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Synthesis of 1,1′- and 2,2′-Bicarbazole Alkaloids by Iron(III)-Catalyzed Oxidative Coupling of 2- and 1-Hydroxycarbazoles**

Christian Brütting,[a] Raphael F. Fritsche,[a] Sebastian K. Kutz,[a] Carsten Börger,[a] Arndt W. Schmidt,[a] Olga Kataeva,[b] and Hans-Joachim Knölker*[a]

Abstract: We describe the synthesis of 1,1′- and 2,2′-bicarbazoles by oxidative homo-coupling of 2- and 1-hydroxycarbazoles. The oxidative coupling using catalytic amounts of F_{16}PcFe can be applied to both groups of substrates. While it generally provides the best yields for the synthesis of 1,1′-bicarbazoles, di-*tert*-butyl peroxide affords better results for the 2,2′-bicarbazoles. In our study, we have achieved the first syntheses of the biscarbalexines A–C, bisglybomine B, 2,2′-dihydroxy-7,7′-dimethoxy-3,3′-dimethyl-1,1′-bicarbazole, bispyrayafoline C, and bisisomahanine. The iron-catalyzed coupling of koenigine led to an improved synthesis of 8,8″-biskoenigine and afforded an unprecedented decacylic product. Oxidative coupling of 1-hydroxycarbazoles led to bisclausenol and to the first total syntheses of bismurrayafoline B and D.

Introduction

Biaryl compounds play a major role as chiral ligands and as catalysts in asymmetric synthesis. They also constitute a unique class of natural products.[1–2] A number of methods has been developed for the synthesis of axially chiral biaryl compounds and for the separation of their atropisomers.[3]

The synthesis of 2,2′-dihydroxy-1,1′-binaphthalenes and *ortho*,*ortho*′-dihydroxybiphenyls by phenolic coupling of the corresponding hydroxyarenes has been extensively investigated.[4–8] However, the corresponding bicarbazoles have been studied scarcely, although a range of 1,1′-, 2,2′-, and unsymmetrical bicarbazoles has been isolated from different natural sources, mainly plants of the genera *Murraya*, *Glycosmis* and *Clausena*.[9–24] Herein, we report the synthesis of the 1,1′-coupled bis-2-hydroxy-3-methylcarbazole (**1**), the methoxy-substituted 1,1′-bicarbazole-2,2′-diols **2**–**5**, bisglybomine B (**6**), the bi(pyrano[3,2-*a*]carbazoles) **7**–**9**, and the 2,2′-bicarbazoles **10**–**12** by oxidative coupling of the corresponding monomeric carbazole alkaloids (Figures 1 and 2). The carbazoles are available by our molybdenum-mediated,[25,26] iron-mediated[27–29] and palladium-catalyzed[30–41] approaches. The present report complements our recent syntheses of methylene-bridged biscarbazoles based on an Ullmann-type coupling of carbazole units as key step.[42,43]

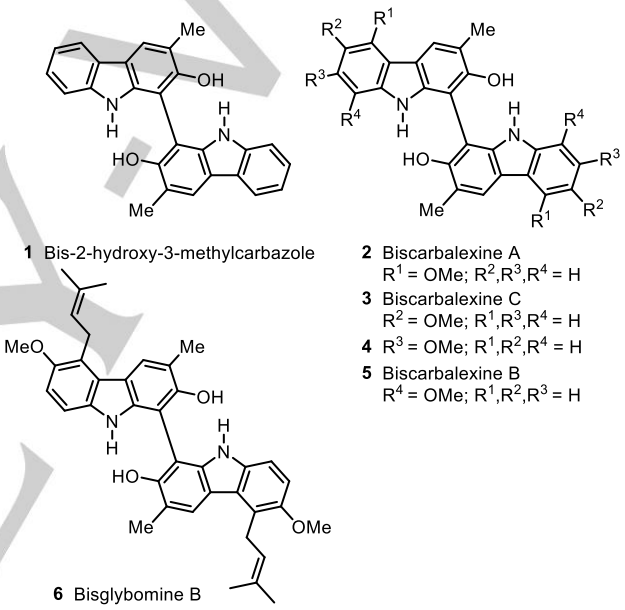

Figure 1. Bis-2-hydroxy-3-methylcarbazole (**1**) and related 1,1′-bicarbazoles.

Results and Discussion

Bis-2-hydroxy-3-methylcarbazole (**1**) has been isolated in 1993 by Furukawa et al. from the roots of *Murraya koenigii*.[44] In 1996, we described the first synthetic access to the 1,1′-bicarbazole **1** by a *p*-chloranil-mediated oxidative coupling of 2-hydroxy-3-methylcarbazole (**14**) (Scheme 1, Table 1).[25,45] Using a similar approach, Dash et al. obtained **1** by a copper(II) chloride-catalyzed coupling of **14**.[46] In our original paper, 2-hydroxy-3-methylcarbazole (**14**) was synthesized by reaction of the arylamine **13** with a cyclohexadienylmolybdenum salt followed by oxidative cyclization and cleavage of the methyl ether.[25] Since then, various synthetic approaches to **14** have been developed.[10,18,46–49]

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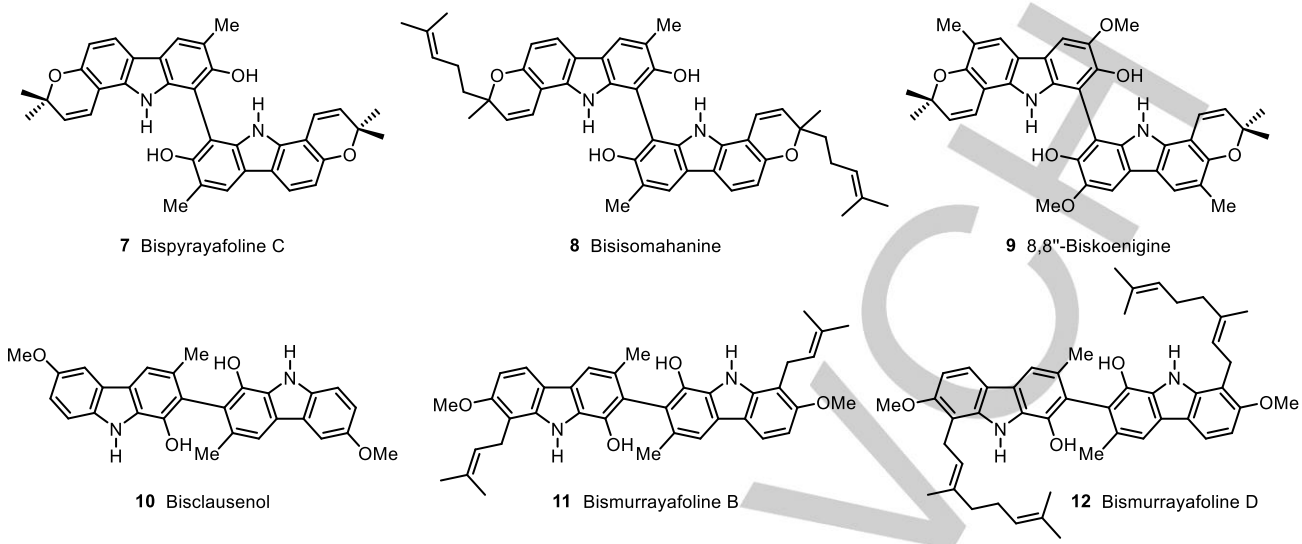
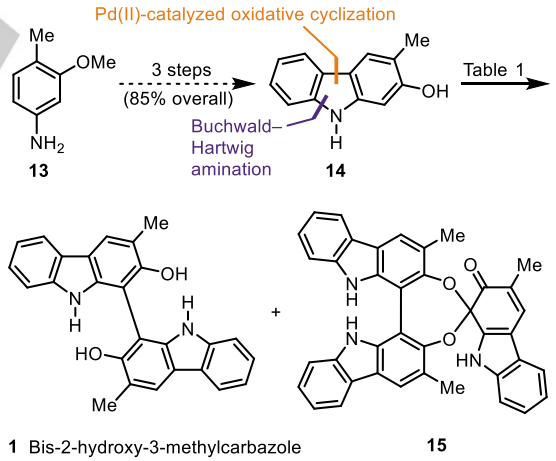


Figure 2. Bipyrano[3,2-*a*]carbazoles and 2,2′-bicarbazoles.

Our approach via Buchwald–Hartwig coupling of the aniline **13** and iodobenzene followed by palladium(II)-catalyzed oxidative cyclization and methyl ether cleavage provided 2-hydroxy-3-methylcarbazole (**14**) in three steps and 85% overall yield on gram scale.[40,48,49] Using **14** as model compound, we screened the performance of various reagents for the oxidative coupling to the 1,1′-bicarbazole **1** (Table 1). Treatment of **14** with a copper(II)–TMEDA complex under air, a method previously used by Koga and co-workers for the oxidative coupling of β-naphthols,[50] provided the 1,1′-bicarbazole **1** in only 12% yield. The major product was the triscarbazole **15** containing a central 1,3-dioxepine unit. The structure of compound **15** has been assigned by 2D NMR spectroscopy (see Supporting Information). The X-ray analysis of a similar compound confirmed the assignment of the heterocyclic framework (vide infra). Analogous compounds have been described by Dryhurst et al. on oxidation of 5-hydroxyindole derivatives.[51,52] Coupling of **14** using catalytic amounts of copper(I) iodide in the presence of *meso*-1,2-diphenyl-1,2-diaminoethane provided the 1,1′-bicarbazole **1** in 43% yield and the triscarbazole **15** in 15% yield. Treatment of **14** with vanadyl acetylacetonate in dichloromethane under oxygen atmosphere, as described by Uang et al. for oxidative coupling of β-naphthols,[53] provided the desired 1,1′-bicarbazole **1** in 52% yield and compound **15** in up to 7% yield.

Oxidative coupling of **1** was accomplished in 80% yield without any formation of compound **15** by treatment of **14** with stoichiometric amounts of di-*tert*-butyl peroxide in chlorobenzene at reflux.[54,55] Recently, iron-catalyzed oxidative coupling reactions have attracted increasing attention because iron compounds represent environmentally benign green catalysts.[56] In this context, we recently described the oxidative C–C coupling of diarylamines using hexadecafluorophthalocyanine–iron (F_{16}PcFe)[57,58] as catalyst and methanesulfonic acid as additive.[59] Under these conditions, the 1,1′-bicarbazole **1** was obtained in 77% yield. A separation of the atropisomers of **1** was not attempted as we did not expect a configurational stability of the pure enantiomers of **1** at room temperature (vide infra). Moreover, Furukawa et al. did not report any chiroptical data for the natural product.



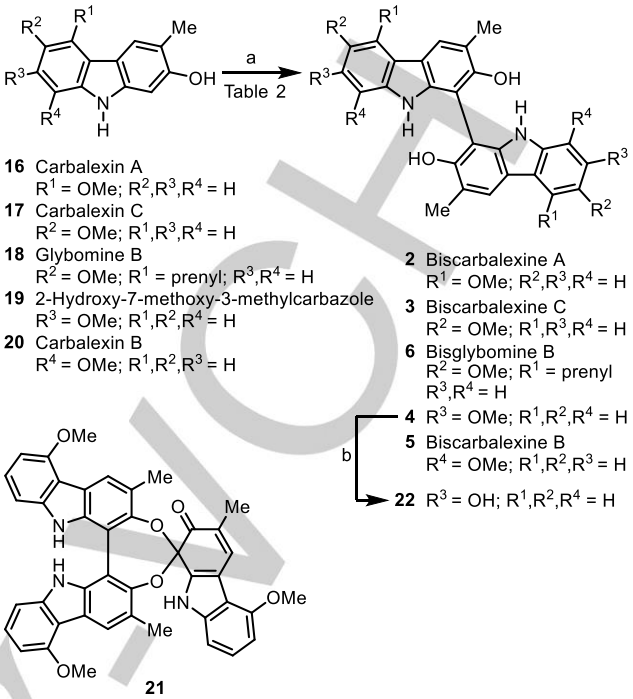
Scheme 1. Synthesis and oxidative coupling of 2-hydroxy-3-methylcarbazole (**14**).

Table 1. Oxidative homo-coupling of 2-hydroxy-3-methylcarbazole (**14**).

Reagents and conditions	Yield [%] **1**	**15**
2.2 equiv *p*-chloranil, MeOH, reflux, 8 h[25]	38	0
0.1 equiv $[CuOH·TMEDA]_2Cl_2$, CH_2Cl_2, RT, air, 1 h	12	18
0.1 equiv CuI, 0.1 equiv 1,2-diphenyl-1,2-diaminoethane, MeCN, 40 °C, 17 h	43	15
0.1 equiv $CuCl_2·2\ H_2O$, 1.5 equiv DBU, MeCN, 100 °C (sealed tube), 26 h[46]	51	n.r.[a]
0.1 equiv $VO(acac)_2$, CH_2Cl_2, RT, 18 h	52	2
0.1 equiv $VO(acac)_2$, CH_2Cl_2–Et_2O (4:1), RT, O_2, 22.5 h	52	7
2.0 equiv $(t\text{-BuO})_2$, PhCl, reflux, 2.5 h	80	0
3.0 mol% $F_{16}PcFe$, 10 mol% MsOH, CH_2Cl_2, RT, air, 6 h	77	0

[a] n.r.: not reported

We then investigated the synthesis of the methoxy-substituted bicarbazoles **2**–**6** by oxidative coupling of the corresponding carbazoles **16**–**20** (Scheme 2). In 2012, Chen et al. obtained biscarbalexine A (**2**), the 5,5′-dimethoxy analog of **1**, from the stem of *G. pentaphylla*.[60] The corresponding precursor, carbalexin A (**16**), was isolated from leaves of the same plant by Greger et al. in 2001.[61] Recently we reported the first total synthesis of carbalexin A (**16**) by pivaloyloxy-directed, regioselective palladium(II)-catalyzed oxidative cyclization of a diarylamine.[62] Treatment of carbalexin A (**16**) with catalytic amounts of $[CuOH·TMEDA]_2Cl_2$ under air provided biscarbalexine A (**2**) in 53% yield (Table 2). In agreement with the oxidative coupling of 2-hydroxy-3-methylcarbazole (**14**), these conditions led to the formation of the triscarbazole **21** as by-product (29% yield). The structure of **21** was assigned based on 2D NMR spectroscopy (see Supporting Information) and unequivocally confirmed by an X-ray analysis of single crystals (Figure 3). Oxidative coupling of **16** using catalytic amounts of vanadyl acetylacetonate under oxygen atmosphere provided exclusively biscarbalexine A (**2**) in 74% yield. The iron(III)-catalyzed oxidative coupling of carbalexin A (**16**) using 1 mol% of $F_{16}PcFe$ in acetic acid afforded biscarbalexine A (**2**) in 70% yield. Although the chirality of biscarbalexine A (**2**) has not been discussed on its isolation,[60] we have separated the atropisomers by chiral HPLC (Figure 4). It was found that the individual enantiomers racemize slowly at room temperature (solvent: MeCN–H_2O, 70:30 + 0.1% TFA). This finding strongly suggests that naturally occurring biscarbalexine A (**2**) is a racemic mixture.



Scheme 2. Synthesis of the 1,1′-bicarbazoles **2**–**6**, the triscarbazole **21** and tetrahydroxy-1,1′-bicarbazole **22**. *Reagents and conditions*: a) see Table 2; b) 4.0 equiv BBr_3, CH_2Cl_2, −78 °C, 2h, 0 °C, 4 h, RT, 44 h (40%).

Table 2. Oxidative homo-coupling of the dioxygenated carbazoles **16**–**20**.

Compd.	Reagents and conditions	Product (yield)
16	0.1 equiv $[CuOH·TMEDA]_2Cl_2$, CH_2Cl_2, RT, air, 45 min	**2** (53%)[a]
16	0.1 equiv $VO(acac)_2$, CH_2Cl_2, RT, O_2, 2.5 h	**2** (74%)
16	1.0 mol% $F_{16}PcFe$, HOAc, RT, air, 20 min	**2** (70%)
17	2.0 equiv $(t\text{-BuO})_2$, PhCl, reflux, 2.25 h	**3** (91%)
17	3.0 mol% $F_{16}PcFe$, 10 mol% MsOH, CH_2Cl_2, RT, air, 80 min	**3** (92%)
18	3.0 equiv $(t\text{-BuO})_2$, PhCl, reflux, 1.5 h	**6** (56%)
18	2.0 mol% $F_{16}PcFe$, HOAc, RT, air, 10 min	**6** (63%)
19	0.1 equiv $VO(acac)_2$, CH_2Cl_2, RT, O_2, 24 h	**4** (50%)
19	3.0 mol% $F_{16}PcFe$, HOAc, RT, air, 30 min	**4** (61%)
20	4.0 equiv $(t\text{-BuO})_2$, PhCl, reflux, 2 h	**5** (23%)
20	2.0 mol% $F_{16}PcFe$, HOAc, RT, air, 30 min	**5** (54%)

[a] The triscarbazole **21** was obtained as by-product in 29% yield.

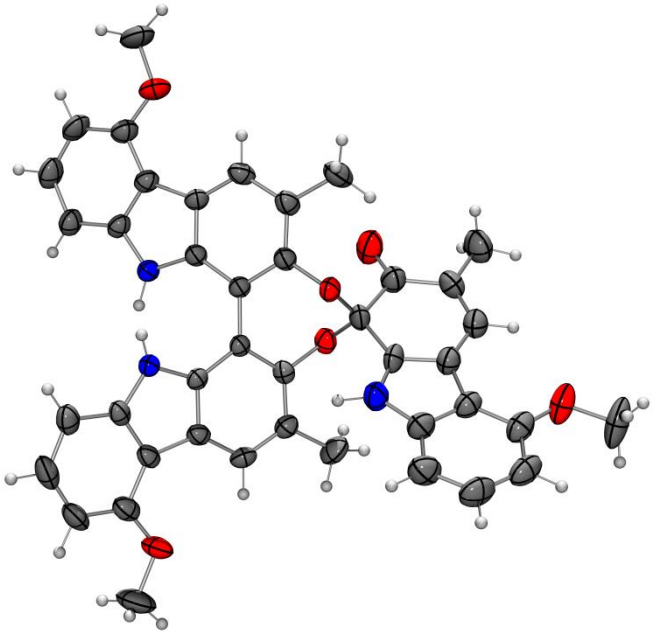


Figure 3. Molecular structure of **21** in the crystal (monoclinic, $C2_c$); ORTEP plot showing thermal ellipsoids at the 50% probability level.

The 6,6′-dimethoxy analog biscarbalexine C (**3**) has not been obtained from natural sources so far. However, in 2012 Chen and co-workers reported the isolation of bisglybomine B (**6**), a closely related 6,6′-dimethoxybicarbazole featuring an additional prenyl substituent at C-5 of the carbazole moieties.[60] In 2009 we described the first total synthesis of carbalexin C (**17**),[41,63] the precursor for **3**, which was isolated in 2001 from *Glycosmis pentaphylla*.[61] We also achieved the first total synthesis of the prenylated analog glybomine B (**18**),[62] which had been isolated from *Glycosmis arborea*.[64] Both 6,6′-dimethoxy substituted 1,1′-bicarbazoles **3** and **6** were synthesized by treatment of **17** and **18** with di-*tert*-butyl peroxide in chlorobenzene at reflux (Table 2). Oxidative homo-coupling of carbalexin C (**17**) provided the corresponding dimer biscarbalexine C (**3**) in 91% yield, whereas the coupling of glybomine B (**18**) required a higher load of the oxidant to provide the natural product **6** in 56% yield. Using our iron(III)-catalyzed oxidative coupling, **3** and **6** were obtained in slightly better yields and considerably shorter reaction times.

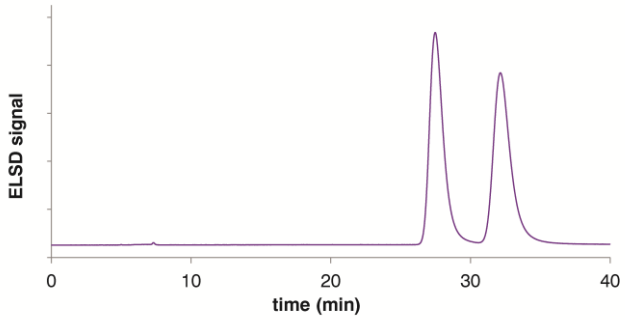
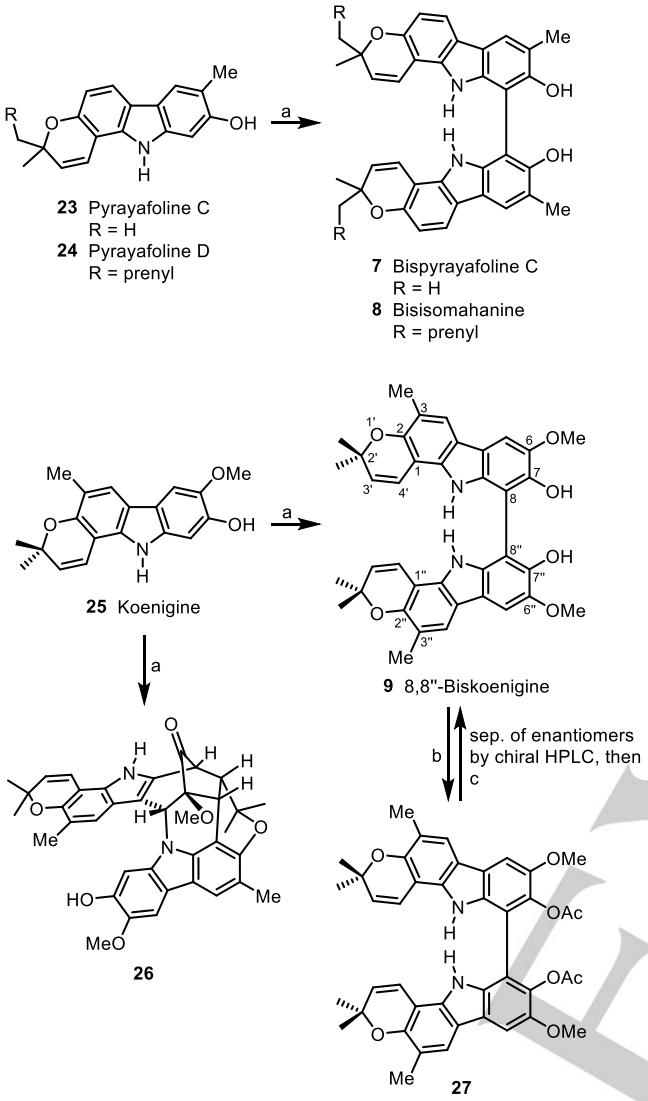


Figure 4. Separation of the atropisomers of biscarbalexine A (**2**) by chiral HPLC (Nucleocel delta RP, isocratic elution, MeCN–H_2O, 70:30 + 0.1% TFA).

The 2,2′,7,7′-tetraoxygenated 1,1′-bicarbazole **4** has not been obtained from natural sources yet. The same is true for the corresponding 2-hydroxy-7-methoxy-3-methylcarbazole (**19**). However, compound **19** has been mentioned as synthetic intermediate by Anwer in 1972,[65] and also served as precursor for our approach to the pyrano[3,2-*a*]carbazoles *O*-methylmurrayamine A and *O*-methylmahanine.[32] Oxidative homo-coupling of **19** using catalytic amounts of vanadyl acetoacetonate under oxygen atmosphere afforded the 1,1′-bicarbazole **4** in 50% yield. Oxidative homo-coupling of **19** using catalytic amounts of F_{16}PcFe in the presence of air led to the 1,1′-bicarbazole **4** in 61% yield. Treatment of compound **4** with boron tribromide provided 2,2′,7,7′-tetrahydroxy-3,3′-dimethyl-1,1′-bicarbazole (**22**). Finally, we also prepared the non-natural biscarbalexine B (**5**). The corresponding carbalexin B (**20**) was first mentioned as synthetic compound by Reisch in 1980,[66] later isolated by Greger from *Glycosmis pentaphylla* in 2001,[61] and obtained by our total synthesis in 2014.[35,36] Treatment of **20** with di-*tert*-butyl peroxide in chlorobenzene at reflux led to the 8,8′-dimethoxy-1,1′-bicarbazole in only 23% yield accompanied by extensive decomposition. The iron(III)-catalyzed oxidative homo-coupling of **20** afforded biscarbalexine B (**5**) in 54% yield.

The successful oxidative homo-coupling of simple 2-hydroxycarbazoles to the corresponding 1,1′-bicarbazoles **1**–**6** encouraged us to apply the approach to the coupling of the pyrano[3,2-*a*]carbazoles **23**–**25** (Scheme 3). Pyrayafoline C (**23**) and D (**24**) were isolated in 1991 by Furukawa from the stem bark of *Murraya euchrestifolia*.[67] In 2014, we described a synthetic route to both compounds.[32] Bispyrayafoline C (**7**) has not been obtained from natural sources yet. Bisisomahanine (**8**), a homo-coupling product of pyrayafoline D, was isolated in 2004 by Cuong et al. from the roots of *Glycosmis stenocarpa* and reported to be optically active ($[\alpha]_D^{20}$ = −13.1, *c* = 0.25, $CHCl_3$).[68] However, the authors did not assign the absolute configuration. Treatment of pyrayafoline C (**23**) and D (**24**) with di-*tert*-butyl peroxide afforded the corresponding dimers **7** and **8** in 85% and 64% yield, respectively (Table 3). The prenyl-substituted compounds **24** and **8** seem to be more sensitive towards decomposition under these reaction conditions. The iron(III)-catalyzed oxidative coupling with 1 mol% of F_{16}PcFe in acetic acid proved to be superior and provided bispyrayafoline C (**7**) and bisisomahanine (**8**) in 93% yield. For compound **8** only one set of signals was observed in the ^{1}H and ^{13}C NMR spectra, although most likely it was obtained as a mixture of diastereoisomers. Since the relative configuration of the natural product is unknown, we did not attempt to separate the atropisomers.



Scheme 3. Synthesis of bispyrayafoline C (**7**), bisisomahanine (**8**), 8,8″-biskoenigine (**9**), compound **26** and *O*,*O*″-diacetyl(8,8″-biskoenigine) (**27**). *Reagents and conditions*: a) see: Table 3; b) 3.0 equiv Ac_2O, 4.0 equiv Et_3N, cat. DMAP, THF, RT, 2 h (93%); c) 8.0 equiv K_2CO_3, MeOH–CH_2Cl_2 (1:1), RT 18 h (100%).

Table 3. Oxidative homo-coupling of the pyrano[3,2-*a*]carbazoles **23**–**25**.

Compd.	Reagents and conditions	Product (yield)
23	2.9 equiv. (*t*-BuO)$_2$, PhCl, reflux, 2.5 h	**7** (85%)
23	1.0 mol% F_{16}PcFe, HOAc, RT, air, 10 min	**7** (93%)
24	2.0 equiv. (*t*-BuO)$_2$, PhCl, reflux, 1.5 h	**8** (64%)
24	1.0 mol% F_{16}PcFe, HOAc, RT, air, 20 min	**8** (93%)
25	0.1 equiv [CuOH·TMEDA]$_2Cl_2$, CH_2Cl_2, RT, air, 20 min	**9** (70%)
25	0.1 equiv. VO(acac)$_2$, CH_2Cl_2, RT, O_2, 1.75 h	**9** (72%)
25	1.0 mol% F_{16}PcFe, HOAc, RT, air, 3 h	**26** (51%)
25	1.0 mol% F_{16}PcFe, CH_2Cl_2, RT, air, 20 min	**9** (90%)

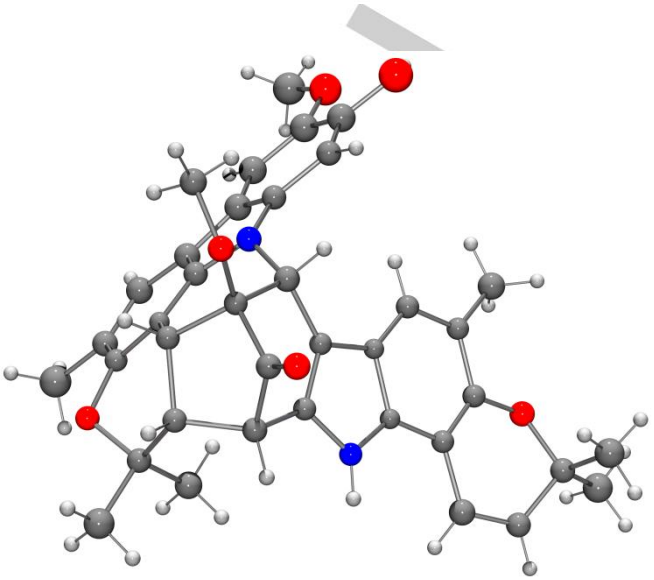
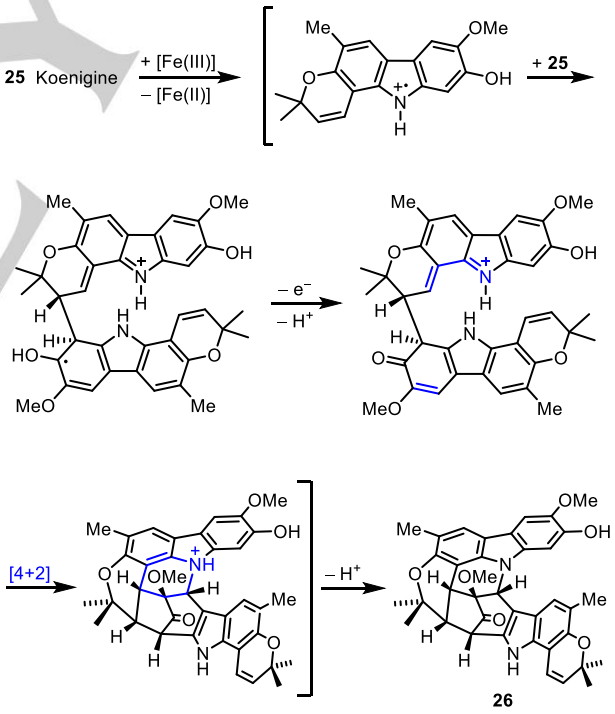


Figure 5. Molecular structure of the decacyclic coupling product **26** in the crystal (triclinic, *P*-1).



Scheme 4. Proposed mechanism for the formation of compound **26**.

The dioxygenated pyrano[3,2-*a*]carbazole koenigine (**25**) was isolated in 1970 by Narasimhan from leaves of *Murraya koenigii*.[69,70] 8,8″-Biskoenigine (**9**) was obtained by Hao more than 30 years later from the dried leaves of the same plant.[71,72] 8,8″-Biskoenigine (**9**) was reported to be optically active: $[\alpha]_D^{24}$ = +139.6 (*c* = 1.00, $CHCl_3$).[72] Hao and co-workers also described

the iron(III) chloride-mediated oxidative coupling of natural koenigine (**25**) to racemic 8,8″-biskoenigine (**9**) in 30% yield.[72] Recently, we described the first total synthesis of koenigine (**25**) by using our palladium-catalyzed approach.[41] Oxidation of synthetic koenigine (**25**) with catalytic amounts of $[CuOH{\cdot}TMEDA]_2Cl_2$ under air led to 8,8″-biskoenigine (**9**) in 70% yield (Table 3). Treatment of **25** with catalytic amounts of vanadyl acetylacetonate under oxygen atmosphere provided 8,8″-biskoenigine (**9**) in 72% yield. The iron(III)-catalyzed oxidative coupling of **25** with 1 mol% of F_{16}PcFe in acetic acid in the presence of air afforded, after an unusually long reaction time of 3 hours, the decacyclic coupling product **26** in 51% yield. The relative configuration of **26** has been assigned by 2D NMR spectroscopy (see Supporting Information) and unambiguously confirmed by an X-ray crystal structure determination (Figure 5). The formation of compound **26** can be rationalized by an iron(III)-catalyzed oxidative homo-coupling of koenigine (**25**) followed by an intramolecular hetero-Diels-Alder cycloaddition (Scheme 4). When the iron(III)-catalyzed homo-coupling of **25** was performed in dichloromethane as solvent, 8,8″-biskoenigine (**9**) was obtained in 90% yield. Synthetic **9** was subjected to chiral HPLC (Figure 6A). Although the two enantiomers were distinguishable, we were unable to establish conditions suitable for the separation of (+)- and (−)-**9** by preparative HPLC. The atropisomers eventually were separated after double O-acetylation to *O*,*O*″-diacetyl(8,8″-biskoenigine) (**27**). Preparative HPLC provided (+)-**27** and (−)-**27** in >98% ee (Figure 6A). The individual enantiomers proved to be stable towards racemization at room temperature and even after heating a solution of (+)- or (−)-**27** (Figure 6B). However, cleavage of the acetyl groups by exposure to potassium carbonate in methanol at room temperature led to racemic 8,8″-biskoenigine (**9**). Base-facilitated racemization of hydroxybiaryls was observed previously by other groups.[73,74]

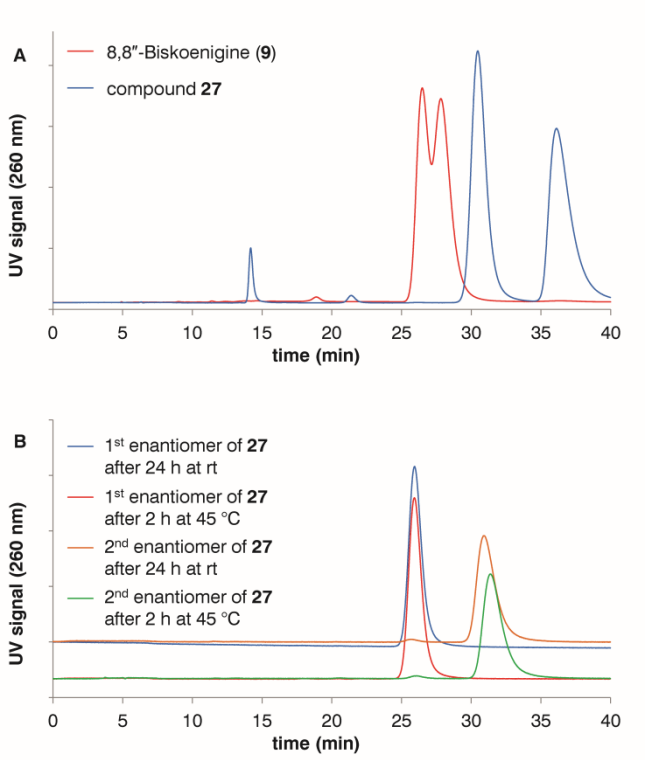
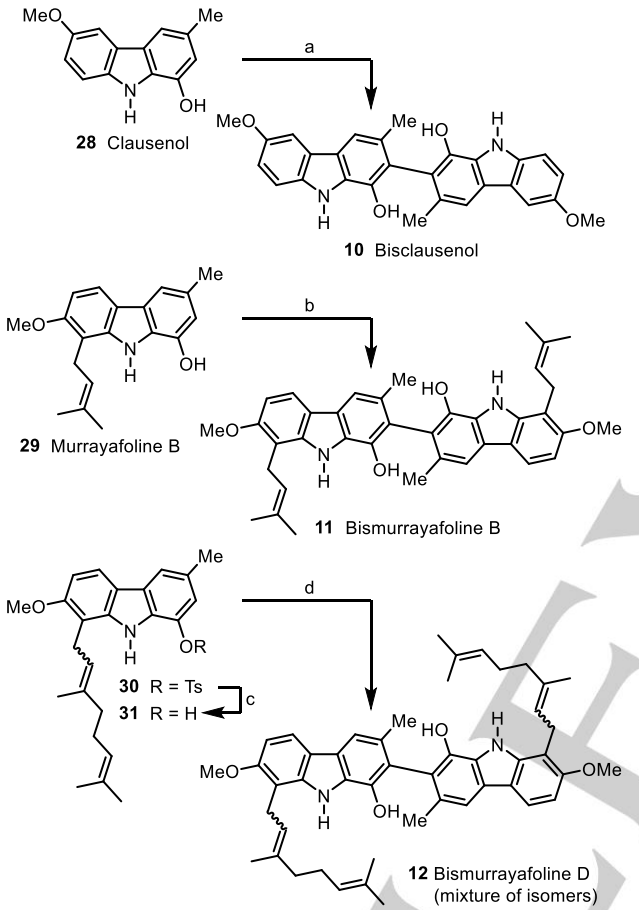


Figure 6. Chiral HPLC separation (Nucleocel delta RP) of the atropisomers of 8,8″-biskoenigine (**9**) (68% eluent B, isocratic) and *O*,*O*″-diacetyl(8,8″-biskoenigine) (**27**) (72% eluent B, isocratic; for details, see exp. section), and thermal stability of the atropisomers of **27** against racemization (Nucleocel delta RP, MeCN–H_2O, 70:30 + 0.1% TFA, rt, 24h and 45 °C, 2 h).

The 2,2′-bicarbazoles **10**–**12** were synthesized by oxidative coupling of the corresponding 1-hydroxycarbazoles **28**, **29** and **31** (Scheme 5) Clausenol (**28**) has been isolated by Chakraborty et al. from *Clausena excavata*.[75] Different synthetic approaches to **28** have been reported[75–78] including our palladium-catalyzed route.[79,80] The oxidative homo-coupling of clausenol (**28**) using di-*tert*-butyl peroxide to the non-natural 2,2′-bicarbazole **10** has already been reported by Lin and Zhang, who also described the separation of the atropisomers.[76,77] We have achieved a yield of 93% for the transformation of clausenol (**28**) to bisclausenol (**10**) with di-*tert*-butyl peroxide. The bismurrayafolines B (**11**) and D (**12**) were isolated by Furukawa from *Murraya euchrestifolia* in 1983 and 1991, respectively.[81,82] Murrayafoline B (**29**), the monomer of **11**, was isolated in 1985 by Furukawa from the same plant.[83] Synthetic approaches to **29** have been reported by Kapil[84] and by our group.[85] Oxidation of synthetic murrayafoline B (**29**)[85] with di-*tert*-butyl peroxide provided bismurrayafoline B (**11**) in 76% yield. The spectroscopic data were in agreement with those reported for the natural compound. The 7-geranyl-substituted carbazole (*E*)-**31** has not yet been isolated from nature. The corresponding *O*-tosyl derivative **30** (*E*:*Z*=1.3:1) was an intermediate of our synthetic approach to murrayaquinone C.[85] Cleavage of the tosyl group afforded the 1-hydroxycarbazole **31** which has been fully characterized as it

represents the presumed natural product murrayafoline D. Oxidation of compound **31** with an excess of di-*tert*-butyl peroxide provided the corresponding dimer **12** as a mixture of diastereoisomers in 99% yield. The iron(III)-catalyzed homo-coupling reaction of the 1-hydroxycarbazoles **28**, **29**, and **31** afforded the corresponding 2,2′-bicarbazoles **10**, **11**, and **12** in 63%, 45% and 38% yield, respectively (see Supporting Information).



Scheme 5. Synthesis of the 2,2′-bicarbazoles **10**, **11** and **12**. *Reagents and conditions*: a) 1.3 equiv (*t*-BuO)$_2$, PhCl, reflux, 2 h (93%); b) 1.5 equiv (*t*-BuO)$_2$, PhCl, reflux, 2 h (76%); c) 8.6 equiv $LiAlH_4$, THF, reflux, 16 h; d) 2.9 equiv (*t*-BuO)$_2$, PhCl, reflux, 3.25 h (99%, 2 steps).

Conclusions

The efficiency of several reagents and catalysts for the oxidative homo-coupling of 2-hydroxy-3-methylcarbazole (**14**) has been investigated. The iron(III)-catalyzed homo-coupling of 2-hydroxycarbazoles by oxidation with catalytic amounts of hexadecafluorophthalocyanine–iron in the presence of air provides overall the best results for the synthesis of 1,1′-bicarbazoles with yields up to 93%. Oxidative coupling with alternative reagents (di-*tert*-butyl peroxide, air in the presence of catalytic amounts of copper(II) chloride, or oxygen and catalytic amounts of vanadyl acetylacetonate) was generally less efficient, but still provided the desired coupling products in reasonable yields. With chiral ligands, the two latter methods offer a possibility to obtain enantiomerically pure bicarbazoles.[4,86] Using the iron(III)-catalyzed homo-coupling as key step, we achieved the first total syntheses of the naturally occurring 1,1′-bicarbazole alkaloids biscarbalexine A (**2**), bisglybomine B (**6**) and bisisomahanine (**8**). Moreover, the iron(III)-catalyzed coupling provided efficient routes to the non-natural 1,1′-bicarbazoles **3**–**5** and the bipyrano[3,2-*a*]carbazole **7**. When using dichloromethane as solvent, the iron(III)-catalyzed coupling could also be applied to an efficient total synthesis of 8,8″-biskoenigine (**9**). Double O-acetylation of **9** enabled the separation of the atropisomers by chiral HPLC of compound **27**. In acetic acid as solvent, the homo-coupling of koenigine (**25**) in the presence of air and catalytic amounts of F_{16}PcFe affords the unprecedented decacylic coupling product **26**. Finally, the oxidative homo-coupling of the 1-hydroxycarbazoles **28**, **29** and **31** afforded the 1,1′-dihydroxy-2,2′-bicarbazoles **10**–**12** and thus led to the first total syntheses of bismurrayafoline B (**11**) and bismurrayafoline D (**12**). In this case, di-*tert*-butyl peroxide as oxidant was superior to the iron(III)-catalyzed coupling reaction.

Experimental Section

General. All reactions were carried out in oven-dried glassware using anhydrous solvents under an argon atmosphere, unless stated otherwise. CH_2Cl_2, THF, and toluene were dried using a solvent purification system (MBraun-SPS). $Pd(OAc)_2$ was recrystallized from glacial AcOH. All other chemicals were used as received from commercial sources. The iron(III)-catalyzed reactions were carried out in non-dried solvents and open to air. Activated carbon on silica gel was prepared by mixing activated carbon powder (50 mg) with silica gel (1.0 g). Hexadecafluorophthalocyanine–iron was prepared following the procedure reported previously.[57a,59] Petroleum ether (PE) refers to the hydrocarbon mixture with a boiling range of 40–65 °C. Flash chromatography was performed using silica gel from Acros Organics (0.035–0.070 mm). TLC was performed with TLC plates from Merck (60 F254) using UV light for visualization. Melting points were measured on a Gallenkamp MPD 350 melting point apparatus. Ultraviolet spectra were recorded on a PerkinElmer 25 UV/Vis spectrometer. IR spectra were recorded on a Thermo Nicolet Avatar 360 FT-IR spectrometer using the ATR method (Attenuated Total Reflectance). NMR spectra were recorded on Bruker DRX 500 and Avance III 600 spectrometers. Chemical shifts δ are reported in parts per million with the solvent signal as internal standard. Standard abbreviations were used to denote the multiplicities of the signals. EI-MS and EI-HRMS were recorded on a Finnigan MAT-95 spectrometer (70 eV) or by GC/MS-coupling using an Agilent Technologies 6890 N GC System equipped with a 5973 Mass Selective Detector (70 eV). ESI-MS spectra were recorded on an Esquire LC with an ion trap detector from Bruker. Positive and negative ions were detected. ESI-HRMS were recorded using an Q-TOF 6538 (Agilent) or LTQ ORBITRAP XL instrument (Thermo Scientific). Elemental analyses were measured on an EuroVector EuroEA3000 elemental analyzer. X-ray crystal structure analyses were performed with a Bruker-Nonius Kappa CCD (for **21**) and a with Bruker AXS Smart APEX diffractometer (for **26**) equipped with a 700 series Cryostream low temperature device from Oxford Cryosystems. SHELXS-97,[87] SADABS version 2.10,[88] SHELXL-97,[89] POV-Ray for Windows version 3.7.0.msvc10.win64, and ORTEP-3 for Windows[90] were used as software. Analytical HPLC was carried out on an Agilent

Model 1100 with G1315B UV-DAD (detection at 215, 260 and 560 nm), G1321A fluorescence and an evaporative light scattering detector (ELS 1000, Polymer Laboratories); column: Macherey-Nagel Nucleocel delta RP (4.6 × 250 mm); flow rate: 0.5 mL min^{-1}; eluent A: H_2O + 0.1% TFA; eluent B: MeCN + 0.1% TFA. Preparative HPLC was carried out using a Varian PrepStar system with a Varian ProStar Model 320 UV and an evaporative light scattering detector (ELS 1000, Polymer Laboratories) connected via a Sunchrom Quick-Split splitter; column: Macherey-Nagel Nucleocel delta RP (21 × 250 mm); flow rate: 8.5 mL min^{-1}; eluent A: H_2O + 0.1% TFA; eluent B: MeCN + 0.1% TFA.

Bis-2-hydroxy-3-methylcarbazole (2,2′-dihydroxy-3,3′-dimethyl-1,1′-bicarbazole) (1): Dichloromethane (5 mL) was added to a mixture of hexadecafluorophthalocyanine–iron (6.44 mg, 7.52 µmol), methanesulfonic acid (2.41 mg, 25.0 µmol) and 2-hydroxy-3-methylcarbazole (**14**) (49.3 mg, 250 µmol). The resulting suspension was stirred at room temperature for 6 h under air. The mixture was filtered through a short pad of silica gel with dichloromethane (20 mL). Removal of the solvent in vacuo provided the 1,1′-bicarbazole **1** (37.8 mg, 96.3 µmol, 77%) as colorless solid. M.p. 259 °C (dec.); UV (MeOH): λ = 213, 236, 257 (sh), 303, 335 nm; IR (KBr): ν = 3529, 3401, 1610, 1460, 1419, 1307, 1216, 1193, 1168, 1132, 887, 749, 739 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.53 (s, 6 H), 5.28 (s, 2 H), 7.22–7.26 (m, 4 H), 7.30–7.33 (m, 2 H), 7.65 (s, 2 H), 7.99 (s, 2 H), 8.03 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 16.73 (2 CH_3), 99.03 (2 C), 110.71 (2 CH), 117.10 (2 C), 117.94 (2 C), 119.47 (2 CH), 119.79 (2 CH), 123.12 (2 CH), 123.62 (2 C), 124.79 (2 CH), 137.69 (2 C), 139.26 (2 C), 151.17 (2 C); ^{1}H NMR (400 MHz, acetone-d_6): δ = 2.45 (s, 6 H), 7.10 (m, 2 H), 7.19 (m, 2 H), 7.27 (d, *J* = 8.0 Hz, 2 H), 7.42 (s, 2 H), 7.89 (s, 2 H), 7.99 (d, *J* = 7.7 Hz, 2 H), 9.62 (br s, 2 H); ^{13}C NMR (100 MHz, acetone-d_6): δ = 18.10 (2 CH_3), 103.29 (2 C), 112.24 (2 CH), 117.62 (2 C), 118.95 (2 C), 120.03 (2 CH), 120.25 (2 CH), 123.11 (2 CH), 125.16 (2 CH), 125.37 (2 C), 140.88 (2 C), 141.65 (2 C), 154.12 (2 C); MS (EI): *m/z* (%) = 392 (100) $[M]^+$, 196 (19); HRMS (EI): *m/z* calcd for $C_{26}H_{20}N_2O_2$: 392.1525; found: 392.1537; elemental analysis (%) calcd for $C_{26}H_{20}N_2O_2$: C 79.57, H 5.14, N 7.14; found: C 79.43, H 5.31, N 7.30.

Triscarbazole 15: *Method A:* $[CuOH{\cdot}TMEDA]_2Cl_2$ (18.8 mg, 40.6 µmol) was added to a solution of 2-hydroxy-3-methylcarbazole (**14**) (80.0 mg, 406 µmol) in dichloromethane (4 mL) and the solution was stirred at room temperature under air for 1 h. The mixture was diluted with dichloromethane and washed with water. The aqueous layer was extracted with dichloromethane, the combined organic layers were dried (sodium sulfate) and the solvent was evaporated. Purification of the residue by column chromatography (silica gel; isohexane/ethyl acetate, 10:1) provided the less polar compound **15** (ochreous solid; 14.7 mg, 25.1 µmol, 18%) and the more polar 1,1′-bicarbazole **1** (colorless solid; 9.4 mg, 24 µmol, 12%). **15**: M.p. 182 °C (dec.); UV (MeOH): λ = 228, 288 nm; fluorescence (MeOH): λ_{ex} = 288 nm, λ_{em} = 362 nm; IR (ATR) ν = 3367, 3055, 2920, 2851, 1663, 1607, 1560, 1492, 1457, 1409, 1370, 1315, 1253, 1206, 1191, 1165, 1127, 1059, 999, 953, 917, 872, 811, 771, 742, 702 cm^{-1}; ^{1}H NMR (600 MHz, acetone-d_6): δ = 1.77 (s, 3 H), 2.00 (d, *J* = 1.4 Hz, 3 H), 2.36 (s, 3 H), 7.16–7.28 (m, 5 H), 7.35 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1 H), 7.40 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1 H), 7.48 (dd, *J* = 7.9, 0.6 Hz, 1 H), 7.52 (d, *J* = 8.0 Hz, 1 H), 7.84–7.86 (m, 1 H), 7.89 (d, *J* = 1.4 Hz, 1 H), 7.96 (s, 1 H), 8.08 (s, 1 H), 8.16 (d, *J* = 7.9 Hz, 2 H), 10.07 (br s, 1 H), 10.13 (br s, 1 H), 10.76 (br s, 1 H); ^{13}C NMR and DEPT (150 MHz, acetone-d_6): δ = 16.65 (CH_3), 15.97 (CH_3), 17.54 (CH_3), 105.61 (C), 110.27 (C), 111.79 (C), 112.32 (2 CH), 113.39 (CH), 113.95 (C), 119.45 (CH), 119.78 (CH), 119.88 (CH), 120.41 (CH), 120.69 (CH), 121.51 (C), 121.59 (CH), 121.75 (CH), 121.87 (CH), 122.58 (C), 123.53 (C), 123.90 (C), 123.98 (CH), 124.02 (2 C), 124.84 (C), 125.63 (C), 125.73 (CH), 126.16 (CH), 136.23 (C), 136.29 (CH), 136.77 (C), 136.89 (C), 137.85 (C), 141.81 (C), 141.93 (C), 146.64 (C), 149.43 (C), 193.20 (C=O); MS (ESI, +10 V): *m/z* = 586.3 $[M+H]^+$; HRMS (ESI): *m/z* calcd for $C_{39}H_{27}N_3O_3$: 585.2052; found: 585.2047.

Biscarbalexine A (2,2′-dihydroxy-5,5′-dimethoxy-3,3′-dimethyl-1,1′-bicarbazole) (2): Hexadecafluorophthalocyanine–iron (2.11 mg, 2.46 µmol) was added to a solution of 2-hydroxy-5-methoxy-3-methylcarbazole (carbalexin A) (**16**) (56.8 mg, 250 µmol) in acetic acid (5 mL) and the solution was stirred at room temperature for 20 min under air. Then argon was bubbled through the reaction mixture and the solvent was removed in vacuo. Then toluene (3 mL) was added to remove the residual acetic acid as an azeotrope in vacuo. The residue was dissolved in dichloromethane (1 mL), filtered through a short pad of activated carbon on silica gel with dichloromethane (20 mL) and the solvent was removed in vacuo. Purification of the residue by column chromatography (silica gel, isohexane/ethyl acetate, 20%–35%) provided the 1,1′-bicarbazole **2** (39.5 mg, 87.3 µmol, 70%) as light yellow solid. The atropisomers were separated by HPLC (70% eluent B, isocratic). M.p. 163–167 °C; UV (MeOH): λ = 242, 256 (sh), 295, 321 (sh), 334 nm; fluorescence (MeOH): λ_{ex} = 295 nm, λ_{em} = 355 nm; IR (ATR): ν = 3527, 3455, 3397, 2917, 2837, 1702, 1607, 1578, 1504, 1417, 1356, 1316, 1262, 1196, 1129, 1093, 1064, 1043, 1019, 971, 888, 782, 758, 728, 697, 653, 622 cm^{-1}; ^{1}H NMR (500 MHz, acetone-d_6): δ = 2.45 (s, 6 H), 4.10 (s, 6 H), 6.68 (d, *J* = 7.9 Hz, 2 H), 6.90 (d, *J* = 7.9 Hz, 2 H), 7.14 (t, *J* = 7.9 Hz, 2 H), 7.28 (s, 2 H), 8.03 (s, 2 H), 9.61 (br s, 2 H); ^{13}C NMR (125 MHz, acetone-d_6): δ = 17.39 (2 CH_3), 55.65 (2 CH_3), 100.42 (2 CH), 102.32 (2 C), 104.82 (2 CH), 113.63 (2 C), 116.43 (2 C), 117.91 (2 C), 125.08 (2 CH), 125.41 (2 CH), 139.27 (2 C), 142.31 (2 C), 152.38 (2 C), 156.23 (2 C); MS (ESI, +10 V): *m/z* = 453.2 $[M+H]^+$, 905.5 $[2\ M+H]^+$; MS (EI): *m/z* = 492 (100) $[M]^+$, 437 (5), 226 (26); HRMS (EI): *m/z* calcd for $C_{28}H_{24}N_2O_4$: 452.1736; found: 452.1739.

Triscarbazole 21: $(CuOH{\cdot}TMEDA)_2Cl_2$ (12.3 mg, 26.4 µmol) was added to a solution of 2-hydroxy-5-methoxy-3-methylcarbazole (carbalexin A) (**16**) (60 mg, 0.26 mmol) in dichloromethane (2.7 mL) and the solution was stirred at room temperature under air for 45 min. The mixture was diluted with dichloromethane and washed with water. The aqueous layer was extracted with dichloromethane. The combined organic layers were dried (magnesium sulfate) and the solvent was evaporated. Purification of the residue by column chromatography (silica gel; pentane/ethyl acetate, 6:1) provided the less polar 1,1′-bicarbazole **2** (31.4 mg, 69.4 µmol, 53%; spectroscopic data: see above) and the more polar compound **21** (17.1 mg, 25.3 µmol, 29%) as orange solid. M.p. >170 °C (dec.); UV (MeOH): λ = 237, 276, 339 nm; fluorescence (MeOH) λ_{ex} = 339 nm, λ_{em} = 361 nm; IR (ATR): ν = 3390, 2920, 2837, 1666, 1605, 1582, 1555, 1505, 1458, 1435, 1406, 1334, 1263, 1200, 1168, 1096, 1064, 998, 951, 910, 881, 765, 725 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.94 (s, 3 H), 2.04 (d, *J* = 1.3 Hz, 3 H), 2.32 (s, 3 H), 4.01 (s, 3 H), 4.12 (s, 3 H), 4.14 (s, 3 H), 6.59 (d, *J* = 7.8 Hz, 1 H), 6.72 (d, *J* = 8.0 Hz, 1 H), 6.75 (d, *J* = 8.0 Hz, 1 H), 6.79 (d, *J* = 8.2 Hz, 1 H), 6.95 (d, *J* = 8.0 Hz, 1 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 7.10 (t, *J* = 8.0 Hz, 1 H), 7.30 (t, *J* = 8.0 Hz, 1 H), 7.36 (t, *J* = 8.0 Hz, 1 H), 7.81 (s, 1 H), 7.94 (s, 1 H), 7.98 (d, *J* = 1.3 Hz, 1 H), 8.08 (s, 1 H), 8.22 (s, 1 H), 8.27 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.65 (CH_3), 16.11 (CH_3), 16.91 (CH_3), 55.23 (CH_3), 55.47 (CH_3), 55.52 (CH_3), 100.91 (2 CH), 101.31 (CH), 103.63 (C), 103.92 (CH), 104.06 (CH), 105.14 (CH), 110.02 (C), 110.26 (C), 112.28 (C), 112.67 (C), 112.99 (C), 113.92 (C), 121.00 (C), 121.25 (C), 123.90 (CH), 124.18 (C), 124.33 (C), 124.47 (CH), 124.52 (CH), 125.66 (C), 126.34 (CH), 127.01 (CH), 133.49 (C), 134.28 (C), 134.46 (C), 137.52 (C), 138.00 (CH), 141.40 (C), 141.50 (C), 145.29 (C), 146.69 (C), 154.93 (C), 156.00 (C), 156.04 (C), 191.34 (C); MS (ESI, +10 V): *m/z* = 676.4 $[M+H]^+$; MS (ESI, −50 V): *m/z* = 674.1 $[M-H]^-$; HRMS (EI): *m/z* calcd for $C_{42}H_{33}N_3O_6$: 675.2369; found: 675.2362.

Crystallographic data for compound **21**: $C_{42}H_{33}N_3O_6$, M = 675.71 g mol^{-1}, crystal size 0.43 × 0.23 × 0.11 mm^3, monoclinic, space group $C2/c$, a = 33.995(7), b = 11.140(2), c = 28.591(6) Å, β = 116.83(3) °, V = 9662(3) Å^3, Z = 8, ρ_{calcd} = 0.929 g cm^{-3}, μ = 0.063 mm^{-1}, λ = 0.71073 Å, T = 198(2) K, θ range = 3.08–25.40°, reflections collected 88289, independent reflections 8877 (R_{int} = 0.0507), 475 parameters. The structure was solved by direct methods and refined by full-matrix least-squares on F^2; final R indices [$I > 2\sigma(I)$] R^1 = 0.0621 and wR^2 = 0.1718; maximal residual electron density 0.477 e Å^{-3}. CCDC 1570474.

Biscarbalexine C (2,2′-dihydroxy-6,6′-dimethoxy-3,3′-dimethyl-1,1′-bicarbazole) (3): Dichloromethane (5 mL) was added to a mixture of hexadecafluorophthalocyanine–iron (6.39 mg, 7.46 µmol), methanesulfonic acid (2.44 mg, 25.3 µmol) and 2-hydroxy-6-methoxy-3-methylcarbazole (carbalexine C) (**17**) (56.8 mg, 250 µmol) and the suspension was stirred at room temperature for 80 min under air. The mixture was filtered through a short pad of silica gel with dichloromethane (40 mL). Removal of the solvent in vacuo provided the 1,1′-bicarbazole **3** (51.8 mg, 115 µmol, 92%) as light yellow solid. M.p >180 °C (dec.); UV (MeOH): λ = 229, 260, 312 nm; fluorescence (MeOH): λ_{ex} = 312 nm, λ_{em} = 383 nm; IR (ATR): v = 3517, 3494, 3402, 3312, 2965, 2937, 2909, 2830, 2050, 2030, 2007, 1970, 1632, 1483, 1461, 1433, 1329, 1293, 1205, 1177, 1113, 1053, 1023, 995, 954, 917, 873, 846, 792, 767, 730, 628 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.42 (s, 6 H), 3.82 (s, 6 H), 6.80 (dd, J = 8.7, 2.5 Hz, 2 H), 7.18 (d, J = 8.7 Hz, 2 H), 7.54 (d, J = 2.5 Hz, 2 H), 7.87 (s, 2 H), 7.91 (s, 2 H), 9.75 (s, 2 H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 17.59 (2 CH_3), 55.50 (2 CH_3), 101.99 (2 CH), 103.75 (2 C), 111.32 (2 CH), 111.91 (2 CH), 115.41 (2 C), 116.49 (2 C), 120.86 (2 CH), 123.63 (2 C), 134.70 (2 C), 139.81 (2 C), 152.15 (2 C), 152.69 (2 C); MS (ESI, +10 V): m/z = 453.2 [M+H]$^+$; MS (ESI, −10 V): m/z = 450.9 [M−H]$^-$; HRMS (ESI): m/z calcd for $C_{28}H_{24}N_2O_4$: 452.1736; found: 452.1733.

2,2′-Dihydroxy-7,7′-dimethoxy-3,3′-dimethyl-1,1′-bicarbazole (4): Hexadecafluorophthalocyanine–iron (3.21 mg, 3.75 µmol) was added to a solution of 2-hydroxy-7-methoxy-3-methylcarbazole (**19**) (28.4 mg, 125 µmol) in acetic acid (4 mL) and the solution was stirred at room temperature for 30 min under air. Subsequently, argon was bubbled through the reaction mixture and the solvent was removed in vacuo. Toluene (3 mL) was added to remove the residual acetic acid as an azeotrope in vacuo. The residue was dissolved in dichloromethane (1 mL), filtered through a short pad of activated carbon on silica gel with dichloromethane (20 mL) and the solvent was removed in vacuo. Purification of the residue by column chromatography (silica gel, isohexane/ethyl acetate, 30%–40%) provided the 1,1′-bicarbazole **4** (17.3 mg, 38.2 µmol, 61%) as colorless solid. M.p. 294.5–296 °C; UV (MeOH): λ = 216 (sh), 237, 266, 312, 322 nm; fluorescence (MeOH): λ_{ex} = 236 nm, λ_{em} = 365 nm; IR (ATR): v = 3414, 2922, 2853, 1610, 1501, 1472, 1446, 1403, 1376, 1321, 1252, 1193, 1156, 1127, 1031, 1018, 946, 883, 817, 740, 657, 631 cm^{-1}; ^{1}H NMR (500 MHz, acetone-d_6): δ = 2.43 (s, 6 H), 3.76 (s, 6 H), 6.75 (dd, J = 8.6, 2.3 Hz, 2 H), 6.85 (d, J = 2.2 Hz, 2 H), 7.26 (s, 2 H), 7.78 (s, 2 H), 7.86 (d, J = 8.5 Hz, 2 H), 9.47 (s, 2 H); ^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 17.38 (2 CH_3), 55.59 (2 CH_3), 95.75 (2 CH), 102.87 (2 C), 108.10 (2 CH), 117.21 (2 C), 118.01 (2 C), 118.58 (2 C), 120.21 (2 CH), 121.66 (2 CH), 140.01 (2 C), 142.25 (2 C), 152.30 (2 C), 158.79 (2 C); MS (ESI, +25 V): m/z = 453.2 [M+H]$^+$; HRMS (ESI): m/z calcd for $C_{28}H_{24}N_2O_4$: 452.1736; found: 452.1726.

2,2′,7,7′-Tetrahydroxy-3,3′-dimethyl-1,1′-bicarbazole (22): Boron tribromide (1 M in CH_2Cl_2, 104 µL, 104 µmol) was added at −78 °C to a solution of 1,1′-bicarbazole **4** (11.7 mg, 25.9 µmol) in dichloromethane (4 mL) and the solution was stirred at −78 °C for 2 h, at 0 °C for 4 h and at room temperature for 44 h. Methanol (2 mL) and water were added, the layers were separated and the aqueous layer was extracted four times with dichloromethane. The combined organic layers were washed with brine, dried ($MgSO_4$) and the solvent was removed. Purification of the residue by column chromatography (silica gel; pentane/ethyl acetate, gradient from 2:1 to 1:1) provided the tetrahydroxy-1,1′-bicarbazole **22** (4.4 mg, 10 µmol, 40%) as ochreous solid. M.p. 254.5–256 °C. UV (MeOH): λ = 219 (sh), 236, 267, 284 (sh), 313, 321 nm; fluorescence (MeOH): λ_{ex} = 313 nm, λ_{em} = 387 nm; IR (ATR): v = 3336, 2920, 2851, 2056, 1701, 1609, 1488, 1362, 1257, 1157, 1048, 1019, 955, 876, 803, 639 cm^{-1}; ^{1}H NMR (500 MHz, acetone-d_6): δ = 2.42 (s, 6 H), 6.68 (dd, J = 8.4, 2.2 Hz, 2 H), 6.76 (s, 2 H), 7.17 (s, 2 H), 7.74 (s, 2 H), 7.78 (d, J = 8.4 Hz, 2 H), 8.07 (s, 2 H), 9.94 (s, 2 H); ^{13}C NMR (125 MHz, acetone-d_6): δ = 17.35 (2 CH_3), 97.62 (2 CH), 102.74 (2 C), 108.61 (2 CH), 117.44 (2 C), 117.63 (2 C), 117.86 (2 C), 120.06 (2 CH), 121.42 (2 CH), 139.76 (2 C), 142.39 (2 C), 151.90 (2 C), 156.00 (2 C); MS (ESI, +25 V): m/z = 425.4 [M+H]$^+$.

Biscarbalexine B (2,2′-dihydroxy-8,8′-dimethoxy-3,3′-dimethyl-1,1′-bicarbazole) (5): Hexadecafluorophthalocyanine–iron (2.15 mg, 2.51 µmol) was added to a solution of 2-hydroxy-8-methoxy-3-methylcarbazole (carbalexin B) (**20**) (28.4 mg, 125 µmol) in acetic acid (5 mL) and the solution was stirred at room temperature for 30 min under air. Then, argon was bubbled through the reaction mixture and most of the acetic acid was removed in vacuo. Toluene (3 mL) was added to remove the residual acetic acid as an azeotrope in vacuo. The residue was dissolved in dichloromethane (10 mL), filtered through a short pad of silica gel with dichloromethane (50 mL) and the solvent was removed in vacuo. Purification of the residue by column chromatography (silica gel, isohexane/ethyl acetate, 20%–50%) provided the 1,1′-bicarbazole **5** (15.2 mg, 33.6 µmol, 54%) as light yellow solid. M.p. >260 °C; UV (MeOH): λ = 238 (sh), 254 (sh), 289 nm; fluorescence (MeOH): λ_{ex} = 289 nm, λ_{em} = 368 nm; IR (ATR): v = 3386, 3064, 2998, 2969, 2939, 2916, 2846, 1728, 1627, 1611, 1575, 1502, 1450, 1384, 1339, 1296, 1256, 1207, 1144, 1085, 997, 922, 869, 807, 781, 728, 695, 653, 618 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.43 (s, 6 H), 3.81 (s, 6 H), 6.82 (d, J = 7.8 Hz, 2 H), 7.03 (t, J = 7.8 Hz, 2 H), 7.60 (d, J = 7.8 Hz, 2 H), 7.86 (s, 2 H), 7.95 (s, 2 H), 9.31 (s, 2 H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 17.64 (2 CH_3), 55.07 (2 CH_3), 104.43 (2 C), 104.71 (2 CH), 111.62 (2 CH), 115.94 (2 C), 117.56 (2 C), 118.93 (2 CH), 120.82 (2 CH), 124.78 (2 C), 129.13 (2 C), 139.03 (2 C), 145.33 (2 C), 152.22 (2 C); MS (ESI, +10 V): m/z = 453.2 [M+H]$^+$; MS (ESI, −50 V): m/z = 450.9 [M−H]$^-$; HRMS (ESI): m/z calcd for $C_{28}H_{24}N_2O_4$: 452.1736; found: 452.1727.

Bisglybomine B (2,2′-dihydroxy-6,6′-dimethoxy-3,3′-dimethyl-5,5′-bis(3-methylbut-2-enyl)-1,1′-bicarbazole) (6): Hexadecafluorophthalocyanine–iron (2.11 mg, 2.46 µmol) was added to a solution of glybomine B (**18**) (36.9 mg, 125 µmol) in acetic acid (2.5 mL) and the solution was stirred at room temperature for 10 min under air. Subsequently, argon was bubbled through the reaction mixture and most of the acetic acid removed in vacuo. Toluene (3 mL) was added to remove the residual acetic acid as an azeotrope in vacuo. The residue was dissolved in dichloromethane (1 mL) and filtered through a short pad of silica gel with dichloromethane (25 mL). Removal of the solvent in vacuo provided the 1,1′-bicarbazole **6** (23.1 mg, 39.2 µmol, 63%) as colorless solid. M.p. >250 °C (dec.); UV (MeOH): λ = 218, 235, 261, 307, 340 nm; fluorescence: λ_{ex} = 307 nm, λ_{em} = 385 nm; IR (ATR): v = 3267, 2985, 2962, 2909, 2850, 2826, 1725, 1607, 1491, 1449, 1391, 1304, 1285, 1252, 1220, 1179, 1133, 1101, 1083, 1026, 1012, 938, 872, 844, 800, 784, 725, 641 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.76 (d, J = 0.7 Hz, 6 H), 1.99 (s, 6 H), 2.51 (s, 6 H), 3.88 (s, 6 H), 3.98 (d, J = 6.1 Hz, 4 H), 5.25 (s, 2 H), 5.35–5.40 (m, 2 H), 6.97 (d, J = 8.7 Hz, 2 H), 7.03 (d, J = 8.6 Hz, 2 H), 7.49 (br s, 2 H), 8.02 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.90 (2 CH_3), 18.30 (2 CH_3), 25.62 (2 CH_2), 25.83 (2 CH_3), 57.84 (2 CH_3), 98.59 (2 C), 108.12 (2 CH), 111.12 (2 CH), 117.21 (2 C), 117.28 (2 C), 122.34 (2 CH), 123.04 (2 C), 124.34 (2 C), 125.79 (2 CH), 132.54 (2

C), 134.82 (2 C), 138.90 (2 C), 150.89 (2 C), 151.15 (2 C); MS (ESI, +10 V): *m/z* = 589.6 $[M+H]^+$, 1177.0 $[2M+H]^+$; MS (ESI, −50 V): *m/z* = 587.4 $[M-H]^-$; HRMS (ESI): *m/z* calcd for $C_{38}H_{40}N_2O_4$: 588.299; found: 588.295.

Bispyrayafoline C (9,9'-Dihydroxy-3,3,3′,3′,8,8′-hexamethyl-3,3′,11,11′-tetrahydro-10,10′-bipyrano[3,2-*a*]carbazole) (7): Hexadecafluorophthalocyanine–iron (1.06 mg, 1.24 µmol) was added to a solution of pyrayafoline C (**23**) (34.9 mg, 125 µmol) in acetic acid (2.5 mL) and the solution was stirred at room temperature for 10 min under air. Then, argon was bubbled through the reaction mixture and most of the acetic acid was removed in vacuo. Toluene (3 mL) was added to remove the residual acetic acid as an azeotrope in vacuo. The residue was dissolved in dichloromethane (1 mL) and filtered through a short pad of activated carbon on silica gel with dichloromethane (50 mL). Removal of the solvent in vacuo provided the bipyrano[3,2-*a*]carbazole **7** (32.4 mg, 58.2 µmol, 93%) as colorless solid. M.p. >205 °C (dec.); UV (MeOH): λ = 221, 239, 283 (sh), 294, 333 nm; fluorescence (MeOH): λ_{ex} = 294 nm, λ_{em} = 368 nm; IR (ATR): ν = 3426, 2973, 2920, 2853, 1723, 1699, 1622, 1587, 1446, 1419, 1372, 1321, 1257, 1188, 1168, 1153, 1131, 1116, 1039, 1000, 944, 897, 849, 804, 778, 719, 693, 633 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 1.35 (s, 12 H), 2.39 (s, 6 H), 5.58 (d, *J* = 9.9 Hz, 2 H), 6.54 (d, *J* = 8.3 Hz, 2 H), 7.07 (d, *J* = 9.9 Hz, 2 H), 7.62 (s, 2 H), 7.69 (d, *J* = 8.3 Hz, 2 H), 7.74 (s, 2 H), 9.97 (s, 2 H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 17.62 (2 CH_3), 27.10 (2 CH_3), 27.30 (2 CH_3), 75.01 (2 C), 104.28 (2 C), 104.72 (2 C), 107.78 (2 CH), 115.80 (2 C), 116.77 (2 C), 118.15 (2 C), 118.60 (2 CH), 118.94 (2 CH), 119.85 (2 CH), 128.04 (2 CH), 136.29 (2 C), 139.66 (2 C), 149.31 (2 C), 151.48 (2 C); MS (ESI, +10 V): *m/z* = 557.4 $[M+H]^+$; MS (ESI, −10 V): 555.1 $[M-H]^-$; elemental analysis (%) calcd for $C_{36}H_{32}N_2O_4$: C 77.68, H 5.79, N 5.03; found: C 77.48, H 5.63, N 5.02.

Bisisomahanine (8): Hexadecafluorophthalocyanine–iron (1.08 mg, 1.26 µmol) was added to a solution of pyrayafoline D (**24**) (43.4 mg, 125 µmol) in acetic acid (4 mL) and the solution was stirred at room temperature for 20 min under air. Then, argon was bubbled through the reaction mixture and most of the acetic acid was removed in vacuo. Toluene (3 mL) was added to remove the residual acetic acid as an azeotrope in vacuo. The residue was dissolved in dichloromethane (1 mL) and filtered through a short pad of activated carbon on silica gel with dichloromethane (40 mL). Removal of the solvent in vacuo provided bisisomahanine (**8**) (40.4 mg, 58.3 µmol, 93%) as yellow solid. M.p. 130–140 °C. UV (MeOH): λ = 224, 239, 287 (sh), 296, 332, 354 (sh) nm; fluorescence (MeOH): λ_{ex} = 296 nm, λ_{em} = 421 nm; UV ($CHCl_3$): λ = 239, 288 (sh), 298, 332 nm; fluorescence ($CHCl_3$): λ_{ex} = 298 nm, λ_{em} = 427 nm; IR (ATR): ν = 3532, 3465, 3339, 3031, 2967, 2917, 2850, 1741, 1636, 1612, 1588, 1473, 1446, 1417, 1374, 1319, 1298, 1257, 1179, 1131, 1083, 1041, 907, 875, 846, 804, 780, 724, 636 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 1.39 (s, 6 H), 1.54 (s, 3 H), 1.55 (s, 3 H), 1.63 (s, 3 H), 1.64 (s, 3 H), 1.65–1.77 (m, 4 H), 2.06–2.15 (m, 4 H), 2.49 (s, 6 H), 5.03–5.09 (m, 2 H), 5.10 (s, 2 H), 5.55 (d, *J* = 9.9 Hz, 2 H), 6.44 (d, *J* = 9.8 Hz, 2 H), 6.74 (d, *J* = 8.4 Hz, 2 H), 7.46 (s, 2 H), 7.72 (d, *J* = 8.4 Hz, 2 H), 7.85 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.69 (2 CH_3), 17.61 (2 CH_3), 22.69 (2 CH_2), 25.64 (2 CH_3), 25.87 (2 CH_3), 40.74 (2 CH_2), 78.24 (2 C), 98.94 (2 C), 104.94 (2 C), 109.91 (2 CH), 117.36 (2 CH), 117.74 (4 C), 117.91 (2 C), 119.45 (2 CH), 122.32 (2 CH), 124.07 (2 CH), 128.81 (2 CH), 131.70 (2 C), 135.97 (2 C), 137.74 (2 C), 150.27 (2 C), 151.09 (2 C); MS (ESI, +25 V): *m/z* = 693.7 $[M+H]^+$; MS (ESI, −75 V): *m/z* = 691.6 $[M-H]^-$; elemental analysis (%) calcd for $C_{46}H_{48}N_2O_4$: C 79.74, H 6.98, N: 4.04; found: C 79.46, H: 7.29, N: 3.69.

8,8″-Biskoenigine (9): Hexadecafluorophthalocyanine–iron (1.07 mg, 1.25 µmol) was added to a solution of koenigine (**25**) (38.7 mg, 125 µmol) in dichloromethane (1 mL) and the solution was stirred at room temperature for 20 min under air. The mixture was filtered through a short pad of activated carbon on silica gel with isohexane/ethyl acetate (2:1, 15 mL). Removal of the solvent in vacuo provided 8,8″-biskoenigine (**9**) (34.8 mg, 56.4 µmol, 90%) as brown solid. M.p. 240–242 °C; UV (MeOH): λ = 225, 301, 344 nm; fluorescence (MeOH): λ_{ex} = 301 nm, λ_{em} = 382 nm; IR (ATR): ν = 3357, 2971, 2931, 1723, 1641, 1610, 1492, 1455, 1419, 1373, 1358, 1282, 1251, 1199, 1126, 1053, 1023, 979, 943, 888, 835, 774, 728, 663, 623 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6): δ = 1.390 (s, 6 H), 1.393 (s, 6 H), 2.29 (s, 6 H), 4.01 (s, 6 H), 5.54 (d, *J* = 9.9 Hz, 2 H), 6.72 (d, *J* = 9.8 Hz, 2 H), 7.23 (s, 2 H), 7.60 (s, 2 H), 7.64 (s, 2 H), 9.55 (br s, 2 H); ^{13}C NMR (125 MHz, acetone-d_6): δ = 16.29 (2 CH_3), 27.59 (2 CH_3), 27.87 (2 CH_3), 57.06 (2 CH_3), 75.97 (2 C), 102.28 (2 CH), 104.92 (2 C), 105.66 (2 C), 115.38 (2 C), 117.45 (2 C), 118.79 (2 C), 119.21 (2 CH), 120.46 (2 CH), 129.18 (2 CH), 135.89 (2 C), 136.06 (2 C), 143.56 (2 C), 144.44 (2 C), 148.97 (2 C); MS (ESI, +25 V): *m/z* = 617.4 $[M+H]^+$; MS (ESI, −50 V): *m/z* = 615.2 $[M-H]^-$; MS (EI): *m/z* = 616 (100) $[M]^+$, 601 (66), 293 (18); HRMS (EI): *m/z* calcd for $C_{38}H_{36}N_2O_6$: 616.2573; found: 616.2563.

Decacyclic coupling product (26): Hexadecafluorophthalocyanine–iron (1.09 mg, 1.25 µmol) was added to a solution of koenigine (**25**) (38.7 mg, 125 µmol) in acetic acid (5 mL) and the solution was stirred at room temperature for 3 h under air. Subsequently, argon was bubbled through the reaction mixture and most of the acetic acid was removed in vacuo. Toluene (3 mL) was added to remove the residual acetic acid as an azeotrope in vacuo. The residue was dissolved in ethyl acetate (1 mL), filtered through a short pad of activated carbon on silica gel with ethyl acetate (10 mL) and the solvent was removed in vacuo. Purification of the residue by column chromatography (silica gel, isohexane/ethyl acetate, 20–45%) provided the decacyclic coupling product **26** (19.6 mg, 31.8 µmol, 51%) as light brown solid. M.p. 154 °C; UV (MeOH): λ = 237, 313 nm; fluorescence (MeOH): λ_{ex} = 237 nm, λ_{em} = 363 nm; IR (ATR): ν = 3349, 2965, 2924, 2850, 2056, 1757, 1691, 1640, 1451, 1433, 1322, 1276, 1202, 1178, 1129, 1084, 1033, 868, 845, 777, 725 cm^{-1}; ^1H NMR (600 MHz, acetone-d_6): 0.86 (s, 3 H), 1.25 (s, 3 H), 1.33 (s, 3 H), 1.72 (s, 3 H), 1.86 (d, *J* = 0.6 Hz, 3 H), 2.19 (s, 3 H), 3.38 (dd, *J* = 11.0, 5.0 Hz, 1 H), 3.62 (d, *J* = 11.0 Hz, 1 H), 3.69 (dd, *J* = 4.9, 1.3 Hz, 1 H), 3.79 (s, 3 H), 3.97 (s, 3 H), 5.57 (d, *J* = 9.8 Hz, 1 H), 6.17 (s, 1 H), 6.49 (s, 1 H), 6.53 (d, *J* = 9.8 Hz, 1 H), 7.31 (s, 1 H), 7.50 (s, 1 H), 7.67 (s, 1 H), 7.83 (s, 1 H), 10.04 (br s, 1 H); ^{13}C NMR (150 MHz, acetone-d_6): 15.40 (CH_3), 16.22 (CH_3), 26.60 (CH_3), 27.67 (CH_3), 27.81 (CH_3), 32.75 (CH_3), 32.82 (CH), 50.08 (CH), 50.12 (CH), 53.48 (CH_3), 57.25 (CH_3), 59.47 (CH), 76.05 (C), 82.79 (C), 88.05 (C), 101.12 (CH), 104.78 (C), 105.14 (CH), 109.58 (C), 110.78 (C), 117.92 (CH), 118.71 (C), 119.08 (CH), 119.85 (C), 120.33 (C), 120.39 (C), 120.80 (C), 122.93 (CH), 129.59 (CH), 132.43 (C), 133.01 (C), 139.90 (C), 141.51 (C), 144.30 (C), 146.71 (C), 147.50 (C), 151.37 (C), 200.90 (C=O); MS (ESI, −10 V): *m/z* = 614.9 $[M-H]^-$; HRMS (ESI): *m/z* calcd for $C_{38}H_{36}N_2O_6$: 616.2573; found: 616.2558.

Crystallographic data for compound **26**: The crystals were obtained from acetone-d_6 as thin weakly diffracting needles. $C_{38}H_{36}N_2O_6$, *M* = 616.69 g mol^{-1}, crystal size 0.68 × 0.06 × 0.04 mm^3, triclinic, space group *P*-1, *a* = 11.052(4), *b* = 26.160(10), *c* = 29.125(12) Å, α = 101.418(12)°, β = 98.247(6)°, γ = 94.891(7)°, *V* = 8113(5) $Å^3$, *Z* = 8, ρ_{calcd} = 1.010 g cm^{-3} (solvent molecules not taken into account) μ = 0.068 mm^{-1}, λ = 0.71073 Å, *T* = 120(2) K, θ range = 1.60–23.53°, reflections collected 59288, independent reflections 23818 (R_{int} = 0.1971), 774 parameters. The structure was solved by direct methods and refined by full-matrix least-squares on F^2; final *R* indices [$I > 2\sigma(I)$] R^1 = 0.1123 and wR^2 = 0.2475. CCDC 1570475.

***O*,*O*′-Diacetyl-8,8″-biskoenigine (9,9′-diacetoxy-8,8′-dimethoxy-3,3,3′,3′,5,5′-hexamethyl-3,3′,11,11′-tetrahydro-10,10′-bipyrano[3,2-*a*]carbazole) (27):** Triethylamine (0.31 mL, 2.2 mmol), acetic anhydride

(0.16 mL, 1.7 mmol) and catalytic amounts of DMAP were added sequentially to a solution of 8,8″-biskoenigine (**9**) (343 mg, 0.556 mmol) in THF (38 mL) and the mixture was stirred at room temperature for 2 h. The mixture was diluted with diethyl ether and extracted with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted with diethyl ether, the combined organic layers were dried (magnesium sulfate) and the solvent was evaporated. Purification of the residue by column chromatography (silica gel; isohexane/ethyl acetate, 3:1) provided the diacetate **27** (363 mg, 0.518 mmol, 93%) as light brown solid. M.p. 173–174 °C; UV (MeOH): λ = 234, 287 (sh), 298, 338, 355 (sh) nm; fluorescence (MeOH): λ_{ex} = 298 nm, λ_{em} = 392 nm; IR (ATR): v = 3409, 2971, 1754, 1642, 1475, 1418, 1366, 1289, 1216, 1165, 1129, 1028, 981, 894, 776, 728 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (s, 6 H), 1.47 (s, 6 H), 1.97 (s, 6 H), 2.33 (s, 6 H), 4.01 (s, 6 H), 5.57 (d, *J* = 9.8 Hz, 2 H), 6.51 (d, *J* = 9.8 Hz, 2 H), 7.60 (s, 2 H), 7.64 (s, 2 H), 7.99 (br s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.12 (2 CH_3), 20.55 (2 CH_3), 27.25 (2 CH_3), 27.90 (2 CH_3), 56.73 (2 CH_3), 75.93 (2 C), 102.80 (2 CH), 104.89 (2 C), 109.93 (2 C), 116.42 (2 C), 117.37 (2 CH), 118.66 (2 C), 120.54 (2 CH), 121.02 (2 C), 129.09 (2 CH), 132.96 (2 C), 135.42 (2 C), 136.33 (2 C), 145.77 (2 C), 149.77 (2 C) 171.16 (2 C=O); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.36 (s, 6 H), 1.37 (s, 6 H), 1.85 (s, 6 H), 2.26 (s, 6 H), 3.89 (s, 6 H), 5.58 (d, *J* = 9.9 Hz, 2 H), 6.95 (d, *J* = 10.0 Hz, 2 H), 7.78 (s, 2 H), 7.80 (s, 2 H), 10.10 (s, 2 H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 16.00 (2 CH_3), 20.22 (2 CH_3), 27.34 (4 CH_3), 56.25 (2 CH_3), 75.30 (2 C), 102.61 (2 CH), 104.63 (2 C), 110.25 (2 C), 116.56 (2 C), 116.63 (2 C), 118.78 (2 CH), 119.99 (2 C), 120.56 (2 CH), 127.95 (2 CH), 133.54 (2 C), 135.70 (2 C), 136.29 (2 C), 145.24 (2 C), 148.62 (2 C), 167.97 (2 C=O); MS (ESI, +25 V): *m/z* = 701.6 $[M+H]^+$; MS (ESI, −25 V): *m/z* = 699.3 $[M-H]^-$; MS (EI): *m/z* = 700 (77) $[M]^+$, 658 (100), 643 (24), 616 (62), 601 (55), 293 (40); HRMS (EI): *m/z* calcd for $C_{42}H_{40}N_2O_8$: 700.2785; found: 700.2771.

The atropisomers of compound **27** were separated by chiral HPLC (72% eluent B, isocratic). Isomer 1: $[\alpha]_D^{20}$ −301 (*c* = 0.073, $CHCl_3$); m.p. 170–171 °C. Isomer 2: $[\alpha]_D^{20}$ +304 (*c* = 0.070, $CHCl_3$); m.p. 174–175 °C.

1,1′-Dihydroxy-6,6′-dimethoxy-3,3′-dimethyl-2,2′-bicarbazole (bisclausenol) (10): Di-*tert*-butyl peroxide (0.06 mL, 0.05 g, 0.3 mmol) was added to a solution of clausenol (1-hydroxy-6-methoxy-3-methylcarbazole) (**28**) (51.6 mg, 0.227 mmol) in chlorobenzene (5 mL) and the mixture was heated at reflux for 2 h. After cooling to room temperature, the solvent was evaporated and the residue was purified by column chromatography (silica gel; hexane/ethyl acetate, 2:1) to provide bisclausenol (**10**) (47.9 mg, 0.106 mmol, 93%) as light yellow crystals. M.p. >250 °C (dec.); UV (EtOH): λ = 228, 254, 293 (sh), 303, 342, 357 nm; fluorescence (EtOH): λ_{ex} = 303 nm; λ_{em} = 388 nm; IR (ATR): v = 3403, 3349, 2920, 2830, 2508, 1686, 1621, 1562, 1542, 1522, 1492, 1474, 1459, 1436, 1384, 1338, 1297, 1260, 1206, 1150, 1089, 1057, 1014, 987, 953, 866, 835, 806, 778, 765 cm^{-1}; ^{1}H NMR (500 MHz, acetone-d_6): δ = 2.09 (s, 6 H), 3.91 (s, 6 H), 7.04 (dd, *J* = 8.7, 2.5 Hz, 2 H), 7.45 (s, 2 H), 7.48 (d, *J* = 8.7 Hz, 2 H), 7.56 (s, 2 H), 7.63 (d, *J* = 2.4 Hz, 2 H), 9.94 (s, 2 H); ^{13}C NMR and DEPT (125 MHz, acetone-d_6): δ = 20.56 (2 CH_3), 56.05 (2 CH_3), 103.34 (2 CH), 112.72 (2 CH), 113.33 (2 CH), 115.50 (2 CH), 118.69 (2 C), 124.69 (2 C), 125.03 (2 C), 129.16 (2 C), 130.20 (2 C), 135.96 (2 C), 141.92 (2 C), 154.57 (2 C); MS (ESI, +25 V): *m/z* = 453.2 $[M+H]^+$; 927.4 $[2M+Na]^+$; MS (ESI, −50 V): *m/z* = 451.0 $[M-H]^-$; 903.1 $[2M-H]^-$; HRMS (ESI): *m/z* calcd for $C_{28}H_{24}N_2O_4$: 452.1736; found: 452.1732.

Bismurrayafoline B (1,1′-dihydroxy-7,7′-dimethoxy-3,3′-dimethyl-8,8′-bis(3-methylbut-2-en-1-yl)-2,2′-bicarbazole) (11): A mixture of murrayafoline-B (**29**) (50.0 mg, 0.170 mmol), di-*tert*-butyl peroxide (37.0 mg, 0.253 mmol) and chlorobenzene (15 mL) was heated at reflux for 2 h. After cooling to room temperature, a saturated aqueous solution of sodium thiosulfate was added and the mixture was extracted twice with ethyl acetate. The combined organic layers were dried (magnesium sulfate) and the solvent was evaporated. Purification of the residue by column chromatography (silica gel; isohexane/ethyl acetate, gradient 15:1 to 10:1) provided bismurrayafoline B (**11**) (37.6 mg, 63.9 µmol, 76%) as as brown solid. M.p. 123 °C; UV (MeOH): λ = 233, 251 (sh), 259, 303, 322 (sh), 335 (sh) nm; fluorescence (MeOH): λ_{ex} = 303 nm, λ_{em} = 369 nm; IR (ATR): v = 3511, 3448, 3408, 2952, 2914, 2853, 2826, 1725, 1696, 1619, 1565, 1474, 1444, 1372, 1326, 1219, 1171, 1081, 1041, 968, 847, 792 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.74 (s, 6 H), 1.90 (s, 6 H), 2.16 (s, 6 H), 3.66 (d, *J* = 6.7 Hz, 4 H), 3.95 (s, 6 H), 4.97 (br s, 2 H), 5.34 (m, 2 H), 6.91 (d, *J* = 8.6 Hz, 2 H), 7.59 (s, 2 H), 7.85 (d, *J* = 8.5 Hz, 2 H), 8.06 (br s, 2 H); ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 18.14 (2 CH_3), 20.12 (2 CH_3), 24.09 (2 CH_2), 25.87 (2 CH_3), 56.79 (2 CH_3), 105.12 (2 CH), 111.64 (2 C), 113.33 (2 CH), 114.74 (2 C), 117.92 (2 C), 118.55 (2 CH), 122.39 (2 CH), 126.00 (2 C), 127.14 (2 C), 129.34 (2 C), 133.12 (2 C), 139.52 (2 C), 140.75 (2 C), 155.94 (2 C); MS (ESI, +25 V): *m/z* = 589.9 $[M+H]^+$; MS (ESI, −75 V): 587.5 $[M-H]^-$; HRMS (ESI): *m/z* calcd for $C_{38}H_{40}N_2O_4$: 588.2988; found: 588.2977.

1-Hydroxy-7-methoxy-3-methyl-8-(3,7-dimethylocta-2,6-dien-1-yl)-carbazole (murrayafoline D) (31): Lithium aluminum hydride (138.2 mg, 3.64 mmol) was added at room temperature to a solution of carbazolyl tosylate **30** (ratio of *E*/*Z* = 1.4:1; 268.8 mg, 519 µmol)[85] in THF (30 mL) and the mixture was heated at reflux for 23 h. After cooling to 0 °C, a saturated aqueous solution of potassium sodium tartrate was added and the mixture was extracted twice with ethyl acetate. The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated. Purification of the residue by column chromatography (silica gel, isohexane/ethyl acetate, 10:1) provided the 1-hydroxycarbazole **31** (84.4 mg, 232 µmol, 45%; light brown, highly viscous oil) as a mixture of diastereoisomers (ratio of *E*/*Z* = 1.4:1). UV (MeOH): λ = 231, 246, 256, 301 nm; fluorescence (MeOH): λ_{ex} = 231 nm, λ_{em} = 368 nm; IR (ATR): v = 3366, 2959, 2915, 2853, 1620, 1590, 1512, 1491, 1448, 1417, 1374, 1350, 1325, 1253, 1220, 1173, 1083, 975, 874, 830, 791 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): 1.55 (*E*, s) and 1.65 (*Z*, s, 3 H), 1.60 (*E*, d, *J* = 0.9 Hz) and 1.70 (*Z*, d, *J* = 0.8 Hz, 3 H), 1.74 (*Z*, d, *J* = 1.2 Hz) and 1.89 (*E*, d, *J* = 0.5 Hz, 3 H), 2.01–2.07 (*E*, m) and 2.31–2.36 (*Z*, m, 2 H), 2.07–2.13 (*E*, m) and 2.17–2.24 (*Z*, m, 2 H), 2.44 (s, 3 H), 3.64 (d, *J* = 6.8 Hz, 2 H), 3.906 (*Z*, s) and 3.912 (*E*, s, 3 H), 4.86 (br. s, 1 H), 5.04–5.09 (*E*, m) and 5.21–5.25 (*Z*, m, 1 H), 5.30–5.36 (m, 1 H), 6.57 (s, 1 H), 6.84 (*Z*, d, *J* = 8.5 Hz) and 6.85 (*E*, d, *J* = 8.5 Hz, 1 H), 7.36 (s, 1 H), 7.768 (*Z*, d, *J* = 8.5 Hz) and 7.771 (*E*, d, *J* = 8.5 Hz, 1 H), 7.96 (*Z*, s) and 7.97 (*E*, s, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): 16.34 (*E*) and 23.34 (*Z*, CH_3), 17.65 (*E*) and 17.71 (*Z*, CH_3), 21.45 (CH_3), 23.62 and 23.86 (CH_2), 25.60 (*E*) and 25.72 (*Z*, CH_3), 26.49 (*E*) and 26.68 (*Z*, CH_2), 32.18 (*Z*) and 39.71 (*E*, CH_2), 56.61 (*Z*) and 56.70 (*E*, CH_3), 104.69 (*Z*) and 104.78 (*E*, CH), 111.32 and 111.35 (CH), 111.40 and 111.43 (C), 112.49 (CH), 118.03 (C), 118.33 (*E*) and 118.35 (*Z*, CH), 122.22 (*E*) and 122.91 (*Z*, CH), 124.12 (*E*) and 124.17 (*Z*, CH), 125.87 and 125.90 (C), 127.25 (C), 129.42 and 129.43 (C), 131.58 and 132.0 (C), 136.56 and 136.77 (C), 140.40 and 140.41 (C), 140.52 and 140.60 (C), 155.51 and 155.56 (C); MS (ESI, +10 V): *m/z* = 364.2 $[M+H]^+$, 727.5 $[2M+H]^+$; MS (ESI, −50 V): *m/z* = 361.9 $[M-H]^-$, 725.1 $[2M-H]^-$; HRMS (ESI): *m/z* calcd for $C_{24}H_{29}NO_2$: 363.2198; found: 363.2192.

1,1′-Dihydroxy-7,7′-dimethoxy-3,3′-dimethyl-8,8′-bis(3,7-dimethylocta-2,6-dien-1-yl)-2,2′-bicarbazole (bismurrayafoline D) (12): Lithium aluminum hydride (2.4 M in THF, 0.6 mL, 1.4 mmol) was added at room temperature to a solution of carbazolyl tosylate **30** (ratio of *E*/*Z* = 1.3:1; 83.9 mg, 0.162 mmol)[85] in THF (10 mL) and the mixture was heated at reflux for 16 h. After cooling to 0 °C, a saturated aqueous solution of potassium sodium tartrate was added and the mixture was extracted with twice ethyl acetate. The combined organic layers were

dried ($MgSO_4$) and the solvent was evaporated. Highly polar compounds were removed by filtration through a short plug of silica gel (isohexane/ethyl acetate, 15:1) to provide the 1-hydroxycarbazole **31** (58.8 mg, 0.162 mmol). A mixture of the 1-hydroxycarbazole **31** (36.0 mg, 99.2 µmol), di-*tert*-butyl peroxide (22.0 mg, 0.151 mmol) and chlorobenzene (7 mL) was heated at reflux for 90 min. A further portion of di-*tert*-butyl peroxide (20.0 mg, 0.137 mmol) was added and the mixture was heated at reflux for further 105 min. After cooling to room temperature, a saturated aqueous solution of sodium thiosulfate was added and the mixture was extracted with twice ethyl acetate. The combined organic layers were dried (magnesium sulfate) and the solvent was evaporated. Purification of the residue by column chromatography (silica gel, isohexane/ethyl acetate, gradient 15:1 to 10:1) provided the 2,2′-bicarbazole **12** (35.8 mg, 49.4 µmol, 99%; light yellow, highly viscous oil) as a mixture of diastereoisomers. UV (MeOH): λ = 232, 251 (sh), 259, 305, 321 (sh), 335 (sh) nm; fluorescence (MeOH): λ_{ex} = 305 nm, λ_{em} = 369 nm; IR (ATR): v = 3511, 3435, 3411, 2959, 2916, 2846, 1726, 1641, 1620, 1566, 1484, 1473, 1444, 1373, 1328, 1236, 1175, 1084, 968, 848, 793 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): 1.54 (*E*, s) and 1.64 (*Z*, s, 6 H), 1.59 (*E*, *s*) and 1.68 (*Z*, s, 6 H), 1.74 (*Z*, d, *J* = 1.1 Hz) and 1.89 (*E*, s, 6 H), 2.01–2.12 (*E*, m, 8 H) and 2.17–2.24 (*Z*, m, 4 H) and 2.31–2.36 (*Z*, m, 4 H), 2.14 (*E*, s) and 2.15 (*Z*, s, 6 H), 3.67 (d, *J* = 6.8 Hz, 4 H), 3.938 (*Z*, s) and 3.942 (*E*, s, 6 H), 5.06 (*E*, m) and 5.22 (*Z*, m, 2 H), 5.36 (t, *J* = 6.8 Hz, 2 H), 6.89 (*Z*, d, *J* = 8.6 Hz) and 6.90 (*E*, d, *J* = 8.5 Hz, 2 H), 7.58 (s, 2 H), 7.842 (*Z*, d, *J* = 8.4 Hz) and 7.844 (*E*, d, *J* = 8.5 Hz, 2 H) 8.08 (br s, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$): 16.32 (*E*) and 23.35 (*Z*, 2 CH_3), 17.63 and 17.69 (2 CH_3), 19.92 and 19.94 (2 CH_3), 23.64 and 23.88 (2 CH_2), 25.58 and 25.70 (2 CH_3), 26.47 and 26.64 (2 CH_2), 32.18 (*Z*) and 39.72 (*E*, 2 CH_2), 56.58 and 56.66 (2 CH_3), 104.91 and 105.00 (2 CH), 111.48 and 111.52 (2 C), 113.13 (2 CH), 114.59 (2 C), 117.79 (2 C), 118.38 (2 CH), 122.15 and 122.85 (2 CH), 124.08 and 124.11 (2 CH), 125.79 and 125.81 (2 C), 127.01 (2 C), 129.17 (2 C), 131.52 and 132.00 (2 C), 136.69 and 136.91 (2 C), 139.40 (2 C), 140.61 and 140.69 (2 C), 155.76 and 155.81 (2 C); MS (ESI, +25 V): 725.7 $[M+H]^+$; MS (ESI, −10 V): 723.3 $[M-H]^-$, 1447.3 $[2M-H]^-$; HRMS (ESI): *m/z* calcd for $C_{48}H_{56}N_2O_4$: 724.4240; found: 724.4228.

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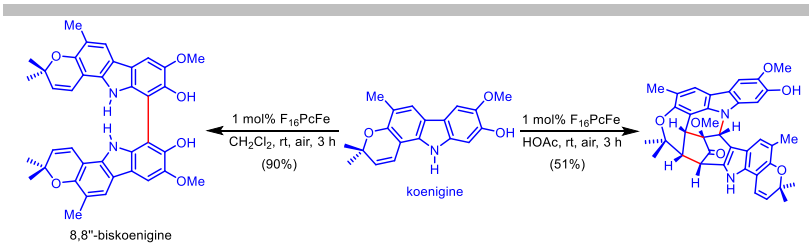

The iron-catalysed oxidative homo-coupling of hydroxycarbazoles to bicarbazoles using hexadecafluorophthalocyanine–iron in the presence of air has been investigated and compared to other methods for biaryl coupling.

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Synthesis of 1,1′- and 2,2′-Bicarbazole Alkaloids by Iron(III)-Catalyzed Oxidative Coupling of 2- and 1-Hydroxycarbazoles