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Roadmap towards N-Heterocyclic [2.2]Paracyclophanes and Their Application in Asymmetric Catalysis

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A novel family of [2.2]paracyclophane derivatives is described. Different substituted pyrazole, triazole and pyrimidine moieties were introduced to the [2.2]paracyclophane scaffold and the products were characterized spectroscopically and by X-ray structure analysis. These compounds are promising ligands for application in asymmetric catalysis. We show here that one of these ligands can catalyze asymmetric conjugate addition. Furthermore a palladium complex was synthesized by using a hydroxy-pyrazolyl[2.2]paracyclophane ligand.

Introduction

[2.2]Paracyclophane and its derivatives are a unique class of compounds due to their rigidity. They can be functionalized easily by following the established routes of arene chemistry,[1] and their application ranges from asymmetric catalysis all the way to surface modification through chemical vapour deposition (CVD). A first breakthrough in paracyclophane chemistry was worked out by Gorham in the mid-1960s, who developed the use of pyrolysis and subsequent polymerization.[2] Those findings allowed the application of [2.2]paracyclophane in surface modification chemistry. For example, coating methods with [2.2]paracyclophane derivatives were reported that led to numerous publications on CVD surface modification.[3] In addition, there are many other applications of [2.2]paracyclophanes in polymer chemistry and materials science.[4]

Another field of application of paracyclophane chemistry is in asymmetric reactions and catalysis. Unlike ferrocene, [2.2]paracyclophane derivatives exhibit planar chirality with just one substituent. A breakthrough in stereoselective paracyclophane chemistry came through the synthesis of the enantiopure C_2-symmetric paracyclophane ligand PhanePhos.[5] Substantial reviews in the field of catalysis have been published by Gibson, Paradies and David.[6–8] Further investigations, for example, by Noyori and Soai,[9,10] showed that catalysis with [2.2]paracyclophane zinc complexes having a nitrogen–oxygen coordination motif is feasible. In recent years, we combined the rigidity of the [2.2]paracyclophane backbone with novel metal coordinating moieties and described the asymmetric conjugate addition (ACA) of diethylzinc to cinnamaldehyde utilizing different [2.2]paracyclophane ligands.[11–13] In this publication we present a series of new [2.2]paracyclophane derivatives bearing N-heterocycles with various substitution patterns. Such structures are possible candidates for the ACA of aldehydes. The synthesis and characterization of novel paracyclophane derivatives is discussed. A few years ago, Thiel et al. published similar systems based on the phenyl analogue.[14,15] We here transferred some of their methods to the [2.2]paracyclophane backbone, improved their methods, and expanded the product spectrum. The main goal of this work was the synthesis of N-heterocycles of types **1**, **2** and **3** (Figure 1). Because all the starting materials are accessible as enantiopure paracyclophane derivatives, translation to chiral, nonracemic products should be possible in all cases, and one such example is discussed here.

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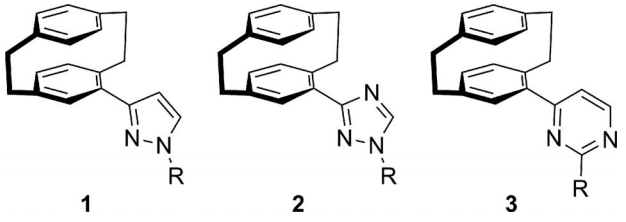
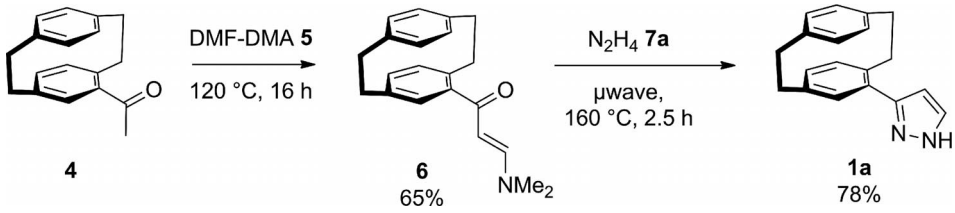


Figure 1. Target structures: pyrazole **1**, triazole **2** and pyrimidine **3** derivatives.

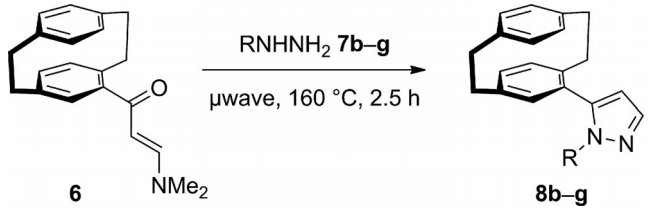


Scheme 1. Synthesis of 3-dimethylaminopropen-2-onyl[2.2]paracyclophane (**6**) and its conversion into pyrazol-3-yl[2.2]paracyclophane (**1a**).

Results and Discussion

Starting from commercially available [2.2]paracyclophane, 4-acetyl[2.2]paracyclophane (**4**) is accessible in good yields through Friedel–Crafts acylation following a reaction pathway reported by Cram.[16] Inspired by Thiel's method to access pyrazole derivatives, 3-dimethyaminoprop-2-enone **6** was synthesized, which underwent ring-closure to pyrazole **1a** upon treatment with hydrazine (Scheme 1). The reaction time could be reduced by conducting the reaction under microwave conditions.

To fully explore the scope of this reaction, a range of hydrazines were employed (Scheme 2, Table 1). As an example for this class of compounds, the crystal structure of **8g** is shown in Figure 2.[17]



Scheme 2. General procedure for the synthesis of pyrazolyl[2.2]-paracyclophanes **8b**–**g**.

Table 1. Summary of the synthesis of pyrazolyl[2.2]paracyclophanes **8b**–**g**.

Entry	Hydrazine	R	Yield [%]	Product
1	**7b**	Me	8	**8b**[a]
2	**7c**	CH_2CF_3	92	**8c**[a]
3	**7d**	cHex	32	**8d**
4	**7e**	Ph	71	**8e**
5	**7f**	Bn	61	**8f**
6	**7g**	4-BrC_6H_4	74	**8g**[a]

[a] Crystal structure given in the Supporting Information.

After the successful synthesis of monofunctionalized pyrazolyl[2.2]paracyclophane derivatives, we focused on hydroxy-pyrazolyl[2.2]paracyclophanes. Rozenberg et al. developed a route to acetyl-hydroxy[2.2]paracyclophane (AHPC, **9**), which is one of the intermediate structures towards hydroxy-pyrazolyl[2.2]paracyclophanes.[18] In this three-step, racemic sequence, with a total yield of 62%, AHPC (**9**) is accessible from formyl[2.2]paracyclophane (Rieche formylation) and subsequent hydroxy[2.2]paracyclophane (Dakin oxidation).[19]

Corresponding to the procedure by Thiel, AHPC (**9**) was treated with *N*,*N*-dimethylformamide–dimethyl acetal

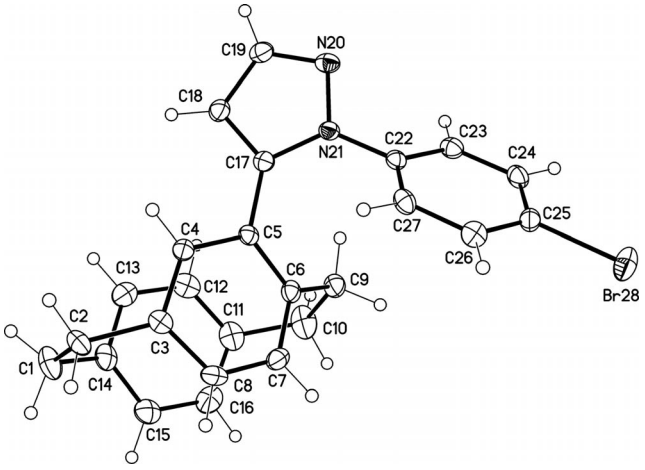


Figure 2. Molecular structure of **8g** (displacement parameters are drawn at 50% probability level).

(DMF–DMA; **5**) leading to hydroxy-dimethylaminopropen-2-onyl[2.2]paracyclophane (**10**). The molecular structure of **10** was determined by single-crystal structure analysis (Figure 3). By implementing similar microwave reaction conditions to those described above, hydroxy-pyrazolyl[2.2]-paracyclophane (**11a**), as the next target structure, could be accessed (Scheme 3).

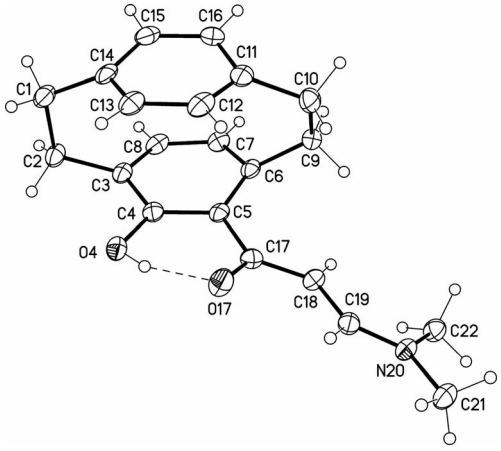
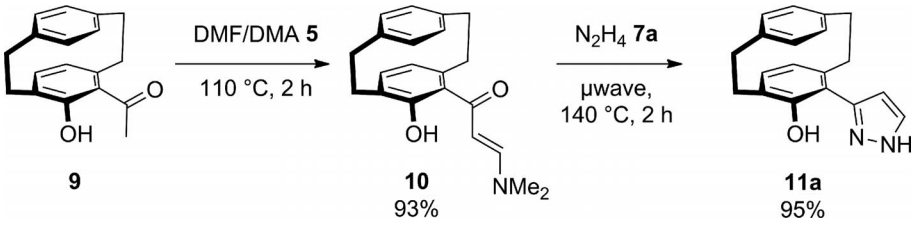
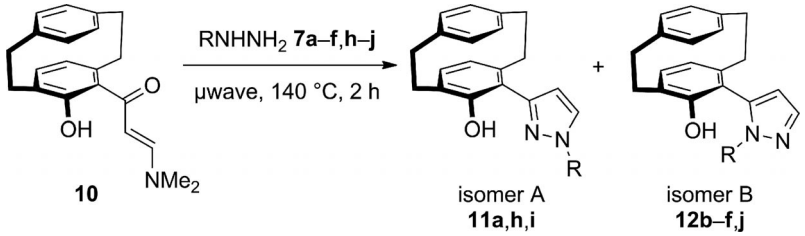


Figure 3. Molecular structure of **10** (displacement parameters are drawn at 50% probability level).

As described for the above intermediates, other hydrazines were applied under microwave conditions to yield further substituted hydroxy-pyrazolyl[2.2]paracyclophanes. Depending on the nature of the hydrazine, two pyrazole



Scheme 3. Synthesis of hydroxy-pyrazolyl[2.2]paracyclophane (**11a**).



Scheme 4. Synthesis of two pyrazole isomers.

isomers were obtained that could not always be separated by using standard purification methods (Scheme 4, Table 2).[20] The isomer ratios A/B were determined by ^{1}H NMR spectroscopic analysis.

Table 2. Comparison of hydroxy-pyrazolyl[2.2]paracyclophanes.

Entry	Hydrazine	R	Yield [%][a]	OH shift [δ, ppm]	Ratio A/B[b]	Major product
1	**7a**	H	95	10.70	1:0	**11a**
2	**7b**	Me	99	5.41	1:13	**12b**
3	**7c**	CH_2CF_3	90	5.35	1:5	**12c**
4	**7d**	cHex	57	5.34	0:1[d]	**12d**
5	**7e**	Ph	79	5.47	0:1	**12e**
6	**7f**	Bn	43	5.28	1:40[c]	**12f**
7	**7h**	*t*Bu	47	11.25	13:1	**11h**
8	**7i**	2-Py	4	10.71	22:1	**11i**
9	**7j**	CH_2-2-Py	63	–[e]	0:1	**12j**

[a] Isolated yield of the major isomer or isomer mixture. [b] Isomer ratio: A: substituent R at the α-nitrogen atom, B: at the β-nitrogen atom (Scheme 4). [c] X-ray data of both isomers were obtained. [d] No solid-state structure was determined; the nature of the isomer was determined on the basis of ^{1}H NMR spectroscopic analysis. [e] No OH signal was detected; isomer structure determined by X-ray crystallography.

As an example for a series of structurally characterized N-functionalized pyrazoles with a [2.2]paracyclophane backbone, the solid-state structures of compounds **12e** and **11h** are presented in Figure 4 and 5, respectively.

Carrying out the reaction with phenylhydrazine (**7e**) led to the formation of isomer A (Entry 5), bearing the phenyl residue at the α-nitrogen atom of the pyrazole with respect to the [2.2]paracyclophane scaffold, whereas the use of hydrazine hydrate (**7a**) gave isomer B (Entry 1). Compounds **11a**, **12d**, **12e** and **12j** were isolated as pure regioisomers, whereas all other derivatives were isolated as mixtures with one dominant isomer. The structures were determined by ^{1}H NMR spectroscopic analysis and supported by X-ray structure analysis. In isomer A, one of the pyrazole nitrogen atoms is sterically capable of taking part in hydrogen bonding with the OH group (Figure 5), leading to a pronounced

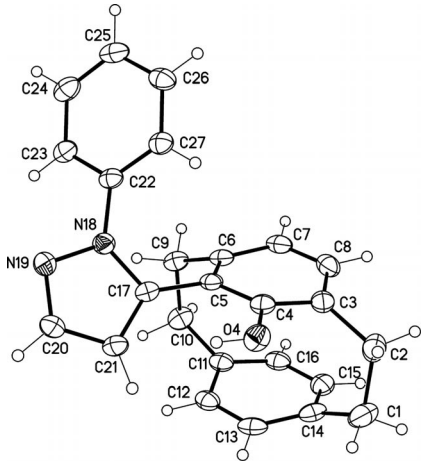


Figure 4. Molecular structure of **12e** in the solid state (displacement parameters are drawn at 50% probability level).

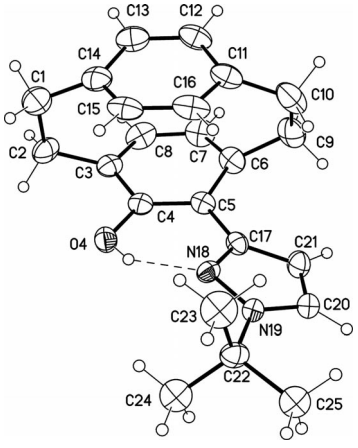
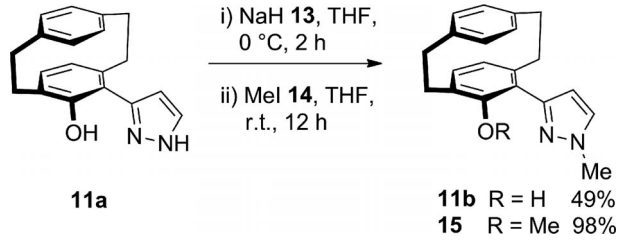


Figure 5. Molecular structure of **11h** in the solid state (displacement parameters are drawn at 50% probability level, partial disordering is omitted for clarity).

shift of the OH resonance to lower field (e.g., δ = 11.25 ppm for **11h**; Entry 7). This is no longer possible for isomer B,

for which this nitrogen atom is functionalized, leading to a high-field shift of the OH resonance (e.g., δ = 5.47 ppm for **11e**).

Coordination of zinc to the hydroxyl group and the α-nitrogen atom of the pyrazole ring is necessary for efficient ACA catalysis, thus, isomers of type B are not suitable for this reason because they cannot coordinate the zinc cation in the required coordination environment. An alternative route to isomers of type A is deprotonation of the NH-moiety of **11a** followed by alkylation (Scheme 5). In this case, isomer A is exclusively formed, probably due to the formation of an O,N chelate complex with the sodium cation, which blocks one of the nitrogen atoms for alkylation. By doubling the amount of base and alkylating agent, this sequence also allows parallel alkylation of both the pyrazole and the OH groups. The solid-state structure of compound **11b** was elucidated by X-ray structure analysis (Figure 6).



Scheme 5. Synthesis of methylated pyrazolyl[2.2]paracyclophanes (**11b** and **15**).

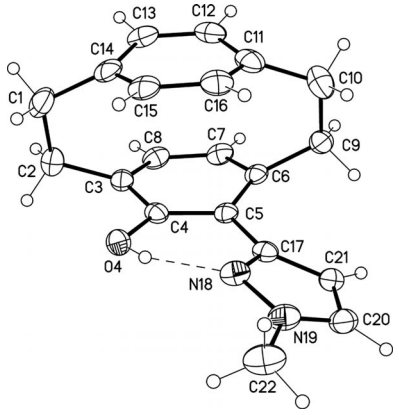


Figure 6. Molecular structure of one of the two independent molecules of **11b** in the solid state (displacement parameters are drawn at 50% probability level).

Because reacting compound **10** with methylhydrazine gave isomer A (**12b**) almost exclusively, we could directly compare the OH resonances of both isomers: whereas **12b** gave an OH resonance at δ = 5.41 ppm, the corresponding resonance of **11b** appeared at δ = 10.90 ppm.

A further example of the deprotonation–alkylation sequence leading to isomer A is the methoxymethyl (MOM) protected pyrazole **11k** (OH resonance at δ = 10.76 ppm). Figure 7 shows the molecular structure of compound **11k**. Analogous arylations are possible by following protocols for S_NAr reactions leading to the nitrophenyl derivatives **16** and **17** and methyl ester **18** (Figure 8). Such systems may be relevant for the formation of various metal complexes.

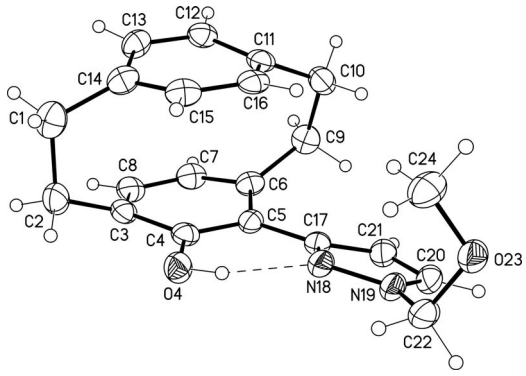


Figure 7. Molecular structure of **11k** in the solid state (displacement parameters are drawn at 50% probability level).

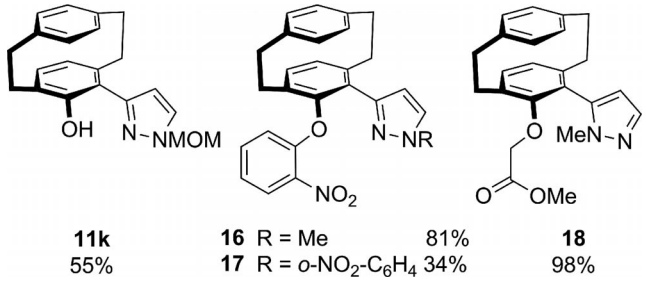
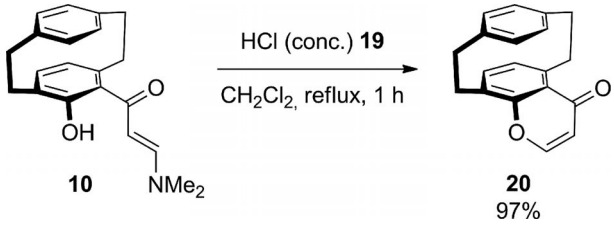


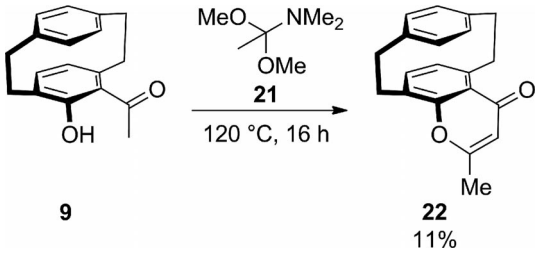
Figure 8. Some further functionalized pyrazolyl[2.2]paracyclophane derivatives **11k**, **16**, **17** and **18**. *Reagents and conditions:* For **11k**: **11a**, DMF, NaH (1.1 equiv.), MOMCl (1.5 equiv.) 30 min, room temp. For **16**: **11b**, DMSO, 1-fluoro-2-nitrobenzene (1.5 equiv.), K_2CO_3 (3.0 equiv.), 180 °C, 5 h. For **17**: **11a**, 1-fluoro-2-nitrobenzene (1.5 equiv.), K_2CO_3 (3.0 equiv.), 180 °C, 4 h. For **18**: **12b**, methyl bromoacetate (2.0 equiv.), 2 d, room temp.

As a minor side product appearing in most of the reactions of hydroxyacetyl[2.2]paracyclophanes with hydrazines, the yellow coloured chromone **20** could be identified (Scheme 6). This compound was selectively accessible in high yields by treatment of **10** with concentrated hydrochloric acid in dichloromethane heated to reflux.



Scheme 6. Synthesis of the paracyclophane-chromone derivative **20**.

Direct conversion AHPC (**9**) into another chromone derivative, **22**, was observed by reacting the former with dimethylacetamide dimethylacetal (**21**) (Scheme 7); Figure 9 shows the molecular structure of **22**.



Scheme 7. Synthesis of the paracyclophane-chromone derivative **22**.

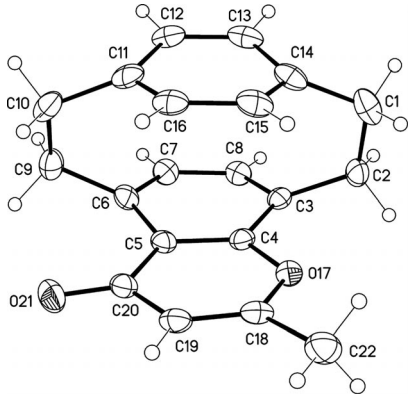


Figure 9. Molecular structure of **22** in the solid state (displacement parameters are drawn at 50% probability level).

Starting with [2.2]paracyclophane amide (**23**), triazolyl functionalized [2.2]paracyclophanes are accessible. Compound **23** was synthesized by following a process developed by Reich et al.,[21] involving treatment of racemic bromo[2.2]paracyclophane with *n*BuLi and then with dry-ice to give carboxy[2.2]paracyclophane.[22] The acid was activated with $SOCl_2$ and the acid chloride was quenched with aqueous ammonia to give **23** in 92% yield.[23] Analogously to AHPC (**9**), **23** was treated with DMF–DMA (**5**), to give **24**, which could not be purified by column chromatography due to decomposition. Reacting **24** with hydrazine **7a** for 1 h at 80 °C in a high-pressure vessel with acetic acid as the solvent led to the formation of triazole **2a** (Scheme 8).[24] Figure 10 shows the molecular structure of triazolyl[2.2]-paracyclophane (**2a**).

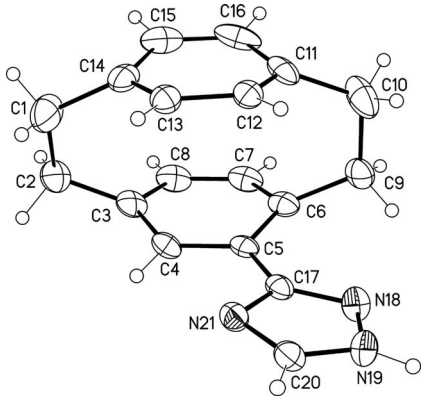
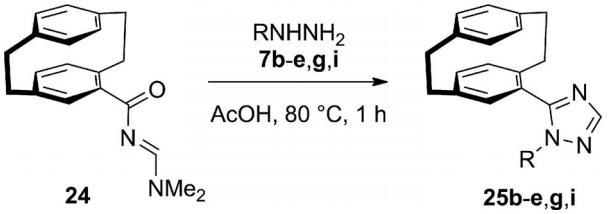


Figure 10. Molecular structure of **2a** in the solid state (displacement parameters are drawn at 50% probability level).

Again, a range of hydrazines were used to explore the scope of this reaction (Scheme 9), and triazole derivatives **25b**–**e**, **25g** and **25i** could be obtained in acceptable yields (Table 3).



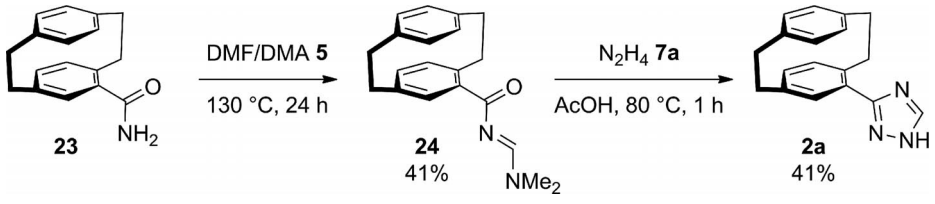
Scheme 9. Synthesis of triazolyl[2.2]paracyclophanes **25b**–**e**, **25g**, and **25i**.

Table 3. Summary of the synthesis of triazolyl[2.2]paracyclophanes.

Entry	Hydrazine	R	Yield [%]	Product
1	**7b**	Me	53	**25b**
2	**7c**	CH_2CF_3	45	**25c**
3	**7d**	cHex	64	**25d**[a]
4	**7e**	Ph	59	**25e**[a]
5	**7g**	4-BrC_6H_4	47	**25g**
6	**7i**	2-Py	49	**25i**[a]

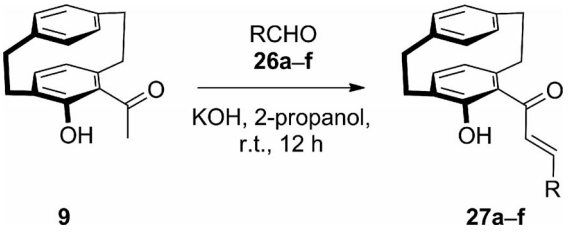
[a] Molecule structure given in the Supporting Information.

We then wanted to develop a method with which to access pyrimidine and pyridine derivatives of [2.2]paracyclophanes. Treating AHPC (**9**) with a range of aldehydes **26a**–**f** in a base-catalyzed aldol reaction generated the six compounds **27a**–**f** in quite low yields (Scheme 10, Table 4).[25]



Scheme 8. Synthesis of compound **2a** from amide[2.2]paracyclophane (**23**).

One illustrative molecular structure of compound **27e** is presented in Figure 11.



Scheme 10. Base-catalyzed aldol reaction with AHPC (**9**).

Table 4. Summary of the base-catalyzed aldol reactions.

Entry	Aldehyde	R	Yield [%]	Product
1	**26a**	Ph	28	**27a**[a]
2	**26b**	4-FC_6H_4	11	**27b**[a]
3	**26c**	4-$CF_3C_6H_4$	16	**27c**
4	**26d**	4-*t*BuC_6H_4	15	**27d**[a]
5	**26e**	3,5-$(OMe)_2$-C_6H_3	19	**27e**[a]
6	**26f**	[2.2]PC	3	**27f**

[a] Molecular structure given in the Supporting Information.

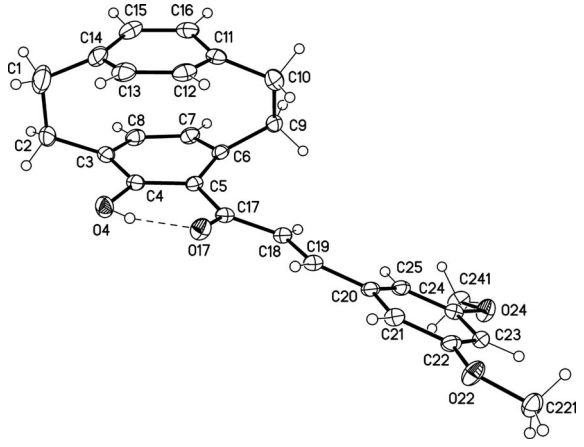
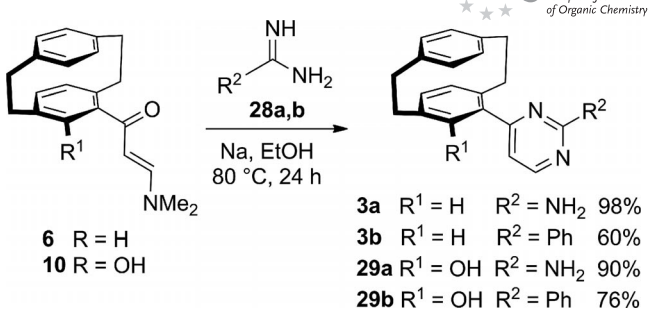


Figure 11. Molecular structure of **27e** in the solid state (displacement parameters are drawn at 50% probability level).

We expected to prepare pyrimidine derivatives from amidines,[26] and pyridines from malononitrile, respectively.[27] Unfortunately it was not possible to purify the products by using conventional separation methods or HPLC. To eliminate the possibility of rotamers, which can complicate the NMR spectra, ^{1}H NMR experiments at increased temperatures were carried out, however, with no satisfying outcome. In all reactions, chromone **20** was formed as a side product. However, reacting precursors **6** and **10** with guanidine (**28a**) or benzamidine (**28b**) resulted in the formation of compounds **3** and **29** in good to excellent yields (Scheme 11).[28] Due to steric hindrance and the fact that guanidine (**28a**) is a better nucleophile than benzamidine (**28b**), the yields of the aminopyrimidines were superior to those of the phenylpyrimidines. These compounds will form part of further research in asymmetric catalysis. Figure 12 shows the molecular structure of **29a**.



Scheme 11. Synthesis of pyrimidine derivatives.

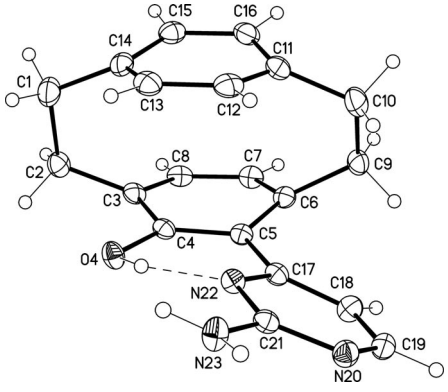
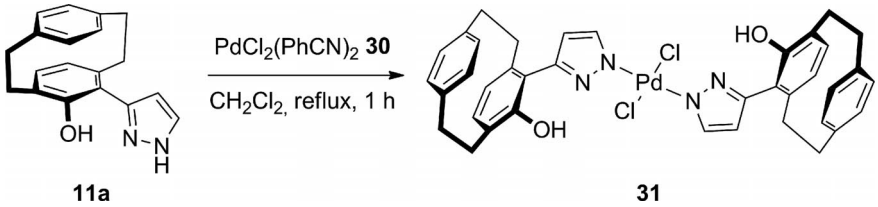


Figure 12. Molecular structure of **29a** in the solid state (displacement parameters are drawn at 50% probability level).

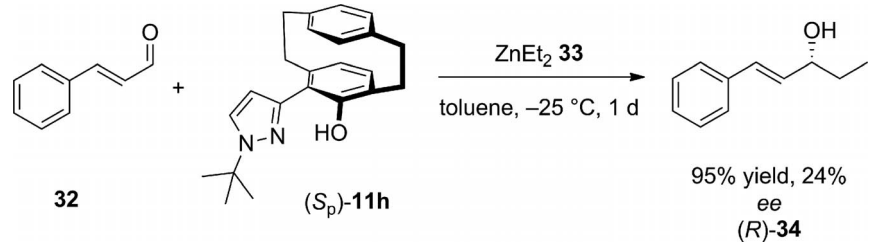
Treating hydroxy-pyrazolyl[2.2]paracyclophane (**11a**) with $PdCl_2(PhCN)_2$ (**30**) gave two diastereomers of the palladium chloride complex **31**, which were characterized by mass spectrometry (see Scheme 12 and the Supporting Information).

The next target was to synthesize an enantiomerically pure ligand for asymmetric conjugate addition (ACA). We focused on isomers A of the pyrazole type ligands **11**. This option gave us three possible structures **11a**, **11h** and **11i**. Although we achieved very good yield in synthesizing **11a**, the application of this compound was ruled out by the possibility that the NH group might interfere in catalysis. The yield of **11i** was too low to continue with this compound as the model catalyst. Therefore, synthesis of (S_p)-**11h**, bearing a *t*Bu group on the pyrazole, was carried out starting from enantiopure (S_p)-formyl[2.2]paracyclophane,[19] following the steps described earlier (Schemes 3 and 4).

To prove the catalytic activity of this new class of compounds, one representative ACA was carried out with (S_p)-**11h**. Cinnamaldehyde (**32**) was treated with diethylzinc (**33**) and a catalytic amount of (S_p)-**11h** (Scheme 13). The 1,2-product was obtained with (S_p)-**11h** in excellent yields; no side product from 1,4-addition was observed. Chiral phase HPLC analysis revealed 24% of enantiomeric excess (*ee*). Although the *ee* value was not as high as expected, ligand (S_p)-**11h** still acted as a catalyst, which opens up possibilities to optimize structures and reaction conditions.



Scheme 12. Reaction of racemic **11a** to form two diastereomers of the 1-hydroxy(2-pyrazol-3-yl)[2.2]paracyclophane palladium complex **31** (only the *rac*-isomer is shown for clarity).



Scheme 13. Asymmetric conjugate addition with ligand (S_p)-**11h** and diethylzinc of cinnamaldehyde (**32**).

Conclusions

We successfully synthesized various pyrazole, triazole and pyrimidine substituted [2.2]paracyclophane derivatives. The X-ray structure analyses and ^{1}H NMR spectra of the pyrazole products proved that different isomers are formed, suggesting that two mechanistic pathways are possible. Regarding the pyrazole structures, we correlated the substitution pattern with the ^{1}H NMR signal of the hydroxyl group. Hydroxy-pyrazolyl[2.2]paracyclophane **11a** is feasible as a ligand for metal complexes and, with one example, we showed that these ligand systems can be used as catalysts in asymmetric conjugate addition.

Experimental Section

General Procedure A for Aldol Derivatives: AHPC (**9**; 1.00 equiv.) and aldehyde (1.00 equiv.) were dissolved in 2-propanol (2 mL) and cooled to 0 °C, then 50% aq. KOH (2.00 equiv.) was added and the mixture was stirred at room temperature for 12 h. The red residue was filtered off, washed with cold 2-propanol and purified by column chromatography (cyclohexane/ethyl acetate, 50:1).

General Procedure B for 1-Hydroxy-2-pyrazol-3-yl)[2.2]paracyclophanes: A 10 mL microwave vessel was charged with **10** (1.00 equiv.), hydrazine (8.00 equiv.) and 2-propanol (2 mL) and the mixture was heated under microwave conditions (140 °C) for 2 h, dried with $MgSO_4$, and purified by column chromatography.

General Procedure C for Pyrazol-3-yl[2.2]paracyclophanes: A 10 mL microwave vessel was charged with **4** (1.00 equiv.), hydrazine (8.00 equiv.) and 2-propanol (2 mL), and the mixture was heated under microwave conditions (160 °C) for 2.5 h, dried with $MgSO_4$, and purified by column chromatography.

General Procedure D for Triazol-3-yl[2.2]paracyclophanes: A 5 mL high-pressure vessel was charged with **24** (1.00 equiv.), hydrazine (8.00 equiv.) and glacial acetic acid (1 mL). The mixture was heated to 80 °C for 1 h, then water was added and the mixture was extracted with ethyl acetate. The combined organic phases were dried with $MgSO_4$ and purified by column chromatography.

General Procedure E for (1-Hydroxy-2-pyrimidine-4-yl)[2.2]paracyclophanes: A 5 mL high-pressure vessel was charged with either **6** or **10** (1.00 equiv.), phenylamidine (1.30 equiv.), sodium (2.00 equiv.) and anhydrous ethanol (3 mL). The mixture was heated to 80 °C overnight, then the mixture was dried with $MgSO_4$ and purified by column chromatography.

Compound 1a: According to general procedure C with **10** (220 mg, 720 μmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 1:1) to give **1a** (188 mg, 95%) as a white crystalline solid. R_f = 0.45 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.71–2.80 (m, 1 H, H_{Pc}), 2.86–3.18 (m, 6 H, H_{Pc}), 3.75–3.82 (m, 1 H, H_{Pc}), 6.47–6.50 (m, 1 H, Pc-H_{Ar}), 6.56–6.70 (m, 7 H, Pc-H_{Ar}), 7.68–7.69 (m, 1 H, Pc-H_{Ar}), 12.35 (br. s, 1 H, NH) ppm. IR (DRIFT): $\tilde{\nu}$ = 3098 (w), 2921 (w), 2848 (w), 1594 (vw), 1540 (vw), 1499 (vw), 1450 (w), 1434 (w), 1399 (w), 1342 (vw), 1299 (vw), 1204 (vw), 111 (w), 1095 (w), 1076 (vw), 1049 (w), 989 (vw), 937 (w), 903 (w), 838 (w), 770 (w), 714 (w), 670 (w), 639 (w), 618 (w), 581 (w), 517 (w), 491 (w) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 274 (36) [M^+], 170 (47) [$C_{11}H_{10}N_2^+$], 104 (16) [$C_8H_8^+$]. HRMS: calcd. for $C_{19}H_{18}N_2$ 274.1469; found 274.1468.

Compound 2a: According to general procedure D with **24** (38.7 mg, 130 μmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **2a** (14.6 mg, 41%) as a white solid. R_f = 0.30 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.86–3.20 (m, 7 H, H_{Pc}), 3.92–4.01 (m, 1 H, H_{Pc}), 6.44–6.52 (m, 2 H, Pc-H_{Ar}), 6.55–6.59 (m, 2 H, Pc-H_{Ar}), 6.60–6.65 (m, 2 H, Pc-H_{Ar}), 7.01 (s, 1 H, Pc-H_{Ar}), 8.23 (s, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.9, 35.0, 35.2, 35.4 (–, 4× CH_2), 128.7 (C_{quat}), 131.0, 132.4, 132.9, 132.9, 133.0, 134.4, 135.6, 136.2 (+, 8× CH), 138.8, 139.4, 139.6, 140.4, 148.8 (5× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3109 (vw), 2926 (vw), 2850 (vw), 1757 (vw), 1593 (vw), 1511 (vw), 1481 (vw), 1450 (vw), 1433 (vw), 1409 (vw), 1383 (vw), 1305 (vw), 1263 (vw), 1177 (vw), 1081 (vw), 1060 (vw), 983 (vw), 940 (vw), 906 (w), 881 (vw), 844 (w), 806 (w), 794 (vw), 765 (vw), 716 (w), 640 (w), 583 (vw), 514 (w), 496 (vw), 479 (vw), 3017 (vw) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 275 (18) [M^+], 171 (5) [$C_{10}H_9N_3^+$], 104 (39) [$C_8H_8^+$], 103 (2) [$C_8H_7^+$], 91 (6) [$C_7H_7^+$]. HRMS: calcd. for $C_{18}H_{17}N_3$ 275.1422; found 275.1420.

Compound 3a: According to general procedure E with **6** (43.0 mg, 140 μmol). The crude product was purified by column chromatog-

raphy (cyclohexane/ethyl acetate, 1:1) to give **3a** (41.3 mg, 98%) as a white solid. R_f = 0.44 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.79–2.85 (m, 1 H, H_{Pc}), 2.94–3.01 (m, 2 H, H_{Pc}), 3.02–3.10 (m, 2 H, H_{Pc}), 3.12–3.22 (m, 2 H, H_{Pc}), 3.73–3.83 (m, 1 H, H_{Pc}), 5.30 (br. s, 2 H, NH_2), 6.49–6.56 (m, 2 H, Pc-H_{Ar}), 6.58–6.61 (m, 4 H, Pc-H_{Ar}), 6.83 (s, 1 H, Pc-H_{Ar}), 6.86 (d, J = 5.27 Hz, 1 H, Pc-H_{Ar}), 8.36 (d, J = 5.27 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.6, 35.2, 35.3, 35.4 (–, 4× CH_2), 111.4, 130.8 (+, 2× CH), 132.0 (C_{quat}), 132.3, 132.6, 132.8, 133.0, 134.5, 136.4 (+, 6× CH), 138.2, 138.9, 139.4, 139.7, 139.9 (5× C_{quat}), 157.4 (+, CH), 162.5 (C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3302 (w), 3138 (w), 3000 (w), 2920 (w), 2849 (w), 1651 (w), 1561 (m), 1544 (w), 1475 (w), 1452 (w), 1433 (w), 1343 (w), 1289 (w), 1217 (w), 1084 (w), 1000 (vw), 931 (vw), 901 (w), 837 (w), 813 (w), 742 (w), 714 (w), 678 (w), 644 (w), 634 (w), 897 (w), 574 (w), 518 (w), 506 (w), 485 (w), 440 (w) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 301 (79) [M^+], 197 (100) [$C_{12}H_{11}N_3^+$], 104 (2) [$C_8H_8^+$]. HRMS: calcd. for $C_{20}H_{19}N_3$ 301.1579; found 301.1578.

Compound 3b: According to general procedure E with **6** (43.0 mg, 140 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **3b** (30.0 mg, 60%) as a white solid. R_f = 0.68 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.69–282 (m, 1 H, H_{Pc}), 2.88–3.15 (m, 6 H, H_{Pc}), 3.75–3.86 (m, 1 H, H_{Pc}), 6.51–6.56 (m, 6 H, Pc-H_{Ar}), 6.92 (s, 1 H, Pc-H_{Ar}), 7.24 (d, J = 5.17 Hz, 1 H, Pc-H_{Ar}), 7.43–7.53 (m, 3 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.7, 35.2, 35.3, 35.5 (–, 4× CH_2), 118.8, 128.3 (2×), 128.7 (2×), 130.7, 131.0, 132.5, 132.6, 133.0, 133.4, 134.5, 136.3 (+, 13× CH), 138.2, 138.3, 139.0, 139.4, 139.6, 140.1 (6× C_{quat}), 157.2 (+, CH), 164.5, 166.0 (2× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3006 (vw), 2922 (w), 2849 (w), 1896 (vw), 1738 (vw), 1674 (vw), 1585 (w), 1559 (w), 1536 (w), 1499 (w), 1456 (w), 1430 (w), 1404 (w), 1369 (w), 1324 (w), 1296 (w), 1238 (w), 1171 (w), 1156 (w), 1096 (vw), 1068 (vw), 1047 (vw), 1025 (w), 986 (vw), 938 (vw), 904 (w), 883 (vw), 865 (w), 849 (w), 798 (w), 765 (w), 731 (w), 712 (w), 696 (w), 672 (w), 649 (w), 634 (w), 578 (w), 512 (w), 497 (w), 463 (vw), 437 (vw) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 362 (29) [M^+], 259 (6) [$C_{19}H_{17}N^+$], 258 (35) [$C_{18}H_{14}N_2^+$], 104 (43) [$C_8H_8^+$], 103 (2) [$C_7H_5N^+$]. HRMS: calcd. for $C_{26}H_{22}N_2$ 362.1781; found 362.1783.

Compound 6: A high-pressure vessel was charged with 4-acetyl[2.2]-paracyclophane (**4**; 1.54 g, 6.16 mmol) and DMF-DMA (**5**; 2.56 mL, 2.20 g, 18.5 mmol) snd the mixture was heated to 120 °C overnight. The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **6** (1.23 g, 65%) as a light-yellow solid. R_f = 0.26 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.83–3.23 (m, 13 H, H_{Pc} and 2× Me), 3.63–3.82 (m, 1 H, H_{Pc}), 5.32 (d, J = 12.6 Hz, 1 H, Pc-H_{Ar}), 6.40 (d, J = 7.3 Hz, 1 H, Pc-H_{Ar}), 6.45 (d, J = 7.8 Hz, 1 H, Pc-H_{Ar}), 6.49–6.57 (m, 3 H, Pc-H_{Ar}), 6.71–6.79 (m, 2 H, Pc-H_{Ar}), 7.58 (d, J = 12.5 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.1, 35.2, 35.3, 35.6 (–, 4× CH_2), 37.1, 44.9 (+, 2× CH_3), 96.8, 131.9, 132.3, 132.3, 132.5, 132.6, 134.4, 135.6 (+, 8× CH), 139.1, 139.4, 139.5, 140.2, 140.5 (5× C_{quat}), 153.4 (+, CH), 191.9 (CO, C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2924 (vw), 2849 (vw), 2325 (vw), 2039 (vw), 1977 (vw), 1892 (vw), 1643 (w), 1567 (w), 1501 (vw), 1431 (vw), 1348 (vw), 1292 (vw), 1237 (vw), 1179 (vw), 1108 (vw), 1086 (vw), 1034 (vw), 978 (vw), 935 (vw), 893 (vw), 854 (vw), 805 (w), 770 (vw), 752 (vw), 719 (w), 670 (vw), 621 (w), 508 (w), 407 (vw) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 305 (28) [M^+], 201 (36) [$C_{13}H_{15}N_2O^+$], 157 (4) [$C_{11}H_9O^+$], 104 (42) [$C_8H_8^+$], 103 (23) [$C_8H_7^+$], 98 (4) [$C_5H_8NO^+$]. HRMS: calcd. for $C_{21}H_{23}NO$ 305.1780; found 305.1783.

Compound 8b: According to general procedure C with **6** (519 mg, 1.70 mmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 3:1) to give **8b** (39.0 mg, 8%) as a light-yellow crystalline solid. R_f = 0.28 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.82–2.91 (m, 3 H, H_{Pc}), 2.99–3.15 (m, 5 H, H_{Pc}), 3.65 (s, 3 H, Me), 6.46 (dd, J = 7.8, 1.3 Hz, 1 H, Pc-H_{Ar}), 6.50–6.52 (m, 2 H, Pc-H_{Ar}), 6.57–6.59 (m, 2 H, Pc-H_{Ar}), 6.62 (dq, J = 7.9, 1.5 Hz, 2 H, Pc-H_{Ar}), 6.70 (dd, J = 7.9, 1.5 Hz, 1 H, Pc-H_{Ar}), 7.63 (d, J = 1.5 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.6, 35.0, 35.2, 35.4 (–, 4× CH_2), 36.7 (+, CH_3), 105.9, 129.9 (+, 2× CH), 130.2 (C_{quat}), 132.3, 132.4, 133.4, 134.2, 135.1 (+, 5× CH), 138.5 (C_{quat}), 138.7 (+, CH), 139.4, 139.5, 140.3, 144.4 (4× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3105 (vw), 2920 (m), 2850 (w), 1894 (vw), 1672 (w), 1592 (w), 1500 (w), 1478 (w), 1451 (w), 1432 (w), 1411 (w), 1397 (m), 1272 (w), 1228 (w), 1184 (w), 1092 (w), 1069 (w), 998 (w), 951 (vw), 928 (w), 899 (m), 839 (m), 813 (m), 793 (m), 733 (m), 710 (m), 679 (w), 666 (w), 649 (m), 638 (m), 585 (m), 518 (m), 494 (m), 466 (w), 403 (w) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 288 (100) [M^+], 184 (86) [$C_{12}H_{12}N_2^+$], 169 (21) [$C_{11}H_9N_2^+$], 104 (42) [$C_8H_8^+$], 103 (9) [$C_8H_7^+$], 78 (5) [$C_5H_4N^+$], 77 (5) [$C_6H_5^+$]. HRMS: calcd. for $C_{20}H_{20}N_2$ 288.1626; found 288.1628.

Compound 8c: According to general procedure C with **6** (35.0 mg, 110 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **8c** (36 mg, 92%) as a white crystalline solid. R_f = 0.53 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.73–2.79 (m, 1 H, H_{Pc}), 2.86–2.92 (m, 2 H, H_{Pc}), 2.94–3.06 (m, 2 H, H_{Pc}), 3.08–3.18 (m, 3 H, H_{Pc}), 4.52 (dq, J = 8.26, 0.67 Hz, 2 H, CH_2CF_3), 6.46 (dd, J = 7.9, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.51 (d, J = 1.7 Hz, 1 H, Pc-H_{Ar}), 6.57–6.59 (m, 1 H, Pc-H_{Ar}), 6.59–6.63 (m, 3 H, Pc-H_{Ar}), 6.65–6.67 (m, 1 H, Pc-H_{Ar}), 6.68–6.71 (m, 1 H, Pc-H_{Ar}), 7.76 (d, J = 1.8 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.2, 35.0, 35.1, 35.4 (–, 4× CH_2), 49.7 (–, q, J = 35.0 Hz, CH_2), 107.1 (+, CH), 122.8 (q, J = 280.7 Hz, C_{quat}), 129.0 (C_{quat}), 129.9, 132.4, 132.4, 133.4, 134.0, 134.8, 135.5 (+, 7× CH), 137.4, 139.2, 139.7, 140.8 (4× C_{quat}), 140.9 (+, CH), 148.8 (C_{quat}) ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ = –70.4 (CF_3) ppm. IR (DRIFT): $\tilde{\nu}$ = 2915 (vw), 2854 (vw), 1594 (vw), 1503 (vw), 1464 (vw), 1414 (w), 1380 (w), 1317 (w), 1269 (w), 1255 (w), 1186 (w), 1146 (w), 1073 (w), 1010 (vw), 926 (w), 908 (w), 882 (vw), 835 (w), 790 (w), 724 (w), 708 (vw), 674 (vw), 661 (w), 646 (w), 587 (w), 532 (vw), 417 (w), 499 (w), 405 (vw) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 356 (37) [M^+], 252 (18) [$C_{13}H_{11}F_3N_2^+$], 183 (3) [$C_{12}H_{11}N_2^+$], 104 (31) [$C_8H_8^+$], 69 (11) [CF_3^+]. HRMS: calcd. for $C_{21}H_{19}F_3N_2$ 356.1500; found 356.1501.

Compound 8d: According to general procedure C with **6** (46.0 mg, 150 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 20:1) to give **8d** (17 mg, 32%) as a white crystalline solid. R_f = 0.53 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93–1.05 (m, 1 H, *c*Hex), 1.14–1.26 (m, 2 H, *c*Hex), 1.32–1.38 (m, 1 H, *c*Hex), 1.53–1.62 (m, 3 H, *c*Hex), 1.87–1.92 (m, 1 H, *c*Hex), 2.05–2.11 (m, 1 H, *c*Hex), 2.15–2.23 (m, 1 H, *c*Hex), 2.83–3.05 (m, 5 H, CH, H_{Pc}), 3.08–3.17 (m, 3 H, H_{Pc}), 3.87–3.95 (m, 1 H, H_{Pc}), 6.46 (dd, J = 7.9, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.49 (d, J = 1.8 Hz, 1 H, Pc-H_{Ar}), 6.50 (s, Pc-H_{Ar}), 6.56–6.57 (m, 2 H, Pc-H_{Ar}), 6.61 (dd, J = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.67 (dd, J = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.71 (dd, J = 7.9, 1.8 Hz, 1 H, Pc-H_{Ar}), 7.68 (d, J = 1.7 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.2, 24.4, 24.8, 30.76, 32.2, 32.8, 34.1 (2×), 34.4 (–, 9× CH_2), 56.7 (+, NCH), 104.7, 128.9 (–, 2× CH_2), 129.3 (C_{quat}), 131.1, 131.5, 132.3, 132.8, 133.1, 134.0 (–, 6× CH_2), 137.4 (C_{quat}), 137.7 (–,CH_2), 138.4, 138.5, 139.1, 142.1 (4× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3088 (vw), 2916 (w), 2846 (w), 1678

(w), 1591 (vw), 1527 (vw), 1500 (vw), 1450 (w), 1396 (w), 1359 (w), 1324 (w), 1260 (w), 1186 (w), 1127 (w), 1099 (w), 1064 (w), 1010 (vw), 999 (w), 956 (vw), 928 (w), 895 (w), 857 (vw), 839 (w), 816 (w), 800 (w), 767 (w), 760 (w), 722 (w), 672 (w), 643 (w), 891 (w), 637 (w), 510 (m), 484 (w), 462 (w), 406 (w) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 256 (100) [$C_{25}H_{28}N_2^+$], 274 (93) [$C_{19}H_{17}N_2^+$], 252 (28) [M^+], 169 (93) [$C_{11}H_9N_2^+$], 104 (41) [$C_8H_8^+$]. HRMS: calcd. for $C_{17}H_{20}N_2$ 356.2252; found 356.2254.

Compound 8f: According to general procedure C with **6** (46.0 mg, 150 μmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 10:1) to give **8f** (33.5 mg, 61%) as a light-yellow crystalline solid. R_f = 0.86 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.87–3.14 (m, 8 H, H_{Pc}), 5.05 (d, *J* = 15.0 Hz, 1 H, CH_2-Ph), 5.20 (d, *J* = 15.0 Hz, 1 H, CH_2-Ph), 6.46–6.49 (m, 2 H, Pc-H_{Ar}), 6.56 (d, *J* = 1.8 Hz, 1 H, Pc-H_{Ar}), 6.63 (dd, *J* = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.73 (dd, *J* = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.74 (dd, *J* = 7.9, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.81–6.86 (m, 2 H, Pc-H_{Ar}), 7.12–7.15 (m, 3 H, Pc-H_{Ar}), 7.69 (d, *J* = 1.8 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.6, 35.1, 35.2, 35.4 (–, 4× CH_2), 52.9 (–, CH_2Ph), 106.2, 127.4, 128.3, 128.6, 128.8 (+, 5× CH), 129.0 (C_{quat}), 129.8, 130.0 (+, 2× CH), 130.1 (C_{quat}), 132.3, 132.4, 133.3, 134.0, 134.3, 135.2 (+, 6× CH), 137.0, 138.3, 139.5 (3× C_{quat}), 139.5 (+, CH), 140.3, 144.4 (2× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3089 (w), 3064 (m), 3030 (m), 3009 (m), 2928 (s), 2891 (m), 2852 (m), 1894 (vw), 1736 (m), 1701 (w), 1626 (w), 1595 (m), 1533 (w), 1497 (m), 1455 (s), 1434 (m), 1399 (s), 1359 (w), 1297 (m), 1270 (m), 1241 (m), 1204 (m), 1181 (w), 1129 (w), 1102 (m), 1061 (w), 1029 (w), 1011 (w), 928 (m), 906 (m), 842 (m), 781 (s), 727 (s), 695 (s), 673 (w), 641 (m), 593 (w), 577 (w), 518 (m), 498 (m), 457 (w) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 364 (1) [M^+], 104 (3) [$C_8H_8^+$], 103 (2) [$C_8H_7^+$], 91 (85) [$C_7H_7^+$], 78 (9) [$C_5H_4N^+$], 77 (48) [$C_6H_5^+$]. HRMS: calcd. for $C_{26}H_{24}N_2$ 364.1939; found 364.1942.

Compound 8g: According to general procedure C with **6** (48.0 mg, 160 μmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 20:1) to give **8g** (51 mg, 74%) as a light-yellow crystalline solid. R_f = 0.53 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41–2.54 (m, 2 H, H_{Pc}), 2.74–2.78 (m, 2 H, H_{Pc}), 3.04–3.13 (m, 4 H, H_{Pc}), 6.32 (d, *J* = 7.8 Hz, 1 H, Pc-H_{Ar}), 6.47 (dd, *J* = 7.9, 1.9 Hz, 1 H, Pc-H_{Ar}), 6.51–6.56 (m, 2 H, Pc-H_{Ar}), 6.59 (d, *J* = 1.8 Hz, 1 H, Pc-H_{Ar}), 6.62 (dd, *J* = 7.8, 1.9 Hz, 1 H, Pc-H_{Ar}), 6.69 (dd, *J* = 7.3, 1.8 Hz, 2 H, Pc-H_{Ar}), 6.96–7.00 (m, 2 H, Pc-H_{Ar}), 7.29–7.33 (m, 2 H, Pc-H_{Ar}), 7.83 (d, *J* = 1.8 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.6, 34.8, 35.1, 35.4 (–, 4× CH_2), 108.2 (+, CH), 120.4 (C_{quat}), 128.88 (2×), 129.6 (+, 3× CH), 129.7 (C_{quat}), 131.5 (2×), 132.2, 132.3, 133.0, 133.3, 134.5, 135.4 (+, 8× CH), 138.7, 139.2, 139.4, 139.6, 140.2 (5× C_{quat}), 140.77 (+, CH), 143.9 (C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2920 (vw), 2849 (vw), 1589 (vw), 1531 (vw), 1488 (w), 1453 (w), 1403 (w), 1377 (w), 1097 (vw), 1072 (w), 1010 (w), 991 (w), 924 (w), 898 (w), 865 (vw), 827 (m), 782 (m), 721 (w), 704 (w), 675 (vw), 638 (w), 589 (w), 552 (vw), 515 (w), 486 (vw), 467 (vw), 454 (w), 411 (vw), 309 (vw) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 428 (82) [M^+], 349 (73) [$C_{25}H_{21}N_2^+$], 324 (36) [$C_{17}H_{13}BrN_2^+$], 245 (73) [$C_{17}H_{13}N_2^+$], 104 (55) [$C_8H_8^+$], 78 (10) [Br]. HRMS: calcd. for $C_{25}H_{21}BrN_2$ 428.0888; found 428.0886.

Compound 10: A high-pressure vessel was charged with AHPC (**9**; 0.470 g, 1.75 mmol) and DMF–DMA (**5**; 0.610 mL, 0.520 g, 4.37 mmol). The mixture was heated to 90 °C for 20 min, then the crude product was purified by column chromatography (cyclohexane/ethyl acetate, 1:1) to give **10** (523 mg, 93%) as a yellow solid; m.p. 220.2 °C. R_f = 0.37 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 2.65–2.72 (m, 1 H, H_{PC}), 2.81–3.03 [m, 8 H, H_{PC} + $N(CH_3)_2$], 3.14–3.21 (m, 4 H, H_{PC}), 3.69–3.77 (m, 1 H, H_{PC}), 5.34 (d, *J* = 12.2 Hz, 1 H, COCH), 6.23 (d, *J* = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.28 (dd, *J* = 17.7, 1.4 Hz, 1 H, Pc-H_{Ar}), 6.39–6.46 (m, 2 H, Pc-H_{Ar}), 6.60 (dd, *J* = 7.8, 1.4 Hz, 1 H, Pc-H_{Ar}), 6.85 (dd, *J* = 7.7, 1.5 Hz, 1 H, Pc-H_{Ar}), 7.78 (d, *J* = 12.2 Hz, 1 H, CHN), 13.47 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, DMSO): δ = 29.5, 33.3, 34.6, 36.6 (–, 4× CH_2), 37.2, 44.8 (+, 2× CH_3), 96.0 (+, CO*C*H), 123.7 (C_{quat}), 126.2, 127.0, 130.7, 131.8, 132.7, 136.9 (+, 6× CH), 138.0, 139.1, 140.5 (3× C_{quat}), 154.3 (+, NCH), 160.1 (C_{quat}, COH), 190.5 (C_{quat}, CO) ppm. IR (DRIFT): $\tilde{\nu}$ = 2941 (vw), 1879 (vw), 1623 (m), 1567 (w), 1538 (w), 1491 (vw), 1423 (w), 1400 (m), 1358 (w), 1329 (w), 1269 (w), 1230 (m), 1156 (w), 1082 (m), 1018 (w), 976 (w), 937 (w), 856 (w), 794 (w), 756 (w), 734 (w), 715 (w), 715 (w), 655 (w), 602 (w), 573 (w), 535 (w), 505 (w), 461 (vw), 402 (vw) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 321 (70) [M^+], 217 (58) [$C_{13}H_{15}NO_2^+$], 104 (100) [$C_8H_8^+$], 98 (8) [C_5H_8NO]. $C_{21}H_{23}NO_2$ (321.17): calcd. C 78.47, H 7.21, N 4.36; found C 77.78, H 7.09, N 4.08.

Compound 11a: According to general procedure B with **10** (1.17 g, 3.64 mmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 3:1) to give **11a** (1.00 g, 95%) as a white solid; m.p. = 155.4 °C. R_f = 0.59 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.55–2.65 (m, 2 H, H_{Pc}), 2.80–2.87 (m, 1 H, H_{Pc}), 2.95–3.09 (m, 2 H, H_{Pc}), 3.17–3.24 (m, 1 H, H_{Pc}), 3.45–3.52 (m, 1 H, H_{Pc}), 3.68–3.74 (m, 1 H, H_{Pc}), 6.31 (dd, *J* = 7.7, 1.9 Hz, 1 H, Pc-H_{Ar}), 6.32 (d, *J* = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.42 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.48 (dd, *J* = 7.9, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.57 (d, *J* = 2.5 Hz, 1 H, H_{Py}), 6.58–6.60 (m, 1 H, H_{Ar}), 7.03 (dd, *J* = 7.8, 1.9 Hz, 1 H, H_{Ar}), 7.63 (d, *J* = 2.5 Hz, 1 H, H_{Py}), 10.23 (br. s, 1 H, NH), 10.70 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.8, 34.0, 34.3, 35.2 (–, 4× CH_2), 106.4 (+, NHCH*C*H), 118.7 (C_{quat}), 126.6, 127.5 (+, 2× CH), 127.6 (C_{quat}), 129.0, 129.9, 132.1, 132.9, 134.4 (+, 5× CH), 138.2, 139.4, 139.9 (3× C_{quat}), 151.0 (C_{quat}, NHN*C*), 154.6 (C_{quat}, CO) ppm. IR (DRIFT): $\tilde{\nu}$ = 3363 (vw), 2940 (w), 1851 (vw), 1608 (vw), 1567 (vw), 1524 (vw), 1501 (vw), 1429 (w), 1278 (vw), 1238 (w), 1182 (w), 1146 (vw), 1088 (w), 1061 (vw), 1012 (w), 985 (vw), 958 (vw), 936 (vw), 925 (vw), 875 (vw), 801 (w), 770 (w), 750 (w), 709 (w), 667 (w), 600 (vw), 566 (w), 513 (w), 466 (vw) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 290 (22) [M^+], 223 (5) [$C_{16}H_{15}O^+$], 186 (27) [$C_{11}H_{10}N_2O^+$], 104 (16) [$C_8H_8^+$], 68 (14) [$C_3H_3N_2^+$ + H], 42 (100). HRMS: calcd. for $C_{19}H_{18}N_2O$ 290.1419; found 290.1420.

Compound 11b: Hydroxy-pyrazolyl[2.2]paracyclophane (**11a**; 100 mg, 340 μmol) was dissolved in anhydrous THF (1 mL), and NaH (**13**; 17.0 mg, 690 μmol) was added at 0 °C. In a period of 2 h, the mixture was warmed to room temperature. MeI (**14**; 40.0 μL, 690 μmol) in anhydrous THF (1 mL) was added slowly and the mixture was stirred for 12 h at room temperature. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate and $NaHCO_3$ was added. The aqueous phase was extracted with ethyl acetate (3× 20 mL) and the combined organic layers were dried with $MgSO_4$ and purified by column chromatography (cyclohexane/ethyl acetate, 3:1) to give **11b** (50.5 mg, 49%) as a white solid. R_f = 0.81 (cyclohexane/ethyl acetate, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.57–2.67 (m, 2 H, H_{Pc}), 2.78–2.86 (m, 1 H, H_{Pc}), 2.95–3.09 (m, 2 H, H_{Pc}), 3.17–3.24 (m, 1 H, H_{Pc}), 3.45–3.52 (m, 1 H, H_{Pc}), 3.70–3.76 (m, 1 H, H_{Pc}), 3.99 (s, 3 H, Me), 3.29 (d, *J* = 7.7 Hz, 1 H, H_{Pc}), 6.33 (dd, *J* = 7.7, 1.9 Hz, 1 H, Pc-H_{Ar}), 6.41 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.48 (d, *J* = 2.3 Hz, 1 H, H_{Py}), 6.49 (dd, *J* = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.59 (dd, *J* = 7.8, 1.8 Hz, 1 H, H_{Ar}), 7.05 (dd, *J* = 7.7, 1.9 Hz, 1 H, H_{Ar}), 7.40 (d, *J* = 2.3 Hz, 1 H, H_{Py}-NMe), 10.89 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz,

$CDCl_3$): δ = 30.8, 34.1, 34.2, 35.3 (–, 4× CH_2), 39.0 (+, CH_3), 106.7 (+, CH), 119.0 (C_{quat}), 126.5, 127.6 (+, 2× CH), 127.6 (C_{quat}), 129.8, 130.7, 132.1, 132.9, 134.1 (+, 5× CH), 138.2, 139.1, 139.9, 150.7, 154.7 (5× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2920 (vw), 2848 (vw), 1604 (vw), 1570 (vw), 1518 (vw), 1491 (vw), 1433 (w), 1412 (w), 1341 (vw), 1309 (vw), 1290 (w), 1225 (w), 1147 (vw), 1127 (vw), 1076 (vw), 1016 (vw), 962 (vw), 931 (vw), 877 (vw), 772 (w), 688 (w), 665 (w), 598 (vw), 578 (vw), 564 (vw), 540 (vw), 512 (w), 464 (vw), 435 (vw) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 304 (75) [M^+], 200 (100) [$C_{12}H_{12}N_2O^+$], 104 (7) [$C_8H_8^+$], 81 (6) [$C_4H_5N_2^+$]. HRMS: calcd. for $C_{20}H_{20}N_2O$ 304.1576; found 304.1578.

Compound 11h: According to general procedure B with **10** (250 mg, 780 μmol). The crude product was purified by column chromatography (pentane/ethyl acetate, 5:1) to give **11h** (127 mg, 47%) as a yellow crystalline solid. R_f = 0.74 (pentane/ethyl acetate, 4:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.70 (s, 9 H, *t*Bu), 2.56–2.66 (m, 2 H, H_{Pc}), 2.77–2.84 (m, 1 H, H_{Pc}), 2.96–3.11 (m, 2 H, H_{Pc}), 3.18–3.26 (m, 1 H, H_{Pc}), 3.44–3.53 (m, 1 H, H_{Pc}), 3.71–3.80 (m, 1 H, H_{Pc}), 6.25 (dd, *J* = 7.7, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.31 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.43 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.47–6.49 (m, 2 H, Pc-H_{Ar}), 6.58 (dd, *J* = 8.0, 1.7 Hz, 1 H, Pc-H_{Ar}), 7.06 (dd, *J* = 7.7, 1.8 Hz, 1 H, Pc-H_{Ar}), 7.07 (d, *J* = 1.8 Hz, 1 H, Pc-H_{Ar}), 11.25 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.7 (+, 3× CH_3), 31.0, 34.0, 34.1, 35.4 (–, 4× CH_2), 58.6 [*C*(CH_3), C_{quat}], 105.7 (+,CH), 119.3 (C_{quat}), 126.4, 126.5, 127.3 (+, 3× CH), 127.6 (C_{quat}), 129.6, 132.0, 133.0, 133.8 (+, 4× CH), 138.2, 139.1, 139.8, 150.0, 154.8 (5× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2972 (w), 2928 (m), 1676 (vw), 1601 (w), 1568 (w), 1498 (w), 1475 (w), 1420 (m), 1364 (m), 1343 (m), 1288 (m), 1231 (m), 1147 (w), 1124 (m), 1099 (w), 1065 (w), 1019 (m), 960 (w), 935 (w), 878 (w), 796 (w), 771 (m), 714 (m), 663 (m), 643 (m), 611 (m), 593 (w), 576 (w), 512 (m), 465 (w), 419 (vw) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 346 (1) [M^+], 268 (23) [$C_{23}H_{26}N_2O^+$], 104 (27) [$C_8H_8^+$], 77 (4) [$C_6H_5^+$], 57 (8) [$C_4H_9^+$]. HRMS: calcd. for $C_{23}H_{26}N_2O$ 346.2045; found 346.2044.

Compound (S_p)-11h: According to general procedure B with (S_p)-**10** (402 mg, 1.25 mmol). The crude product was purified by column chromatography (ethyl acetate/cyclohexane, 50:1) to give (S_p)-**11h** (190 mg, 44%) as a yellow crystalline solid; $[\alpha]_D^{20}$ = –208 (*c* = 1.6 mg/mL, EtOAc); R_f = 0.47 (ethyl acetate/cyclohexane, 5:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.70 (s, 9 H, *t*Bu), 2.51–2.64 (m, 2 H, H_{Pc}), 2.72–2.83 (m, 1 H, H_{Pc}), 2.91–3.10 (m, 2 H, H_{Pc}), 3.14–3.24 (m, 1 H, H_{Pc}), 3.43–3.50 (m, 1 H, H_{Pc}), 3.68–3.81 (m, 1 H, H_{Pc}), 6.24 (dd, *J* = 7.7, 1.5 Hz, 1 H, Pc-H_{Ar}), 6.29 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.41 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.44–6.48 (m, 2 H, Pc-H_{Ar}), 6.54–6.57 (m, 1 H, Pc-H_{Ar}), 7.01–7.04 (m, 1 H, Pc-H_{Ar}), 7.56 (d, *J* = 2.45 Hz, 1 H, Pc-H_{Ar}), 11.22 (br. s, 1 H, OH) ppm.

Compound 11i: According to general procedure B with **10** (168 mg, 520 μmol). The crude product was purified by column chromatography (pentane/ethyl acetate, 5:1) to give **11i** (7.7 mg, 4%) as an orange crystalline solid. R_f = 0.90 (pentane/ethyl acetate, 2:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.60–2.68 (m, 2 H, H_{Pc}), 2.84–2.92 (m, 1 H, H_{Pc}), 2.98–3.11 (m, 2 H, H_{Pc}), 3.19–3.26 (m, 1 H, H_{Pc}), 3.46–3.53 (m, 1 H, H_{Pc}), 3.70–3.77 (m, 1 H, H_{Pc}), 6.35 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.38 (dd, *J* = 7.8, 1.9 Hz, 1 H, Pc-H_{Ar}), 6.47 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.50 (dd, *J* = 7.8, 1.6 Hz, 1 H, Pc-H_{Ar}), 6.60 (dd, *J* = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 6.73 (d, *J* = 2.7 Hz, 1 H, Pc-H_{Ar}), 7.76 (dd, *J* = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 7.24–7.27 (m, 1 H, Pc-H_{Ar}), 7.89–7.94 (m, 1 H, Pc-H_{Ar}), 8.01 (d, *J* = 8.2 Hz, 1 H, Pc-H_{Ar}), 8.47–8.48 (m, 1 H, Pc-H_{Ar}), 8.65 (d, *J* = 2.7 Hz, 1 H, Pc-H_{Ar}), 10.71 (s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.8, 34.0, 34.3, 35.4 (–, 4× CH_2), 109.3, 112.0 (+, 2× CH), 118.3 (C_{quat}), 121.6, 126.7, 127.4 (+, 3× CH), 127.7 (C_{quat}), 127.8, 129.8, 132.2, 132.9, 134.9 (+, 5× CH), 138.2 (C_{quat}), 139.0 (+,CH), 139.8, 139.9 (2× C_{quat}), 148.3 (+,CH), 153.2, 154.7 (2× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3147 (vw), 3013 (vw), 2925 (w), 2850 (w), 1742 (vw), 1594 (m), 1577 (m), 1521 (m), 1470 (m), 1447 (s), 1413 (m), 1348 (m), 1293 (m), 1236 (w), 1147 (w), 1123 (w), 1087 (w), 1055 (m), 1018 (m), 992 (w), 969 (w), 954 (w), 931 (w), 907 (w), 878 (w), 771 (s), 730 (m), 715 (s), 662 (m), 620 (w), 582 (m), 512 (m), 464 (w), 405 (w) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 367 (100) [M^+], 263 (100) [$C_{16}H_{13}N_3O^+$], 185 (10) [$C_{11}H_9N_2O^+$], 119 (5) [$C_8H_7O^+$], 104 (56) [$C_8H_8^+$], 78 (16) [$C_5H_4N^+$], 77 (6) [$C_6H_5^+$]. HRMS: calcd. for $C_{24}H_{21}N_3O$ 367.1685; found 367.1682.

Compound 11k: In a high-pressure vessel, **11a** (127 mg, 440 μmol) was dissolved in anhydrous DMF (2 mL), and NaH (**13**; 12.0 mg, 480 μmol) and MOMCl (50.0 μL, 660 μmol) were added. The mixture was stirred at room temperature for 30 min and quenched with water. The solution was extracted with ethyl acetate (3× 20 mL) and dried with $MgSO_4$. The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 3:1) to give **11k** (80 mg, 55%) as a white solid. R_f = 0.50 (cyclohexane/ethyl acetate, 3:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.56–2.65 (m, 2 H, H_{Pc}), 2.80–2.87 (m, 1 H, H_{Pc}), 2.97–3.10 (m, 2 H, H_{Pc}), 3.17–3.24 (m, 1 H, H_{Pc}), 3.44 (s, 3 H, Me), 3.46–3.53 (m, 1 H, H_{Pc}), 3.68–3.74 (m, 1 H, H_{Pc}), 5.48 (q, *J* = 10.9, 6.1 Hz, 2 H, OCH_2), 6.30 (dd, *J* = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.32 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.43 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.49 (dd, *J* = 7.9, 1.6 Hz, 1 H, Pc-H_{Ar}), 6.59 (dd, *J* = 8.8, 2.5 Hz, 2 H, Pc-H_{Ar}), 7.05 (dd, *J* = 7.7, 1.7 Hz, 1 H, Pc-H_{Ar}), 7.62 (d, *J* = 2.5 Hz, 1 H, Pc-H_{Ar}), 10.76 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.8, 34.0, 34.3, 35.3 (–, 4× CH_2), 57.0 (+, OCH_3), 81.9 (–, CH_2), 108.2 (+, CH), 118.6 (C_{quat}), 126.6, 127.5 (+, 2× CH), 127.7 (C_{quat}), 129.7, 130.6, 132.1, 133.0, 134.4 (+, 5× CH), 138.1, 139.4, 139.9, 151.5, 154.7 (5× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2930 (w), 1733 (vw), 1598 (w), 1567 (w), 1516 (w), 1498 (w), 1484 (w), 1412 (m), 1327 (w), 1291 (w), 1240 (w), 1214 (w), 1188 (w), 1149 (w), 1108 (m), 1059 (m), 1042 (w), 1018 (w), 989 (w), 962 (vw), 940 (w), 919 (w), 880 (w), 778 (m), 740 (m), 715 (m), 687 (m), 659 (m), 624 (w), 601 (w), 579 (w), 563 (w), 513 (m), 437 (vw) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 334 (53) [M^+], 230 (46) [$C_{13}H_{14}N_2O_2^+$], 185 (18) [$C_{11}H_9N_2O^+$], 104 (25) [$C_8H_8^+$], 45 (100) [$C_2H_5O^+$]. HRMS: calcd. for $C_{21}H_{22}N_2O_2$ 334.1681; found 334.1682.

Compound 12b: According to general procedure B with **10** (965 mg, 300 μmol). The reaction gave **12b** (869 mg, 95%) as a white crystalline solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.45–2.54 (m, 1 H, H_{Pc}), 2.61–2.73 (m, 1 H, H_{Pc}), 2.82–2.92 (m, 3 H, H_{Pc}), 3.10–3.17 (m, 2 H, H_{Pc}), 3.37–3.45 (m, 1 H, H_{Pc}), 3.59 (s, 3 H, Me), 5.41 (br. s, 1 H, OH), 6.33 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.52 (d, *J* = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.60–6.70 (m, 4 H, Pc-H_{Ar}), 6.91–6.95 (m, 1 H, Pc-H_{Ar}), 7.73 (d, *J* = 1.9 Hz, 1 H, Pc-H_{Ar}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2924 (w), 2851 (vw), 1591 (vw), 1566 (vw), 1500 (vw), 1459 (vw), 1433 (vw), 1410 (w), 1386 (w), 1283 (vw), 1243 (vw), 1175 (w), 1138 (vw), 1087 (vw), 1046 (vw), 1011 (vw), 979 (vw), 931 (vw), 876 (vw), 843 (vw), 780 (w), 710 (w), 680 (vw), 651 (w), 581 (vw), 515 (w), 566 (vw), 438 (vw) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 304 (80) [M^+], 199 (100) [$C_{12}H_{12}N_2O^+$], 104 (15) [$C_8H_8^+$]. HRMS: calcd. for $C_{20}H_{20}N_2O$ 304.1576; found 304.1577.

Compound 12c: According to general procedure B with **10** (300 mg, 930 μmol). The crude product was purified by column chromatography (pentane/ethyl acetate, 5:1) to give **12c** (12 mg, 90%) as a yellow crystalline solid. R_f = 0.80 (pentane/ethyl acetate, 2:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.39–2.47 (m, 1 H, H_{Pc}), 2.66–2.74 (m, 1 H, H_{Pc}), 2.83–2.89 (m, 3 H, H_{Pc}), 3.10–3.17 (m, 2 H, H_{Pc}), 3.36–3.46 (m, 1 H, H_{Pc}), 4.47 (m, 2 H, CH_2), 5.36 (br. s, 1 H, OH),

6.35 (d, J = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.56 (d, J = 7.9 Hz, 1 H, Pc-H_{Ar}), 6.64–6.71 (m, 3 H, Pc-H_{Ar}), 6.74 (d, J = 1.8 Hz, 1 H, Pc-H_{Ar}), 6.92–6.94 (m, 1 H, Pc-H_{Ar}), 7.85 (d, J = 1.8 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.6, 32.8, 34.0, 34.8 (–, 4× CH_2), 49.5 (q, J = 35 Hz, CH_2CF_3), 106.6 (+, CH), 115.3 (C_{quat}), 122.8 (q, J = 280 Hz, CF_3), 126.8 (+, CH), 126.9 (C_{quat}), 128.0, 129.6, 132.7, 133.7, 137.6 (+, 5× CH), 138.4, 139.4, 140.1, 140.5 (4× C_{quat}), 141.3 (+, CH), 152.1 (C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2929 (w), 2854 (w), 1596 (w), 1568 (w), 1501 (w), 1460 (w), 1411 (m), 1382 (m), 1318 (m), 1251 (s), 1181 (m), 1151 (s), 1104 (m), 1030 (m), 994 (w), 927 (m), 834 (w), 781 (m), 718 (m), 670 (m), 642 (m), 582 (m), 515 (m), 438 (w), 402 (w) cm^{-1}. MS (70 eV, EI): m/z (%) = 372 (58) [M^+], 268 (23) [$C_{13}H_{11}F_3N_2O^+$], 267 (60) [$C_{13}H_{10}F_3N_2O^+$], 185 (3) [$C_{11}H_9N_2O^+$], 104 (100) [$C_8H_8^+$], 83 (2) [$C_2H_2F_3^+$], 77 (7) [$C_6H_5^+$]. HRMS: calcd. for $C_{21}H_{19}F_3N_2O$ 372.1449; found 372.1447.

Compound 12d: According to general procedure B with **10** (55.0 mg, 170 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 10:1) to give **12d** (36 mg, 57%) as a yellow crystalline solid. R_f = 0.38 (cyclohexane/ethyl acetate, 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92–1.07 (m, 1 H, *c*Hex), 1.13–1.26 (m, 2 H, *c*Hex), 1.35–1.43 (m, 1 H, *c*Hex), 1.51–1.66 (m, 3 H, *c*Hex), 1.79–1.87 (m, 1 H, *c*Hex), 1.95–2.09 (m, 2 H, *c*Hex), 2.47–2.59 (m, 1 H, *c*Hex), 2.62–2.72 (m, 1 H, H_{Pc}), 2.78–2.92 (m, 3 H, H_{Pc}), 3.08–3.16 (m, 2 H, H_{Pc}), 3.34–3.45 (m, 1 H, H_{Pc}), 3.67–3.80 (m, 1 H, H_{Pc}), 5.34 (s, 1 H, OH), 6.32 (d, J = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.52 (d, J = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.61–6.71 (m, 4 H, Pc-H_{Ar}), 6.91 (d, J = 7.9 Hz, 1 H, Pc-H_{Ar}), 7.77 (d, J = 1.6 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.1, 25.4, 25.7, 30.7 (–, 4× CH_2), 32.0, 32.9, 33.6, 34.1, 34.9 (–, 4× CH_2, *c*Hex), 57.6 (+, CH, *c*Hex), 104.4 (+, CH), 116.4, 126.2 (2× C_{quat}), 126.3, 128.0, 129.8, 132.5, 133.7 (+, 5× CH), 135.9 (C_{quat}), 137.1 (+, CH), 138.5 (C_{quat}), 139.3 (+, CH), 140.4, 141.0, 151.7 (3× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3502 (vw), 2924 (w), 2851 (w), 1596 (vw), 1567 (vw), 1500 (vw), 1449 (w), 1409 (w), 1356 (vw), 1319 (vw), 1261 (vw), 1206 (vw), 1167 (vw), 1142 (vw), 1121 (vw), 1098 (vw), 1029 (vw), 994 (vw), 979 (vw), 929 (vw), 893 (vw), 875 (vw), 781 (w), 760 (vw), 717 (vw), 684 (vw), 661 (vw), 581 (vw), 518 (w), 446 (vw), 422 (vw), 401 (vw) cm^{-1}. MS (70 eV, EI): m/z (%) = 372 (100) [M^+], 268 (27) [$C_{17}H_{20}N_2O^+$], 289 (3) [$C_{19}H_{17}N_2O^+$], 185 (74) [$C_{11}H_9N_2O^+$], 104 (12) [$C_8H_8^+$], 83 (100) [$C_6H_{11}^+$]. HRMS: calcd. for $C_{25}H_{28}N_2O$ 372.2202; found 372.2201.

Compound 12e: According to general procedure B with **10** (300 mg, 930 µmol). The crude product was purified by column chromatography (pentane/ethyl acetate, 10:1) to give **12e** (268 mg, 79%) as an orange crystalline solid. R_f = 0.72 (pentane/ethyl acetate, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.25–2.33 (m, 1 H, H_{Pc}), 2.35–2.42 (m, 1 H, H_{Pc}), 2.61–2.80 (m, 3 H, H_{Pc}), 3.06–3.20 (m, 2 H, H_{Pc}), 3.36–3.46 (m, 1 H, H_{Pc}), 5.47 (br. s, 1 H, OH), 6.04 (d, J = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.45 (d, J = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.58 (s, 2 H, Pc-H_{Ar}), 6.70 (d, J = 8.0 Hz, 1 H, Pc-H_{Ar}), 6.84 (d, J = 1.8 Hz, 1 H, Pc-H_{Ar}), 6.94 (d, J = 8.0 Hz, 1 H, Pc-H_{Ar}), 7.03–7.08 (m, 2 H, Pc-H_{Ar}), 7.16–7.20 (m, 3 H, Pc-H_{Ar}), 7.93 (d, J = 1.8 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.7, 33.0, 34.1, 34.6 (–, 4× CH_2), 106.5 (+,CH), 116.3 (C_{quat}), 124.77 (+, 2× CH), 126.1 (C_{quat}), 126.5, 127.2, 128.0, 128.4, 129.4, 132.5, 133.7, 137.1 (+, 9× CH), 137.4, 138.7, 139.5, 140.2 (4× C_{quat}), 140.8 (+,CH), 141.2, 151.3 (2× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3503 (w), 2936 (w), 1744 (vw), 1597 (w), 1568 (vw), 1497 (w), 1453 (vw), 1433 (vw), 1408 (w), 1380 (w), 1308 (w), 1253 (vw), 1197 (w), 1161 (w), 1143 (w), 1087 (w), 1069 (vw), 1047 (vw), 1016 (w), 989 (vw), 972 (vw), 921 (w), 874 (vw), 834 (vw), 803 (w), 765 (m), 720 (w), 693 (w), 651 (w), 583 (w), 514 (w), 448 (m), 420 (w) cm^{-1}. MS (70 eV, EI): m/z (%) = 366 (64) [M^+], 262 (68) [$C_{17}H_{14}N_2O^+$], 261 (100) [$C_{17}H_{13}N_2O^+$], 245 (3) [$C_{17}H_{13}N_2^+$], 104 (20) [$C_8H_8^+$], 102 (1) [$C_8H_6^+$], 77 (5) [$C_6H_5^+$]. HRMS: calcd. for $C_{25}H_{22}N_2O$ 366.1732; found 366.1733.

Compound 12f: According to general procedure B with **10** (158 mg, 490 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 10:1) to give **12f** (80 mg, 43%) as a yellow crystalline solid. R_f = 0.32 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41–2.49 (m, 1 H, H_{Pc}), 2.61–2.68 (m, 1 H, H_{Pc}), 2.70–2.77 (m, 1 H, H_{Pc}), 2.78–2.86 (m, 2 H, H_{Pc}), 3.08–3.16 (m, 2 H, H_{Pc}), 3.33–3.43 (m, 1 H, H_{Pc}), 4.93 (d, J = 14.8 Hz, 1 H, CH_2-Ph), 5.09 (d, J = 14.8 Hz, 1 H, CH_2-Ph), 5.27 (s, 1 H, OH), 6.33 (d, J = 7.8 Hz, 1 H, Pc-H_{Ar}), 6.52 (d, J = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.63 (dq, J = 7.8, 1.7 Hz, 2 H, Ph), 6.66 (d, J = 1.9 Hz, 1 H, Pc-H_{Ar}), 6.71 (dd, J = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 6.85–6.89 (m, 2 H, Pc-H_{Ar}), 6.92 (dd, J = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 7.14–7.14 (m, 3 H, Pc-H_{Ar}), 7.77 (d, J = 1.8 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.7, 33.1, 34.0, 34.8, 53.0 (–, 5× CH_2), 105.3 (+, CH), 116.3, 126.4 (2× C_{quat}), 126.5, 127.6, 128.0, 129.7, 132.6, 133.6 (+, 10× CH), 136.4 (C_{quat}), 137.2 (+, CH), 137.3, 138.6 (2× C_{quat}), 139.8 (+, CH), 140.4, 140.9, 151.8 (3× C_{quat}), 148.3 (+, CH), 153.2, 154.7 (2× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2920 (w), 2849 (w), 1886 (vw), 1640 (w), 1567 (w), 1497 (w), 1454 (w), 1432 (w), 1410 (w), 1297 (w), 1275 (w), 1241 (w), 1207 (w), 1144 (w), 1098 (vw), 1083 (w), 1032 (w), 998 (vw), 979 (vw), 933 (w), 873 (vw), 842 (vw), 778 (w), 707 (m), 694 (w), 663 (w), 588 (w), 516 (w), 467 (w), 436 (vw) cm^{-1}. MS (70 eV, EI): m/z (%) = 380 (41) [M^+], 289 (2) [$C_{19}H_{17}N_2O^+$], 276 (65) [$C_{18}H_{16}N_2O^+$], 185 (13) [$C_{11}H_9N_2O^+$], 157 (1) [$C_{10}H_9N_2^+$], 104 (60) [$C_8H_8^+$], 91 (18) [$C_7H_7^+$], 78 (12) [$C_5H_4N^+$], 77 (11) [$C_6H_5^+$]. HRMS: calcd. for $C_{26}H_{24}N_2O$ 380.1889; found 380.1887.

Compound 12j: According to general procedure B with **10** (62.0 mg, 190 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 2:1) to give **12j** (45.7 mg, 63%) as a yellow crystalline solid. R_f = 0.13 (cyclohexane/ethyl acetate, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.59–2.67 (m, 2 H, H_{Pc}), 2.77–2.84 (m, 1 H, H_{Pc}), 2.68–2.95 (m, 2 H, H_{Pc}), 3.04–3.18 (m, 2 H, H_{Pc}), 3.33–3.43 (m, 1 H, H_{Pc}), 5.07 (dd, J = 15.7 Hz, 2 H, CH_2Py), 6.27 (d, J = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.46 (d, J = 7.7 Hz, 1 H, Pc-H_{Ar}), 6.61 (dd, J = 7.8, 1.7 Hz, 1 H, Pc-H_{Ar}), 6.67 (dd, J = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.72 (d, J = 1.8 Hz, 1 H, Pc-H_{Ar}), 6.77 (dd, J = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 6.82 (d, J = 7.8 Hz, 1 H, Pc-H_{Ar}), 6.91 (dd, J = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 7.06–7.11 (m, 1 H, Pc-H_{Ar}), 7.52 (dt, J = 15.4, 7.7, 1.8 Hz, 1 H, Pc-H_{Ar}), 7.78 (d, J = 1.8 Hz, 1 H, Pc-H_{Ar}), 8.39 (d, J = 4.8 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4, 33.0, 34.2, 35.0 (–, 4× CH_2), 54.0 (–, CH_2Py), 105.5 (+, CH), 117.4 (C_{quat}), 121.7, 122.6, 126.4 (+, 3× CH), 127.3 (C_{quat}), 128.3, 130.0, 132.5, 133.5, 136.9, 137.1 (+, 6× CH), 138.5, 139.0 (2× C_{quat}), 140.3 (+, CH), 140.4, 141.0 (2× C_{quat}), 149.0 (+, CH), 152.5, 156.1 (2× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3015 (vw), 2961 (vw), 2936 (w), 1597 (vw), 1559 (w), 1527 (vw), 1503 (vw), 1477 (w), 1435 (w), 1415 (w), 1396 (w), 1300 (w), 1271 (w), 1243 (vw), 1211 (w), 1192 (w), 1104 (w), 1091 (w), 1072 (vw), 1053 (vw), 1004 (vw), 995 (w), 978 (w), 942 (w), 926 (w), 884 (w), 868 (w), 840 (vw), 818 (w), 795 (w), 776 (w), 757 (w), 744 (w), 720 (w), 672 (w), 632 (w), 594 (w), 585 (w), 524 (w), 508 (w), 467 (vw), 442 (vw), 407 (vw), 2855 (vw), 1891 (vw) cm^{-1}. MS (70 eV, EI): m/z (%) = 381 (100) [M^+], 303 (3) [$C_{20}H_{19}N_2O^+$], 289 (2) [$C_{19}H_{17}N_2O^+$], 199 (59) [$C_{12}H_{11}N_2O^+$], 185 (11) [$C_{11}H_9N_2O^+$], 104 (9) [$C_8H_8^+$], 92 (2) [$C_6H_6N_2^+$], 80 (3) [$C_4H_4N_2^+$], 78 (3) [$C_5H_4N^+$]. HRMS: calcd. for $C_{25}H_{23}N_3O$ 381.1841; found 381.1840.

Compound 15: Hydroxy-pyrazolyl[2.2]paracyclophane (**11a**; 76.0 mg, 260 µmol) was dissolved in anhydrous THF (1 mL), and

NaH (**13**; 35.0 mg, 1.44 mmol) was added at 0 °C. In a period of 2 h, the mixture was warmed to room temperature. MeI (**14**; 30.0 μL, 520 μmol) in anhydrous THF (1 mL) was added slowly and the mixture was stirred for 12 h at room temperature. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate and $NaHCO_3$ was added. The aqueous phase was extracted with ethyl acetate (3× 20 mL) and the combined organic layers were dried with $MgSO_4$ and purified by column chromatography (cyclohexane/ethyl acetate, 3:1) to give **15** (80.9 mg, 98%) as a white solid. R_f = 0.19 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.62–2.75 (m, 2 H, H_{Pc}), 2.76–2.82 (m, 1 H, H_{Pc}), 2.85–2.09 (m, 1 H, H_{Pc}), 3.00–3.06 (m, 1 H, H_{Pc}), 3.13–3.20 (m, 1 H, H_{Pc}), 3.30–3.36 (m, 1 H, H_{Pc}), 3.38 (s, 3 H, NMe), 3.60–3.67 (m, 1 H, H_{Pc}), 3.96 (s, 3 H, OMe), 6.45 (q, J = 7.8 Hz, 2 H, Pc-H_{Ar}), 6.54–6.60 (m, 2 H, Pc-H_{Ar}), 6.66–6.68 (m, 1 H, Pc-H_{Ar}), 6.67 (d, J = 2.2 Hz, 1 H, H_{Py}), 6.86 (dd, J = 7.9, 1.6 Hz, 1 H, Pc-H_{Ar}), 7.63 (d, J = 2.2 Hz, 1 H, H_{Py}-NMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.8, 33.2, 33.5 (–, 4× CH_2), 37.9 (+, NCH_3), 59.5 (+, OCH_3), 106.5 (+, CH), 127.1 (C_{quat}), 128.1, 128.8, 129.2, 129.8 (+, 4× CH), 130.4 (C_{quat}), 131.6, 131.7, 133.6 (+, 3× CH), 138.4, 138.6, 140.4, 147.4, 156.0 (5× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2923 (m), 2850 (w), 1596 (vw), 1558 (vw), 1511 (w), 1501 (w), 1460 (w), 1432 (w), 1407 (m), 1386 (m), 1330 (w), 1302 (vw), 1240 (m), 1223 (m), 1183 (w), 1145 (w), 1123 (w), 1073 (w), 1035 (m), 997 (w), 987 (w), 956 (vw), 928 (w), 892 (w), 873 (w), 801 (m), 772 (m), 757 (m), 715 (m), 690 (w), 672 (w), 610 (w), 581 (w), 520 (m), 468 (w), 450 (vw), 408 (vw) cm^{-1}. MS (70 eV, EI): m/z (%) = 318 (100) [M^+], 214 (20) [$C_{13}H_{14}N_2O^+$], 81 (26) [$C_4H_5N_2^+$]. HRMS: calcd. for $C_{21}H_{22}N_2O$ 318.1732; found 318.1734.

Compound 16: A high-pressure vessel was charged with **11b** (320 mg, 1.05 mmol), 1-fluoro-2-nitrobenzene (170 μL, 1.58 mmol), anhydrous K_2CO_3 (436 mg, 3.16 mmol) and anhydrous DMSO (2 mL). The mixture was heated at 180 °C for 5 h, then water was added and the mixture was extracted with ethyl acetate (3× 20 mL). The combined organic layers were dried with $MgSO_4$ and purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **16** (360 mg, 81%) as a brown solid. R_f = 0.23 (cyclohexane/ethyl acetate, 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.57–2.68 (m, 2 H, H_{Pc}), 2.81–2.92 (m, 2 H, H_{Pc}), 2.94–3.02 (m, 1 H, H_{Pc}), 3.03–3.14 (m, 1 H, H_{Pc}), 3.18–3.28 (m, 1 H, H_{Pc}), 3.71–3.81 (m, 1 H, H_{Pc}), 3.85 (s, 3 H, Me), 6.42–6.48 (m, 1 H, Pc-H_{Ar}), 6.54–6.64 (m, 3 H, Pc-H_{Ar}), 6.65–6.74 (m, 2 H, Pc-H_{Ar}), 6.75–6.79 (m, 1 H, Pc-H_{Ar}), 6.89–6.95 (m, 1 H, Pc-H_{Ar}), 7.12–7.17 (m, 1 H, Pc-H_{Ar}), 7.18–7.23 (m, 1 H, Pc-H_{Ar}), 7.28–7.33 (m, 1 H, Pc-H_{Ar}), 7.86–7.93 (m, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.2, 34.2, 34.3, 34.4 (–, 4× CH_2), 38.9 (+, NCH_3), 107.6, 116.6, 120.7, 125.4 (+, 4× CH), 128.8 (C_{quat}), 129.7, 130.1, 130.3 (+, 3× CH), 132.1 (C_{quat}), 132.7, 132.9, 133.0, 134.1, 134.9 (+, 5× CH), 138.5, 139.3, 139.6, 142.7, 147.0, 148.9, 151.5 (7× C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2928 (w), 2852 (vw), 1734 (vw), 1603 (w), 1519 (m), 1476 (w), 1451 (w), 1414 (w), 1389 (w), 1344 (m), 1307 (w), 1250 (m), 1232 (m), 1159 (w), 1145 (w), 1122 (w), 1088 (w), 1040 (w), 1010 (w), 967 (w), 938 (w), 884 (w), 858 (w), 830 (w), 796 (w), 770 (w), 740 (m), 715 (w), 675 (w), 635 (w), 582 (w), 518 (w), 467 (vw), 429 (vw) cm^{-1}. MS (70 eV, EI): m/z (%) = 425 (100) [M^+], 321 (3) [$C_{18}H_{15}N_3O_3^+$], 275 (44) [$C_{18}H_{15}N_2O^+$], 199 (17) [$C_{12}H_{11}N_2O^+$], 104 (9) [$C_8H_8^+$]. HRMS: calcd. for $C_{26}H_{23}N_3O_3$ 425.1739; found 425.1736.

Compound 17: A high-pressure vessel was charged with **11a** (320 mg, 1.10 mmol), 1-fluoro-2-nitrobenzene (170 μL, 1.65 mmol), anhydrous K_2CO_3 (457 mg, 3.31 mmol) and anhydrous DMSO (2 mL). The mixture was heated at 180 °C for 4 h, then water was added and the mixture was extracted with ethyl acetate (3× 20 mL). The combined organic layers were dried with $MgSO_4$ and purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **17** (200 mg, 34%) as a yellow solid. R_f = 0.26 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.59–2.66 (m, 1 H, H_{Pc}), 2.72–2.80 (m, 1 H, H_{Pc}), 2.83–2.90 (m, 1 H, H_{Pc}), 2.95–3.02 (m, 2 H, H_{Pc}), 3.04–3.12 (m, 1 H, H_{Pc}), 3.19–3.28 (m, 1 H, H_{Pc}), 3.71 (m, 1 H, H_{Pc}), 6.45 (d, J = 8.4 Hz, 1 H, Pc-H_{Ar}), 6.54–6.58 (m, 1 H, H_{Ar}), 6.60–6.65 (m, 2 H, H_{Ar}), 6.70 (d, J = 7.9 Hz, 1 H, Pc-H_{Ar}), 6.75 (dd, J = 7.8, 1.7 Hz, 1 H, Pc-H_{Ar}), 6.92–6.96 (m, 1 H, H_{Ar}), 7.04 (d, J = 2.5 Hz, 1 H, Pc-H_{Ar}), 7.15–7.22 (m, 2 H, H_{Ar}), 7.44–7.52 (m, 2 H, H_{Ar}), 7.60–7.65 (m, 1 H, H_{Ar}), 7.71 (d, J = 7.7 Hz, 1 H, Pc-H_{Ar}), 7.87 (dd, J = 8.0, 1.2 Hz, 1 H, Pc-H_{Ar}), 7.91 (dd, J = 8.2, 1.6 Hz, 1 H, Pc-H_{Ar}) ppm. MS (70 eV, EI): m/z (%) = 532 (87) [M^+], 306 (10) [$C_{17}H_{12}N_3O_3^+$], 104 (9) [$C_8H_8^+$]. HRMS: calcd. for $C_{31}H_{24}N_4O_5$ 532.1747; found 532.1750.

Compound 18: A high-pressure vessel was charged with **12b** (40.0 mg, 0.130 mmol), methyl bromoacetate (25.0 μL, 40.0 mg, 260 μmol), potassium carbonate (36.0 mg, 260 μmol) and DMF (1 mL). The mixture was stirred for 2 d at room temperature, then the crude product was purified by column chromatography (cyclohexane/ethyl acetate, 3:1) to give **18** (98%) as a yellow compound. R_f = 0.42 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50–2.60 (m, 1 H, H_{Pc}), 2.69–2.92 (m, 4 H, H_{Pc}), 3.07–3.21 (m, 2 H, H_{Pc}), 3.44–3.55 (m, 1 H, H_{Pc}), 3.61 (s, 3 H, NMe), 3.62 (s, 3 H, OMe), 3.91 (q, J = 15.1 Hz, 2 H, OCH_2), 6.40–6.47 (m, 1 H, Pc-H_{Ar}), 6.51–6.57 (m, 1 H, Pc-H_{Ar}), 6.62–6.63 (m, 2 H, Pc-H_{Ar}, H_{Py}), 6.68–6.72 (m, 2 H, Pc-H_{Ar}), 6.84–6.91 (m, 1 H, Pc-H_{Ar}), 7.61–7.66 (m, 1 H, H_{Py}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.3, 33.0, 34.4, 34.7 (–, 4× CH_2), 36.7 (+, NCH_3), 51.8 (+, OCH_3), 70.1 (–, OCH_2), 107.7, 129.6, 129.9, 130.4, 132.1 (+, 5× CH), 132.5 (C_{quat}), 133.3, 136.8, 138.3 (+, 3× CH), 138.7, 139.1, 140.2, 141.9, 155.4 (5× C_{quat}), 169.4 (C_{quat}, CO) ppm. IR (DRIFT): $\tilde{\nu}$ = 2929 (w), 2853 (w), 1762 (m), 1678 (vw), 1595 (vw), 1557 (vw), 1500 (w), 1459 (w), 1428 (m), 1400 (m), 1282 (w), 1261 (w), 1174 (m), 1103 (w), 1079 (m), 1011 (w), 993 (w), 964 (w), 948 (w), 926 (m), 896 (w), 848 (w), 795 (m), 764 (w), 714 (m), 664 (w), 651 (w), 605 (w), 585 (w), 519 (m), 474 (w), 420 (w) cm^{-1}. MS (70 eV, EI): m/z (%) = 376 (100) [M^+], 272 (4) [$C_{15}H_{16}N_2O_3^+$], 257 (5) [$C_{14}H_{13}N_2O_3^+$], 198 (6) [$C_{12}H_{10}N_2O^+$], 183 (7) [$C_{12}H_{11}N_2^+$], 104 (37) [$C_8H_8^+$]. HRMS: calcd. for $C_{23}H_{24}N_2O_3$ 376.1787; found 376.1789.

Compound 20: Compound **10** (200 mg, 620 μmol) was solved in anhydrous dichloromethane (2 mL) and added to a high-pressure vessel charged with conc. HCl (1.5 mL). The mixture was heated to 40 °C for1 h, then quenched with distilled H_2O (3 mL). The mixture was extracted with dichloromethane (3× 5 mL) and the organic layers were dried with $MgSO_4$. The solvent was removed under reduced pressure to give **20** (165 mg, 97%). R_f = 0.48 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.79–2.88 (m, 2 H, H_{PC}), 2.97–3.05 (m, 1 H, H_{PC}), 3.07–3.12 (m, 2 H, H_{PC}), 3.15–3.20 (m, 1 H, H_{PC}), 3.56–3.63 (m, 1 H, H_{PC}), 4.57–4.62 (m, 1 H, H_{PC}), 6.23–6.27 (m, 2 H, Pc-H_{Ar}), 6.38–6.40 (m, 1 H, Pc-H_{Ar}), 6.42–6.44 (m, 1 H, Pc-H_{Ar}), 6.54–6.56 (m, 1 H, Pc-H_{Ar}), 6.63 (d, J = 7.6 Hz, 1 H, COCH), 6.79 (d, J = 7.6 Hz, 1 H, OCH), 7.80 (d, J = 5.8 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4, 33.9, 34.0, 35.4 (–, 4× CH_2), 114.1 (+, *C*HCO), 126.7 (C_{quat}), 126.8 (+, CH), 128.8 (C_{quat}), 130.5, 131.5, 133.1, 133.7, 137.6 (+, 5× CH), 138.8, 139.9, 143.4 (3× C_{quat}), 152.9 (+, *C*HOC), 156.5 (C_{quat}, CHO*C*), 179.2 (C_{quat}, CO) ppm. IR (DRIFT): $\tilde{\nu}$ = 2923 (m), 2851 (w), 1632 (s), 1578 (m), 1499 (w), 1474 (s), 1430 (m), 1410 (m), 1391 (m), 1342 (s), 1300 (m), 1240 (m), 1210 (m), 1122 (w), 1056 (m), 999 (w), 981 (w), 941 (m), 893 (w), 867 (m), 827 (m), 797

(s), 718 (m), 663 (m), 618 (w), 593 (m), 555 (m), 539 (w), 540 (m), 456 (w), 439 (w) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 276 (20) [M^+], 172 (35) [$C_{11}H_8O_2^+$], 104 (18) [$C_8H_8^+$], 43 (100). HRMS: calcd. for $C_{19}H_{16}O_2$ 276.1150; found 276.1152. $C_{19}H_{16}O_2$ (276.12): calcd. C 82.58, H 5.84; found C 81.39, H 5.99.

Compound 22: A high-pressure vessel was charged with **9** (1.06 g, 3.99 mmol) and *N*,*N*-dimethylacetamide-dimethylacetal (**21**; 1.75 mL, 1.60 g, 12.0 mmol) and the mixture was heated to 120 °C overnight. The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **22** (131 mg, 11%) as a yellow solid. R_f = 0.70 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, Me), 2.78–2.87 (m, 2 H, H_{Pc}), 2.99–3.20 (m, 4 H, H_{Pc}), 3.58–3.68 (m, 1 H, H_{Pc}), 4.52–4.64 (m, 1 H, H_{Pc}), 6.10 (s, 1 H, Pc-H_{Ar}), 6.27 (d, *J* = 6.9 Hz, 1 H, Pc-H_{Ar}), 6.38 (t, *J* = 8.4 Hz, 2 H, Pc-H_{Ar}), 6.54 (d, *J* = 7.9 Hz, 1 H, Pc-H_{Ar}), 6.62 (d, *J* = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.78 (d, *J* = 7.6 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.2 (+, CH_3), 30.6, 33.9, 34.0, 35.3 (–, 4× CH_2), 111.6 (+, CH), 125.3 (C_{quat}), 127.0 (+, CH), 128.4 (C_{quat}), 130.4, 131.2, 133.1, 133.6, 137.3 (+, 5× CH), 138.7, 139.9, 143.2, 156.5, 163.4 (5× C_{quat}), 179.9 (C_{quat}, CO) ppm. IR (DRIFT): $\tilde{\nu}$ = 2925 (vw), 2850 (vw), 1639 (w), 1617 (w), 1580 (w), 1568 (w), 1499 (vw), 1474 (w), 1429 (vw), 1405 (vw), 1386 (w), 1362 (w), 1290 (vw), 1249 (vw), 1290 (vw), 1249 (vw), 1224 (vw), 1180 (vw), 1159 (vw), 1127 (vw), 1034 (vw), 1017 (vw), 959 (vw), 935 (w), 878 (w), 865 (w), 822 (vw), 793 (vw), 768 (vw), 714 (w), 679 (vw), 659 (w), 592 (w), 567 (vw), 539 (vw), 502 (w), 463 (vw), 439 (vw), 3058 (vw) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 290 (100) [M^+], 186 (37) [$C_{12}H_{10}O_2^+$], 104 (1) [$C_8H_8^+$]. HRMS: calcd. for $C_{20}H_{18}O_2$ 290.1307; found 290.1309.

Compound 24: A high-pressure vessel was charged with **23** (560 mg, 2.23 mmol) and DMF-DMA (**5**; 5.10 mL, 4.38 g, 2.23 mmol) and the mixture was heated to 130 °C for 24 h. The reaction gave **24** (280 mg, 41%) as a white solid.

Compound 25b: According to general procedure D with **24** (39.1 mg, 130 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **25b** (20.0 mg, 53%) as a white solid. R_f = 0.30 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.85–2.91 (m, 1 H, H_{Pc}), 2.94–2.98 (m, 2 H, H_{Pc}), 3.02–3.09 (m, 3 H, H_{Pc}), 3.12–3.22 (m, 2 H, H_{Pc}), 3.70 (s. 3 H, Me), 6.57–6.64 (m, 5 H, Pc-H_{Ar}), 6.81–6.83 (m, 1 H, Pc-H_{Ar}), 6.83–6.86 (m, 1 H, Pc-H_{Ar}), 8.08 (s, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.8, 35.2, 35.3, 35.4 (–, 4× CH_2), 35.8 (+, CH_3), 127.2 (C_{quat}), 131.9, 132.0, 132.8, 133.4, 133.8, 135.3, 135.4 (+, 7× CH), 139.0, 139.0, 139.4, 140.7 (4× C_{quat}), 151.0 (+, CH), 155.1 (C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2925 (w), 2850 (w), 1896 (vw), 1718 (vw), 1670 (vw), 1593 (w), 1518 (vw), 1490 (w), 1443 (w), 1411 (w), 1369 (w), 1278 (w), 1175 (w), 1153 (w), 1093 (w), 1047 (vw), 1004 (w), 976 (w), 942 (vw), 903 (w), 870 (w), 847 (w), 794 (w), 734 (w), 711 (m), 684 (w), 664 (m), 640 (m), 588 (w), 516 (w), 505 (w), 462 (vw), 3109 (vw), 3012 (vw) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 289 (37) [M^+], 185 (100) [$C_{11}H_{11}N_3^+$], 170 (1) [$C_{10}H_8N_3^+$], 104 (25) [$C_8H_8^+$], 103 (6) [$C_8H_7^+$]. HRMS: calcd. for $C_{19}H_{19}N_3$ 289.1579; found 289.1577.

Compound 25c: According to general procedure D with **24** (41.0 mg, 130 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **25c** (21.0 mg, 45%) as a white solid. R_f = 0.42 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.79–2.86 (m, 1 H, H_{Pc}), 2.94–3.10 (m, 5 H, H_{Pc}), 3.12–3.26 (m, 2 H, H_{Pc}), 4.51 (q, *J* = 8.0 Hz, 2 H, CH_2CF_3), 6.53 (dd, *J* = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 6.59 (d, *J* = 7.9 Hz, 1 H, Pc-H_{Ar}), 6.61 (qd, *J* = 16.1, 7.8, 1.7 Hz, 2 H, Pc-H_{Ar}), 6.66 (dd, *J* = 7.9, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.70 (d, *J* = 1.8 Hz, 1 H, Pc-H_{Ar}), 6.99 (dd, *J* = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 8.16 (s, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.5, 35.2, 35.2, 35.3 (–, 4× CH_2), 49.0 (q, *J* = 36 Hz, CH_2CF_3), 122.4 (q, *J* = 280 Hz, CF_3), 125.9 (C_{quat}), 132.0, 132.2, 132.7, 133.3, 133.8, 135.6, 135.8 (+, 7× CH), 138.7, 139.1, 139.4, 141.0 (4× C_{quat}), 152.2 (+, CH), 156.8 (C_{quat}) ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ = –70.05 ppm. MS (70 eV, EI): *m/z* (%) = 357 (53) [M^+], 253 (100) [$C_{12}H_{10}F_3N_3^+$], 104 (28) [$C_8H_8^+$], 103 (6) [$C_8H_7^+$]. HRMS: calcd. for $C_{20}H_{18}F_3N_3$ 357.1453; found 357.1454.

Compound 25d: According to general procedure D with **24** (33.0 mg, 110 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **25d** (25.3 mg, 64%) as a white solid. R_f = 0.70 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.01–1.08 (m, 1 H, H_{cHex}), 1.10–1.29 (m, 3 H, H_{cHex}), 1.46–1.51 (m, 1 H, H_{cHex}), 1.59–1.72 (m, 3 H, H_{cHex}), 1.83–1.90 (m, 1 H, H_{cHex}), 1.98–2.11 (m, 2 H, H_{cHex}), 2.86–2.94 (m, 2 H, H_{Pc}), 2.97–3.06 (m, 3 H, H_{Pc}), 3.14–3.22 (m, 2 H, H_{Pc}), 3.85–3.96 (m, 1 H, H_{Pc}), 6.55–6.60 (m, 4 H, Pc-H_{Ar}), 6.62 (d, *J* = 1.7 Hz, 1 H, Pc-H_{Ar}), 6.73 (d, *J* = 1.7 Hz, 1 H, Pc-H_{Ar}), 6.93 (dd, *J* = 7.9, 1.8 Hz, 1 H, Pc-H_{Ar}), 8.07 (s, 1 H, Pc-H_{Ar}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3109 (w), 3011 (m), 2930 (s), 2855 (s), 2238 (w), 1896 (w), 1869 (w), 1728 (s), 1683 (s), 1595 (m), 1557 (w), 1502 (m), 1454 (s), 1385 (s), 1358 (m), 1325 (m), 1279 (s), 1240 (s), 1179 (s), 1100 (m), 1086 (m), 1047 (m), 1029 (m), 1000 (m), 974 (m), 939 (m), 902 (m), 845 (m), 817 (m), 794 (m), 761 (m), 760 (s), 678 (m), 643 (m), 595 (w), 512 (m), 488 (w) cm^{-1}. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.0, 25.3, 25.5, 31.9, 33.4 (–, 4× CH_2), 33.5, 35.2, 35.3, 35.4 (–, 4× CH_2), 57.4 (+, CH), 127.7 (C_{quat}), 131.8, 132.3, 132.7, 133.4, 133.8, 135.2, 135.2 (–, 7× CH_2), 139.0, 139.1, 139.4, 140.4 (4× C_{quat}), 151.0 (+, CH), 153.8 (C_{quat}) ppm. MS (70 eV, EI): *m/z* (%) = 357 (3) [M^+], 253 (1) [$C_{16}H_{19}N_3^+$], 104 (2) [$C_8H_8^+$], 83 (100) [$C_6H_{11}^+$]. HRMS: calcd. for $C_{24}H_{27}N_3$ 357.2205; found 357.2203.

Compound 25e: According to general procedure D with **24** (40.0 mg, 130 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **25e** (26.8 mg, 59%) as a white solid. R_f = 0.68 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.44–2.51 (m, 1 H, H_{Pc}), 2.61–2.66 (m, 1 H, H_{Pc}), 2.76–2.89 (m, 2 H, H_{Pc}), 2.99–3.05 (m, 2 H, H_{Pc}), 3.07–3.21 (m, 2 H, H_{Pc}), 6.32 (d, *J* = 7.8 Hz, 1 H, Pc-H_{Ar}), 6.50 (dd, *J* = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.54–6.60 (m, 3 H, Pc-H_{Ar}), 6.83 (dd, *J* = 7.5, 1.4 Hz, 1 H, Pc-H_{Ar}), 6.86 (d, *J* = 1.8 Hz, 1 H, Pc-H_{Ar}), 7.11–7.13 (m, 1 H, Pc-H_{Ar}), 7.13 (d, *J* = 2.2 Hz, 1 H, Pc-H_{Ar}), 7.26–7.23 (m, 3 H, Pc-H_{Ar}), 8.22 (s, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.8, 35.1, 35.2, 35.4 (–, 4× CH_2), 115.5, 124.3 (+, 2× CH), 127.3 (C_{quat}), 128.0, 128.8, 129.6, 131.8, 131.9, 132.7, 133.2, 133.7, 135.3, 135.5 (+, 10× CH), 137.9, 139.2, 139.2, 139.3, 140.3 (5× C_{quat}), 151.8 (+, CH), 154.3 (C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2926 (w), 2852 (w), 1734 (w), 1596 (w), 1498 (m), 1451 (m), 1372 (m), 1240 (m), 1174 (w), 1133 (w), 1105 (w), 1068 (w), 1045 (w), 1005 (m), 970 (w), 902 (w), 843 (m), 794 (w), 762 (m), 733 (m), 719 (m), 692 (m), 668 (m), 640 (m), 591 (w), 558 (w), 514 (m) cm^{-1}. MS (70 eV, EI): *m/z* (%) = 351 (1) [M^+], 247 (1) [$C_{16}H_{13}N_3^+$], 104 (1) [$C_8H_8^+$]. HRMS: calcd. for $C_{24}H_{21}N_3$ 351.1735; found 351.1737.

Compound 25g: According to general procedure D with **24** (41 mg, 130 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 10:1) to give **25g** (26 mg, 47%) as a white solid. R_f = 0.45 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.51–2.61 (m, 2 H, H_{Pc}), 2.77–2.93 (m, 2 H, H_{Pc}), 2.98–3.07 (m, 2 H, H_{Pc}), 3.11–3.19 (m, 2 H, H_{Pc}), 6.37 (d, *J* = 7.8 Hz, 1 H, Pc-H_{Ar}), 6.51–6.53 (m, 1 H, Pc-H_{Ar}), 6.59 (d, *J* =

8.1 Hz, 3 H, Pc-H_{Ar}), 6.79–6.83 (m, 1 H, Pc-H_{Ar}), 6.85–6.86 (m, 1 H, Pc-H_{Ar}), 7.02 (d, J = 8.6 Hz, 2 H, Pc-H_{Ar}), 7.38 (d, J = 8.7 Hz, 2 H, Pc-H_{Ar}), 8.24 (s, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.9, 35.1, 35.1, 35.3 (–, 4× CH_2), 115.4 (+, CH), 121.9 (C_{quat}), 125.7 (+, CH), 126.9 (C_{quat}), 129.7, 131.8, 131.9, 132.0, 132.7, 133.2, 133.6, 135.5, 135.7 (+, 9× CH), 168.8, 139.1, 139.1, 139.4, 140.6 (+, 5× CH),151.9 (+, CH), 154.4 (C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 3012 (m), 2928 (s), 2853 (m), 1897 (vw), 1736 (m), 1593 (m), 1492 (s), 1406 (m), 1374 (s), 1242 (s), 1174 (m), 1046 (m), 1001 (s), 970 (w), 901 (m), 844 (m), 829 (s), 755 (m), 736 (s), 719 (m), 693 (w), 670 (m), 641 (m), 592 (w), 556 (vw), 512 (m), 457 (w) cm^{-1}. MS (70 eV, EI): m/z (%) = 429 (11) [M^+], 350 (23) [$C_{24}H_{20}N_3^+$], 325 (15) [$C_{16}H_{12}BrN_3^+$], 104 (7) [$C_8H_8^+$]. HRMS: calcd. for $C_{24}H_{20}BrN_3$ 429.0841; found 429.0841.

Compound 25i: According to general procedure D with **24** (33.0 mg, 110 µmol). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to give **25i** (18.9 mg, 49%) as a white solid. R_f = 0.20 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.47–2.56 (m, 1 H, H_{Pc}), 2.74–2.93 (m, 3 H, H_{Pc}), 2.97–3.06 (m, 2 H, H_{Pc}), 3.10–3.22 (m, 2 H, H_{Pc}), 6.36 (d, J = 7.8 Hz, 1 H, Pc-H_{Ar}), 6.50–6.53 (m, 1 H, Pc-H_{Ar}), 6.55–6.60 (m, 3 H, Pc-H_{Ar}), 6.81–6.84 (m, 1 H, Pc-H_{Ar}), 6.86 (d, J = 1.7 Hz, 1 H, Pc-H_{Ar}), 7.07 (d, J = 8.1 Hz, 1 H, Pc-H_{Ar}), 7.22–7.25 (m, 1 H, Pc-H_{Ar}), 7.63 (td, J = 15.6, 7.7, 1.8 Hz, 1 H, Pc-H_{Ar}), 8.26 (s, 1 H, Pc-H_{Ar}), 8.43 (dd, J = 4.7, 1.4 Hz, 1 H, Pc-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.8, 35.1, 35.4, 35.4 (–, 4× CH_2), 119.0, 123.3 (+, 2× CH), 127.5 (C_{quat}), 131.8, 132.0, 132.7, 133.2, 133.7, 135.2, 135.4, 138.0 (+, 8× CH), 139.3, 139.3, 139.3, 140.2 (4× C_{quat}), 149.0 (+, CH), 150.5 (C_{quat}), 152.1 (+, CH), 154.8 (C_{quat}) ppm. IR (DRIFT): $\tilde{\nu}$ = 2920 (w), 2852 (w), 1631 (vw), 1591 (w), 1572 (w), 1519 (vw), 1473 (m), 1463 (m), 1434 (m), 1410 (w), 1391 (w), 1375 (m), 1261 (w), 1211 (w), 1170 (w), 1149 (w), 1136 (w), 1083 (w), 1045 (vw), 1014 (w), 999 (w), 971 (w), 956 (vw), 942 (vw), 901 (w), 888 (w), 842 (w), 789 (m), 734 (m), 717 (m), 670 (w), 638 (w), 619 (w), 590 (w), 561 (w), 514 (m), 491 (w), 411 (w) cm^{-1}. MS (70 eV, EI): m/z (%) = 352 (7) [M^+], 248 (38) [$C_{15}H_{12}N_4^+$], 104 (38) [$C_8H_8^+$], 103 (2) [$C_8H_7^+$], 78 (1) [$C_5H_4N^+$]. HRMS: calcd. for $C_{23}H_{20}N_4$ 352.1688; found 352.1690.

Compound 27a: According to general procedure A with AHPC (**9**; 300 mg, 1.13 mmol), to give **27a** (111 mg, 28%). R_f = 0.74 (cyclohexane/ethyl acetate, 1:1). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3, 33.4, 33.9, 36.24 (–, 4× CH_2), 123.3 (C_{quat}), 126.9, 127.0, 127.3, 127.8, 128.6, 128.7, 128.9 (+, 7× CH), 129.0 (C_{quat}), 130.1 (+, CH), 130.1 (C_{quat}), 130.7, 131.2, 132.2, 132.8 (+, 4× CH), 132.8, 139.5 (2× C_{quat}), 143.1 (+, CH), 145.4 (C_{quat}), 161.9 (C_{quat}, COH), 194.7 (C_{quat}, CO) ppm. IR (DRIFT): $\tilde{\nu}$ = 3058 (vw), 3027 (w), 2926 (w), 2851 (w), 1734 (w), 1663 (w), 1632 (m), 1570 (m), 1494 (w), 1448 (w), 1433 (w), 1409 (m), 1336 (m), 1218 (m), 1154 (w), 1100 (w), 1073 (m), 1021 (m), 990 (w), 935 (w), 910 (w), 861 (w), 795 (m), 751 (m), 694 (m), 664 (m), 585 (w), 565 (m), 546 (w), 511 (m), 483 (w), 461 (w) cm^{-1}. MS (70 eV, EI): m/z (%) = 354 (2) [M^+], 43 (100). HRMS: calcd. for $C_{25}H_{22}O_2$ 354.1620; found 354.1622.

Compound 27b: According to general procedure A with AHPC (**9**; 1.5 g, 5.63 mmol) in 2-propanol (20 mL), yield 234 mg (11%); m.p. 154.7 °C. R_f = 0.67 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.54–2.60 (m, 1 H, H_{PC}), 2.69–2.79 (m, 1 H, H_{PC}), 3.02–3.08 (m, 3 H, H_{PC}), 3.16–3.23 (m, 1 H, H_{PC}), 3.41–3.48 (m, 1 H, H_{PC}), 3.52–3.57 (m, 1 H, H_{PC}), 6.35 (d, J = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.40 (dd, J = 7.8, 1.9 Hz, 1 H, Pc-H_{Ar}), 6.49 (dd, J = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 6.58 (d, J = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.63 (dd, J = 7.9, 1.9 Hz, 1 H, Pc-H_{Ar}), 7.04 (dd, J = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 7.07–7.14 (m, 3 H, H_{Ar} + COCH), 7.58–7.62 (m, 2 H, H_{Ar}), 7.71 (d, J = 15.7 Hz, 1 H, COCHC*H*), 12.37 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3, 33.9, 35.4, 37.5 (–, 4× CH_2), 116.2, 116.4 (+, 2× CH), 123.2 (C_{quat}), 126.7, 126.7, 127.0, 127.8 (+, 4× CH), 129.1 (C_{quat}), 130.4, 130.5 (+, 2× CH), 131.0 (C_{quat}), 131.2, 132.2, 132.8 (+, 3× CH), 137.8 (C_{quat}), 139.9 (+, CH), 140.1, 142.3 (2× C_{quat}), 161.9 (C_{quat}, COH), 165.4 (C_{quat}, CF), 194.5 (C_{quat}, CO) ppm. IR (DRIFT): $\tilde{\nu}$ = 2921 (w), 2851 (vw), 1889 (vw), 1630 (w), 1597 (w), 1569 (w), 1556 (w), 1505 (w), 1453 (w), 1433 (w), 1409 (w), 1339 (w), 1292 (w), 1213 (w), 1155 (w), 1099 (w), 1073 (w), 1018 (w), 991 (w), 935 (w), 872 (vw), 856 (vw), 826 (w), 979 (w), 915 (w), 689 (w), 660 (w), 596 (vw), 580 (w), 529 (w), 496 (w), 452 (w), 428 (vw) cm^{-1}. MS (70 eV, EI): m/z (%) = 372 (33) [M^+], 268 (27) [$C_{17}H_{13}FO_2^+$], 104 (100) [$C_8H_8^+$]. HRMS: calcd. for ($C_{25}H_{21}FO_2$) 372.1526; found 372.1523. $C_{25}H_{21}FO_2$ (372.15): calcd. C 80.62, H 5.68; found C 80.03, H 5.72.

Compound 27c: According to general procedure A with AHPC (**9**; 200 mg, 750 µmol), yield 49.8 mg (16%). R_f = 0.4 (cyclohexane/ethyl acetate, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.54–2.61 (m, 1 H, H_{PC}), 2.70–2.78 (m, 1 H, H_{PC}), 3.01–3.09 (m, 3 H, H_{PC}), 3.17–3.23 (m, 1 H, H_{PC}), 3.40–3.54 (m, 2 H, H_{PC}), 6.30 (d, J = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.31 (dd, J = 7.8, 1.9 Hz, 1 H, Pc-H_{Ar}), 6.42 (dd, J = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 6.54 (m, 2 H, Pc-H_{Ar}), 6.95 (dd, J = 7.8, 1.9 Hz, 1 H, Pc-H_{Ar}), 7.23 (d, J = 15.9 Hz, 1 H, COCH), 7.67–7.72 (m, 4 H, H_{Ar}), 7.73 (d, J = 15.9 Hz, 1 H, COCHC*H*), 12.25 (br. s, 1 H, OH) ppm. IR (DRIFT): $\tilde{\nu}$ = 2929 (w), 2854 (w), 1639 (w), 1574 (m), 1449 (vw), 1409 (m), 1319 (m), 1254 (w), 1218 (w), 1159 (m), 1104 (m), 1060 (m), 1015 (m), 982 (m), 953 (w), 937 (w), 877 (w), 836 (m), 824 (m), 798 (m), 732 (m), 718 (w), 694 (w), 663 (w), 592 (w), 580 (w), 534 (w), 513 (w), 472 (w), 411 (vw) cm^{-1}. MS (70 eV, EI): m/z (%) = 422 (5) [M^+], 318 (4) [$C_{18}H_{13}F_3O_2^+$], 104 (100) [$C_8H_8^+$]. HRMS: calcd. for $C_{26}H_{21}F_3O_2$ 422.1494; found 422.1494.

Compound 27d: According to general procedure A with AHPC (**9**; 2.0 g, 7.50 mmol) in 2-propanol (20 mL), yield 456 mg (15%); m.p. 159.6 °C. R_f = 0.72 (cyclohexane/ethyl acetate, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 [s, 9 H, $C(CH_3)_3$], 2.54–2.61 (m, 1 H, H_{PC}), 2.68–2.77 (m, 1 H, H_{PC}), 2.98–3.08 (m, 3 H, H_{PC}), 3.16–3.25 (m, 1 H, H_{PC}), 3.41–3.48 (m, 1 H, H_{PC}), 3.55–3.61 (m, 1 H, H_{PC}), 6.36 (d, J = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.39 (dd, J = 7.8, 1.9 Hz, 1 H, Pc-H_{Ar}), 6.48 (dd, J = 7.8, 7.1 Hz, 1 H, Pc-H_{Ar}), 6.57 (d, J = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.61 (dd, J = 7.9, 2.0 Hz, 1 H, Pc-H_{Ar}), 7.04 (dd, J = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 7.13 (d, J = 15.7 Hz, 1 H, COCH), 7.45 (d, J = 8.4 Hz, 2 H, H_{Ar}), 7.55 (d, J = 8.4 Hz, 2 H, H_{Ar}), 7.72 (d, J = 15.8 Hz, 1 H, COCHC*H*), 12.43 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.2 (–, CH_2), 31.2 [+, $C(CH_3)_3$], 33.9 (–, CH_2), 35.0 [C_{quat}, $C(CH_3)_3$], 35.4, 37.5 (–, 2× CH_2), 123.3 (C_{quat}), 126.1, 126.2, 126.9, 127.8, 128.5 (+, 5× CH), 129.0 (C_{quat}), 131.2 (+, CH), 132.0 (C_{quat}), 132.15, 132.8 (+, 2× CH), 137.9 (C_{quat}), 139.8 (+, CH), 140.1, 142.4 (2× C_{quat}), 143.2 (+, CH), 154.4 (C_{quat}), 161.8 (C_{quat}, COH), 194.9 (C_{quat}, CO) ppm. IR (DRIFT): $\tilde{\nu}$ = 2962 (vw), 2927 (vw), 1626 (w), 1571 (w), 1556 (w), 1502 (vw), 1455 (vw), 1410 (w), 1333 (w), 1269 (vw), 1218 (w), 1152 (vw), 1100 (vw), 1070 (w), 994 (w), 935 (vw), 876 (vw), 832 (w), 793 (w), 753 (vw), 716 (vw), 668 (w), 595 (vw), 581 (vw), 555 (w), 535 (vw), 509 (w), 475 (vw), 453 (vw) cm^{-1}. MS (70 eV, EI): m/z (%) = 410 (94) [M^+], 305 (100) [$C_{21}H_{22}O_2^+$ – H], 104 (64) [$C_8H_8^+$]. HRMS: calcd. for $C_{29}H_{30}O_2$ 410.2246; found 410.2245. $C_{29}H_{30}O_2$ (410.22): calcd. C 84.84, H 7.37; found C 83.39, H 7.50.

Compound 27e: According to general procedure A with AHPC (**9**; 200 mg, 750 µmol), yield 59.3 mg (19%). R_f = 0.40 (cyclohexane/ethyl acetate, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.54–2.61 (m,

1 H, H_{Pc}), 2.68–2.77 (m, 1 H, H_{Pc}), 2.99–3.07 (m, 3 H, H_{Pc}), 3.16–3.23 (m, 1 H, H_{Pc}), 3.41–3.47 (m, 1 H, H_{Pc}), 3.52–3.57 (m, 1 H, H_{Pc}), 3.84 (s, 6 H, 2× OCH_3), 6.36 (d, J = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.39 (dd, J = 7.9, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.49 (dd, J = 7.9, 1.5 Hz, 1 H, Pc-H_{Ar}), 6.54 [t, J = 2.2 Hz, 1 H, C*H*($COCH_3$)$_2$], 6.58 (d, J = 7.6 Hz, 1 H, Pc-H_{Ar}), 6.61 (dd, J = 7.9, 1.8 Hz, 1 H, Pc-H_{Ar}), 6.74 (d, J = 2.2 Hz, 2 H, H_{Ar}), 7.03 (dd, J = 7.9, 1.7 Hz, 1 H, Pc-H_{Ar}), 7.12 (d, J = 15.7 Hz, 1 H, COCH), 7.65 (d, J = 15.7 Hz, 1 H, COCHC*H*), 12.34 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.2, 33.8, 35.4, 37.5 (–, 4× CH_2), 55.5 (+, 2× CH_3), 102.8 [+, *C*($COCH_3$)$_2$], 106.5 [+, 2× $CO(CH_2)_2C(CH)_2$], 123.2 (C_{quat}), 126.9, 127.5, 127.8 (+, 3× CH), 129.0 (C_{quat}), 131.2, 132.2, 132.8 (+, 3× CH), 136.6, 137.9 (2× C_{quat}), 139.9 (+, CH), 140.1, 142.5 (2× C_{quat}), 143.1 (+, CH), 161.1 (C_{quat}, 2× *C*OCH_3), 161.9 (C_{quat}, COH), 194.7 (C_{quat}, CO) ppm. IR (DRIFT): $\tilde{\nu}$ = 3005 (vw), 2935 (w), 2845 (vw), 1636 (w), 1585 (w), 1498 (vw), 1448 (w), 1404 (w), 1357 (w), 1324 (w), 1294 (w), 1245 (w), 1199 (w), 1151 (w), 1101 (w), 1059 (w), 981 (w), 935 (w), 921 (vw), 873 (vw), 825 (w), 772 (w), 714 (w), 693 (vw), 674 (w), 658 (w), 645 (vw), 594 (w), 530 (vw), 511 (w), 486 (vw), 443 (vw) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 414 (100) [M^+], 309 (50) [$C_{19}H_{18}O_4^+$ – H], 279 (9) [$C_{18}H_{15}O_3^+$], 104 (18) [$C_8H_8^+$]. HRMS: calcd. for $C_{27}H_{26}O_4$ 414.1831; found 414.1828.

Compound 27f: According to general procedure A with AHPC (**9**; 200 mg, 750 μmol), yield 12.4 mg (3%). R_f = 0.70 (cyclohexane/ethyl acetate 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.56–2.71 (m, 2 H, H_{Pc}), 2.94–3.24 (m, 11 H, H_{Pc}), 3.41–3.55 (m, 2 H, H_{Pc}), 3.64–3.77 (m, 1 H, H_{Pc}), 6.30–6.32 (m, 1 H, Pc-H_{Ar}), 6.37–6.40 (m, 2 H, Pc-H_{Ar}), 6.45–6.48 (m, 2 H, Pc-H_{Ar}), 6.52–6.55 (m, 3 H, Pc-H_{Ar}), 6.60–6.63 (m, 3 H, Pc-H_{Ar}), 6.70–6.72 (m, 1 H, Pc-H_{Ar}), 6.96 (d, J = 15.5 Hz, 1 H, COCH), 7.05 (dd, J = 7.8, 1.8 Hz, 1 H, Pc-H_{Ar}), 7.91 (d, J = 15.5 Hz, 1 H, COCHC*H*), 12.49 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3, 33.8, 33.8, 35.1, 35.3 (–, 5× CH_2), 35.4 (–, 2× CH_2), 37.5 (–,CH_2), 123.6 (C_{quat}), 126.6, 126.9, 127.8 (+, 3× CH), 129.1 (C_{quat}), 131.2, 131.2, 131.3, 131.8, 132.2, 132.8, 132.9, 133.1 (+, 8× CH), 134.8 (C_{quat}), 135.0, 135.4 (+, 2× CH), 137.9, 139.2, 139.3 (3× C_{quat}), 139.8 (+, CH), 140.1 (C_{quat}), 140.5 (+, CH), 140.6, 141.9, 142.4 (3× C_{quat}), 161.8 (C_{quat}, COH), 194.6 (C_{quat}, CO) ppm. MS (70 eV, EI): *m*/*z* (%) = 484 (11) [M^+], 277 (11) [$C_{19}H_{16}O_2^+$ + H], 206 (16) [$C_{16}H_{14}^+$], 119 (25) [$C_8H_7O^+$], 104 (100) [$C_8H_8^+$], 103 (13) [$C_8H_7^+$]. HRMS: calcd. for $C_{35}H_{32}O_2$ 484.2402; found 484.2404.

Compound 31: A high-pressure vessel was charged with hydroxypyrazolyl[2.2]paracyclophane (156 mg, 540 μmol), [$PdCl_2$(PhCN)$_2$] (**30**; 103 mg, 270 μmol) and dichloromethane (2 mL). The mixture was stirred at 45 °C for 1 h then the organic precipitate was filtered and washed with dichloromethane. The simulated mass spectra was in accordance with the experimental spectrum (see the Supporting Information).

Compound (*R*)-34: Ligand (S_p)-**11h** (3.5 mg, 10.1 μmol) was treated with $ZnEt_2$ (1.5 M in toluene, 1.27 mmol, 0.85 mL) for 30 min at room temperature. The mixture was cooled to –25 °C and cinnamaldehyde (0.08 mL, 640 μmol) was added. After one day, the reaction was quenched at room temperature with 2 M aqueous HCl (1 mL). The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 20:1) to give the secondary alcohol (*R*)-**34** (98 mg, 95%). R_f = 0.09 (cyclohexane/ethyl acetate, 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.4 Hz, 3 H, CH_3), 1.18–1.26 (m, 1 H, CH_2), 1.60–1.62 (m, 1 H, CH_2), 4.08–4.21 (m, 1 H, C*H*COH), 6.13 (dd, J = 15.9, 6.8 Hz, Ph-CH-C*H*), 6.50 (d, J = 15.9 Hz, Ph-CH), 7.16–7.33 (m, 5 H, Ph) ppm. See the Supporting Information for chiral phase HPLC analytics for determining the *ee* of 24%.

X-ray Crystallographic Data: Crystallographic Data (excluding structure factors) for the structures reported in this work have been deposited with the Cambridge Crystallographic Data Centre under registration numbers CCDC-919988 (for **10**), -918989 (for **27a**), -918990 (for **27b**), -918991 (for **27d**), -918992 (for **27e**), -918993 (for **11b**), -918994 (for **11k**), -918995 (for **12e**), -918996 (for **12c**), -918997 (for **11h**), -918998 (for **11i**), -918999 (for **22**), -919000 (for **12j**), -919001 (for **18**), -919002 (for **12f**), -919003 (for **2a**), -919004 (for **25i**), -919005 (for **25e**), -919006 (for **25d**), -919007 (for **8c**), -919008 (for **8g**), -919009 (for **29a**), and -919010 (for **8b**). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Crystal structure determinations and NMR spectra.

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