C₂q.), 138.40 (C₂q.), 137.15 (C₂q.), 135.67 (C₂q.), 135.02 (+, C₃A_H), 132.37 (+, C₃A_H), 131.49 (+, C₃A_H), 130.11 (C₂q.), 129.54 (+, C₃A_H), 129.18 (+, C₃A_H), 128.86 (+, C₃A_H), 128.56 (+, C₃A_H), 128.48 (+, C₃A_H), 127.80 (+, C₃A_H), 126.31 (+, C₃A_H), 118.91 (+, C₃A_H), 115.60 (+, C₃A_H), 33.98 (--, CH₂), 33.41 (--, CH₂), 33.33 (--, CH₂), 33.09 (--, CH₂) ppm.

IR (ATR) ᶦ = 3378 (vw), 2922 (vw), 2849 (vw), 1729 (vw), 1590 (vw), 1557 (vw), 1496 (w), 1480 (vw), 1431 (vw), 1311 (vw), 1249 (vw), 1174 (vw), 1074 (vw), 1030 (vw), 886 (vw), 795 (vw), 769 (vw), 745 (vw), 693 (vw), 641 (vw), 598 (vw), 524 (vw), 486 (vw), 421 (vw) cm⁻¹.

MS (EI, 70 eV) m/z (%) = 375 (4) [M]⁺, 270 (7) [C₂₈H₁₇N–H]⁺, 166 (47) [C₁₃H₈N]⁺, 105 (10) [C₅H₉]⁺.

HRMS (EI, C₂₈H₂₅N): calcd. 375.1987; found 375.1988.
Figure S5. $^1$H NMR of 3a.

Figure S6. $^{13}$C NMR of 3a.
The crude product was purified by column chromatography (silica, n-pentane/ethyl acetate/dichloromethane; 10:1:1) to yield the title compound (69.3 mg, 173 µmol, 35%) as a yellow, fluorescent solid.

\[ R_f = 0.17 \ (n\text{-hexane}/\text{ethyl acetate}; \ 10:1). \]

$^1$H NMR (400 MHz, CDCl$_3$) δ = 7.75 (d, $J = 8.4$ Hz, 2H), 7.58 (d, $J = 8.0$ Hz, 2H), 7.46 – 7.35 (m, 1H), 7.29 (d, $J = 7.9$ Hz, 1H), 7.10 (dd, $J = 7.8$, 1.8 Hz, 1H), 7.01 (d, $J = 7.9$ Hz, 2H), 6.96 (d, $J = 7.3$ Hz, 1H), 6.63 – 6.51 (m, 3H), 6.47 (dd, $J = 7.9$, 1.8 Hz, 1H), 6.03 (s, 1H), 5.68 (s, 1H), 3.30 (ddd, $J = 13.1$, 10.0, 2.5 Hz, 1H), 3.22 – 3.08 (m, 2H), 3.08 – 2.98 (m, 1H), 2.86 (ddd, $J = 12.7$, 10.2, 2.6 Hz, 1H), 2.81 – 2.67 (m, 2H), 2.59 (ddd, $J = 12.6$, 9.9, 5.5 Hz, 1H) ppm.

$^{13}$C NMR (101 MHz, CDCl$_3$) δ = 145.9 (C$_q$), 142.6 (C$_q$), 141.3 (C$_q$), 139.2 (C$_q$), 139.2 (C$_q$), 138.4 (C$_q$), 135.4 (+, C$_{Ar}$H), 134.3 (C$_q$), 132.5 (+, C$_{Ar}$H), 132.5 (+, C$_{Ar}$H), 131.5 (+, C$_{Ar}$H), 130.0 (+, C$_{Ar}$H), 129.5 (+, C$_{Ar}$H), 129.4 (C$_q$), 128.2 (+, C$_{Ar}$H), 127.1 (+, C$_{Ar}$H), 121.3 (+, C$_{Ar}$H), 119.4 (C$_q$), 117.5 (+, C$_{Ar}$H), 110.0 (C$_q$), 34.6 (−, CH$_2$), 33.7 (−, CH$_2$), 33.6 (−, CH$_2$), 33.3 (−, CH$_2$) ppm.

IR (ATR) $\tilde{v}$ = 3369 (m), 3036 (w), 3007 (w), 2941 (w), 2928 (w), 2905 (w), 2859 (w), 2225 (s), 1601 (w), 1585 (vs), 1557 (vs), 1513 (w), 1497 (vs), 1477 (vs), 1462 (m), 1436 (w), 1411 (m), 1394 (m), 1324 (vs), 1313 (vs), 1285 (s), 1249 (m), 1242 (m), 1203 (w), 1176 (m), 1160 (w), 1133 (w), 1109 (w), 1094 (w), 1078 (w), 1027 (w), 999 (w), 993 (w), 969 (w), 956 (w), 935 (w), 907 (m), 895 (w), 878 (m), 851 (m), 836 (vs), 805 (w), 795 (m), 744 (vs), 728 (vs), 715 (vs), 697 (s), 686 (vs), 645 (w), 620 (w), 613 (w), 595 (m), 572 (s), 554 (w), 535 (m), 510 (vs), 477 (vs), 458 (vs), 424 (s), 409 (s), 392 (m), 382 (s) cm$^{-1}$.

MS (FAB, 3-NBA) $m/z = 400$ [M]$^+$. – HRMS (FAB, 3-NBA, C$_{29}$H$_{24}$N$_2$): calcd. 400.1939; found 400.1940.

HRMS (ESI, C$_{29}$H$_{24}$N$_2$): calcd. 400.1939; found 400.1923.
Figure S7. $^1$H NMR of 3b.

Figure S8. $^{13}$C NMR of 3b.
(rac)-4-N-Phenylamino-7-(4-methoxy)phenyl[2.2]paracyclophane (3c)

The crude product was purified by column chromatography (silica, 
$n$-hexane/ethyl acetate; 20:1) to yield the title compound (82.0 mg,
202 µmol, 39%) as a white solid.

$R_f = 0.19$ ($n$-hexane/ethyl acetate; 20:1).

$^1$H NMR (500 MHz, C$_6$D$_6$) δ = 7.45 (d, $J = 8.6$ Hz, 2H), 7.16 – 7.13 (m, 2H), 7.02 – 6.96 (m, 3H), 6.94 – 6.88 (m, 2H), 6.85 (t, $J = 7.3$ Hz, 1H), 6.81 (dd, $J = 7.9$, 1.9 Hz, 1H), 6.50 (s, 1H), 6.40 (dd, $J = 7.8$, 1.8 Hz, 1H), 6.26 (dd, $J = 7.8$, 1.9 Hz, 1H), 5.68 (s, 1H), 5.14 (s, 1H), 3.43 (s, 3H), 3.42 – 3.38 (m, 1H), 2.97 (ddd, $J = 13.7$, 9.2, 2.0 Hz, 1H), 2.91 – 2.78 (m, 2H), 2.67 – 2.47 (m, 3H), 2.39 (ddd, $J = 13.7$, 10.1, 7.2 Hz, 1H) ppm.

$^{13}$C NMR (126 MHz, C$_6$D$_6$) δ = 159.20 (C$_q$), 144.15 (C$_q$), 139.54 (C$_q$), 139.41 (C$_q$), 139.38 (C$_q$), 138.08 (C$_q$), 137.42 (C$_q$), 135.61 (+, C$_{Ar}$H), 134.41 (C$_q$), 133.00 (+, C$_{Ar}$H), 131.61 (+, C$_{Ar}$H), 131.27 (C$_q$), 130.92 (+, C$_{Ar}$H), 130.42 (+, C$_{Ar}$H), 129.55 (+, C$_{Ar}$H), 128.88 (+, C$_{Ar}$H), 128.35 (+, C$_{Ar}$H), 128.16 (+, C$_{Ar}$H), 120.57 (+, C$_{Ar}$H), 116.63 (+, C$_{Ar}$H), 114.45 (+, C$_{Ar}$H), 54.90 (+, OCH$_3$), 34.65 (–, CH$_2$), 34.04 (–, CH$_2$), 33.89 (–, CH$_2$), 33.78 (–, CH$_2$) ppm.

IR (ATR) $\tilde{\nu} =$ 3361 (vw), 2930 (w, NH), 2635 (vw), 2534 (vw), 2291 (vw), 2167 (vw), 2086 (vw), 1901 (vw), 1781 (vw), 1605 (w), 1484 (w), 1241 (w), 1174 (w), 1035 (w), 836 (w), 750 (w), 620 (w), 487 (w) cm$^{-1}$.

MS (FAB, 3-NBA) $m/z = 405$ [M]$^+$. 

HRMS (FAB, 3-NBA, C$_{29}$H$_{27}$N): calcd. 405.2093; found 405.2093.
Figure S9. $^1$H NMR of 3c.

Figure S10. $^{13}$C NMR of 3c.
The crude product was purified by column chromatography (silica, n-hexane/ethyl acetate; 10:1) to yield the title compound (88.3 mg, 218 µmol, 44%) as a white solid. An analytically pure sample was obtained by recrystallization from heptane.

R_f = 0.26 (n-hexane/ethyl acetate; 10:1).

^1^H NMR (500 MHz, C_6D_6) δ = 7.64 (dd, J = 7.5, 1.8 Hz, 1H), 7.29 – 7.22 (m, 1H), 7.15 – 7.08 (m, 2H), 7.01 (dd, J = 7.8, 2.0 Hz, 1H), 6.92 – 6.86 (m, 2H), 6.85 – 6.80 (m, 2H), 6.69 (dd, J = 8.3, 1.1 Hz, 1H), 6.53 (s, 1H), 6.40 (dd, J = 7.9, 1.9 Hz, 1H), 6.26 (dd, J = 7.8, 1.9 Hz, 1H), 5.63 (s, 1H), 5.13 (s, 1H), 3.30 (s, 3H), 2.95 – 2.84 (m, 1H), 2.79 (dd, J = 13.1, 9.4, 7.0 Hz, 1H), 2.71 (dd, J = 13.2, 9.9, 5.1 Hz, 1H), 2.65 – 2.59 (m, 2H), 2.40 (dd, J = 13.8, 10.2, 7.1 Hz, 1H) ppm.

^13^C NMR (126 MHz, C_6D_6) δ = 156.7 (C_q.), 143.6 (C_q.), 140.5 (C_q.), 139.5 (C_q.), 139.2 (C_q.), 138.8 (C_q.), 135.7 (+, C_AH), 132.9 (+, C_AH), 132.2 (C_q.), 131.3 (C_q.), 131.1 (+, C_AH), 131.0 (C_q.), 130.0 (+, C_AH), 129.7 (+, C_AH), 129.1 (+, C_AH), 128.1 (+, C_AH), 128.0 (+, C_AH), 127.6 (+, C_AH), 126.8 (+, C_AH), 120.9 (+, C_AH), 120.1 (+, C_AH), 116.5 (+, C_AH), 111.1 (+, C_AH), 54.8 (+, OCH_3), 34.6 (–, CH_2), 33.7 (–, CH_2), 33.4 (–, CH_2), 33.4 (–, CH_2) ppm.

IR (ATR) ν = 3390 (m), 3014 (w), 2995 (w), 2955 (w), 2893 (w), 2830 (w), 1589 (vs), 1500 (vs), 1458 (vs), 1449 (m), 1429 (vs), 1407 (w), 1388 (w), 1313 (s), 1285 (m), 1259 (m), 1235 (vs), 1203 (w), 1173 (m), 1162 (m), 1142 (w), 1129 (w), 1106 (m), 1075 (w), 1050 (w), 1024 (s), 992 (w), 977 (w), 960 (w), 948 (w), 895 (s), 875 (w), 851 (w), 822 (w), 800 (m), 790 (w), 754 (vs), 718 (s), 710 (s), 697 (v), 636 (m), 616 (w), 599 (m), 571 (w), 538 (w), 526 (w), 510 (s), 501 (vs), 480 (s), 462 (m), 438 (m), 402 (vs), 380 (vs) cm⁻¹.

MS (FAB, 3-NBA) m/z = 405 [M]+.

HRMS (FAB, 3-NBA, C_{29}H_{27}ON): calcd. 405.2093; found 405.2093.
Figure S11. $^1$H NMR of 3d.

Figure S12. $^{13}$C NMR of 3d.
(rac)-4-N-Phenylamino-7-(2,5-dimethyl)phenyl[2.2]paracyclophane (3e)

The crude product was purified by column chromatography (silica, n-hexane/ethyl acetate; 20:1) to yield the title compound (166 mg, 411 µmol, 82%) as a white solid.

R_f = 0.36 (n-hexane/ethyl acetate; 20:1).

_1H NMR (500 MHz, C_6D_6) δ = 7.71 (s, 1H), 7.25 – 7.20 (m, 3H), 7.17 (dd, J = 7.7, 1.8 Hz, 1H), 7.13 (dd, J = 7.8, 1.9 Hz, 1H), 7.05 – 6.98 (m, 3H), 6.94 (t, J = 7.3 Hz, 1H), 6.59 (s, 1H), 6.55 (dd, J = 7.9, 1.8 Hz, 1H), 6.34 (dd, J = 7.8, 1.9 Hz, 1H), 5.63 (s, 1H), 5.23 (s, 1H), 5.05 (s, 1H), 4.05 (dd, J = 13.8, 9.4, 1.9 Hz, 1H), 2.99 – 2.84 (m, 3H), 2.78 – 2.57 (m, 3H), 2.54 (s, 3H, Me), 2.48 (ddd, J = 13.9, 10.2, 7.0 Hz, 1H), 2.30 (s, 3H, Me) ppm.

_13C NMR (126 MHz, C_6D_6) δ = 143.81 (C_q.), 141.72 (C_q.), 139.84 (C_q.), 139.53 (C_q.), 139.46 (C_q.), 139.19 (C_q.), 136.04 (+, C_ArH), 135.91 (C_q.), 135.45 (C_q.), 133.83 (C_q.), 133.33 (+, C_ArH), 131.39 (+, C_ArH), 130.83 (C_q.), 130.59 (+, C_ArH), 130.13 (+, C_ArH), 129.52 (+, C_ArH), 128.35 (+, C_ArH), 128.16 (+, C_ArH), 127.97 (+, C_ArH), 126.90 (+, C_ArH), 120.63 (+, C_ArH), 116.76 (+, C_ArH), 34.94 (−, CH_2), 33.75 (−, CH_2), 33.73 (−, CH_2), 33.10 (−, CH_2), 21.48 (+, CH_3), 20.23 (+, CH_3) ppm.

IR (ATR) ν = 3988 (w), 3836 (w), 3607 (w), 3372 (w), 2921 (w, NH), 2849 (w), 2322 (w), 2171 (vw), 1741 (w), 1588 (w), 1495 (m), 1308 (w), 1247 (w), 1076 (w), 881 (w), 820 (m), 750 (m), 605 (m), 461 (m) cm⁻¹.

MS (FAB, 3-NBA) m/z = 403 [M]^+.

HRMS (FAB, 3-NBA, C_{30}H_{29}N): calcd. 403.2300; found 403.2299.
Figure S13. $^1$H NMR of 3e.

Figure S14. $^{13}$C NMR of 3e.
The crude product was purified by column chromatography (silica, n-hexane/dichloromethane; 5:1) to yield the title compound (32.6 mg, 284 µmol, 12%) as a white solid.

\[ R_f = 0.29 \text{ (n-hexane/dichloromethane; 5:1).} \]

\(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta = 7.76\) (s, 1H), 7.40 (d, \(J = 8.6\) Hz, 2H), 7.37 – 7.32 (m, 4H), 7.17 (dd, \(J = 8.5, 7.2\) Hz, 2H), 7.12 – 7.02 (m, 9H), 6.97 – 6.88 (m, 2H), 6.79 – 6.72 (m, 1H), 6.62 – 6.53 (m, 2H), 6.52 – 6.45 (m, 2H), 6.02 (s, 1H), 3.06 – 2.91 (m, 2H), 2.90 – 2.74 (m, 2H), 2.71 – 2.57 (m, 2H), 2.50 – 2.41 (m, 2H) ppm.

\(^{13}\)C NMR (101 MHz, DMSO-\(d_6\)) \(\delta = 147.24\) (C\(_q\)), 145.42 (C\(_q\)), 143.85 (C\(_q\)), 139.83 (C\(_q\)), 138.91 (C\(_q\)), 138.41 (C\(_q\)), 137.07 (C\(_q\)), 135.30 (C\(_q\)), 135.24 (C\(_q\)), 134.76 (+, C\(_{Ar}\)H), 132.23 (+, C\(_{Ar}\)H), 131.49 (+, C\(_{Ar}\)H), 130.11 (C\(_q\)), 130.04 (+, C\(_{Ar}\)H), 129.61 (+, C\(_{Ar}\)H), 129.57 (+, C\(_{Ar}\)H), 128.81 (+, C\(_{Ar}\)H), 128.49 (+, C\(_{Ar}\)H), 127.86 (+, C\(_{Ar}\)H), 123.98 (+, C\(_{Ar}\)H), 123.16 (+, C\(_{Ar}\)H), 123.03 (+, C\(_{Ar}\)H), 118.78 (+, C\(_{Ar}\)H), 115.47 (+, C\(_{Ar}\)H), 33.98 (–, CH\(_2\)), 33.62 (–, CH\(_2\)), 33.38 (–, CH\(_2\)), 33.06 (–, CH\(_2\)) ppm.

IR (ATR) \(\tilde{\nu} = 3371\) (m), 3050 (w), 3026 (w), 3006 (w), 2949 (w), 2922 (m), 2888 (w), 2850 (w), 1591 (s), 1562 (m), 1492 (vs), 1483 (vs), 1451 (m), 1434 (vs), 1408 (m), 1391 (w), 1305 (s), 1278 (s), 1237 (m), 1207 (w), 1173 (m), 1150 (m), 1113 (w), 1091 (m), 1075 (w), 1027 (w), 996 (w), 976 (w), 945 (w), 938 (w), 897 (m), 881 (s), 875 (s), 839 (w), 813 (w), 800 (m), 741 (vs), 715 (vs), 693 (vs), 659 (s), 642 (s), 629 (m), 615 (m), 588 (w), 572 (w), 509 (vs), 492 (s), 453 (m), 438 (s), 432 (s), 407 (s), 382 (vs), 375 (vs) cm\(^{-1}\).

MS (FAB, 3-NBA, %) \(m/z = 542\) (87) [M]\(^+\), 299 (80) [C\(_{22}\)H\(_{21}\)N]\(^+\).

HRMS (FAB, [M]\(^+\), C\(_{40}\)H\(_{34}\)N\(_2\)): calcd. 542.2722; found 542.2723.
Figure S15. $^1$H NMR of 3f.

Figure S16. $^{13}$C NMR of 3f.
(rac)-4-N-Phenlamino-7-(2-anthracenyl)phenyl[2.2]paracyclophane (3g)

The crude product was purified by column chromatography (silica, n-hexane/ethyl acetate; 20:1) to yield the title compound (134 mg, 284 µmol, 57%) as a white solid.

$R_f = 0.28$ (n-hexane/ethyl acetate; 20:1).

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta = 8.71$ (s, 1H), 8.61 (s, 1H), 8.21 – 8.15 (m, 2H), 8.14 – 8.09 (m, 2H), 7.84 (s, 1H), 7.67 (dd, $J = 8.7, 1.7$ Hz, 1H), 7.56 – 7.49 (m, 2H), 7.20 (dd, $J = 8.5, 7.2$ Hz, 2H), 7.10 (dd, $J = 7.8, 1.8$ Hz, 1H), 7.01 – 6.93 (m, 2H), 6.78 (m, 2H), 6.72 (s, 1H), 6.65 – 6.60 (m, 1H), 6.51 (dd, $J = 7.8, 1.8$ Hz, 1H), 6.11 (s, 1H), 3.48 – 3.37 (m, 1H), 3.11 – 3.00 (m, 2H), 2.91 (ddd, $J = 12.8, 9.3, 6.9$ Hz, 1H), 2.85 – 2.69 (m, 3H), 2.44 – 2.37 (m, 1H) ppm.

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta = 143.69$ (C$q$), 140.46 (C$q$), 139.01 (C$q$), 138.40 (C$q$), 137.93 (C$q$), 137.58 (C$q$), 135.27 (C$q$), 135.24 (+, C$_{Ar}$H), 132.41 (+, C$_{Ar}$H), 131.71 (C$q$), 131.50 (+, C$_{Ar}$H), 131.45 (C$q$), 131.13 (C$q$), 130.10 (C$q$), 129.99 (C$q$), 129.62 (+, C$_{Ar}$H), 128.83 (+, C$_{Ar}$H), 128.73 (+, C$_{Ar}$H), 128.68 (+, C$_{Ar}$H), 128.15 (+, C$_{Ar}$H), 125.69 (+, C$_{Ar}$H), 125.59 (+, C$_{Ar}$H), 125.36 (+, C$_{Ar}$H), 119.03 (+, C$_{Ar}$H), 115.81 (+, C$_{Ar}$H), 34.00 (–, CH$_2$), 33.61 (–, CH$_2$), 33.33 (–, CH$_2$), 33.13 (–, CH$_2$) ppm.

IR (ATR) $\tilde{\nu} = 3051$ (vw), 2921 (w, NH), 2851 (w), 1621 (w), 1449 (w), 1271 (w), 1147 (w), 956 (w), 882 (m), 724 (m), 602 (w), 473 (m) cm$^{-1}$.

MS (FAB, 3-NBA) $m/z = 475$ [M]+.

HRMS (FAB, 3-NBA, $C_{36}H_{29}$N): calcd. 475.2300; found 475.2300.
Figure S17. $^1$H NMR of 3g.

Figure S18. $^{13}$C NMR of 3g.
(rac)-4-N-Phenylamino-7-(4-N-carbazolyl)phenyl[2.2]paracyclophane (3h)

The crude product was purified by column chromatography (silica, n-hexane/ethyl acetate; 20:1) to yield the title compound (32.6 mg, 284 µmol, 12%) as a white solid.

$R_f = 0.29$ (n-hexane/ethyl acetate; 20:1).

$^1$H NMR (500 MHz, C$_6$D$_6$) δ = 8.13 (dd, $J = 7.6$, 1.0 Hz, 2H), 7.57 – 7.49 (m, 4H), 7.42 – 7.34 (m, 4H), 7.32 – 7.27 (m, 2H), 7.19 – 7.16 (m, 2H), 7.02 (dd, $J = 7.8$, 1.9 Hz, 1H), 6.97 – 6.92 (m, 2H), 6.88 (t, $J = 7.3$ Hz, 1H), 6.78 (dd, $J = 7.9$, 1.9 Hz, 1H), 6.53 (s, 1H), 6.39 (dd, $J = 7.9$, 1.8 Hz, 1H), 6.28 (dd, $J = 7.9$, 1.9 Hz, 1H), 5.72 (s, 1H), 5.18 (s, 1H), 3.38 (ddd, $J = 12.7$, 10.2, 3.0 Hz, 1H), 3.00 – 2.87 (m, 2H), 2.70 – 2.61 (m, 1H), 2.61 – 2.48 (m, 2H), 2.43 (ddd, $J = 13.8$, 10.1, 7.1 Hz, 1H) ppm.

$^{13}$C NMR (126 MHz, C$_6$D$_6$) δ = 143.64 (C$_{q}$), 141.55 (C$_{q}$), 140.86 (C$_{q}$), 140.50 (C$_{q}$), 139.32 (C$_{q}$), 139.28 (C$_{q}$), 138.30 (C$_{q}$), 136.51 (C$_{q}$), 136.20 (C$_{q}$), 135.76 (+, C$_{Ar}$H), 133.02 (+, C$_{Ar}$H), 131.66 (+, C$_{Ar}$H), 131.04 (+, C$_{Ar}$H), 130.53 (C$_{q}$), 130.41 (+, C$_{Ar}$H), 129.61 (+, C$_{Ar}$H), 128.35 (+, C$_{Ar}$H), 128.26 (+, C$_{Ar}$H), 127.45 (+, C$_{Ar}$H), 126.40 (+, C$_{Ar}$H), 124.15 (C$_{q}$), 121.09 (+, C$_{Ar}$H), 120.84 (+, C$_{Ar}$H), 120.52 (+, C$_{Ar}$H), 117.26 (+, C$_{Ar}$H), 110.33 (+, C$_{Ar}$H), 34.80 (–, CH$_2$), 33.97 (–, CH$_2$), 33.81 (–, CH$_2$), 33.67 (–, CH$_2$) ppm.

IR (ATR) $\tilde{\nu} = 3990$ (w), 3891 (w), 3729 (w), 3532 (w), 3378 (w), 3035 (w), 2922 (m, NH), 2325 (w), 1727 (w), 1590 (m), 1449 (m), 1313 (m), 1228 (m), 1017 (w), 906 (w), 837 (w), 746 (s), 498 (m), 422 (m) cm$^{-1}$.

MS (FAB, 3-NBA) $m/z = 540$ [M]$^+$. 

HRMS (FAB, 3-NBA, C$_{40}$H$_{32}$N$_2$): calcd. 540.2565; found 540.2566.
Figure S19. $^1$H NMR of 3h.

Figure S20. $^{13}$C NMR of 3h.
**\((\text{rac})-4,N,N\text{-Diphenylamino}-7\text{-phenyl}[2.2]\text{paracyclophane (4)}\)**

In a sealable vial, \((\text{rac})-4\text{-phenylamino}[2.2]\text{paracyclophane}\) (150 mg, 500 µmol, 1.00 equiv.), potassium tert-butoxide (112 mg, 1.00 mmol, 2.00 equiv.) and Pd(PPh\(_3\))\(_4\) (28.9 mg, 25.0 µmol, 5.0 mol%) were added. The vial was evacuated and purged with argon three times. Then, 3 mL of dry toluene and bromobenzene (160 µL, 236 mg, 1.50 mmol, 3.00 equiv.) were added via syringe. The reaction mixture was stirred at 120 °C for 16 h. It was quenched with sat. NH\(_4\)Cl solution (5 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over Na\(_2\)SO\(_4\) and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica, \(n\)-hexane/ethyl acetate; 10:1) to yield the title compound (20.3 mg, 45.0 µmol, 9%) as a white solid. An analytically pure sample was obtained by recrystallization from ethanol.

\(R_f = 0.52\) (\(n\)-hexane/ethyl acetate; 10:1).

\(^1\text{H NMR (}500\text{ MHz, CDCl}_3\) \(\delta = 7.51\) (d, \(J = 6.7\) Hz, 2H), 7.45 (t, \(J = 7.7\) Hz, 2H), 7.35 – 7.30 (m, 5H), 7.25 – 7.22 (m, 4H), 7.17 (dd, \(J = 7.8, 1.8\) Hz, 1H), 7.15 – 7.10 (m, 2H), 6.75 (qd, \(J = 7.8, 1.8\) Hz, 2H), 6.45 (s, 1H), 6.39 – 6.35 (dd, \(J = 8.0, 1.8\) Hz, 1H), 5.82 (s, 1H), 3.46 – 3.39 (m, 1H), 3.15 (ddd, \(J = 13.2, 9.5, 5.6\) Hz, 1H), 3.01 (ddd, \(J = 13.4, 9.9, 3.8\) Hz, 1H), 2.83 (ddd, \(J = 13.6, 9.5, 3.8\) Hz, 1H), 2.77 – 2.69 (m, 1H), 2.61 – 2.46 (m, 3H) ppm.

\(^{13}\text{C NMR (}126\text{ MHz, CDCl}_3\) \(\delta = 149.2\) (2C, C\(_q\)), 145.7 (C\(_q\)), 140.8 (C\(_q\)), 140.0 (C\(_q\)), 139.1 (C\(_q\)), 137.3 (C\(_q\)), 137.0 (C\(_q\)), 135.8 (+, C\(_\text{Ar}\)H), 132.1 (+, C\(_\text{Ar}\)H), 131.6 (+, C\(_\text{Ar}\)H), 130.7 (+, C\(_\text{Ar}\)H), 129.9 (+, C\(_\text{Ar}\)H), 129.6 (+, C\(_\text{Ar}\)H), 129.5 (+, C\(_\text{Ar}\)H), 129.5 (+, 4C, C\(_\text{Ar}\)H), 128.6 (+, 2C, C\(_\text{Ar}\)H), 126.5 (+, C\(_\text{Ar}\)H), 126.3 (+, 4C, C\(_\text{Ar}\)H), 125.6 (+, C\(_\text{Ar}\)H), 124.3 (+, 2C, C\(_\text{Ar}\)H), 35.2 (2C, CH\(_2\)), 34.4 (–, 2C, CH\(_2\)), 34.2 (–, CH\(_3\)) ppm.

IR (ATR) \(\tilde{\nu} = 3054\) (vw), 3030 (w), 2922 (w), 2891 (w), 2850 (w), 1585 (m), 1482 (vs), 1446 (m), 1442 (m), 1434 (m), 1411 (m), 1289 (m), 1264 (m), 1244 (m), 1201 (w), 1177 (w), 1154 (w), 1109 (w), 1089 (w), 1072 (w), 1028 (w), 1009 (w), 959 (w), 933 (w), 918 (w), 892 (w), 866 (w), 846 (w), 824 (w), 807 (w), 795 (w), 748 (vs), 717 (m), 694 (vs), 654 (m), 626 (m), 612 (m), 591 (w), 560 (w), 552 (w), 507 (s), 494 (m), 480 (m), 463 (m), 456 (m), 449 (m), 409 (w), 388 (w), 380 (w) cm\(^{-1}\).

MS (FAB, 3-NBA) \(m/z = 451\) [M]\(^+\).

HRMS (FAB, 3-NBA, C\(_{34}\)H\(_{29}\)N): calcd. 451.2300; found 451.2298.
Figure S21. $^1$H NMR of 4.

Figure S22. $^{13}$C NMR of 4.
2,5-Dimethyl-N-phenylaniline (5)

In a sealable vial, 2-bromo-1,4-dimethylbenzene (1.00 g, 746 μL, 5.40 mmol, 1.00 equiv.), aniline (1.21 g, 1.18 mL, 13.0 mmol, 2.40 equiv.), sodium tert-butanolate (1.45 g, 15.1 mmol, 2.80 equiv.), XPhos (51.5 mg, 108 μmol, 2.0 mol%) and Pd$_2$dba$_3$ (24.7 mg, 27.0 μmol, 0.5 mol%) was dissolved in dry dioxane (22 mL). The mixture was heated to 100 °C for 12 h. After cooling to room temperature, ammonium chloride (sat. aq. solution, 20 mL). The phases were separated and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over sodium sulfate and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (silica, n-pentane/EtOAc, 6:1) to obtain the title compound (1.05 g, 5.32 mmol, 98%) as a yellow oil that crystallized upon prolonged standing.

R$_f$ = 0.68 (n-pentane/ethyl acetate; 6:1).

$^1$H NMR (500 MHz, CDCl$_3$) δ = 7.33 – 7.28 (m, 2H, $H_Ar$), 7.13 (d, $J$ = 7.7 Hz, 1H, $H_Ar$), 7.12 (d, $J$ = 1.7 Hz, 1H, $H_Ar$), 7.02 – 6.98 (m, 2H, $H_Ar$), 6.95 (tt, $J$ = 7.3, 1.1 Hz, 1H, $H_Ar$), 6.81 (dd, $J$ = 7.6, 1.8 Hz, 1H, $H_Ar$), 6.74 (s, 1H, NH), 2.33 (s, 3H, CH$_3$) ppm.

$^{13}$C NMR (126 MHz, CDCl$_3$) δ = 144.2 (C$_q$), 141.1 (C$_q$), 136.6 (C$_q$), 130.9 (+, C$_A$H), 129.4 (+, 2C, C$_A$H), 125.4 (C$_q$), 122.9 (+, C$_A$H), 120.4 (+, C$_A$H), 119.6 (+, C$_A$H), 117.5 (+, 2C, C$_A$H), 21.3 (+, CH$_3$), 17.6 (+, CH$_3$) ppm.

IR (ATR) $\tilde{\nu}$ = 3479 (w), 3471 (w), 3461 (w), 3452 (w), 3438 (w), 3429 (w), 3388 (w), 3369 (w), 3361 (w), 3037 (w), 1598 (w), 1553 (w), 1455 (m), 1441 (m), 1417 (s), 1306 (w), 1259 (m), 1241 (w), 1154 (w), 1120 (w), 1058 (w), 1034 (w), 1017 (m), 1007 (m), 960 (w), 902 (w), 885 (w), 799 (w), 759 (vs), 724 (vs), 656 (s), 646 (m), 592 (w), 582 (w), 567 (w), 552 (w), 530 (w), 516 (w), 509 (w), 496 (m), 486 (m), 473 (w), 453 (w), 442 (s), 424 (s), 395 (m), 382 (m) cm$^{-1}$.

MS (EI, 70 eV) m/z = 197 [M]$^+$.  
HRMS (EI, 70 eV, C$_{14}$H$_{15}$N): calcd. 197.1204; found 197.1204.
Figure S23. $^1$H NMR of 5.

Figure S24. $^{13}$C NMR of 5
2,5-Dimethyl-N,N-diphenylaniline (6)

In a sealable vial, 2,5-dimethyl-N-phenylaniline (150 mg, 760 μmol, 1.00 equiv.), potassium tert-butoxide (107 mg, 950 μmol, 1.25 equiv.) and Pd(PPh₃)₄ (43.9 mg, 38.0 μmol, 5.0 mol%) were added. The vial was evacuated and purged with argon three times. Then, 4.5 mL dry toluene and bromobenzene (176 mg, 131 μL, 950 μmol, 1.25 equiv.) was added via syringe. The reaction mixture was stirred at 120 °C for 16 h. It was quenched with sat. NH₄Cl solution (5 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica, n-pentane/EtOAc, 50:1) to obtain the title compound (63.0 mg, 231 μmol, 22%) as a colorless solid.

Rᵣ = 0.65 (n-pentane/ethyl acetate; 50:1).

¹H NMR (400 MHz, CDCl₃) δ = 7.24 – 7.17 (m, 4H, HAᵣ), 7.13 (d, J = 7.6 Hz, 1H, HAᵣ), 7.02 – 6.94 (m, 6H, HAᵣ), 6.94 – 6.88 (m, 2H, HAᵣ), 2.27 (s, 3H, CH₃), 1.99 (s, 3H, CH₃) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 147.6 (C₀, 2C), 145.2 (C₀), 137.2 (C₀), 133.5 (C₀), 131.6 (+, CA₂H), 130.3 (+, CA₂H), 129.1 (+, CA₂H), 127.0 (+, CA₂H), 121.6 (+, CA₂H), 121.3 (+, CA₂H), 21.0 (+, CH₃), 18.2 (+, CH₃) ppm.

IR (ATR) ν = 3060 (w), 3034 (w), 3019 (w), 2917 (w), 2850 (w), 2835 (vw), 1863 (vw), 1717 (vw), 1704 (vw), 1584 (s), 1487 (vs), 1458 (m), 1448 (m), 1404 (w), 1375 (w), 1327 (m), 1306 (s), 1292 (vs), 1276 (s), 1266 (vs), 1215 (m), 1173 (m), 1153 (w), 1123 (m), 1077 (w), 1027 (m), 997 (w), 967 (w), 952 (w), 922 (w), 899 (w), 888 (w), 827 (w), 812 (s), 755 (vs), 747 (vs), 728 (vs), 691 (vs), 639 (m), 628 (m), 618 (w), 585 (w), 555 (w), 524 (w), 504 (s), 483 (s), 458 (s), 416 (w), 404 (w), 377 (w) cm⁻¹.

MS (EI, 70 eV) m/z = 273 [M]+.

HRMS (EI, 70 eV, C₂₀H₁₉N): calcd. 273.1517; found 273.1515.
Figure S25. $^{13}$C NMR of 6.

Figure S26. $^{13}$C NMR of 6
4 GC Analysis

Table S1. GC calibration data for the starting material 1 with biphenyl as standard.

| standard /g | standard /mmol | 1 /g | 1 /mmol | molar ratio 1/standard | GC Signal ratio 1/standard |
|-------------|----------------|------|---------|------------------------|----------------------------|
| 0.0174      | 0.1128         | 0.0331 | 0.1105 | 0.98                   | 3.25                       |
| 0.0192      | 0.1245         | 0.0298 | 0.0995 | 0.80                   | 2.66                       |
| 0.0140      | 0.0908         | 0.0238 | 0.0795 | 0.88                   | 2.49                       |
| 0.0179      | 0.1161         | 0.0178 | 0.0594 | 0.51                   | 1.46                       |
| 0.0148      | 0.0960         | 0.0119 | 0.0397 | 0.41                   | 0.98                       |
| 0.0155      | 0.1005         | 0.0066 | 0.0220 | 0.22                   | 0.63                       |

Figure S27. Calibration line for the starting material 1.

The calibration line is given by the equation:

\[ y = 3.4392x - 0.2667 \]
Table S2. GC calibration data for the product 3a with biphenyl as standard.

| standard /g | standard /mmol | 3a /g | 3a /mmol | molar ratio 3a /standard | GC Signal ratio 3a/standard |
|-------------|----------------|-------|----------|-------------------------|---------------------------|
| 0.0078      | 0.0506         | 0.0143 | 0.0381   | 0.75                    | 3.53                      |
| 0.0087      | 0.0564         | 0.0104 | 0.0277   | 0.49                    | 1.72                      |
| 0.0070      | 0.0454         | 0.0085 | 0.0226   | 0.50                    | 1.82                      |
| 0.0075      | 0.0486         | 0.0069 | 0.0184   | 0.38                    | 1.40                      |
| 0.0083      | 0.0538         | 0.0029 | 0.0077   | 0.14                    | 0.35                      |

Figure S28. GC calibration line for product 3a.
4. Controlling Selectivity and Optimization of Reaction Conditions

The initial screening was focused on temperature. Additionally, three halobenzenes were tested to get an insight on the halide preferences (Table 1). The differences between chloro, bromo, and iodobenzene were insignificant. Upon lowering the reaction temperature to 100 °C (entry 2), the conversion slightly improved. Upon further decreasing the temperature to 80 °C (entry 3), the conversion for chlorobenzene reaches a moderate conversion of 60%, while the conversions for the bromo- and iodobenzene stay the same. At 60 °C, the conversions significantly drop to the 21–31% range. The monitoring of TLC showed that side product 4 is no longer formed at this temperature. Lowering the temperature to 40 °C (entry 5) and room temperature (entry 6), the conversion falls off to the 11–16% range.

Table 1. Screening of temperature dependence and halide on the conversion rate and yield to 3a:

All reactions were performed on a 250 µmol scale with biphenyl as internal standard and the conversions were determined by gas chromatography.\textsuperscript{[139]}

\begin{table}[h]
\centering
\begin{tabular}{cccccc}
\hline
Entry & Temperature & Halide & Conversion & Halide & Conversion & Halide & Conversion \\
      & [°C]        &       & [%]       &       & [%]       &       & [%]       \\
\hline
1    & 120         & PhCl  & 43        & PhBr  & 45        & PhI   & 37        \\
2    & 100         & PhCl  & 40        & PhBr  & 47        & PhI   & 48        \\
3    & 80          & PhCl  & 60        & PhBr  & 46        & PhI   & 49        \\
4    & 60          & PhCl  & 21        & PhBr  & 30        & PhI   & 31        \\
5    & 40          & PhCl  & 16        & PhBr  & 14        & PhI   & 15        \\
6    & r.t.        & PhCl  & 11        & PhBr  & 11        & PhI   & 11        \\
\hline
\end{tabular}
\end{table}

Next, the catalyst source was screened as shown in Table 2. The temperature was fixed to 60 °C so that the formation of sequential coupling product 4 could be excluded. This was accompanied by an increase of the equivalents of the bromobenzene to three. While the initial catalyst system Pd\textsubscript{2}dba\textsubscript{3}/SPhos gave a nearly identical conversion as during the temperature screening with 31% (entry 1), the tetrakis(triphenylphosphine)palladium(0) catalyst in entry 2 gave a conversion of 52%. All other tested catalysts, such as Pd(OAc)\textsubscript{2}, [Pd(dppf)]Cl\textsubscript{2}, [Pd(PPh\textsubscript{3})\textsubscript{3}]Cl\textsubscript{2}, and PEPPSI-IPr (entries 3–6) gave no conversion. From this screening it can be concluded, that Pd(0) catalysts do promote the C–H activation, while all
Pd(II) catalysts are inactive in both C–H activation and C–N cross-coupling, which was monitored by TLC.

**Table 2. Screening of Catalyst Systems:**
All reactions were performed on a 250 μmol scale with biphenyl as an internal standard and the conversions were determined by gas chromatography.

Next, the influence of monodentate phosphine ligands was evaluated in Table 3 with Pd3dba3 as a palladium source. Both, the already tested SPhos (entry 1) and XPhos (entry 2), perform with identical conversions of 31%, while RuPhos gives a lower conversion of 22% and tBuPhos is nearly inactive with only 2%. In summary, the Pd(PPh3)4 catalyst system (Table 2, entry 2) is superior to all of the tested Pd3dba3/ligand systems.

**Table 3. Screening of Phosphine Ligands:**
All reactions were performed on a 250 μmol scale with biphenyl as an internal standard and the conversions were determined by gas chromatography.
The next parameter to screen was the influence of the solvent as summarized in Table 4. Again, the initial solvent toluene was superior to all other polar solvents examined.

**Table 4. Screening of Solvents:**

All reactions were performed on a 250 µmol scale with biphenyl as an internal standard and the conversions were determined by gas chromatography.

| Entry | Solvent  | Conversion [%] |
|-------|----------|----------------|
| 1     | Toluene  | 46             |
| 2     | THF      | 3              |
| 3     | DMF      | 4              |
| 4     | Dioxane  | 4              |

The influence of the base was evaluated next (Table 5). Once more, the initially used KOtBu (entry 1) was the best base with 51% conversion, while Cs₂CO₃ gave only trace amounts. KOH and K₃PO₄ were inactive in promoting the C–H activation.

**Table 5. Screening of Bases:**

All reactions were performed on a 250 µmol scale with biphenyl as an internal standard and the conversions were determined by gas chromatography.

| Entry | Base       | Conversion [%] |
|-------|------------|----------------|
| 1     | KOtBu      | 51             |
| 2     | Cs₂CO₃     | 2              |
Finally, the influence of equivalents of KO'Bu was screened as the last variable to influence the conversion (Table 6). While an excess of the base with 8 and 4 equivalents (entries 1–2) impede the reaction with conversions of 15% and 32%, respectively, the optimal number of equivalents is slightly above equimolar amounts (entries 3–5) giving conversions of 51–46%. Equimolar and sub-equimolar amounts of KO'Bu (entries 6–7) again hamper the reaction with 29% and 23% respectively. The absence of base (entry 8) prohibits the reaction completely. Therefore, a decrease of the base to 1.25 equivalents was chosen in further investigation.

**Table 6. Screening of equivalents of KO'Bu:**

All reactions were performed on a 250 µmol scale with biphenyl as an internal standard and the conversions were determined by gas chromatography.

| Entry | Equivalents of KO'Bu | Conversion [%] |
|-------|---------------------|----------------|
| 1     | 8.0                 | 15             |
| 2     | 4.0                 | 32             |
| 3     | 2.0                 | 51             |
| 4     | 1.5                 | 47             |
| 5     | 1.25                | 46             |
| 6     | 1.0                 | 29             |
| 7     | 0.75                | 23             |
| 8     | 0                   | 0              |

**Generality, compatibility and synthetic scope of PCP derivatives:**

With the optimized reaction conditions, a series of aromatic bromides were screened (Table 7). Electron poor bromoarenes (entries 1–5) such as 4-nitro, 4-nitrile, 4-trifluoromethyl, or 4-acetyl did not give the desired products. Unfortunately, the 4-triazinyl phenyl did not give any product either. Next, electron-donating bromo-arenes were tested (entries 6–11), which yielded the desired respective products in varying yields. In each case, the target structure was either verified by single-crystal analysis or the presence of the N–H band in IR spectroscopy.
Table 7. Summary of the synthetic screening and scope of PCP derivatives.

![Chemical structures](image)

| Entry | R-Br          | Code | Isolated yield [%] |
|-------|---------------|------|---------------------|
| 1     | O₂N-Br        | b    | –                   |
| 2     | NC-Br         | c    | –                   |
| 3     | F₃C-Br        | d    | –                   |
| 4     | Me-O-Br       | e    | –                   |
| 5     | Ph₂N-Br       | f    | –                   |
| 6     | phenyl-Br     | g    | 57                  |
| 7     | Ph₂N-Br       | h    | 43                  |
| 8     | phenyl-Br     | i    | 12                  |
| 9     | methyl-Br     | j    | 82                  |
| 10    | MeO-Br        | k    | 39                  |
| 11    | Ph-O-Br       | l    | 44                  |
| 12    | N-Br          | m    | –                   |
13

14

15

16

n
–
o
–
p
–
q
–
5 Crystallographic Data

3a: yellow crystals, C$_2$H$_2$N, $M_t$ = 375.49, crystal size 0.16 × 0.12 × 0.03 mm, monoclinic, space group $P2_1/c$ (No. 14), $a = 12.8987(8)$ Å, $b = 9.8224(6)$ Å, $c = 16.9910(9)$ Å, $\beta = 109.710(4)^\circ$, $V = 2026.6(2)$ Å$^3$, $Z = 4$, $\rho = 1.313$ Mg/m$^3$, $\mu$(Cu-K$\alpha$) = 0.53 mm$^{-1}$, $F(000) = 800$, $T = 123(2)$ K, $2\theta_{\text{max}}$ = 145.0$^\circ$, 18099 reflections, of which 3939 were independent ($R_{\text{int}}$ = 0.086), 250 parameters, 64 restraints, $R_1 = 0.115$ (for 2892 I > 2σ(I)), $wR_2 = 0.232$ (all data), $S = 1.11$, largest diff. peak / hole = 0.49 / -0.46 e Å$^{-3}$, one CH$_2$ atom in each C$_2$H$_4$ link is disordered, the unsubstituted cyclophane phenyl ring disordered (see cif-file for details).

3c: colorless crystals, C$_2$H$_2$NO, $M_t$ = 405.51, crystal size 0.12 × 0.08 × 0.04 mm, monoclinic, space group $P2_1/c$ (No. 14), $a = 25.0150(10)$ Å, $b = 10.2604(4)$ Å, $c = 17.4735(7)$ Å, $\beta = 108.614(2)^\circ$, $V = 4250.2(3)$ Å$^3$, $Z = 8$, $\rho = 1.267$ Mg/m$^3$, $\mu$(Cu-K$\alpha$) = 0.58 mm$^{-1}$, $F(000) = 1728$, $T = 123(2)$ K, $2\theta_{\text{max}}$ = 145.8$^\circ$, 43462 reflections, of which 8367 were independent ($R_{\text{int}}$ = 0.074), 567 parameters, 2 restraints, $R_1 = 0.069$ (for 6623 I > 2σ(I)), $wR_2 = 0.188$ (all data), $S = 1.03$, largest diff. peak / hole = 0.69 / -0.28 e Å$^{-3}$.

3d: colorless crystals, C$_2$H$_2$NO, $M_t$ = 405.51, crystal size 0.16 × 0.08 × 0.04 mm, orthorhombic, space group $Pna2_1$ (No. 33), $a = 18.3783(7)$ Å, $b = 7.5162(3)$ Å, $c = 31.1693(11)$ Å, $V = 4305.6(3)$ Å$^3$, $Z = 8$, $\rho = 1.251$ Mg/m$^3$, $\mu$(Cu-K$\alpha$) = 0.58 mm$^{-1}$, $F(000) = 1728$, $T = 123(2)$ K. Due to the bad quality of the data of 3d the data were not deposited with The Cambridge Crystallographic Data Centre.

4: colorless crystals, C$_3$H$_9$N, $M_t$ = 451.58, crystal size 0.16 × 0.12 × 0.03 mm, monoclinic, space group $P2_1/c$ (No. 14), $a = 8.0629(2)$ Å, $b = 14.9366(5)$ Å, $c = 20.2733(6)$ Å, $\beta = 97.692(2)^\circ$, $V = 2419.59(12)$ Å$^3$, $Z = 4$, $\rho = 1.240$ Mg/m$^3$, $\mu$(Cu-K$\alpha$) = 0.54 mm$^{-1}$, $F(000) = 960$, $T = 123(2)$ K, $2\theta_{\text{max}}$ = 144.6$^\circ$, 16489 reflections, of which 4719 were independent ($R_{\text{int}}$ = 0.048), 316 parameters, $R_1 = 0.057$ (for 3706 I > 2σ(I)), $wR_2 = 0.126$ (all data), $S = 1.10$, largest diff. peak / hole = 0.23 / -0.25 e Å$^{-3}$.

6: colorless crystals, C$_3$H$_9$N, $M_t$ = 273.36, crystal size 0.24 × 0.06 × 0.03 mm, monoclinic, space group $P2_1/n$ (No. 14), $a = 17.9205(7)$ Å, $b = 9.9891(4)$ Å, $c = 36.7210(14)$ Å, $\beta = 104.030(2)^\circ$, $V = 6377.3(4)$ Å$^3$, $Z = 16$, $\rho = 1.139$ Mg/m$^3$, $\mu$(Cu-K$\alpha$) = 0.550 mm$^{-1}$, $F(000) = 2236$, $T = 298(2)$ K, $2\theta_{\text{max}}$ = 144.4$^\circ$, 69630 reflections, of which 12551 were independent ($R_{\text{int}}$ = 0.036), 765 parameters, 648 restraints (general RIGU restraint), $R_1 = 0.046$ (for 10026 I > 2σ(I)), $wR_2 = 0.132$ (all data), $S = 1.01$, largest diff. peak / hole = 0.15 / -0.18 e Å$^{-3}$.

CCDC 2009020 (3a), 2009021 (3c), 2009022 (4), and 2009023 (6) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Due to the bad quality of the data of 3d (esp542) the data were not deposited with The Cambridge Crystallographic Data Centre.
Figure S29. Molecular structure of 3a (minor disordered parts omitted for clarity; displacement parameters are drawn at 50 % probability level).

Figure S30. Molecular structure of 3c (displacement parameters are drawn at 50 % probability level).
Figure S31. Molecular structure of the first crystallographic independent molecules of 3c (displacement parameters are drawn at 50 % probability level).

Figure S32. Molecular structure of the second crystallographic independent molecules of 3c (displacement parameters are drawn at 50 % probability level).
Figure S33. Molecular structure of 3d (Mercury plot).

Figure S34. Molecular structure of the second crystallographic independent molecules of 3d (isotropic displacement parameters are drawn at 50 % probability level).
Figure S35. Molecular structure of 4 (displacement parameters are drawn at 50 % probability level).

Figure S36. Molecular structure of 6 (displacement parameters are drawn at 30 % probability level).
Figure S37. Molecular structure the first crystallographic independent molecule of 6 (displacement parameters are drawn at 30 % probability level).
6 References

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[2] P. Lennartz, G. Raabe, C. Bolm, Isr. J. Chem. 2012, 52, 171–179.