Synthetic Approach for Constructing the 1-Oxygenated Carbazole Core and Its Application to the Preparation of Natural Alkaloids

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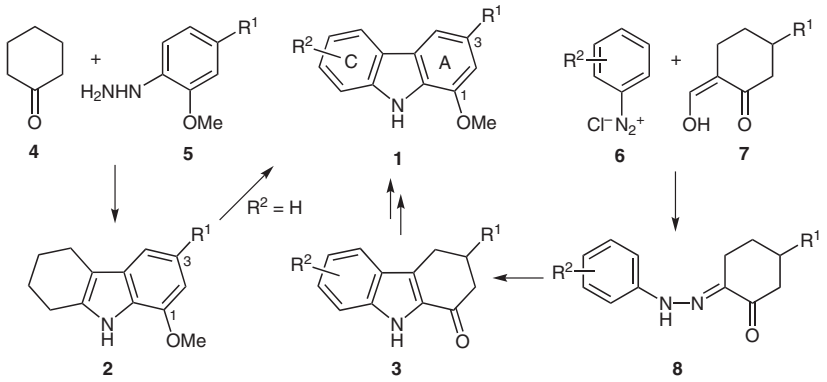
Abstract: An efficient synthetic approach for the construction of the 1-oxygenated carbazole core is described. The condensation of cyclohexane-1,2-diones with a series of anilines yielded the corresponding 2-anilinocyclohex-2-en-1-ones, followed by the one-pot aromatization/methylation process of the latter to provide *N*-aryl-2-methoxyanilines. A palladium(II)-catalyzed cyclization of these *N*-aryl-2-methoxyanilines afforded the desired 1-methoxycarbazole frame in high overall yields. This protocol was implemented for the total synthesis of the naturally occurring glycozolicine and 6-methoxymurrayanine.

Key words: 1-methoxycarbazoles, α-ketoenamines, palladium(II), cyclization, glycozolicine

Intense efforts have been focused on the development of new and efficient synthetic routes for building the carbazole framework.[1] The great interest in this framework is due to the wide structural variety of these naturally occurring alkaloids, and to their broad range of potent pharmacological activities, such as antimicrobial, anticancer, antioxidant, antihypertensive, inhibitory platelet aggregation, cardiotonic, immunosuppressive, and antimicotic.[1] In particular, diverse biological activity is exhibited by 1-oxygenated carbazole alkaloids **1**, extracted from leaves, stem bark, and root of higher plant species of the genera *Clausena*, *Glycosmis* and *Murraya*.[2]

Among the numerous protocols reported[3] for the preparation of such compounds,[1,4] the Fischer indolization strategy has been useful for the construction of the tricyclic scaffold **2** or **3**, which by subsequent dehydrogenation (and methylation) leads to the corresponding carbazoles **1** (Scheme 1).[5] The preparation of the hydrazone precursors follows two methods: (1) the traditional acid-catalyzed condensation between cyclohexanone (**4**) and an arylhydrazine **5**;[6] or (2) the Japp–Klingemann reaction between diazonium salt **6** and 2-formylcyclohexanone **7** leading to hydrazone **8**.[6a,7]

We previously described a general synthetic approach for the preparation of the carbazole scaffold,[8] on the basis of a regioselective Diels–Alder reaction of *exo*-oxazolidin-2-one dienes as the key step.[9] This approach was recently applied to the total synthesis of naturally occurring 1-methoxycarbazoles, such as glycozolicine (**1a**), mukolidine (**1b**), and mukoline (**1c**) (Figure 1).[10] Since the success of this strategy was due in part to the efficient palladium-catalyzed cyclization reaction of a correctly functionalized diarylamine,[11] we herein attempted a new route for the preparation of the 1-methoxycarbazole scaffold through two alternative protocols (Scheme 2): (1) based on the dehydrogenation of intermediates **2** or **3** to afford **1** (Scheme 1),[12] compounds **9** may be available precursors of **1** by a palladium(II)-catalyzed cyclization of α-ketoenamines **11**, as was carried out in a similar way with 2-(arylamino)-1,4-benzoquinones[13] or *N*-arylenaminones;[1b] and (2) direct aromatization of intermediates **11** to furnish diarylamines **10**, followed by palladium(II)-catalyzed cyclization to yield the desired carbazoles **1**.



Scheme 1 Fischer indolization approaches for the synthesis of carbazoles

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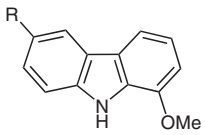


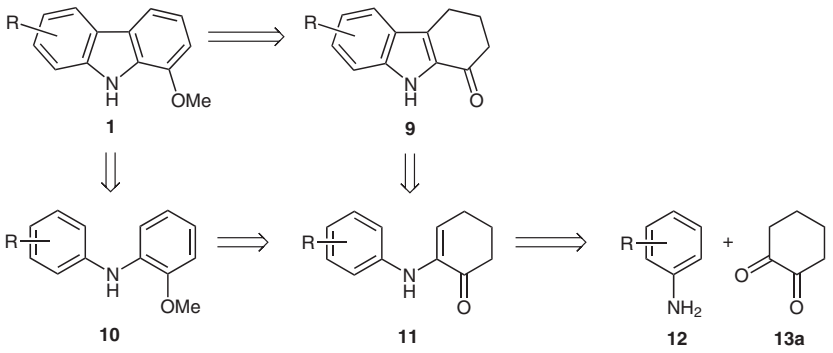
1a, R = Me
1b, R = CHO
1c, R = CH_2OH

Figure 1 Glycozolicine (**1a**), mukolidine (**1b**), and mukoline (**1c**)

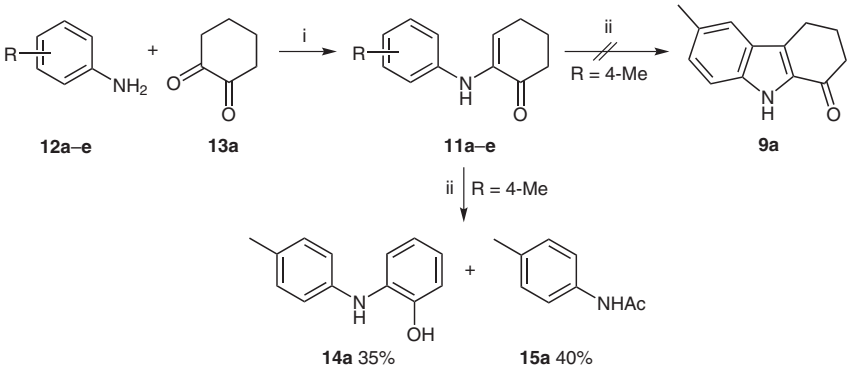
The preparation of 2-anilinocyclohex-2-en-1-ones **11a–e** was easily accomplished in high yields (82–95%) (Table 1) by the catalysis-free condensation of cyclohexane-1,2-dione (**13a**) with a series of anilines **12a–e** (Scheme 3). Since the direct cyclization of substrates analogous to compounds **11** has been reported by palladium(II)-catalyzed insertion,[1b,13] we investigated the catalysis by palladium(II) acetate in acetic acid under thermal conditions (140 °C). Although the desired carbazole frame **9a** was not furnished when the reaction was carried out under these conditions with **11a**, a ca. 1:1 ratio of a mixture of **14a**/**15a** was isolated (Scheme 3). Presumably, the catalyst promoted the aromatization of the cyclohexenone moiety of **11a** to give **14a**, while **15a** was generated by decomposition of **11a** to aniline **12a**, followed by acetylation due to the presence of acetic acid. The known procedures were modified by using a stoichiometric amount of palladium(II) acetate in acetonitrile or in copper(II) acetate, but the expected ring closure, from **11a** to **9a**, did not take place.

Considering that these conditions mainly led to the formation of diarylamine **14a**, we selected protocol (2) (Scheme 2) to build the carbazole framework. Although palladium(II) acetate (30 mol%) was the most efficient catalyst for dehydrogenation, giving rise to the desired diarylamines **14**, the latter were not stable enough under the reaction and purification conditions to significantly increase the yields. The use of other catalysts such as palladium on carbon (5% or 10%), mercury(II) acetate, or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone did not afford better yields. Due to these shortcomings and taking into account that most of the 1-oxygenated carbazoles are methylated, we designed a one-pot, two-step procedure to carry out both the dehydrogenation and methylation processes (Table 2). Thus, the series **10a–e** was prepared in high yields (80–85%).

Finally, the palladium(II)-catalyzed cyclization of diarylamines **10a–e** was successfully carried out by following the protocol originally developed by Knölker and coworkers[11b–d] and optimized for the synthesis of natural carbazoles **1a–c**.[10] In spite of different substituents in the benzene ring, the conversion of the series **10a–e** into the

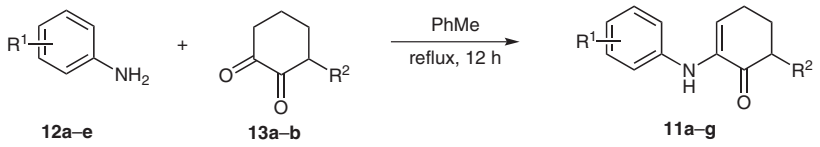


Scheme 2 Alternative protocols for the synthesis of carbazoles **1** starting from anilines **12** and cyclohexane-1,2-dione (**13a**)

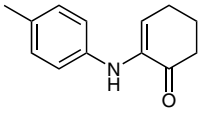
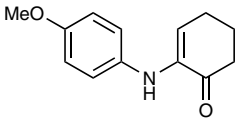
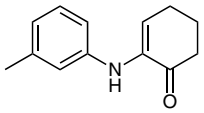
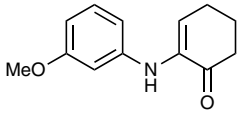
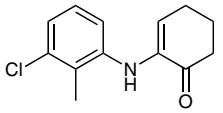
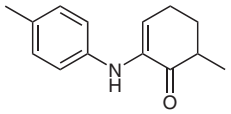
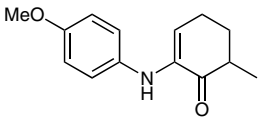


Scheme 3 *Reaction conditions:* (i) **12** (1.78 mmol), **13** (1.78 mmol), toluene (150 mL), reflux, 12 h; (ii) $Pd(OAc)_2$, AcOH, 140 °C.

Table 1 Scope of the Reaction between Anilines **12a–e** and Cyclohexane-1,2-diones **13a**,**b**[a]



12a–e **13a–b** **11a–g**

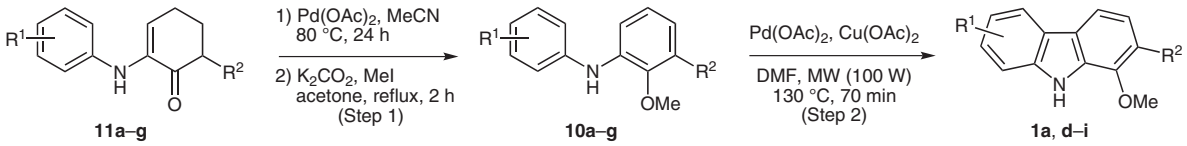
Entry	Aniline	R^1	Cyclohexene-1,2-dione	R^2	Product	Yield[b] (%)
1	**12a**	4-Me	**13a**	H	 **11a**	85
2	**12b**	4-OMe	**13a**	H	 **11b**	95
3	**12c**	3-Me	**13a**	H	 **11c**	82
4	**12d**	3-OMe	**13a**	H	 **11d**	90
5	**12e**	3-Cl-2-Me	**13a**	H	 **11e**	90
6	**12a**	4-Me	**13b**	Me	 **11f**	91
7	**12b**	4-OMe	**13b**	Me	 **11g**	92

[a] Standard conditions: **12** (1.78 mmol), **13** (1.78 mmol), toluene (150 mL), reflux, 12 h.
[b] Isolated yields.

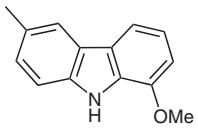
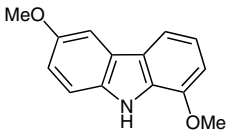
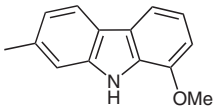
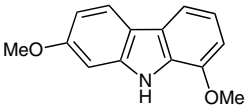
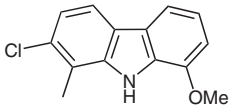
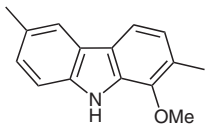
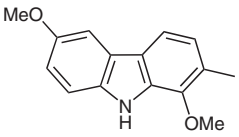
carbazole derivatives **1a**,**d–g** proceeded well and in good yields (70–78%) (Table 2). It is also noteworthy that glycozolicine (**1a**) can be readily transformed into two natural carbazoles mukolidine (**1b**) and mukoline (**1c**)[10] (Figure 1).

With the aim of evaluating the scope of this methodology and of testing the regioselectivity of the formation step of 2-anilinocyclohex-2-en-1-ones **11**, the non-symmetrical cyclohexane-1,2-dione **13b** was treated with anilines **12a**,**b** under the same reaction conditions (Scheme 4). Of the two possible isomers, **11f**,**g** and **16a**,**b**, the former were obtained in high yield (Table 1, entries 6 and 7). This selectivity may be associated with the well-known behavior of secondary or sterically hindered amines in the presence of the non-symmetrical 2-methylcyclohexanone, resulting in the formation of the more stable unsubstituted enamine.[14] Hence, enamine **11** should be more stable than **16**, probably because the latter is destabilized by the inhibition of the resonance between the nitrogen lone-pair and the double bond (Scheme 4).

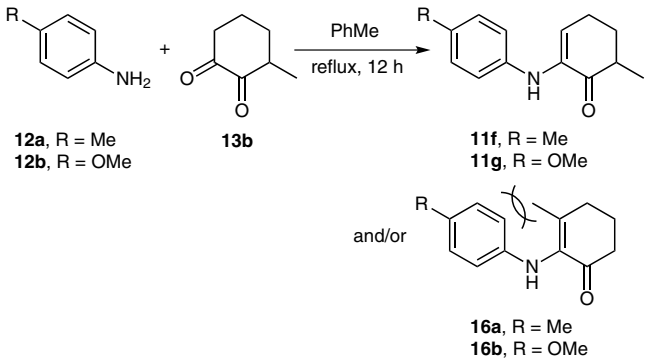
Table 2 Scope of the Conversion of 2-Anilinocyclohexa-2-en-1-ones **11a–g** into Carbazoles **1a**,**d–i**



11a–g **10a–g** **1a, d–i**

Entry	Substrate	R^1	R^2	Step 1		Step 2	
				Product	Yield[a] (%) of **10**	Product	Yield[b] (%) of **1**
1	**11a**	4-Me	H	**10a**	80	 **1a**	75
2	**11b**	4-OMe	H	**10b**	85	 **1d**	77
3	**11c**	3-Me	H	**10c**	80	 **1e**	72
4	**11d**	3-OMe	H	**10d**	83	 **1f**	78
5	**11e**	3-Cl-2-Me	H	**10e**	81	 **1g**	70
6	**11f**	4-Me	Me	**10f**	93	 **1h**	71
7	**11g**	4-OMe	Me	**10g**	86	 **1i**	78

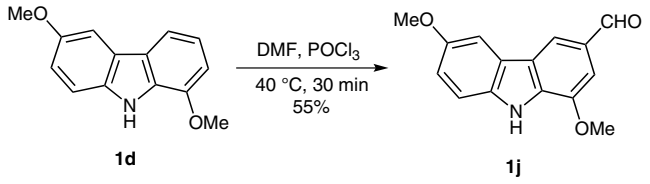
[a] Standard conditions: (1) **11** (0.86–1.24 mmol), $Pd(OAc)_2$ (30 mol%), 80 °C, 24 h; (2) K_2CO_3 (1.5 equiv), MeI (2.0 equiv), reflux, 2 h; isolated yields.
[b] Standard conditions: **10** (0.32–0.47 mmol), $Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (2.5 equiv), MW (100 W), 130 °C, 70 min; isolated yields.



Scheme 4 Regioselective formation of α-ketoenamine **11g**

The dehydrogenation of **11f**,**g** proceeded efficiently to give diarylamines **10f**,**g** (Table 2, entries 6 and 7, step 1), as well as the palladium(II)-catalyzed cyclization of the latter, giving rise to the corresponding 2-methylcarbazoles **1h**,**i** in good yields (Table 2, entries 6 and 7, step 2).

Experimental evidence supports the idea that the biogenetic routes for the formyl or carboxylic functionalized carbazoles at the A- and C-rings consist of an in vivo oxidation of the corresponding methyl-substituted carbazoles.[1c] An example of this is the aforementioned transformation of glycozolicine (**1a**) into the natural carbazoles mukolidine (**1b**) and mukoline (**1c**) (Figure 1), which occurs in the laboratory[10] and probably in nature as well, via an oxidative pathway. However, the direct Vilsmeier–Haack formylation of the carbazole skeleton has seldom been used as an approach for the synthesis of formyl, or after a further oxidative step, of carboxylic carbazoles.[15] This is probably due to the poor selectivity shown by this procedure.[16] However, we investigated the synthesis of the naturally occurring carbazole 6-methoxymurrayanine (**1j**),[17] starting from the herein prepared **1d** (Scheme 5), up to now being reported only as an unnatural carbazole.[4h,18] Thus, by treating the latter with a mixture of *N*,*N*-dimethylformamide/phosphoryl chloride, carbazole **1j** was obtained in 55% yield, recovering unreacted **1d** (21%). The spectral data of the obtained product agreed with those described for the natural[17] and synthetic[18] products.



Scheme 5 Synthesis of 6-methoxymurrayanine (**1j**) by formylation of carbazole **1d**

All the structures of intermediates and products described in these synthetic sequences were characterized by ^{1}H and ^{13}C NMR spectroscopy, with the help of 2D (HMQC and HMBC) experiments, and mass spectrometric techniques (MS and HRMS).

In summary, a short and efficient synthetic approach for the construction of 1-methoxycarbazoles is described, including the naturally occurring alkaloid glycozolicine (**1a**). This approach was accomplished through a three-step reaction sequence with high overall yields (47–62%), starting from cyclohexene-1,2-diones **13a**,**b** and the respective anilines **12a**–**e**, to provide α-ketoenamines **11a**–**g**. The latter proved to be easily available precursors for conversion into diarylamines **10a**–**g**, which were cyclized to the desired carbazoles **1**. A synthetic application of the latter was also carried out by transforming **1d** into the natural carbazole **1j** by direct formylation. The use of this methodology for the synthesis of further carbazole systems is currently under study and will be reported in due course.

Melting points (uncorrected) were determined with an Electrothermal capillary melting point apparatus. IR spectra were recorded on a Perkin-Elmer 2000 spectrophotometer. ^{1}H (300 or 500 MHz) and ^{13}C (75 or 125 MHz) NMR spectra were recorded on Varian Mercury-300 or Varian VNMR System instruments, with TMS as internal standard. MS and HRMS were obtained in EI mode (70 eV) mode on Thermo-Finnigan Polaris Q and on Jeol JSM-GcMateII spectrometers, respectively. Microwave (MW) irradiation was performed on a CEM MW reactor. Analytical TLC was carried out using E. Merck silica gel 60 F254 coated 0.25 plates, visualized by a long- and short-wavelength UV lamp. Flash column chromatography was performed over Natland International Co. silica gel (230–400 mesh). All air moisture sensitive reactions were carried out under N_2 using oven-dried glassware. Toluene was freshly distilled over Na, and CH_2Cl_2 over CaH_2, prior to use. Acetone was dried by distillation after treatment with $KMnO_4$, followed by a second distillation over anhyd Na_2SO_4. K_2CO_3 was dried overnight at 200 °C prior to use. All other reagents were used without further purification.

2-(4-Tolylamino)cyclohex-2-en-1-one (11a); Typical Procedure

In a 250-mL, 3-necked, round-bottomed flask equipped with a magnetic stirring bar, rubber septum, water condenser, and Dean–Stark trap, under N_2, a mixture of **13a** (0.20 g, 1.8 mmol) and **12a** (0.19 g, 1.8 mmol) in dry toluene (150 mL) was stirred at reflux for 12 h. The solvent was removed under vacuum, and the residue purified by column chromatography (silica gel, 10 g/g of crude, hexane–EtOAc, 98:2) to give **11a** (0.30 g, 85%) as a pale yellow solid; mp 58–59 °C [Lit.[19] 58–59 °C]; R_f = 0.74 (hexane–EtOAc, 4:1).

IR (KBr): 3363, 2922, 1671, 1611, 1521, 1308, 1181, 1128, 804 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.00 (q, *J* = 6.5 Hz, 2 H, H5), 2.28 (s, 3 H, CH_3Ar), 2.42 (dt, *J* = 6.5, 5.0 Hz, 2 H, H4), 2.55 (t, *J* = 6.5 Hz, 2 H, H6), 6.24 (br s, 1 H, NH), 6.31 (t, *J* = 5.0 Hz, 1 H, H3), 6.91–6.96 (m, 2 H, H2′), 7.04–7.10 (m, 2 H, H3′).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.6 (*C*H_3Ar), 23.0 (C5), 24.5 (C4), 37.7 (C6), 115.3 (C3), 119.4 (C2′), 129.7 (C3′), 130.8 (C4′), 136.8 (C2), 139.3 (C1′), 195.6 (C1).

MS (70 eV): *m*/*z* (%) = 201 ([M$^+$], 63), 186 (19), 172 (47), 144 (92), 130 (76), 118 (32), 91 (100), 77 (27), 65 (49), 54 (40).

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{13}H_{15}NO$: 201.1154; found: 201.1153.

2-(4-Methoxyphenylamino)cyclohex-2-en-1-one (11b)

Following the procedure for **11a**, with **13a** (0.20 g, 1.8 mmol) and **12b** (0.22 g, 1.8 mmol), **11b** (0.37 g, 95%) was obtained as a pale yellow solid; mp 48–49 °C [Lit.[19] 48–49 °C]; R_f = 0.72 (hexane–EtOAc, 4:1).

IR (film): 3372, 1667, 1628, 1523, 1467, 1334, 1301, 1254, 1182, 1128, 1032, 820, 802 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.98 (q, *J* = 6.6 Hz, 2 H, H5), 2.33–2.41 (m, 2 H, H4), 2.53 (t, *J* = 6.6 Hz, 2 H, H6), 3.76 (s, 3 H, CH_3O), 6.10 (br s, 1 H, NH), 6.13 (t, *J* = 4.6 Hz, 1 H, H3), 6.79–6.86 (m, 2 H, H3′), 6.95–7.02 (m, 2 H, H2′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.0 (C5), 24.3 (C4), 37.6 (C6), 55.3 (CH_3O), 113.9 (C3), 114.3 (C3′), 122.0 (C2′), 134.7 (C1′), 137.5 (C2), 154.7 (C4′), 195.5 (C1).

MS (70 eV): *m*/*z* (%) = 217 ([M^+], 100), 202 (52), 188 (13), 160 (21), 146 (12), 134 (14), 117 (6), 92 (8), 77 (9).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{13}H_{15}NO_2$: 217.1103; found: 217.1109.

2-(3-Tolylamino)cyclohex-2-en-1-one (11c)
Following the procedure for **11a**, with **13a** (0.20 g, 1.8 mmol) and **12c** (0.19 g, 1.8 mmol), **11c** (0.29 g, 82%) was obtained as a pale yellow oil; R_f = 0.74 (hexane–EtOAc, 4:1).

IR (KBr): 3341, 2913, 1675, 1605, 1534, 1492, 1450, 1312, 1176, 1126, 993, 876, 764, 691 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.00 (q, *J* = 6.6 Hz, 2 H, H5), 2.30 (s, 3 H, CH_3Ar), 2.44 (dt, *J* = 6.6, 4.8 Hz, 2 H, H4), 2.54 (t, *J* = 6.6 Hz, 2 H, H6), 6.32 (br s, 1 H, NH), 6.40 (t, *J* = 4.8 Hz, 1 H, H3), 6.73 (br d, *J* = 7.2 Hz, 1 H, H6′), 6.83 (br s, 1 H, H2′), 6.81–6.88 (m, 1 H, H4′), 7.10–7.18 (m, 1 H, H5′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5 (*C*H_3Ar), 22.8 (C5), 24.5 (C4), 37.6 (C6), 115.6 (C4′), 116.3 (C3′), 119.3 (C2′), 121.8 (C6′), 128.9 (C5′), 136.2 (C2), 139.0 (C3′), 141.8 (C1′), 195.5 (C1).

MS (70 eV): *m*/*z* (%) = 201 ([M^+], 100), 186 (14), 172 (41), 158 (27), 144 (57), 130 (29), 118 (11), 91 (32), 77 (6), 65 (18).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{13}H_{15}NO$: 201.1154; found: 201.1155.

2-(3-Methoxyphenylamino)cyclohex-2-en-1-one (11d)
Following the procedure for **11a**, with **13a** (0.20 g, 1.8 mmol) and **12d** (0.22 g, 1.8 mmol), **11d** (0.35 g, 90%) was obtained as a pale yellow solid; mp 59–60 °C; R_f = 0.72 (hexane–EtOAc, 4:1).

IR (film): 3363, 2938, 1672, 1600, 1523, 1494, 1455, 1334, 1274, 1211, 1162, 1047, 764, 688 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.93–2.04 (m, 2 H, H5), 2.40–2.47 (m, 2 H, H4), 2.54 (dd, *J* = 7.5, 6.0 Hz, 2 H, H6), 3.76 (s, 3 H, CH_3O), 6.39 (br s, 1 H, NH), 6.44 (t, *J* = 4.8 Hz, 1 H, H3), 6.44–6.50 (m, 1 H, H6′), 6.57–6.66 (m, 2 H, H2′, H4′), 7.15 (t, *J* = 8.1 Hz, 2 H, H5′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7 (C5), 24.4 (C4), 37.5 (C6), 55.0 (CH_3O), 104.1 (C2′), 105.8 (C6′), 110.8 (C4′), 117.2 (C3), 129.8 (C5′), 135.8 (C1′), 143.1 (C2), 160.3 (C3′), 195.4 (C1).

MS (70 eV): *m*/*z* (%) = 217 ([M^+], 79), 188 (29), 174 (38), 160 (100), 146 (36), 130 (48), 117 (33), 92 (72), 77 (74), 64 (59), 54 (68).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{13}H_{15}NO_2$: 217.1103; found: 217.1108.

2-(3-Chloro-2-methylphenylamino)cyclohex-2-en-1-one (11e)
Following the procedure for **11a**, with **13a** (0.20 g, 1.8 mmol) and **12e** (0.25 g, 1.8 mmol), **11e** (0.38 g, 90%) was obtained as a white solid; mp 63–64 °C; R_f = 0.75 (hexane–EtOAc, 4:1).

IR (KBr): 3384, 2951, 1664, 1631, 1568, 1508, 1461, 1435, 1335, 1302, 1120, 1008, 768 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.97–2.07 (m, 2 H, H5), 2.26 (s, 3 H, CH_3Ar), 2.37–2.45 (m, 2 H, H4), 2.57 (dd, *J* = 7.2, 6.3 Hz, 2 H, H6), 6.00 (t, *J* = 4.7 Hz, 1 H, H3), 6.12 (br s, 1 H, NH), 7.02–7.09 (m, 3 H, H4′, H5′, H6′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5 (*C*H_3Ar), 23.0 (C5), 24.4 (C4), 37.6 (C6), 116.9 (C3), 118.7 (C6′), 123.3 (C4′), 126.7 (C5′), 128.1 (C2′), 135.3 (C3′), 136.8 (C2), 141.3 (C1′), 195.5 (C1).

MS (70 eV): *m*/*z* (%) = 237 ([M^+ + 2], 35), 235 ([M^+], 100), 220 (12), 206 (36), 178 (54), 164 (54), 144 (16), 117 (12), 89 (20).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{13}H_{14}ClNO$: 235.0764; found: 235.0760.

6-Methyl-2-(4-tolylamino)cyclohex-2-en-1-one (11f)
Following the procedure for **11a**, with **13b** (0.200 g, 1.59 mmol) and **12a** (0.170 g, 1.59 mmol), **11f** (0.31 g, 91%) was obtained as a pale yellow oil; R_f = 0.75 (hexane–EtOAc, 4:1).

IR (film): 3361, 1671, 1632, 1613, 1519, 1452, 1337, 1302, 1015, 809 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.21 (d, *J* = 7.0 Hz, 3 H, CH_3-C6), 1.71–1.80 (m, 1 H, H5), 2.02–2.08 (m, 1 H, H5), 2.28 (s, 3 H, CH_3Ar), 2.37–2.47 (m, 2 H, H4), 2.47–2.54 (m, 1 H, H6), 6.24 (br s, 1 H, NH), 6.26 (dd, *J* = 6.0, 3.0 Hz, 1 H, H3), 6.92–6.95 (m, 2 H, H3′), 7.05–7.08 (m, 2 H, H2′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.5 (*C*H_3C6), 20.6 (*C*H_3Ar), 23.5 (C4), 31.0 (C5), 41.4 (C6), 114.5 (C3), 119.4 (C2′), 129.7 (C3′), 130.7 (C4′), 136.2 (C2), 139.5 (C1′), 198.4 (C1).

MS (70 eV): *m*/*z* (%) = 215 ([M^+], 100), 200 (36), 186 (21), 172 (15), 144 (63), 130 (18), 118 (13), 91 (15), 77 (4).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{14}H_{17}NO$: 215.1310; found: 215.1312.

2-(4-Methoxyphenylamino)-6-methylcyclohex-2-en-1-one (11g)
Following the procedure for **11a**, with **13b** (0.200 g, 1.59 mmol) and **12b** (0.196 g, 1.59 mmol), **11g** (0.34 g, 92%) was obtained as a pale yellow oil; R_f = 0.73 (hexane–EtOAc, 4:1).

IR (film): 3362, 1670, 1630, 1512, 1460, 1297, 1241, 1035, 823 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.21 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.66–1.82 (m, 1 H, H5), 1.99–2.10 (m, 1 H, H5), 2.35–2.44 (m, 2 H, H4), 2.45–2.56 (m, 1 H, H6), 3.77 (s, 3 H, MeO), 6.10 (dd, *J* = 5.1, 4.2 Hz, 2 H, H3, NH), 6.80–6.89 (m, 2 H, H3′), 6.96–7.03 (m, 2 H, H2′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.4 (CH_3), 23.4 (C4), 31.1 (C5), 41.3 (C6), 55.4 (CH_3O), 113.3 (C3), 114.4 (C3′), 122.1 (C2′), 135.0 (C1′), 137.1 (C2), 154.8 (C4′), 198.4 (C1).

MS (70 eV): *m*/*z* (%) = 231 ([M^+], 100), 216 (39), 202 (24), 188 (17), 160 (22), 134 (16), 122 (7), 92 (7), 77 (6).

HRMS (EI): *m*/*z* [$M - CH_2$]$^+$ calcd for $C_{13}H_{15}NO_2$: 217.1103; found: 217.1110.

2-Methoxy-*N*-(4-tolyl)aniline (10a); Typical Procedure
In a threaded ACE glass pressure tube with a sealed Teflon screw cap, under N_2, a mixture of **11a** (0.250 g, 1.24 mmol) and $Pd(OAc)_2$ (0.083 g, 0.37 mmol) in anhyd MeCN (2.5 mL) was stirred at 80 °C for 24 h. The solvent was removed under vacuum, the residue mixed with dry K_2CO_3 (0.26 g, 1.9 mmol) and MeI (0.352 g, 2.48 mmol) in dry acetone (20 mL), and the mixture heated to reflux for 2 h. The solvent was removed under vacuum and the residue purified by column chromatography (silica gel, 20 g/g of crude, hexane–EtOAc, 80:20), to give **10a** (0.21 g, 80%) as a pale yellow oil;[20] R_f = 0.65 (hexane–EtOAc, 7:3).

IR (film): 3411, 1599, 1518, 1458, 1297, 1242, 1114, 1028, 741 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3Ar), 3.89 (s, 3 H, CH_3O), 6.06 (br s, 1 H, NH), 6.81 (td, *J* = 7.5, 1.5 Hz, 1 H, H4), 6.85 (td, *J* = 7.5, 2.0 Hz, 1 H, H5), 6.87 (dd, *J* = 7.5, 2.0 Hz, 1 H, H3), 7.04–7.11 (m, 4 H, H2′, H3′), 7.20 (dd, *J* = 7.5, 1.5 Hz, 1 H, H6).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.7 (*C*H_3Ar), 55.5 (CH_3O), 110.2 (C3), 113.5 (C6), 119.1 (C4), 119.5 (C2′), 120.8 (C5), 129.7 (C3′), 130.9 (C4′), 133.7 (C1), 139.8 (C1′), 147.7 (C2).

MS (70 eV): *m*/*z* (%) = 213 ([M$^+$], 90), 198 (36), 183 (100), 154 (25), 128 (8), 91 (7), 77 (8), 65 (7).

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{14}H_{15}NO$: 213.1154; found: 213.1161.

2-Methoxy-*N*-(4-methoxyphenyl)aniline (10b)
Following the procedure for **10a**, with **11b** (0.200 g, 0.92 mmol), $Pd(OAc)_2$ (0.063 g, 0.28 mmol), K_2CO_3 (0.190 g, 1.38 mmol), and MeI (0.261 g, 1.84 mmol), **10b** (0.18 g, 85%) was obtained as a white solid; mp 70–71 °C [Lit.[21] 71–72 °C]; R_f = 0.67 (hexane–EtOAc, 4:1).

IR (KBr): 3379, 1601, 1526, 1239, 1174, 1110, 735 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, CH_3O), 3.86 (s, 3 H, CH_3O), 5.97 (br s, 1 H, NH), 6.72–6.90 (m, 5 H, H3, H3′, H4, H5), 7.00–7.07 (m, 1 H, H6′), 7.07–7.15 (m, 2 H, H2′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (2 CH_3O), 110.1 (C3), 112.4 (C6), 114.5 (C3′), 118.4 (C4), 120.8 (C5), 122.6 (C2′), 134.9 (C1), 135.3 (C1′), 147.2 (C2), 155.2 (C4′).

MS (70 eV): *m*/*z* (%) = 229 ([M$^+$], 23), 214 (17), 179 (28), 170 (26), 154 (23), 130 (13), 77 (100), 51 (34).

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{14}H_{15}NO_2$: 229.1103; found: 229.1103.

2-Methoxy-*N*-(3-tolyl)aniline (10c)
Following the procedure for **10a**, with **11c** (0.200 g, 0.99 mmol), $Pd(OAc)_2$ (0.067 g, 0.30 mmol), K_2CO_3 (0.210 g, 1.52 mmol), and MeI (0.280 g, 1.97 mmol), **10c** (0.17 g, 80%) was obtained as a pale yellow oil;[22] R_f = 0.65 (hexane–EtOAc, 4:1).

IR (film): 3409, 1585, 1523, 1493, 1243, 1115, 1028, 741 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3), 3.85 (s, 3 H, CH_3O), 6.01 (br s, 1 H, NH), 6.75 (dm, *J* = 7.5, 1.6 Hz, 1 H, H4′), 6.82–6.90 (m, 3 H, H3, H4, H5), 6.93–6.98 (m, 2 H, H2′, H6′), 7.16 (dd, *J* = 8.7, 7.5 Hz, 1 H, H5′), 7.27–7.32 (m, 1 H, H6).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5 (CH_3), 55.5 (CH_3O), 110.4 (C3), 114.6 (C6), 115.5 (C2′), 119.2 (C6′), 119.7 (C4), 120.7 (C5), 121.9 (C4′), 129.0 (C5′), 133.0 (C1), 139.0 (C3′), 142.6 (C1′), 148.1 (C2).

MS (70 eV): *m*/*z* (%) = 213 ([M$^+$], 100), 198 (42), 183 (98), 154 (26), 128 (8), 91 (6), 65 (8).

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{14}H_{15}NO$: 213.1154; found: 213.1163.

2-Methoxy-*N*-(3-methoxyphenyl)aniline (10d)
Following the procedure for **10a**, with **11d** (0.200 g, 0.92 mmol), $Pd(OAc)_2$ (0.063 g, 0.28 mmol), K_2CO_3 (0.190 g, 1.38 mmol), and MeI (0.261 g, 1.84 mmol), **10d** (0.175 g, 83%) was obtained as a pale yellow oil;[23] R_f = 0.67 (hexane–EtOAc, 4:1).

IR (film): 3401, 1591, 1494, 1461, 1245, 1156, 1028, 743 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, CH_3O), 3.85 (s, 3 H, CH_3O), 6.14 (br s, 1 H, NH), 6.47 (ddd, *J* = 8.5, 2.0, 1.0 Hz, 1 H, H4′), 6.69–6.73 (m, 2 H, H2′, H6′), 6.82–6.91 (m, 3 H, H3, H4, H5), 7.16 (t, *J* = 7.5 Hz, 1 H, H5′), 7.30–7.34 (m, 1 H, H6).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.1 (CH_3O), 55.5 (CH_3O), 103.9 (C2′), 106.3 (C4′), 110.5 (C3), 110.8 (C6′), 115.3 (C6), 120.1 (C4), 120.7 (C5), 129.9 (C5′), 132.6 (C1), 144.1 (C1′), 148.4 (C2), 160.6 (C3′).

MS (70 eV): *m*/*z* (%) = 229 ([M$^+$], 100), 217 (10), 200 (12), 189 (6), 170 (11), 154 (12), 142 (9), 115 (5), 77 (4).

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{14}H_{15}NO_2$: 229.1103; found: 229.1107.

3-Chloro-*N*-(2-methoxyphenyl)-2-methylaniline (10e)
Following the procedure for **10a**, with **11e** (0.250 g, 1.06 mmol), $Pd(OAc)_2$ (0.071 g, 0.32 mmol), K_2CO_3 (0.22 g, 1.6 mmol), and MeI (0.30 g, 2.1 mmol), **10e** (0.21 g, 81%) was obtained as a white solid; mp 64–65 °C; R_f = 0.68 (hexane–EtOAc, 4:1).

IR (KBr): 3405, 1589, 1507, 1454, 1239, 1113, 1026, 732 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, CH_3), 3.88 (s, 3 H, CH_3O), 5.89 (br s, 1 H, NH), 6.80–6.91 (m, 3 H, H3, H4, H5), 6.95 (dd, *J* = 5.7, 3.9 Hz, 1 H, H6), 7.00–7.07 (m, 2 H, H4′, H5′), 7.16–7.21 (m, 1 H, H6′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5 (CH_3), 55.5 (CH_3O), 110.4 (C3), 114.9 (C6), 118.0 (C6′), 119.9 (C4), 120.8 (C5), 123.0 (C4′), 126.8 (C5′), 127.6 (C2′), 133.3 (C1), 135.2 (C3′), 142.3 (C1′), 148.1 (C2).

MS (70 eV): *m*/*z* (%) = 247 ([M$^+$], 100), 232 (5), 217 (16), 214 (18), 197 (91).

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{14}H_{14}ClNO$: 247.0764; found: 247.0767.

2-Methoxy-3-methyl-*N*-(4-tolyl)aniline (10f)
Following the procedure for **10a**, with **11f** (0.200 g, 0.93 mmol), $Pd(OAc)_2$ (0.062 g, 0.28 mmol), K_2CO_3 (0.192 g, 1.39 mmol), and MeI (0.264 g, 1.86 mmol), **10f** (0.196 g, 93%) was obtained as a pale yellow solid; mp 68–69 °C; R_f = 0.74 (hexane–EtOAc, 4:1).

IR (KBr): 3400, 1603, 1588, 1518, 1474, 1328, 1251, 1207, 1001, 767 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3-C3), 2.31 (s, 3 H, CH_3-C4′), 3.75 (s, 3 H, CH_3O), 6.04 (br s, 1 H, NH), 6.66 (dd, *J* = 8.0, 1.0 Hz, 1 H, H4), 6.88 (t, *J* = 8.0 Hz, 1 H, H5), 7.03–7.06 (m, 2 H, H2′), 7.07 (dd, *J* = 8.0, 1.0 Hz, 1 H, H6), 7.08–7.11 (m, 2 H, H3′).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.9 (CH_3-C3), 20.7 (CH_3-C4′), 59.6 (CH_3O), 112.9 (C6), 119.4 (C2′), 121.7 (C4), 124.1 (C5), 129.8 (C3′), 131.0 (C3), 131.1 (C4′), 137.3 (C1), 140.0 (C1′), 146.9 (C2).

MS (70 eV): *m*/*z* (%) = 227 ([M$^+$], 100), 212 (26), 197 (62), 168 (11), 154 (4), 77 (5).

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{15}H_{17}NO$: 227.1310; found: 227.1307.

2-Methoxy-*N*-(4-methoxyphenyl)-3-methylaniline (10g)
Following the procedure for **10a**, with **11g** (0.200 g, 0.87 mmol), $Pd(OAc)_2$ (0.058 g, 0.26 mmol), K_2CO_3 (0.178 g, 1.29 mmol), and MeI (0.247 g, 1.74 mmol), **10g** (0.18 g, 86%) was obtained as a pale yellow oil; R_f = 0.65 (hexane–EtOAc, 4:1).

IR (film): 3351, 1603, 1515, 1471, 1327, 1242, 1168, 1037, 997, 827, 774 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 3.75 (s, 3 H, CH_3O), 3.76 (s, 3 H, CH_3O), 5.98 (br s, 1 H, NH), 6.60 (d, *J* = 7.2 Hz, 1 H, H4), 6.80–6.94 (m, 4 H, H3′, H5, H6), 7.05–7.13 (m, 2 H, H2′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.8 (CH_3), 55.4 (CH_3O), 59.4 (CH_3O), 111.5 (C6), 114.5 (C3′), 120.9 (C4), 122.5 (C2′), 124.1 (C5), 130.8 (C3), 135.3 (C1′), 138.4 (C1), 146.1 (C2), 155.1 (C4′).

MS (70 eV): *m*/*z* (%) = 243 ([M$^+$], 100), 228 (54), 213 (19), 197 (64), 184 (19), 168 (7), 154 (6).

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{15}H_{17}NO_2$: 243.1259; found: 243.1266.

1-Methoxy-6-methyl-9*H*-carbazole (Glycozolicine, 1a); Typical Procedure
A mixture of **10a** (0.106 g, 0.50 mmol), $Pd(OAc)_2$ (0.011 g, 0.05 mmol), and $Cu(OAc)_2$ (0.22 g, 1.2 mmol) in dry DMF (0.5 mL), under N_2, was stirred and heated at 130 °C for 70 min under microwave irradiation (100 W). The solvent was removed under vacuum

and the residue purified by column chromatography (silica gel, 10 g/g of crude, hexane–EtOAc, 95:5), to give **1a** (0.079 g, 75%) as a white solid; mp 145–146 °C [Lit.[10] 145–146 °C; Lit.[6c] 137–138 °C; Lit.[7a] 150 °C]; R_f = 0.60 (hexane–EtOAc, 7:3).

1,6-Dimethoxy-9*H*-carbazole (1d)
Following the procedure for **1a**, with **10b** (0.100 g, 0.44 mmol), $Pd(OAc)_2$ (0.0099 g, 0.044 mmol), and $Cu(OAc)_2$ (0.2 g, 1.1 mmol), **1d** (0.076 g, 77%) was obtained as a white solid;[4h] mp 118–119 °C [Lit.[18a] 118–120 °C]; R_f = 0.62 (hexane–EtOAc, 7:3).

IR (KBr): 3416, 1615, 1578, 1482, 1459, 1429, 1298, 1259, 1217, 1175, 1031, 796, 737 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.90 (s, 3 H, CH_3O-C6), 3.96 (s, 3 H, CH_3O-C1), 6.85 (br d, *J* = 7.5 Hz, 1 H, H2), 7.04 (dd, *J* = 8.5, 2.5 Hz, 1 H, H7), 7.11 (t, *J* = 7.5 Hz, 1 H, H3), 7.30 (d, *J* = 8.5 Hz, 1 H, H8), 7.51 (d, *J* = 2.5 Hz, 1 H, H5), 7.62 (d, *J* = 7.5 Hz, 1 H, H4), 8.13 (br s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.4 (CH_3O-C1), 56.0 (CH_3O-C6), 103.2 (C5), 105.7 (C2), 111.6 (C8), 112.7 (C4), 115.0 (C7), 119.3 (C3), 124.0 (C4b), 124.3 (C4a), 130.6 (C9a), 134.1 (C8a), 145.7 (C1), 153.8 (C6).

MS (70 eV): *m*/*z* (%) = 227 ([M^+], 100), 212 (48), 196 (4), 184 (80), 169 (30), 141 (33), 126 (7), 77 (23).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{14}H_{13}NO_2$: 227.0946; found: 227.0950.

1-Methoxy-7-methyl-9*H*-carbazole (1e)
Following the procedure for **1a**, with **10c** (0.106 g, 0.50 mmol), $Pd(OAc)_2$ (0.011 g, 0.05 mmol), and $Cu(OAc)_2$ (0.226 g, 1.25 mmol), **1e** (0.076 g, 72%) was obtained as a white solid; mp 172–173 °C [Lit.[24] 172.6–176.4 °C]; R_f = 0.61 (hexane–EtOAc, 7:3).

IR (KBr): 3404, 1618, 1577, 1504, 1436, 1322, 1260, 1243, 1101, 1027, 809, 776, 723 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.48 (s, 3 H, CH_3Ar), 3.96 (s, 3 H, CH_3O), 6.84 (d, *J* = 8.0 Hz, 1 H, H2), 7.03 (br d, *J* = 8.0 Hz, 1 H, H6), 7.12 (t, *J* = 8.0 Hz, 1 H, H3), 7.16 (br s, 1 H, H8), 7.62 (d, *J* = 8.0 Hz, 1 H, H4), 7.90 (d, *J* = 8.0 Hz, 1 H, H5), 8.10 (br s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.0 (CH_3), 55.4 (CH_3O), 105.5 (C2), 111.0 (C8), 112.6 (C4), 119.6 (C3), 120.1 (C5), 120.9 (C6), 121.4 (C4b), 124.4 (C4a), 129.6 (C9a), 135.8 (C7), 139.6 (C8a), 145.6 (C1).

MS (70 eV): *m*/*z* (%) = 211 ([M^+], 100), 196 (72), 168 (85), 153 (12), 139 (13), 115 (6), 77 (13).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{14}H_{13}NO$: 211.0997; found: 211.0990.

1,7-Dimethoxy-9*H*-carbazole (1f)
Following the procedure for **1a**, with **10d** (0.100 g, 0.44 mmol), $Pd(OAc)_2$ (0.0099 g, 0.044 mmol), and $Cu(OAc)_2$ (0.20 g, 1.1 mmol), **1f** (0.077 g, 78%) was obtained as a white solid; mp 164–165 °C [Lit.[25] 164–166 °C]; R_f = 0.62 (hexane–EtOAc, 7:3).

IR (KBr): 3431, 1630, 1577, 1503, 1445, 1382, 1320, 1262, 1245, 1192, 1157, 1095, 1011, 825, 778 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.87 (s, 3 H, CH_3O-C7), 3.98 (s, 3 H, CH_3O-C1), 6.83 (dd, *J* = 7.5, 0.5 Hz, 1 H, H2), 6.84 (dd, *J* = 8.5, 2.5 Hz, 1 H, H6), 6.90 (d, *J* = 2.5 Hz, 1 H, H8), 7.12 (t, *J* = 7.5 Hz, 1 H, H3), 7.57 (d, *J* = 7.5, 1 H, H4), 7.89 (d, *J* = 8.5 Hz, 1 H, H5), 8.17 (br s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.5 (CH_3O-C1), 55.6 (CH_3O-C7), 94.8 (C8), 105.0 (C2), 108.3 (C6), 112.2 (C4), 117.6 (C4b), 119.8 (C3), 121.2 (C5), 124.5 (C4a), 129.6 (C9a), 140.5 (C8a), 145.4 (C1), 159.0 (C7).

MS (70 eV): *m*/*z* (%) = 227 ([M^+], 100), 212 (40), 184 (65), 169 (23), 149 (37), 141 (26), 77 (13).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{14}H_{13}NO_2$: 227.0946; found: 227.0949.

2-Chloro-8-methoxy-1-methyl-9*H*-carbazole (1g)
Following the procedure for **1a**, with **10e** (0.10 g, 0.4 mmol), $Pd(OAc)_2$ (0.009 g, 0.04 mmol), and $Cu(OAc)_2$ (0.18 g, 1.0 mmol), **1g** (0.07 g, 70%) was obtained as a white solid; mp 98–99 °C; R_f = 0.63 (hexane–EtOAc, 7:3).

IR (KBr): 3439, 1580, 1506, 1432, 1323, 1256, 1130, 1059, 1014, 774, 730 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.60 (s, 3 H, CH_3), 4.03 (s, 3 H, CH_3O), 6.90 (d, *J* = 8.0 Hz, 1 H, H7), 7.16 (t, *J* = 8.0 Hz, 1 H, H6), 7.23 (d, *J* = 8.0 Hz, 1 H, H3), 7.62 (d, *J* = 8.0 Hz, 1 H, H5), 7.79 (d, *J* = 8.0 Hz, 1 H, H4), 8.16 (br s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1 (CH_3), 55.5 (CH_3O), 105.9 (C7), 112.8 (C5), 118.1 (C2), 118.7 (C4), 120.3 (C6), 120.8 (C3), 121.8 (C4a), 124.5 (C4b), 129.9 (C8a), 131.0 (C1), 139.3 (C9a), 145.7 (C8).

MS (70 eV): *m*/*z* (%) = 245 ([M^+], 3), 230 (11), 202 (27), 179 (26), 167 (27), 140 (25), 91 (10), 77 (100), 51 (40).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{14}H_{12}ClNO$: 245.0607; found: 245.0607.

1-Methoxy-2,6-dimethyl-9*H*-carbazole (1h)
Following the procedure for **1a**, with **10f** (0.100 g, 0.44 mmol), $Pd(OAc)_2$ (0.0099 g, 0.044 mmol), and $Cu(OAc)_2$ (0.197 g, 1.09 mmol), **1h** (0.07 g, 71%) was obtained as a white solid; mp 159–158 °C; R_f = 0.65 (hexane–EtOAc, 7:3).

IR (KBr): 3329, 1604, 1572, 1515, 1487, 1284, 1228, 1085, 1006, 800 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, CH_3-C2), 2.50 (s, 3 H, CH_3-C6), 3.93 (s, 3 H, CH_3O), 6.99 (d, *J* = 8.0 Hz, 1 H, H3), 7.20 (dd, *J* = 8.3, 1.5 Hz, 1 H, H7), 7.30 (d, *J* = 8.3 Hz, 1 H, H8), 7.66 (d, *J* = 8.0 Hz, 1 H, H4), 7.79 (s, 1 H, H5), 8.07 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.7 (CH_3-C2), 21.4 (CH_3-C6), 60.3 (CH_3O), 110.4 (C8), 115.7 (C4), 120.1 (C5), 122.3 (C3), 123.5 (C4a), 124.1 (C4b), 126.8 (C7), 128.7 (C6), 134.0 (C9a), 137.7 (C8a), 143.1 (C1).

MS (70 eV): *m*/*z* (%) = 225 ([M^+], 100), 210 (92), 184 (20), 182 (35), 167 (18), 152 (5), 140 (5), 77 (3).

HRMS (EI): *m*/*z* [M^+] calcd for $C_{15}H_{15}NO$: 225.1154; found: 225.1155.

1,6-Dimethoxy-2-methyl-9*H*-carbazole (1i)
Following the procedure for **1a**, with **10g** (0.100 g, 0.41 mmol), $Pd(OAc)_2$ (0.0092 g, 0.041 mmol), and $Cu(OAc)_2$ (0.187 g, 1.03 mmol), **1i** (0.077 g, 78%) was obtained as a white solid; mp 167–168 °C; R_f = 0.62 (hexane–EtOAc, 7:3).

IR (film): 3382, 1572, 1488, 1461, 1439, 1291, 1211, 1173, 1028, 1005, 806 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, CH_3), 3.91 (s, 3 H, CH_3O-C6), 3.93 (s, 3 H, CH_3O-C1), 6.99 (d, *J* = 7.8 Hz, 1 H, H3), 7.03 (dd, *J* = 8.9, 2.3 Hz, 1 H, H7), 7.31 (d, *J* = 8.9 Hz, 1 H, H8), 7.49 (d, *J* = 2.3 Hz, 1 H, H5), 7.66 (d, *J* = 7.8 Hz, 1 H, H4), 8.09 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.7 (CH_3), 56.0 (CH_3O-C6), 60.3 (CH_3O-C1), 103.0 (C5), 111.4 (C8), 114.6 (C7), 115.7 (C4), 122.1 (C3), 123.6 (C4a), 124.4 (C4b), 126.9 (C2), 134.0 (C9a), 134.3 (C8a), 143.1 (C1), 153.8 (C6).

MS (70 eV): *m*/*z* (%) = 241 ([M^+], 93), 226 (100), 211 (12), 198 (19), 183 (20), 167 (16), 154 (17), 127 (6), 77 (3).

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{15}H_{15}NO_2$: 241.1103; found: 241.1112.

3-Formyl-1,6-dimethoxy-9*H*-carbazole (6-Methoxymurrayanine) (1j)

In a 25-mL, 2-necked, round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and water condenser, under N_2, a mixture of dry DMF (0.472 g, 6.47 mmol) and $POCl_3$ (0.050 g, 0.33 mmol) was stirred at 0 °C for 20 min. Afterward, a soln of **1d** (0.050 g, 0.22 mmol) in dry DMF (0.5 mL) was added, and the mixture stirred at r.t. for 10 min, then at 40 °C for 30 min. The mixture was poured into H_2O (2 mL) and 2 M aq NaOH soln was added until neutral. The organic layer was purified by column chromatography (silica gel, 20 g/g of crude, hexane–EtOAc, 9:1) to give **1j** (0.031 g, 55%) as a pale yellow solid; mp 231–233 °C [Lit.[17] 231–233 °C; Lit.[18a] 230–232 °C]; R_f = 0.69 (hexane–EtOAc, 7:3).

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