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Synthesis of Planar Chiral Carbazole Derivatives Bearing a [2.2]Paracyclophane Skeleton

Petra Lennartz,[a] Gerhard Raabe,[a] and Carsten Bolm*[a]

Abstract: The synthesis of planar chiral carbazoles bearing a [2.2]paracyclophane backbone is described. Starting from readily available 4-bromo[2.2]paracyclophane planar chiral carbazoles are obtained in a two-step synthesis by Pd-catalyzed C–N cross-coupling and subsequent oxidative cyclization.

Keywords: carbazoles · cyclophanes · oxidative cyclization · palladium · planar chirality

1. Introduction

Since the first directed synthesis of [2.2]paracyclophane (**1a**, Figure 1) by Cram and Steinberg in 1951[1] there has been an ongoing interest in the unique chemistry of this class of compounds.[2] In general, [2.2]paracyclophanes have two benzene rings, which are connected by two ethylene bridges, resulting in a boat-like shape of the arenes.[3] Aryl substitution can lead to planar chiral compounds, which have successfully been applied as ligands, auxiliaries or catalysts in stereoselective reactions.[4] Although many [2.2]paracyclophanes with heterocyclic substituents have been described,[5] only a few compounds with heterocycles fused to one of the benzene rings are known.[5,6] This may not be surprising considering that the synthesis of 4,5-disubstituted [2.2]paracyclophanes is mainly restricted to the use of 4-hydroxy-[2.2]paracyclophane derivatives as starting materials.[7,8] Regioisomeric mixtures have often been obtained when other monosubstituted [2.2]paracyclophanes were applied.[9] For the functionalization of more "classical" arenes efficient *ortho*-directing groups have been found, which opened new pathways for metal-catalyzed direct C–H arylations.[10] Both inter- and intramolecular coupling reactions have been developed, and among the latter oxidative biaryl couplings have proved particularly useful for the preparation of heterocycles including carbazoles.[11]

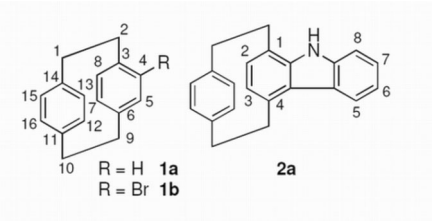

Figure 1. [2.2]Paracyclophane (**1a**) and planar chiral carbazole **2a**.

In continuation of our studies on the synthesis of disubstituted [2.2]paracyclophanes[7f–h,9c,12] we became interested in planar chiral carbazoles such as **2a** (Figure 1), which we hypothesized to be relevant for polymer and materials science due to the extended π-system of the carbazole core.[13] From a synthetic point of view, their preparation by metal-catalyzed direct functionalization/arylation was expected to provide new insights and opportunities in the chemistry of [2.2]paracyclophane modifications.

2. Results

Carbazoles **2** were envisaged to be accessible by two approaches: First, direct *ortho*-arylation of amide **4** followed by intramolecular oxidative C–N bond formation (Scheme 1, path a),[14] or, second, via diarylamine **5** and subsequent oxidative C–C coupling reaction (path b).[15]

Initial attempts to directly arylate 4-amido-[2.2]paracyclophanes **4** (with $R^1 = O$*t*Bu or Et; Scheme 1, path a) under conditions similar to those reported for the direct arylation of anilides[16] remained unsuccessful. It was therefore decided to follow path b (Scheme 1). As first step diarylamine syntheses by palladium-catalyzed

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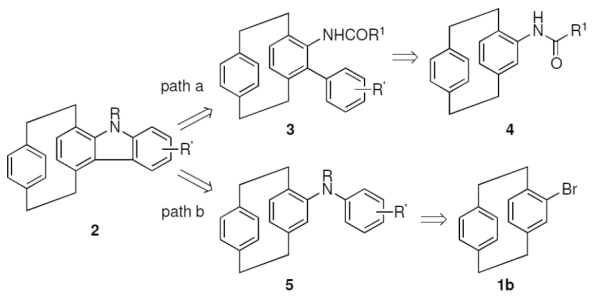


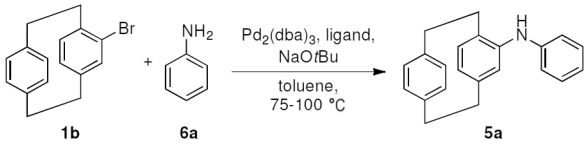
Scheme 1. Retrosynthetic approaches to carbazoles **2**.

Buchwald–Hartwig aminations were investigated. Although such cross-couplings are common for C–N bond formations,[17] only a few examples of this reaction using [2.2]paracyclophanes as aryl components are known.[6c,d,18] Moreover, to the best of our knowledge, only a single report covered the use of aniline derivatives as *N*-nucleophiles.[6h] For our study, the readily available 4-bromo-[2.2]paracyclophane (**1b**, Scheme 1)[19] was chosen as aryl halide. Although **1b** can also be prepared in its enantiomerically pure form,[7b,18b] each experiment reported here was carried out using racemic substrates. In the presence of NaO*t*Bu as base and aniline (**6a**) as nitrogen nucleophile, 4-*N*-(phenyl)amino[2.2]paracyclophane (**5a**) was formed in good yields within 4 h using $Pd_2(dba)_3$ and 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (X-Phos) as ligand in toluene (Table 1, entries 1–7). Starting with 5 mol% of $Pd_2(dba)_3$ and 15% of the ligand the product was formed in 79% yield. A brief screening of the reaction conditions revealed that a reduction of the $Pd_2(dba)_3$ loading to 3 mol% was possible (entry 2). With less than 3 mol% of $Pd_2(dba)_3$ the yield decreased (entries 3 and 4), and neither raising the temperature nor extending the reaction time improved the results (entries 5–7). Two other ligands, BINAP and dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (S-Phos), were tested. In the presence of BINAP no product was formed, and when S-Phos was used similar results than obtained with X-Phos (entries 8,9) were achieved. Noteworthy, in the absence of a ligand no product was formed (entry 10).

Under the optimized reaction conditions, both electron-rich (R = Me, *i*Pr) and electron-poor (R = F, CF_3, CO_2Me) anilines could be coupled to the [2.2]paracyclophane backbone in good to excellent yields (Table 2, entries 1–7). Attempts to directly couple 2-aminophenol failed. However, after protection of the hydroxyl group with triisopropylsilyl chloride,[20] the corresponding amino[2.2]paracyclophane **5h** was formed in 64% yield (entry 8).

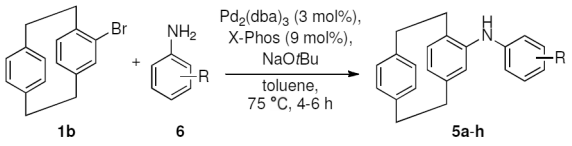
With phenylamino[2.2]paracyclophanes **5a–h** in hand their oxidative cyclizations to give the corresponding carbazoles **2a–h** were investigated. Amine **5a** was chosen as model compound (Table 3). Initial studies were conducted using a stoichiometric amount of $Pd(OAc)_2$ (1 equiv)[21] and acetic acid (AcOH) as solvent. With air as oxidant, carbazole **2a** was formed in 61% yield

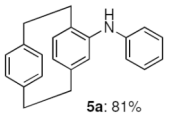
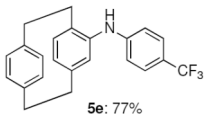
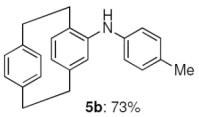
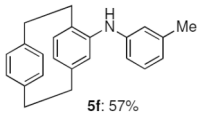
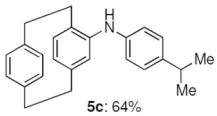
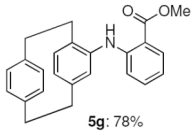
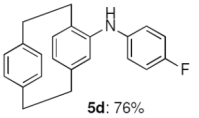
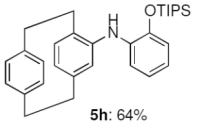
Table 1. Optimization of the Pd-catalyzed C–N cross-coupling of 4-bromo[2.2]paracyclophane (**1b**) with aniline (**6a**).



Entry	$Pd_2(dba)_3$/ligand (mol%)	Ligand	*t* (h)	*T* (°C)	Yield (%)
1	5/15	X-Phos	4	75	79
2	3/9	X-Phos	4	75	81
3	2/6	X-Phos	4	75	66
4	1/3	X-Phos	4	75	45
5	1/3	X-Phos	16	75	51
6	1/3	X-Phos	16	100	68
7	1/3	X-Phos	24	100	68
8	3/9	S-Phos	4	75	78
9	3/9	BINAP	4	75	0
10	3/0	–	4	75	0

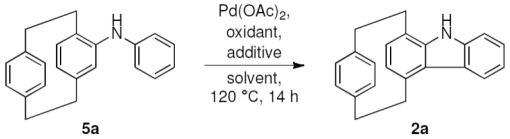
Table 2. Pd-catalyzed C–N cross-coupling of 4-bromo-[2.2]paracyclophane (**1b**) with anilines **6**.[a]



Entry	Product/yield	Entry	Product/yield
1	 **5a**: 81%	5	 **5e**: 77%
2	 **5b**: 73%	6	 **5f**: 57%
3	 **5c**: 64%	7	 **5g**: 78%
4	 **5d**: 76%	8	 **5h**: 64%

[a] Reaction conditions: **1b** (1.0 equiv), aniline derivative **6** (1.2 equiv), $Pd_2(dba)_3$ (0.03 equiv), X-Phos (0.09 equiv), NaO*t*Bu (1.4 equiv) in toluene (4 mL mmol^{-1} of **1b**) at 75 °C.

Table 3. Optimization of the oxidative cyclization of 4-*N*-(phenyl)amino[2.2]paracyclophane (**5a**).[a]



Entry	Solv.	$Pd(OAc)_2$ (mol%)	Oxidant	Yield (%)
1	AcOH	100	air	61[b]
2	AcOH	20	air	49
3	AcOH[c]	20	air	35
4	AcOH[d]	20	air	22
5	PivOH	20	air	traces
6	TFA	20	air	0
7	DMF	20	O_2 (1 atm)	traces
8	DMSO	20	O_2 (1 atm)	0
9	AcOH/ toluene	20	air	42
10	AcOH[e]	20	air	35
11	AcOH	20	O_2 (1 atm)	35
12	AcOH	20	benzoquinone	37
13	AcOH	20	$K_2S_2O_8$	13
14	AcOH	20	$PhI(OAc)_2$	0
15	AcOH	20	$Cu(OAc)_2$	0
16	AcOH	20	AgOAc	25
17	AcOH	20	air[f]	60
18	AcOH	10	air[f]	29

[a] The reactions were performed in a 10 mL round bottom flask using 0.4 mmol of **5a** and 4 mL of the given solvent. [b] For 2 h. [c] At 100 °C. [d] For 18 h. [e] Molecular sieve 4 Å (50 mg) was added. [f] Air was introduced into the solution, and the reaction time was reduced to 8 h.

(entry 1). The regioselectivity of the oxidative C–C bond formation was confirmed by ^1H and ^{13}C NMR spectroscopy as well as X-ray crystal structure analysis. For the latter, single crystals of **2a** were obtained from a benzene/pentane solvent mixture. An ORTEP plot of **2a** is given in Figure 2. The [2.2]paracylophane unit of the molecule shows the typical structural features of this class of compounds. Thus both phenyl rings deviate significantly from planarity, and the sum of bond angles in the rings amount to about 717°. The deviation of the *para* carbon atoms (C18, C21 and C8, C11) from the least squares plane defined by the remaining four atoms of each ring (C16, C17, C19, C20 and C7, C9, C10, C12) is 0.15–0.16 Å. These values coincide with the one obtained for parent [2.2]paracyclophane in an ab initio calculation (MP2/6-31 + G*).[9c] The exocyclic C_6H_5N unit, which forms a carbazole moiety with one of the aromatic rings of the [2.2]paracyclophane, is essentially planar, and no atom of this group deviates from the best plane defined by its atoms (N, C1–C6) by more than 0.02 Å.

Encouraged by this first result (Table 3, entry 1), the catalyst loading was reduced. In the presence of 20 mol% of $Pd(OAc)_2$ **5a** was formed in 49% yield after 14 h

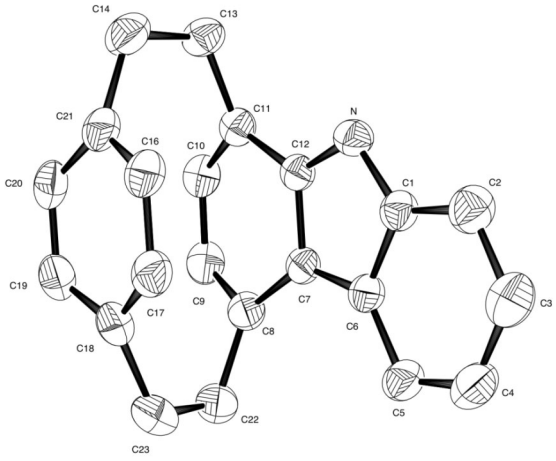


Figure 2. Structure of racemic **2a** in the solid state.

(entry 2). Increasing the reaction time or decreasing the temperature resulted in lower yields (entries 3 and 4). In the absence of $Pd(OAc)_2$ no product was formed. In a control experiment it was shown that **2a** was not stable under the reaction conditions (AcOH, 10 mol% of $Pd(OAc)_2$, 120 °C). After 24 h only 45% of **2a** was recovered. Unfortunately, the decomposition products could not be identified. To avoid the harsh reaction conditions and the decomposition of **2a** several solvents were tested (entries 5–8). Whereas in pivalic acid (PivOH), DMF and DMSO no reaction took place or only traces of **2a** were formed, use of trifluoroacetic acid led to complete decomposition of **5a** (entry 6). To increase the solubility of **5a** a 1:1 mixture of AcOH/toluene was tested, but no positive influence on the reaction outcome was observed (entry 9). Also the presence of water did not affect the reaction. Neither the addition of molecular sieves (entry 10) nor the use of dry acetic acid improved the previous results. Next, the oxidant was varied. Oxygen, benzoquinone, $K_2S_2O_8$, $PhI(OAc)_2$, $Cu(OAc)_2$ and AgOAc were tested (entries 11–16), but none was superior to air. Direct introduction of the oxidant air into the solution led to full conversion of **5a** after only 8 h, and carbazole **2a** was obtained in 60% yield (Table 3, entry 17). A decrease of the amount of $Pd(OAc)_2$ to 10 mol% lowered the yield of **2a** to 29% (entry 18).

Because additives had a positive impact on the catalyst performance in other C–H activation processes,[14c,22,23] and with the goal to further improve the yield of **2a**, the effects of various acids and donor ligands on the oxidative cyclizations of **5a** under the optimized conditions were examined (Table 4). Whereas the presence of trifluoracetic acid, 1,10-phenanthroline, X-Phos and S-Phos blocked the catalysis or led to a lower yield of **2a** (entries 1–4), addition of pivalic acid and 3,4,5-trifluorobenzoic acid (TFBA) resulted in an improvement (entries 5–8). Hence,

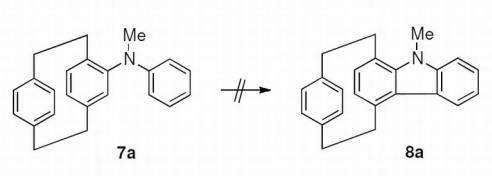
Table 4. Effect of additives on the oxidative cyclization of 4-*N*-phenylamino[2.2]paracyclophane (**5a**).[a]

Entry	$Pd(OAc)_2$ (mol%)	Additive (mol%)	Yield (%) of **2a**
1	10	trifluoroacetic acid (30)	0
2	10	1,10-phenanthroline (10)	0
3	10	X-Phos (15)	0
4	10	S-Phos (15)	25
5	10	pivalic acid (30)	30
6	10	pivalic acid (30)	37[b]
7	20	pivalic acid (60)	62
8	10	3,4,5-trifluorobenzoic acid (30)	50

[a] The reactions were performed on a 0.4 mmol scale in a 10 mL Schlenk tube with 4 mL of AcOH at 120 °C for 8 h, and compressed air was introduced into the solution. [b] Reaction time of 30 h.

the best yields of **2a** was observed, when either 30 mol% of TFBA (with 10 mol% of $Pd(OAc)_2$) or 60 mol% of pivalic acid (with 20 mol% of $Pd(OAc)_2$) were present in the reaction mixture (Table 4, entries 7 and 8). Then, the yields for **2a** were 50% and 62%, respectively, which compared well to the 29% yield under identical conditions in the absence of an additive (Table 3, entry 18).

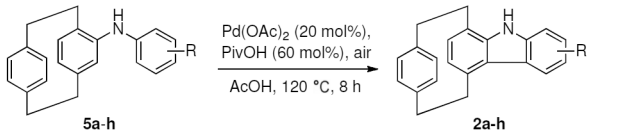
Hypothesizing that a N-substituted product was more stable under the oxidative reaction condition, N-methylated diaryl amine **7a** was submitted to the palladium catalysis (Scheme 2). However, no C–C bond formation occurred, and the corresponding carbazole **8a** was not detected.



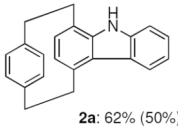
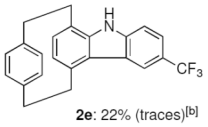
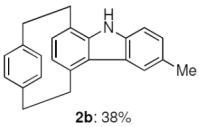
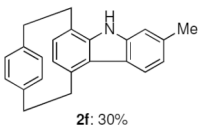
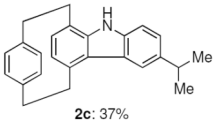
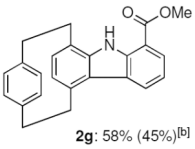
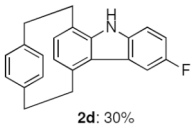
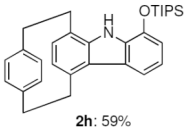
Scheme 2. Attempted conversion of N-methylated [2.2]paracyclophanyl amine (**7a**) into the corresponding carbazole **8a**.

Next, the substrate scope was investigated (Table 5). On the basis of the previous results, the catalysis reactions were performed under conditions as described in Table 4, entry 7, using 60 mol% of pivalic acid as additive. To our delight, all aryl [2.2]paracyclophanyl amines (**5b–h**) underwent oxidative cyclizations providing the corresponding planar chiral carbazoles **2b–h** in moderate to good yields. Even the sterically more hindered *ortho*-substituted substrates **5g** and **5h** reacted well, and carbazoles **2g** and **2h** were obtained in similar yields than unsubstituted **2a** (entries 7 and 8 versus entry 1). Electronic variations of the aryl core had a more pronounced impact and both electron-rich (**2b**, **2c** and **2f**; entries 2, 3 and 6) as well as electron-poor carbazoles (**2d** and **2e**; entries 4 and 5) were only formed in moderate yields. Probably

Table 5. Scope of the oxidative cyclization.[a]



5a-h 2a-h

Entry	Product/yield	Entry	Product/yield
1	 **2a**: 62% (50%)[b]	5	 **2e**: 22% (traces)[b]
2	 **2b**: 38%	6	 **2f**: 30%
3	 **2c**: 37%	7	 **2g**: 58% (45%)[b]
4	 **2d**: 30%	8	 **2h**: 59%

[a] Reaction conditions: Aryl [2.2]paracyclophanyl amines **5a–h** (0.4 mmol), $Pd(OAc)_2$ (0.2 equiv), pivalic acid (0.6 equiv) in acetic acid (4 mL) at 120 °C for 8 h; compressed air was introduced into the solution. [b] Use of $Pd(OAc)_2$ (10 mol%) and TFBA (30 mol%) as additive.

due to steric reasons only a single regioisomer (**2f**) was observed starting from amine **5f**.[15b,24]

As demonstrated before, the $Pd(OAc)_2$/TFBA combination could also be used, but generally this catalyst system led to lower yields as compared to the application of 20% and 60% of $Pd(OAc)_2$ and pivalic acid, respectively (Table 5, entries 1, 5 and 7).

3. Summary

An access to carbazoles with fused [2.2]paracyclophane skeletons has been developed. The reaction sequence is short and involves only two palladium-catalyzed synthetic steps. Starting from 4-bromo[2.2]paracyclophane (**1b**) Buchwald-Hartwig aminations provide intermediates that undergo aerobic oxidative cyclizations leading to the targeted carbazoles in moderate to good yields. Although the catalyst loading in the second step is still high (10–20 mol%), the general strategy is appealing due to the conceptional simplicity of the one-step double C–H activation/functionalization. The expertise gained in these *in-*

*tra*molecular direct arylations of [2.2]paracyclophanes will now serve as the basis for subsequent studies focusing on *inter*molecular variants. Those shall provide a range of 4,5-disubstituted [2.2]paracyclophane derivatives that are otherwise difficult to prepare. Since many of those are planar chiral, stereochemical implications and resulting opportunities will finally be investigated.

Experimental Section

General Methods

Unless otherwise stated, all starting reagents were commercially available and used as received. Toluene was freshly distilled with sodium/benzophenone ketyl radical under nitrogen. NaO*t*Bu was grinded with a mortar before use. 4-Bromo[2.2]paracyclophane (**1b**) was synthesized as described in the literature[19] and purified by column chromatography (pentane/DCM = 9:1). All paracyclophane derivatives are used and prepared as racemates. Reactions were monitored by thin layer chromatography (TLC) using silica gel 60 F254 plates and visualized with UV radiation at 254 nm. Column chromatography was performed using silica gel (Acros, 35–70 μm, 60 Å). Melting points were measured with a Büchi Melting Point B-540 apparatus. ^{1}H, ^{13}C and ^{19}F NMR were recorded either on a Varian Mercury 300, a Varian Inova 400 or Varian VNMR 600 spectrometer in $CDCl_3$ using TMS as internal standard. Chemical shifts (δ) are reported in ppm and coupling constants (J) are given in Hz. IR spectra were acquired on a PerkinElmer Spectrum FT-IR 100 spectrometer. Mass spectra were recorded on a Finnigan SSQ 7000 spectrometer. HRMS were recorded on a Finnigan MAT 95. Elemental analyses were performed on an Elementar Vario EL instrument.

General Procedure for the N-Arylation: GP1 (Tables 1 and 2)

A Schlenk tube containing a stir bar was dried under vacuum and charged with $Pd_2(dba)_3$ (0.03 equiv), X-Phos (0.09 equiv), bromide **1b** (1–4 mmol), NaO*t*Bu (1.4 equiv) and amine (1.2 equiv), if solid. The tube was sealed with a rubber septum, evacuated and backfilled with argon three times. Amine (1.2 equiv), if liquid, and toluene (0.25 M) were added by syringe, and the septum was replaced by a glass stopper. The solution was stirred at 75 °C (preheated oil bath) for 4–6 h, then cooled to room temperature, diluted with ethyl acetate and filtered over a pad of Celite. The solvent was removed under reduced pressure and the product purified by column chromatography.

4-*N*-(Phenyl)amino[2.2]paracyclophane (5a): The title compound was prepared according to GP1 using $Pd_2(dba)_3$ (82 mg, 0.090 mmol), X-Phos (129 mg, 0.270 mmol), bromide **1b** (862 mg, 3.00 mmol), NaO*t*Bu (404 mg, 4.20 mmol) and aniline (335 mg, 3.60 mmol) in toluene (12 mL) at 75 °C for 4.5 h. Purification by column chromatography (gradient: pentane/Et_2O = 19:5 to pentane/DCM = 7:3) provided the title compound as a white solid (724 mg, 81 %): m.p. 184–186 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.21 (m, 2H), 7.01 (dd, J = 7.7 and 1.7 Hz, 1H), 6.95–6.92 (m, 2H), 6.90–6.86 (m, 1H), 6.60 (dd, J = 8.0 and 1.9 Hz, 1H), 6.48–6.43 (m, 3H), 6.38 (dd, J = 9.0 and 1.6 Hz, 1H), 5.87 (d, J = 1.9 Hz, 1H), 5.55 (br s, 1H), 3.12–2.87 (m, 7H), 2.73–2.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.5, 141.1, 140.0, 139.4, 138.9, 135.7, 133.4, 132.6, 131.2, 131.1, 129.0 (2C), 127.3, 126.8, 125.8, 120.0, 115.9 (2C), 35.3, 34.9, 33.9, 33.8; IR (KBr): $\tilde{\nu}$ = 3373, 2925, 2852, 1592, 1565, 1491, 1433, 1306, 1284, 881 cm^{-1}; MS (EI): *m/z* (%) = 299 ([M]$^+$, 76), 194 (100), 180 (13); elemental analysis calcd for $C_{22}H_{21}N$: C 88.25, H 7.07, N 4.68; found: C 87.88, H 7.09, N 4.64.

4-*N*-(4′-Methylphenyl)amino[2.2]paracyclophane (5b): The title compound was prepared according to GP1 using $Pd_2(dba)_3$ (56 mg, 0.061 mmol), X-Phos (86 mg, 0.18 mmol), bromide **1b** (574 mg, 2.00 mmol), NaO*t*Bu (269 mg, 2.80 mmol) and 4-methylaniline (257 mg, 2.40 mmol) in toluene (8 mL) at 75 °C for 5.5 h. The product was purified by column chromatography (pentane/Et_2O = 49:1) providing the title compound as a pale orange solid (489 mg, 78 %): m.p. 130–131 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.06–7.00 (m, 3H), 6.88 (d, J = 8.4 Hz, 2H), 6.59 (dd, J = 7.8 and 1.7 Hz, 1H), 6.46–6.40 (m, 3H), 6.33 (dd, J = 7.7 and 1.5 Hz, 1H), 5.83 (d, J = 1.2 Hz, 1H), 5.46 (br s, 1H), 3.12–2.83 (m, 7H), 2.73–2.63 (m, 1H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.2, 140.9, 140.9, 139.4, 139.0, 135.8, 133.4, 132.6, 131.2, 130.2, 129.8, 129.6 (2C), 127.4, 126.1, 124.8, 116.8 (2C), 35.2, 35.0, 33.7, 33.7, 20.6; IR (KBr): $\tilde{\nu}$ = 3370, 2922, 2852, 1612, 1590, 1512, 1475, 1412, 1300, 890, 804, 714 cm^{-1}; MS (EI): *m/z* (%) = 313 ([M]$^+$, 84), 312 (54), 209 (89), 208 (100), 194 (44), 193 (49), 104 (21), 91 (12), 78 (10); elemental analysis calcd for $C_{23}H_{23}N$: C 88.13 H 7.40, N 4.47; found: C 87.91, H 7.49, N 4.39.

4-*N*-(4′-Isopropylphenyl)amino[2.2]paracyclophane (5c): The title compound was prepared according to GP1 using $Pd_2(dba)_3$ (55 mg, 0.060 mmol), X-Phos (86 mg, 0.180 mmol), bromide **1b** (575 mg, 2.00 mmol), NaO*t*Bu (269 mg, 2.80 mmol) and 4-isopropylaniline (326 mg, 2.41 mmol) in toluene (8 mL) at 75 °C for 4.5 h. Purification by column chromatography (pentane/ethyl acetate = 97:3) provided the title compound as a pale yellow solid (489 mg, 78 %): m.p. 143–144 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.11 (d, J = 8.4 Hz, 2H), 7.04 (dd, J = 7.8 and 1.5 Hz, 1H), 6.91 (d, J = 8.4 Hz, 2H), 6.61 (dd, J = 7.9 and 1.7 Hz, 1H), 6.48–6.42 (m, 3H), 6.34 (dd, J = 8.1 and 1.5 Hz, 1H), 5.85 (d, J = 1.5 Hz, 1H), 5.48 (br s, 1H), 3.15–2.82 (m, 8H), 2.74–2.65 (m, 1H), 1.26 (d, J = 6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.2, 141.1, 140.9, 140.8, 139.4, 139.0, 135.7, 133.4, 132.6, 131.2, 130.3, 127.5, 127.0 (2C), 126.2, 124.9, 116.6 (2C), 35.2, 34.9, 33.7, 33.6, 33.3, 24.1 (2C); IR (KBr): $\tilde{\nu}$ = 3387, 3017, 2955, 2926, 2888, 2855, 1594, 1512, 1478, 1418, 1296, 825, 714 cm^{-1}; MS (EI): *m/z* (%) = 341 ([M]$^+$, 100), 326 (18), 237 (26), 194 (89), 104 (20); elemental analysis calcd for $C_{25}H_{27}N$: C 87.93, H 7.97, N 4.10; found: C 87.75, H 8.11, N 4.06.

4-*N*-(4′-Fluorophenyl)amino[2.2]paracyclophane (5d): The title compound was prepared according to GP1 using $Pd_2(dba)_3$ (55 mg, 0.060 mmol), X-Phos (86 mg, 0.18 mmol), bromide **1b** (575 mg, 2.00 mmol), NaO*t*Bu (270 mg, 2.80 mmol) and 4-fluoroaniline (266 mg, 2.40 mmol) in toluene (8 mL) at 75 °C for 5 h. The product was purified by column chromatography (pentane/DCM = 7:3) providing the title compound as a white solid (485 mg, 76 %): m.p. 176–178 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (dd, J = 7.8 and 2.0 Hz, 1H), 6.97–6.88 (m, 4H), 6.60 (dd, J = 8.0 and 2.0 Hz, 1H), 6.47–6.41 (m, 3H), 6.36 (dd, J = 7.8 and 2.0 Hz, 1H), 5.79 (d, J = 1.7 Hz, 1H), 5.44 (br s, 1H), 3.10–2.85 (m, 7H), 2.73–2.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4 (d, J_{CF} = 239 Hz), 141.3, 140.8, 139.7, 139.3, 138.9, 135.8, 133.5, 132.7, 131.2, 130.4, 127.4, 126.5, 125.0, 118.0 (d, J_{CF} = 7 Hz) (2C), 115.6 (d, J_{CF} = 23 Hz) (2C), 35.2, 34.9, 33.7, 33.6; ^{19}F NMR (376 MHz): δ = −123.8; IR (KBr): $\tilde{\nu}$ = 3359, 2924, 2851, 1593, 1503, 1413, 1302, 1213, 886, 820, 716 cm^{-1}; MS (EI): *m/z* (%) = 317 ([M]$^+$, 56), 213 (95), 212 (100), 198 (12), 104 (14), 91 (12); elemental analysis calcd for $C_{22}H_{20}FN$: C 83.25, H 6.35, N 4.41; found: C 83.10, H 6.46, N 4.36.

4-*N*-(4′-Trifluoromethylphenyl)amino[2.2]paracyclophane (5e): The title compound was prepared according to GP1 using $Pd_2(dba)_3$ (55 mg, 0.060 mmol), X-Phos (86 mg, 0.18 mmol), bromide **1b** (574 mg, 2.00 mmol), NaO*t*Bu (270 mg, 2.81 mmol) and 4-trifluoromethylaniline (387 mg, 2.40 mmol) in toluene (8 mL) at 75 °C for 5 h. Purification by column chromatography (gradient: pentane/DCM = 3:1 to 7:3) provided the title compound as a white solid (563 mg, 77 %): m.p. 185–187 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44 (d, J = 8.5 Hz, 2H), 6.95 (dd, J = 7.9 and 1.7 Hz, 1H), 6.89 (d, J = 8.5 Hz, 2H), 6.61 (dd, J = 7.9 and 1.7 Hz, 1H), 6.53–6.44 (m, 4H), 5.90 (d, J = 1.5 Hz, 1H), 5.74 (br s, 1H), 3.11–2.88 (m, 7H), 2.77–2.67 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.9, 141.5, 139.5, 139.1, 138.3, 136.0, 133.7, 133.3, 132.9, 131.2, 128.8, 127.7, 127.3, 126.5 (q, J_{CF} = 4 Hz) (2C), 121.1 (q, J_{CF} = 33 Hz), 114.1 (2C), 35.2, 34.8, 34.0, 33.8, CF_3 was not observed; ^{19}F NMR (282 MHz): δ = −61.3; IR (KBr): $\tilde{\nu}$ = 3364, 2929, 2852, 1616, 1523, 1483, 1322, 1284, 1103, 1063, 827 cm^{-1}; MS (EI): *m/z* (%) = 367 ([M]$^+$, 65), 263 (100), 262 (98), 248 (10), 194 (30), 193 (38), 104 (25), 78 (10); elemental analysis calcd for $C_{23}H_{20}F_3N$: C 75.19, H 5.49, N 3.81; found: C 75.26, H 5.52, N 3.59.

4-*N*-(3′-Methylphenyl)amino[2.2]paracyclophane (5f): The title compound was prepared according to GP1 using $Pd_2(dba)_3$ (55 mg, 0.060 mmol), X-Phos (86 mg, 0.18 mmol), bromide **1b** (575 mg, 2.00 mmol), NaO*t*Bu (271 mg, 2.82 mmol) and 3-methylaniline (257 mg, 2.40 mmol) in toluene (8 mL) at 75 °C for 6.5 h. Purification by column chromatography (gradient: pentane/Et_2O = 97:3 to pentane/DCM = 7:3) provided the title compound as a pale yellow solid (354 mg, 57 %): m.p. 169–171 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17–7.11 (m, 1H), 7.03 (dd, J = 7.9 and 2.0 Hz, 1H), 6.78–6.71 (m, 3H), 6.62 (dd, J = 7.9 and 2.0 Hz, 1H), 6.50–6.37 (m, 4H), 5.87 (d, J = 1.7 Hz, 1H), 5.52 (br s, 1H), 3.16–2.89 (m, 7H), 2.76–2.66 (m, 1H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.5, 141.1, 140.2, 139.5, 138.9, 138.9, 135.8, 133.5, 132.7, 131.3, 131.2, 128.9, 127.4, 126.7, 125.8, 120.9, 116.7, 113.0, 35.2, 34.8, 33.8, 33.7, 21.5; IR (KBr): $\tilde{\nu}$ = 3369, 2925, 2855, 1591, 1477, 1303, 1161, 873, 768, 703 cm^{-1}; MS (EI): *m/z* (%) = 313 ([M]$^+$, 100), 208 (91), 193 (37), 104 (19), 91 (11), 78 (10); elemental analysis calcd for $C_{23}H_{23}N$: C 88.13, H 7.40, N 4.47; found: C 87.86, H 7.70, N 4.34.

4-*N*-(2′-methoxycarbonylphenyl)amino[2.2]paracyclophane (5g): The title compound was prepared according to GP1 using $Pd_2(dba)_3$ (54 mg, 0.059 mmol), X-Phos (86 mg, 0.18 mmol), bromide **1b** (574 mg, 2.00 mmol), NaO*t*Bu (269 mg, 2.80 mmol) and methyl anthranilate (362 mg, 2.39 mmol) in toluene (8 mL) at 75 °C for 5 h. The product was purified by column chromatography (pentane/ethyl acetate = 19:1) providing the title compound as a yellow solid (621 mg, 87 %): m.p. 159–161 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.42 (br s, 1H), 8.00 (dd, J = 8.0 and 1.7 Hz, 1H), 7.23 (ddd, J = 8.3, 7.0 and 2.0 Hz, 1H), 7.14 (dd, J = 8.3 and 1.7 Hz, 1H), 6.91 (d, J = 8.1 Hz, 1H), 6.69 (ddd, J = 8.1, 7.0 and 1.0 Hz, 1H), 6.59–6.45 (m, 5H), 6.08 (d, J = 1.7 Hz, 1H), 4.01 (s, 3H), 3.15–2.92 (m, 7H), 2.74–2.67 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 147.7, 141.3, 139.6, 139.0, 138.5, 135.6, 134.3, 134.2, 133.5, 132.8, 131.6, 131.4, 129.8, 128.6, 127.8, 116.5, 113.4, 110.6, 51.8, 35.2, 34.8, 33.8, 33.7; IR (KBr): $\tilde{\nu}$ = 3309, 2931, 1674, 1588, 1513, 1491, 1449, 1233, 1086, 749 cm^{-1}; MS (EI): *m/z* (%) = 357 ([M]$^+$, 64), 253 (78), 221 (51), 194 (83), 193 (100), 165 (15), 104 (52), 78 (19), 59 (10); elemental analysis calcd for $C_{24}H_{23}NO_2$: C 80.64, H 6.49, N 3.92; found: C 80.27, H 6.69, N 3.86.

4-*N*-(2′-triisoproylsilyloxy)amino[2.2]paracyclophane (5h): The title compound was prepared according to GP1 using $Pd_2(dba)_3$ (55 mg, 0.060 mmol), X-Phos (86 mg, 0.18 mmol), bromide **1b** (575 mg, 2.00 mmol), NaO*t*Bu (269 mg, 2.80 mmol) and 2-(triisopropylsilyloxy)aniline[20] (637 mg, 2.40 mmol) in toluene (8 mL) at 75 °C for 4 h. Purification by column chromatography (pentane/ethyl acetate = 97:3) provided a mixture of the title compound and X-Phos. The latter compound was removed by a second column chromatography (pentane/DCM = 9:1) to provide the title compound as a white solid (606 mg, 64 %): m.p. 99–101 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.05 (dd, J = 7.9 and 1.7 Hz, 1H), 6.88 (dt, J = 7.9 and 1.6 Hz, 2H), 6.79 (td, J = 7.9 and 1.5 Hz, 1H), 6.70–6.61 (m, 2H), 6.50 (d, J = 7.7 Hz, 2H), 6.43–6.38 (m, 2H), 6.15 (br s, 1H), 5.94 (d, J = 1.7 Hz, 1H), 3.19–2.90 (m, 7H), 2.81–2.71 (m, 1H), 1.57–1.42 (m, 3H), 1.28 (d, J = 7.0 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.0, 141.1, 139.7, 139.5, 139.0, 135.6, 135.0, 133.5, 132.7, 132.7, 131.3, 127.6, 127.6, 127.1, 121.1, 118.3, 117.3, 112.4, 35.3, 34.9, 33.9, 33.8, 18.2 (6C), 13.1 (3C); IR (KBr): $\tilde{\nu}$ = 3419, 2940, 2863, 1591, 1509, 1441, 1251, 1200, 913, 880, 749 cm^{-1}; MS (EI): *m/z* (%) = 471 ([M]$^+$, 100), 428 (18), 367 (42), 238 (11), 193 (16), 104 (18), 59 (15); elemental analysis calcd for $C_{31}H_{41}NOSi$: C 78.93, H 8.76, N 2.97; found: C 78.85, H 8.95, N 2.84.

4-(*N*-Methyl-*N*-phenyl)amino[2.2]paracyclophane (7a):[25] Under an argon atmosphere **5a** (299 mg, 1.00 mmol) was dissolved in DMF (5 mL), and NaH (125 mg, 3.13 mmol) was added in small portions at 0 °C. The solution was warmed to room temperature and stirred for 2 h. MeI (444 mg, 3.13 mmol) was slowly added and the solution was stirred over night. Water (20 mL) was added and the product was extracted with ethyl acetate (3× 25 mL), dried over Na_2SO_4 and the solvent removed in vacuo. Purification by column chromatography (pentane/ethyl acetate = 19:1) provided the title compound as a white solid (256 mg, 82 %): m.p. 142–143 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24–7.18 (m, 2H), 7.01–6.98 (m, 2H), 6.90 (tt, J = 7.4 and 1.2 Hz, 1H), 6.78 (dd, J = 7.8 and 2.0 Hz, 1H), 6.60 (dd, J = 7.8 and 1.7 Hz, 1H), 6.51 (dd, J = 7.9 and 1.7 Hz, 2H), 6.38–6.31 (m, 2H), 6.01 (d, J = 1.5 Hz, 1H), 3.42 (s, 3H), 3.13–2.87 (m, 6H), 2.69–2.60 (m, 1H), 2.54–2.44 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.7, 145.6, 140.9, 140.1, 138.8, 136.2, 133.6, 132.9, 132.8, 131.1, 129.4, 129.0 (2C), 127.5, 123.8, 121.0, 119.4 (2C), 40.6, 35.4, 35.3, 34.9, 34.5; IR (KBr): $\tilde{\nu}$ = 1702, 1596, 1479, 1340, 1283, 1113, 1054, 835, 749 cm^{-1}; MS (EI): *m/z* (%) = 313 ([M]$^+$, 100), 208 (69), 194 (20), 104 (24), 78 (14); elemental analysis calcd for $C_{23}H_{23}N$: C 88.13, H 7.40, N 4.47; found: C 87.88, H 7.30, N 4.34.

General Procedure for the Oxidative Cyclization: GP2 (Tables 4 and 5)

A 10 mL Schlenk tube equipped with a reflux condenser, and a stir bar was dried under vacuum. The tube was charged with $Pd(OAc)_2$ (0.20 equiv), PivOH (0.6 equiv) and AcOH (2 mL). The solution was stirred for 5 min. Aryl [2.2]paracyclophanyl amines **5a–h** (0.4 mmol) and AcOH (2 mL) were added to the yellow solution. Dry air was introduced into the solution with a Teflon tube, and the solution was stirred at 120 °C. After approximately 15–30 min the solution turned black. After 8 h the solution was cooled to room temperature, diluted with ethyl acetate (50 mL), washed with $NaHCO_3$ (50 mL) and water (50 mL), dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by column chromatography.

[2]Paracyclo[2](1,4)carbazolophane (2a): The title compound was prepared according to GP2 using $Pd(OAc)_2$ (18 mg, 0.080 mmol), PivOH (25 mg, 0.24 mmol) and amine **5a** (120 mg,

0.401 mmol) in AcOH (4 mL) for 8 h. Purification by column chromatography (pentane/Et_2O = 9:1) provided the title compound as a white solid (75 mg, 62 %): m.p. 239–241 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, J = 8.0 Hz, 1 H), 7.87 (br s, 1 H), 7.46 (d, J = 8.0 Hz, 1 H), 7.40 (dt, J = 7.6 and 1.1 Hz, 1 H), 7.28–7.24 (m, 1 H), 6.63 (d, J = 7.4 Hz, 1 H), 6.56 (d, J = 7.4 Hz, 1 H), 6.50 (dd, J = 7.9 and 1.9 Hz, 1 H), 6.36 (dd, J = 7.7 and 1.9 Hz, 1 H), 5.94 (dd, J = 7.7 and 1.9 Hz, 1 H), 5.23 (dd, J = 7.7 and 1.9 Hz, 1 H), 4.03–3.98 (m, 1 H), 3.40–3.31 (m, 1 H), 3.16–2.91 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.0, 138.8, 137.9, 137.3, 135.7, 132.0, 131.5, 131.0, 126.4, 126.3, 125.4, 125.3, 124.8, 124.5, 122.4, 122.2, 119.6, 110.6, 33.9, 33.7, 33.2, 31.1; IR (ATR): $\tilde{\nu}$ = 3392, 2924, 1592, 1572, 1499, 1456, 1394, 1322, 1299, 1247, 1026, 905, 871, 805, 747 cm^{-1}; MS (EI): *m/z* (%) = 297 ([M]$^+$, 39), 193 (100), 192 (11), 165 (4), 149 (4), 104 (2); HRMS (EI) calcd for $C_{22}H_{19}N$: 297.1512; found: 297.1510 [M]$^+$.

[2]Paracyclo[2]6-methyl(1,4)carbazolophane (2b): The title compound was prepared according to GP2 using $Pd(OAc)_2$ (18 mg, 0.080 mmol), PivOH (25 mg, 0.24 mmol) and amine **5b** (126 mg, 0.402 mmol) in AcOH (4 mL) for 8 h. The product was purified by column chromatography (pentane/Et_2O = 9:1) providing the title compound as a light yellow solid (47 mg, 38 %): m.p. 208–210 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.86 (d, J = 0.5 Hz, 1 H), 7.75 (br s, 1 H), 7.35 (d, J = 8.2 Hz, 1 H), 7.23 (dm, J = 8.2 Hz, 1 H), 6.61 (d, J = 7.4 Hz, 1 H), 6.56–6.50 (m, 2 H), 6.37 (dd, J = 7.8 and 1.9 Hz, 1 H), 5.96 (dd, J = 7.7 and 2.0 Hz, 1 H), 5.29 (dd, J = 7.7 and 1.9 Hz, 1 H), 4.05–3.98 (m, 1 H), 3.38–3.26 (m, 1 H), 3.17–2.93 (m, 6 H), 2.58 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.3, 137.9, 137.3, 137.0, 135.7, 131.9, 131.4, 130.8, 128.8, 126.3, 126.2, 126.1, 125.4, 125.2, 124.5, 122.2, 122.1, 110.2, 33.9, 33.7, 33.2, 31.0, 21.3; IR (ATR): $\tilde{\nu}$ = 3399, 2923, 2855, 1591, 1500, 1470, 1437, 1389, 1308, 1246, 1184, 905, 873, 797, 725 cm^{-1}; MS (EI): *m/z* (%) = 311 ([M]$^+$, 40), 207 (100), 206 (17), 204 (6), 191 (6), 104 (7); HRMS (ESI) calcd for $C_{23}H_{22}N$: 312.1747; found: 312.1753 [M + H]$^+$.

[2]Paracyclo[2]6-isopropyl(1,4)carbazolophane (2c): The title compound was prepared according to GP2 using $Pd(OAc)_2$ (18 mg, 0.080 mmol), PivOH (25 mg, 0.24 mmol) and amine **5c** (137 mg, 0.401 mmol) in AcOH (4 mL) for 8 h. Purification by column chromatography (gradient pentane/Et_2O = 9:1 to 17:3 to 4:1) provided the title compound as a white solid (51 mg, 37 %): m.p. 128–130 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (s, 1 H), 7.74 (br s, 1 H), 7.38 (d, J = 8.0 Hz, 1 H), 7.31 (dd, J = 8.2 and 1.7 Hz, 1 H), 6.63 (d, J = 7.4 Hz, 1 H), 6.57 (d, J = 7.4 Hz, 1 H), 6.53 (dd, J = 7.9 and 2.0 Hz, 1 H), 6.37 (dd, J = 7.9 and 2.0 Hz, 1 H), 5.95 (dd, J = 7.7 and 2.0 Hz, 1 H), 5.24 (dd, J = 7.7 and 2.0 Hz, 1 H), 4.09–4.02 (m, 1 H), 3.37–2.91 (m, 8 H), 1.43 (d, J = 6.9 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.3, 140.3, 137.8, 137.3, 137.2, 135.5, 131.9, 131.3, 130.6, 126.2, 126.2, 125.4, 125.3, 124.4, 123.6, 122.1, 119.6, 110.3, 34.3, 33.9, 33.8, 33.2, 31.0, 24.9, 24.8; IR (ATR): $\tilde{\nu}$ = 3396, 2954, 2928, 2861, 1591, 1501, 1470, 1388, 1317, 1245, 907, 876, 803, 725 cm^{-1}; MS (EI): *m/z* (%) = 339 ([M]$^+$, 57), 235 (100), 220 (40), 204 (11), 104 (13); HRMS (ESI) calcd for $C_{25}H_{26}N$: 340.2060; found: 340.2064 [M + H]$^+$.

[2]Paracyclo[2]6-fluoro(1,4)carbazolophane (2d): The title compound was prepared according to GP2 using $Pd(OAc)_2$ (18 mg, 0.080 mmol), PivOH (25 mg, 0.24 mmol) and amine **5d** (127 mg, 0.400 mmol) in AcOH (4 mL) for 8 h. Purification by column chromatography (gradient pentane/Et_2O = 9:1 to 4:1) provided the title compound as a light yellow solid (44 mg, 35 %): m.p. 181–184 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80 (br s, 1 H), 7.73 (dd, J = 9.7 and 2.5 Hz, 1 H), 7.39–7.35 (m, 1 H), 7.16 (td, J = 9.0 and 2.5 Hz, 1 H), 6.65 (d, J = 7.4 Hz, 1 H), 6.57 (d, J = 7.4 Hz, 1 H), 6.52 (dd, J = 7.9 and 2.0 Hz, 1 H), 6.37 (dd, J = 7.9 and 2.0 Hz, 1 H), 5.94 (dd, J = 7.7 and 2.0 Hz, 1 H), 5.29 (dd, J = 7.7 and 2.0 Hz, 1 H), 3.95–3.88 (m, 1 H), 3.37–3.26 (m, 1 H), 3.19–2.91 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.6 (d, J_{CF} = 233 Hz), 141.1, 137.8, 137.3, 135.8, 135.1 (2C), 132.1, 131.5, 126.4, 126.3, 125.4 (d, J_{CF} = 10 Hz), 125.2 (d, J_{CF} = 5 Hz), 124.5, 122.4, 112.7 (d, J_{CF} = 26 Hz), 111.1 (d, J_{CF} = 10 Hz), 107.7 (d, J_{CF} = 24 Hz), 33.8, 33.5, 33.2, 31.0; ^{19}F NMR (282 MHz): δ = −124.2; IR (ATR): $\tilde{\nu}$ = 3397, 2925, 1581, 1477, 1388, 1309, 1275, 1247, 1176, 1021, 961, 909, 862, 803, 731 cm^{-1}; MS (EI): *m/z* (%) = 315 ([M]$^+$, 37), 211 (100), 210 (12), 183 (5), 157 (5), 104 (9); HRMS (ESI) calcd for $C_{22}H_{19}FN$: 316.1496; found: 316.1498 [M + H]$^+$.

[2]Paracyclo[2]6-trifluoromethyl(1,4)carbazolophane (2e): The title compound was prepared according to GP2 using $Pd(OAc)_2$ (18 mg, 0.080 mmol), PivOH (25 mg, 0.24 mmol) and amine **5e** (147 mg, 0.400 mmol) in AcOH (4 mL) for 8 h. The product was purified by column chromatography (gradient pentane/Et_2O = 4:1 to 7:3) providing the title compound as a light yellow solid (32 mg, 22 %): m.p. 189–191 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.32 (s, 1 H), 8.03 (br s, 1 H), 7.66 (d, J = 8.4 Hz, 1 H), 7.52 (d, J = 8.9 Hz, 1 H), 6.70 (d, J = 7.4 Hz, 1 H), 6.64 (d, J = 7.4 Hz, 1 H), 6.53 (dd, J = 7.7 and 1.8 Hz, 1 H), 6.39 (dd, J = 7.7 and 1.8 Hz, 1 H), 5.92 (dd, J = 7.7 and 1.8 Hz, 1 H), 5.22 (dd, J = 7.7 and 2.0 Hz, 1 H), 4.02–3.98 (m, 1 H), 3.36–3.30 (m, 1 H), 3.20–3.00 (m, 5 H), 2.96–2.91 (m 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 140.6, 140.2, 137.8, 137.3, 136.0, 132.2, 131.9, 131.7, 127.3, 126.3, 125.4 (q, J_{CF} = 271 Hz), 125.0, 124.7, 124.6, 122.5, 121.9 (q, J_{CF} = 32 Hz) 121.9 (q, J_{CF} = 3 Hz), 119.7 (q, J_{CF} = 5 Hz), 110.7, 33.8, 33.6, 33.1, 31.0; ^{19}F (564 MHz): δ = −59.9; IR (ATR): $\tilde{\nu}$ = 3390, 2929, 1623, 1588, 1391, 1323, 1261, 1163, 1109, 1070, 886, 808, 716 cm^{-1}; MS(EI): *m/z* (%) = 365 ([M]$^+$, 60), 261 (100), 191 (10), 104 (18), 78 (6); HRMS (ESI) calcd for $C_{23}H_{19}NF_3$: 366.1464; found: 366.1464 [M + H]$^+$.

[2]Paracyclo[2]7-methyl(1,4)carbazolophane (2f): The title compound was prepared according to GP2 using $Pd(OAc)_2$ (18 mg, 0.080 mmol), PivOH (25 mg, 0.24 mmol) and amine **5f** (125 mg, 0.399 mmol) in AcOH (4 mL) for 8 h. Purification by column chromatography (pentane/Et_2O = 9:1) followed by a second column chromatography (pentane/$CHCl_3$ = 3:7) provided the title compound as a white solid (37 mg, 30 %): m.p. 206–209 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93 (d, J = 7.9 Hz, 1 H), 7.72 (br, 1 H), 7.23 (s, 1 H), 7.09 (d, J = 7.6 Hz, 1 H), 6.60 (d, J = 7.7 Hz, 1 H), 6.54 (d, J = 7.7 Hz, 1 H), 6.50 (dd, J = 7.9 and 2.0 Hz, 1 H), 6.37 (dd, J = 7.9 and 2.0 Hz, 1 H), 5.95 (dd, J = 7.7 and 2.0 Hz, 1 H), 5.28 (dd, J = 7.7 and 2.0 Hz, 1 H), 4.01–3.94 (m, 1 H), 3.38–3.26 (m, 1 H), 3.16–2.90 (m, 6 H), 2.56 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.9, 139.3, 137.9, 137.2, 135.3, 134.9, 131.9, 131.4, 130.4, 126.3, 126.2, 125.5, 124.5, 123.1, 122.0, 122.0, 121.2, 110.7, 33.9, 33.6, 33.2, 31.1, 22.0; IR (ATR): $\tilde{\nu}$ = 3400, 3028, 2924, 2856, 1734, 1625, 1594, 1500, 1444, 1399, 1317, 1249, 1022, 926, 857, 800 cm^{-1}; MS(EI): *m/z* (%) = 311 ([M]$^+$, 71), 207 (100), 206 (25), 191 (6), 104 (11); HRMS (EI) calcd for $C_{23}H_{21}N$: 311.1669; found: 311.1668 [M]$^+$.

[2]Paracyclo[2]8-methoxycarbonyl(1,4)carbazolophane (2g): The title compound was prepared according to GP2 using $Pd(OAc)_2$ (18 mg, 0.080 mmol), PivOH (25 mg, 0.24 mmol) and amine **5g** (143 mg, 0.400 mmol) in AcOH (4 mL) for 8 h. Purification by column chromatography (pentane/Et_2O = 9:1) provided the title compound as a light yellow solid (83 mg, 58 %): m.p. 207–209 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.88 (br s, 1 H), 8.27 (d, J = 7.7 Hz, 1 H), 8.09 (dd, J = 7.7 and 1.2 Hz, 1 H), 7.30 (t, J = 7.8 Hz, 1 H), 6.71 (d, J = 7.7 Hz, 1 H), 6.63 (d, J = 7.7 Hz, 1 H), 6.52 (dd, J = 7.8 and 1.9 Hz, 1 H), 6.39 (dd, J = 7.8 and 1.9 Hz, 1 H), 5.96

(dd, $J=7.7$ and 2.0 Hz, 1H), 5.19 (dd, $J=7.7$ and 2.0 Hz, 1H), 4.08 (s, 3H), 4.03–3.96 (m, 1H), 3.52–3.41 (m, 1H), 3.20–3.05 (m, 5H), 2.97–2.89 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=168.2$, 140.4, 139.5, 137.5 (2C), 135.7, 132.1, 131.6, 131.5, 127.6, 126.9, 126.5, 126.3, 126.0, 124.6, 124.5, 122.8, 118.6, 111.3, 51.9, 33.8, 33.6, 33.0, 31.0; IR (ATR): $\tilde{\nu}=3419$, 2939, 1695, 1592, 1502, 1434, 1392, 1293, 1266, 1236, 1195, 1145, 867, 800, 743, 714 cm^{-1}; MS (EI): m/z (%) = 355 ([M]$^+$, 53), 251 (100), 219 (48), 190 (21), 164 (16), 104 (15); HRMS (ESI) calcd for $C_{24}H_{22}NO_2$: 356.1645; found: 356.1643 [M+H]$^+$.

[2]Paracyclo[2]8-triisopropylsilyloxy(1,4)carbazolophane (2h): The title compound was prepared according to GP2 using $Pd(OAc)_2$ (18 mg, 0.080 mmol), PivOH (25 mg, 0.24 mmol) and amine **5h** (189 mg, 0.401 mmol) in AcOH (4 mL) for 7.5 h. Purification by column chromatography (gradient pentane/Et_2O = 49:1 to 19:1) provided the title compound as a light yellow solid (111 mg, 59%): m.p. 125–129 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.90$ (br s, 1H), 7.69 (d, $J=8.2$ Hz, 1H), 7.12 (t, $J=7.8$ Hz, 1H), 6.93 (dd, $J=7.7$ and 0.7 Hz, 1H), 6.64 (d, $J=7.4$ Hz, 1H), 6.57 (d, $J=7.4$ Hz, 1H), 6.52 (dd, $J=7.9$ and 1.7 Hz, 1H), 6.38 (dd, $J=7.7$ and 2.0 Hz, 1H), 5.99 (dd, $J=7.7$ and 2.0 Hz, 1H), 5.27 (dd, $J=7.7$ and 1.9 Hz, 1H), 4.05–3.96 (m, 1H), 3.40–3.31 (m, 1H), 3.17–2.91 (m, 6H), 1.54–1.42 (m, 3H), 1.25 (dd, $J=7.4$ and 3.0 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=141.5$, 139.6, 137.9, 137.2, 135.8, 131.9, 131.4, 131.4, 130.8, 126.7, 126.3, 126.2, 126.1, 124.4, 122.4, 120.0, 115.3, 113.1, 34.0, 33.6, 33.2, 31.1, 18.1 (6C), 12.9 (3C); IR (ATR): $\tilde{\nu}=3430$, 2939, 2862, 1620, 1572, 1495, 1458, 1391, 1306, 1260, 1106, 1061, 1006, 974, 879, 785, 726 cm^{-1}; MS (EI): m/z (%) = 469 ([M]$^+$, 44), 365 (100), 322 (11), 252 (8), 236 (12), 104 (13); HRMS (ESI) calcd for $C_{31}H_{40}ONSi$: 470.2874; found: 470.2868 [M+H]$^+$.

Crystal structure analysis of racemic 2a: Crystals of **2a** suitable for X-ray structure determination were obtained from a benzene/pentane mixture at room temperature. The compound crystallizes in the centrosymmetric trigonal space group $R\bar{3}$ (148, hexagonal axes) with cell constants $a=b=22.6870(6)$, $c=17.5427(5)$ Å, and cell volume of $V=7819.5(5)$ Å^3. $Z=18$ and a molecular weight of 328.45 (vide infra) result in a calculated density of $\rho_{calcd}=1.255$ Mg m^{-3} and an absorption coefficient of $\mu=0.547$ mm^{-1} (CuK_α radiation, $\lambda=1.54178$ Å) A total number of 40818 data were collected at ambient temperature on a Bruker APEX DUO CCD diffractometer. The structure was solved employing direct methods as implemented in the SHELXTL program package.[26] The data set was merged ($r_{eq}=0.032$) to give 2667 reflections with $I>2\sigma(I)$, which were included into the final full-matrix least-squares refinement on F employing XTAL3.7.[27] The refinement converged at $r=0.076$ ($r_w=0.090$), a goodness of fit $S=1.430$, a final maximum shift/error of $0.26\cdot10^{-3}$, and a residual electron density of $-0.87/+0.59$e. All but two (vide infra) non-hydrogen atoms were refined anisotropically. The hydrogen atoms were calculated in idealized positions and their U values were fixed at 1.5 times the U_{eq} of the relevant heavy atom prior to final refinement. No refinement of hydrogen parameters. The compound crystallizes together with one molecule of benzene and a probably non-stoichiometric amount of severely disordered pentane. While the benzene unit could be refined as described above, this was not possible for the pentane unit. Thus the corresponding density was absorbed by two carbon and two hydrogen atoms, where the carbon parameters could be refined isotropically. Additional crystallographic data for the structure of **2a** have been deposited with the Cambridge Crystallographic Data Centre (CCDC-832923). Copies can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB12 1EZ, United Kingdom (Fax: 44-1223-336033 or email: deposit@ccdc.cam.ac.uk).

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References

[1] a) D. J. Cram, H. Steinberg, *J. Am. Chem. Soc.* **1951**, *73*, 5691–5704; b) for the initial discovery, see: C. J. Brown, A. C. Farthing, *Nature* **1949**, *164*, 915–916.
[2] *Modern Cyclophane Chemistry*, (Eds: R. Gleiter, H. Hopf) Wiley-VCH, New York, **2004**.
[3] H. Hopf, *Naturwiss.* **1983**, *70*, 349–358.
[4] a) S. E. Gibson, J. D. Knight, *Org. Biomol. Chem.* **2003**, *1*, 1256–1269; b) V. Rozenberg, E. Sergeeva, H. Hopf, in Ref. [2], pp. 453–462; c) S. Bräse, S. Dahmen, S. Höfener, F. Lauterwasser, M. Kreis, R. E. Ziegert, *Synlett* **2004**, 2647–2669.
[5] A. A. Aly, A. B. Brown, *Tetrahedron* **2009**, *65*, 8055–8089.
[6] For examples of fused heterocyclic [2.2]paracyclophanes, see: a) U. Wörsdörfer, F. Vögtle, F. Glorius, A. Pfalz, *J. Prakt. Chem.* **1999**, *341*, 445–448; b) F. Fringuelli, O. Piermatti, F. Pizzo, R. Ruzziconi, *Chem. Lett.* **2000**, 38–39; c) B. Ortner, R. Waibel, P. Gmeiner, *Angew. Chem.* **2001**, *113*, 1323–1325; *Angew. Chem. Int. Ed.* **2001**, *40*, 1283–1285; d) B. Ortner, H. Hübner, P. Gmeiner, *Tetrahedron: Asymmetry* **2001**, *12*, 3205–3208; e) V. Rozenberg, T. Danilova, E. Sergeeva, E. Vorontsov, Z. Starikova, A. Korlyukov, H. Hopf, *Eur. J. Org. Chem.* **2002**, 468–477; f) A. Cipiciani, F. Fringuelli, O. Piermatti, F. Pizzo, R. Ruzziconi, *J. Org. Chem.* **2002**, *67*, 2665–2670; g) L. Minuti, A. Marrocchi, I. Tesei, E. Gacs-Baitz, *Tetrahedron Lett.* **2005**, *46*, 8789–8792; h) P. B. Hitchcock, A. C. C. Hodgson, G. J. Rowlands, *Synlett* **2006**, 2625–2628; i) N. De Rycke, J. Marrot, F. Couty, O. R. P. David, *Eur. J. Org. Chem.* **2011**, 1980–1984.
[7] a) H. Hopf, D. G. Barrett, *Liebigs Ann.* **1995**, 449–451; b) A. Cipiciani, F. Fringuelli, V. Mancini, O. Piermatti, F. Pizzo, *J. Org. Chem.* **1997**, *62*, 3744–3747; c) V. Rozenberg, T. Danilova, E. Sergeeva, E. Vorontsov, Z. Starikova, K. Lysenko, Y. Belokon, *Eur. J. Org. Chem.* **2000**, 3295–3303; d) T. Focken, H. Hopf, V. Snieckus, I. Dix, P. G. Jones, *Eur. J. Org. Chem.* **2001**, 2221–2228; e) V. I. Rozenberg, T. I. Danilova, E. V. Sergeeva, I. A. Shouklov, Z. A. Starikova, H. Hopf, K. Kühlein, *Eur. J. Org. Chem.* **2003**, 432–440; f) C. Bolm, D. K. Whelligan, *Adv. Synth. Catal.* **2006**, *348*, 2093–2100; g) D. K. Whelligan, C. Bolm, *J. Org. Chem.* **2006**, *71*, 4609–4618; h) N. Hermanns, S. Dahmen, C. Bolm, S. Bräse, *Angew. Chem.* **2002**, *114*, 3844–3846; *Angew. Chem. Int. Ed.* **2002**, *41*, 3692–3694; i) V. Rozenberg, R. Zhuravsky, E. Sergeeva, *Chirality* **2006**, *18*, 95–102.
[8] For *tert*-butylsulfinyl as directing group, see: P. B. Hitchcock, G. J. Rowlands, R. J. Seacome, *Org. Biomol. Chem.* **2005**, *3*, 3873–3876.
[9] a) X.-L. Hou, X.-W. Wu, L.-X. Dai, B.-X. Cao, J. Sun, *Chem. Commun.* **2000**, 1195–1196; b) A. Pelter, B. Mootoo, A. Maxwell, A. Reid, *Tetrahedron Lett.* **2001**, *42*, 8391–8394; c) C. Bolm, K. Wenz, G. Raabe, *J. Organomet. Chem.*

2002, *662*, 23–33; d) G. J. Rowlands, *Org. Biomol. Chem.* **2008**, *6*, 1527–1534.

[10] For selected reviews about direct arylation see: a) L.-C. Campeau, K. Fagnou, *Chem. Commun.* **2006**, 1253–1264; b) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174–238; c) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem.* **2009**, *121*, 5196–5217; *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115; d) G. P. McGlacken, L. M. Bateman, *Chem. Soc. Rev.* **2009**, *38*, 2447–2464; e) O. Daugulis, *Top. Curr. Chem.* **2010**, *292*, 57–84; f) C.-L. Sun, B.-J. Li, Z.-J. Shi, *Chem. Commun.* **2010**, *46*, 677–685; g) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147–1169; h) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780–1824.

[11] a) H.-J. Knölker, K. R. Reddy, *Chem. Rev.* **2002**, *102*, 4303–4428; b) H.-J. Knölker, *Top. Curr. Chem.* **2005**, *244*, 115–148; c) S.-L. You, J.-B. Xia, *Top. Curr. Chem.* **2010**, *292*, 165–194.

[12] a) C. Bolm, T. Focken, G. Raabe, *Tetrahedron: Asymmetry* **2003**, *14*, 1733–1746; b) T. Focken, G. Raabe, C. Bolm, *Tetrahedron: Asymmetry* **2004**, *15*, 1693–1706; c) T. Focken, J. Rudolph, C. Bolm, *Synthesis* **2005**, 429–436.

[13] H. Hopf, *Angew. Chem.* **2008**, *120*, 9954–9958; *Angew. Chem. Int. Ed.* **2008**, *47*, 9808–9812.

[14] a) W. C. P. Tsang, N. Zheng, S. L. Buchwald, *J. Am. Chem. Soc.* **2005**, *127*, 14560–14561; b) W. C. P. Tsang, R. H. Munday, G. Brasche, N. Zheng, S. L. Buchwald, *J. Org. Chem.* **2008**, *73*, 7603–7610; c) J. A. Jordan-Hore, C. C. C. Johansson, M. Gulias, E. M. Beck, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 16184–16186; d) B.-J. Li, S.-L. Tian, Z. Fang, Z.-J. Shi, *Angew. Chem.* **2008**, *120*, 1131–1134; *Angew. Chem. Int. Ed.* **2008**, *47*, 1115–1118; e) S. H. Cho, J. Yoon, S. Chang, *J. Am. Chem. Soc.* **2011**, *133*, 5996–6005.

[15] For recent examples on the Pd^{II}-catalyzed synthesis of carbazoles by double aromatic C–H bond activation, see: a) B. Liégault, D. Lee, M. P. Huestis, D. R. Stuart, K. Fagnou, *J. Org. Chem.* **2008**, *73*, 5022–5028; b) T. Watanabe, S. Oishi, N. Fujii, H. Ohno, *J. Org. Chem.* **2009**, *74*, 4720–4726; c) R. Forke, K. K. Gruner, K. E. Knott, S. Auschill, S. Agarwal, R. Martin, M. Böhl, S. Richter, G. Tsiavaliaris, R. Fedorov, D. J. Manstein, H. O. Gutzeit, H.-J. Knölker, *Pure Appl. Chem.* **2010**, *82*, 1975–1991, and references cited herein.

[16] For selected examples of direct arylation of anilides, see: a) Y. Kametani, T. Satoh, M. Miura, M. Nomura, *Tetrahedron Lett.* **2000**, *41*, 2655–2658; b) D. Kalyani, N. R. Deprez, L. V. Desai, M. S. Sanford, *J. Am. Chem. Soc.* **2005**, *127*, 7330–7331; c) O. Daugulis, V. G. Zaitsev, *Angew. Chem.* **2005**, *117*, 4114–4116; *Angew. Chem. Int. Ed.* **2005**, *44*, 4046–4048; d) S. Yang, B. Li, X. Wan, Z. Shi, *J. Am. Chem. Soc.* **2007**, *129*, 6066–6067; e) D. Shabashov, O. Daugulis, *J. Org. Chem.* **2007**, *72*, 7720–7725.

[17] a) A. R. Muci, S. L. Buchwald, *Top. Curr. Chem.* **2002**, *219*, 131–209; b) J. F. Hartwig, *Synlett* **2006**, 1283–1294.

[18] a) K. Rossen, P. J. Pye, A. Maliakal, R. P. Volante, *J. Org. Chem.* **1997**, *62*, 6462–6463; b) M. Kreis, C. J. Friedmann, S. Bräse, *Chem. Eur. J.* **2005**, *11*, 7387–7394; c) M. Kreis, M. Nieger, S. Bräse, *J. Organomet. Chem.* **2006**, *691*, 2171–2181; d) B. Qu, Y. Ma, Q. Ma, X. Liu, F. He, C. Song, *J. Org. Chem.* **2009**, *74*, 6867–6869.

[19] D. J. Cram, A. C. Day, *J. Org. Chem.* **1966**, *31*, 1227–1232.

[20] Y. Kondo, S. Kojima, T. Sakamoto, *J. Org. Chem.* **1997**, *62*, 6507–6511.

[21] For precedent syntheses of carbazoles reported in the literature, substoichiometric or stoichiometric amounts of $Pd(OAc)_2$ have been used. For examples, see Ref. [11c].

[22] For examples of additive effects in metal-catalyzed C–H activations, see: a) M. Lafrance, K. Fagnou, *J. Am. Chem. Soc.* **2006**, *128*, 16496–16497; b) O. René, K. Fagnou, *Adv. Synth. Catal.* **2010**, *352*, 2116–2120; c) C.-L. Sun, H. Li, D.-G. Yu, M. Yu, X. Zhou, X.-Y. Lu, K. Huang, S.-F. Zheng, B.-J. Li, Z.-J. Shi, *Nat. Chem.* **2010**, *2*, 1044–1049.

[23] For the beneficial effect of TFBA, see: K.-S. Masters, T. R. M. Rauws, A. K. Yadav, W. A. Herrebout, B. Van der Veken, B. U. W. Maes, *Chem. Eur. J.* **2011**, *17*, 6315–6320.

[24] For examples with similar regioselectivity, see: R. Forke, A. Jäger, H.-J. Knölker, *Org. Biomol. Chem.* **2008**, *6*, 2481–2483.

[25] For a similar N-methylation, see: W. Bi, X. Yun, Y. Fan, X. Qi, Y. Du, J. Huang, *Synlett* **2010**, 2899–2904.

[26] a) G. M. Sheldrick, *Acta Crystallogr.* **2008**, *A64*, 112–122; b) Version 6.10. Bruker AXS Inc. Madison, Wisconsin, USA.

[27] S. R. Hall, D. J. du Boulay, R. Olthof-Hazekamp, Eds., **2000**, Xtal3.7 System. University of Western Australia.

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