Regular Article

Total Synthesis of Carbazomycins A and B

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Total syntheses of carbazomycins A and B were demonstrated using a ytterbium-catalyzed Diels–Alder reaction with (silyloxyvinyl)indole as a diene. The densely substituted benzene ring of the target compound was successfully constructed by functionalization of a hydrocarbazolone intermediate and subsequent aromatization using *N*-bromosuccinimide.

Key words total synthesis; carbazomycin; Diels–Alder reaction; ytterbium; carbazole

Carbazole is a tricyclic skeleton that is frequently seen as a core structure in biologically active compounds.[1–6] Among them, carbazomycins have a simple structure, but attractive biological activities. Especially, carbazomycins A and B, which were isolated from the extract of cultured mycelia of *Streptoverticillium ehimensis* strain H1051-MY10[7–9] (Chart 1), show inhibitory activity against 5-lipoxygenase, and have weak antibacterial and antiyeast activities. Carbazomycin B is also active against malaria.[10,11] Therefore, carbazomycins have been receiving considerable attention, and there have been several reports on their total synthesis.[12–23] In the synthesis of these compounds, the methods used to construct the fully substituted benzene ring in their structure have been the main subject of synthetic strategies, because it is generally difficult to construct a fully substituted benzene ring from benzene derivatives by aromatic substitution and/or cross-coupling strategies due to a shortage of reliable methods for installing a functional group at the desired position.[24]

Our group has been focusing on the stereo- and regioselective synthesis of the hydrocarbazole skeleton by the catalytic Diels–Alder reaction using highly acid-sensitive 3-(silyloxyvinyl)indole as a diene[25,26] (Chart 2). An asymmetric version of this reaction was promoted by a chiral holmium catalyst, and the optically active hydrocarbazole **6** with three contiguous chiral centers was obtained in a single step. Concise total syntheses of (−)-minovincine[27] and natural alkaloid (+)-**8**[28] demonstrated the synthetic utility of **6**.

During the synthesis of **8**, stereoselective hydroxylation of hydrocarbazolone intermediate **9** derived from **6** was the key step. We noticed that the aromatization of **8** would lead a total synthesis of carbazomycins. However, aromatization of **8** itself was unsuccessful because of its instability. Therefore, we explored aromatization methods using the substrates **10** and **12**, which were equivalent to compound **8**, to obtain the carbazomycin skeleton (Chart 3).

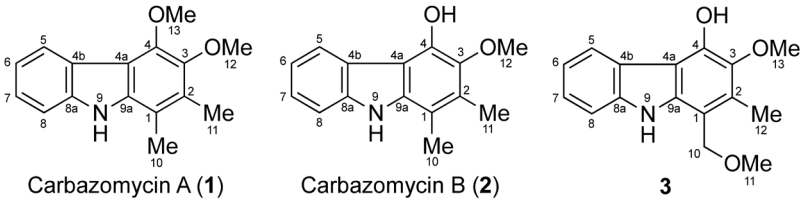

Chart 1. Structures of Carbazomycins A and B, and Related Carbazole Alkaloid **3**

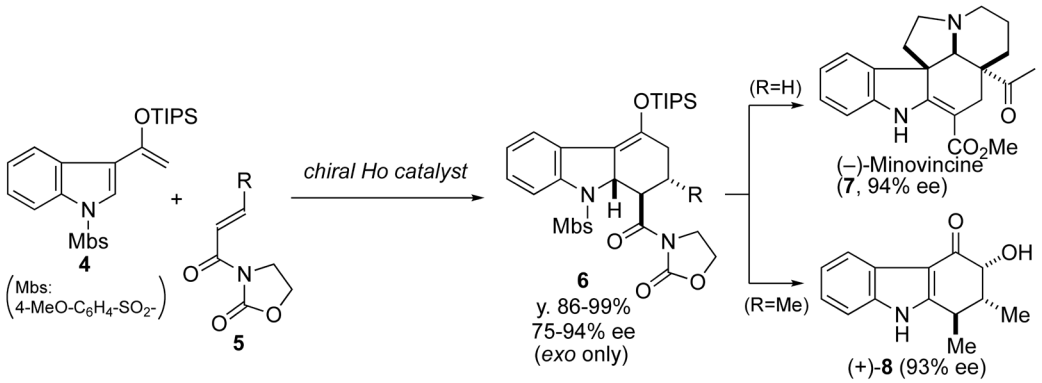

Chart 2. Enantioselective Synthesis of Chiral Hydrocarbazole **6**, and Its Application to the Asymmetric Total Syntheses of Natural Compounds **7** and **8**

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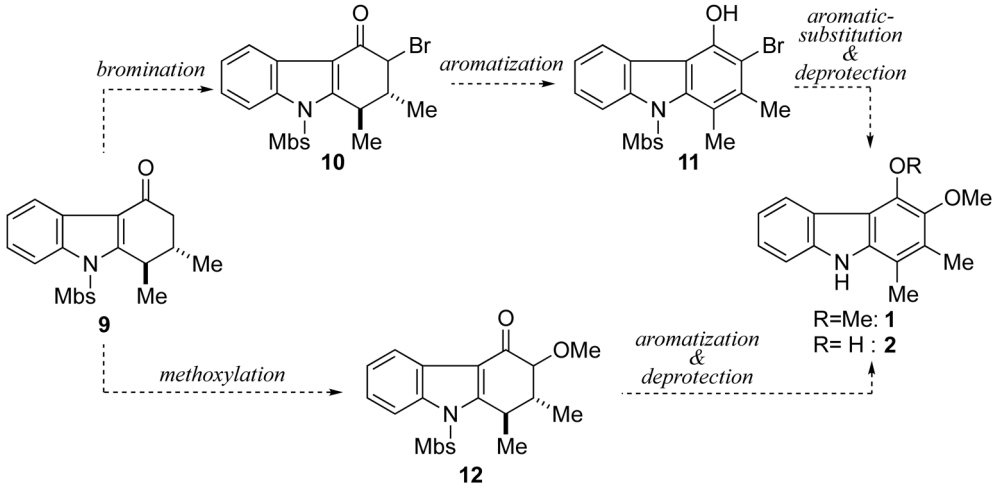

Chart 3. Plan for the Synthesis of Carbazomycins

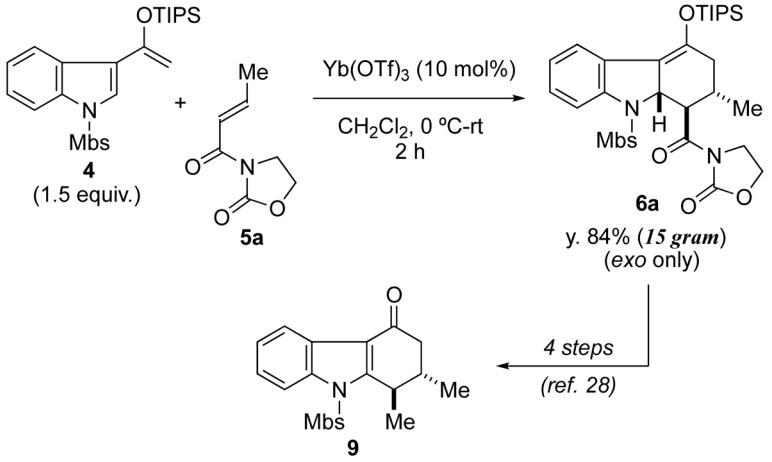

Chart 4. Catalytic Diels–Alder Reaction of Silyloxyvinylindole **4**, and Derivatization to Hydrocarbazolone **9**

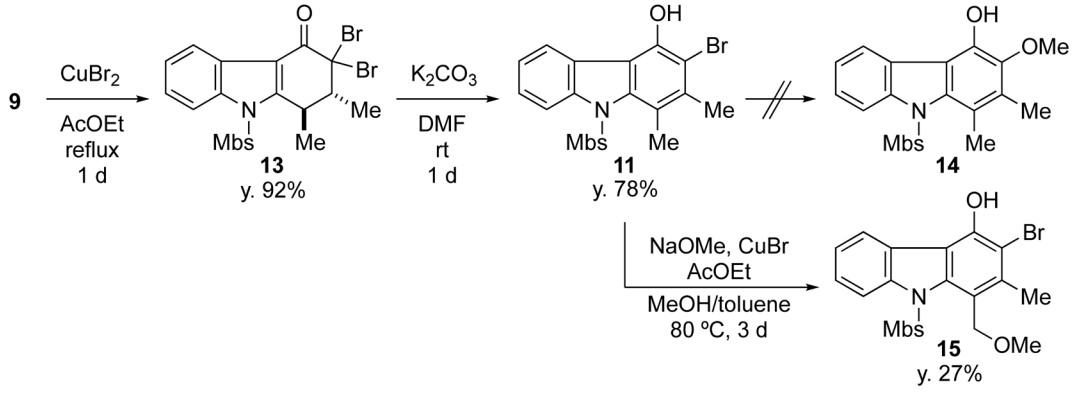

Chart 5. Bromination of Hydrocarbazolone **9**, and Attempts to Introduce a Methoxy Group at C3

Results and Discussion

The synthesis began with our Diels–Alder reaction between silyloxyvinylindole **4** and dienophile **5a**.[25] The racemic reaction of **4** and **5a** was promoted by ytterbium triflate,[29–31] and the *exo*-adduct **6a** was obtained in 84% yield as a single diastereomer on a 15-g scale[32] (Chart 4). From **6a**, hydrocarbazolone **9** was synthesized by following the synthetic route to (+)-**8** in our previous report,[28] *via* reductive cleavage of the acyl oxazolidinone moiety to a methyl group at C10 and subsequent oxidative conversion of triisopropylsilyl (TIPS) enol ether to enone.

Bromination of **9** with copper bromide[33] gave dibrominated product **13** in 92% yield (Chart 5). Treatment with potassium carbonate gave aryl bromide **11**. We examined its aromatic substitution with a methoxy group.[34] We tried several conditions using copper catalysis for the synthesis of **14**, however, only complex mixtures were obtained. Meanwhile, we isolated compound **15**, which had a methoxy group at C10, under the

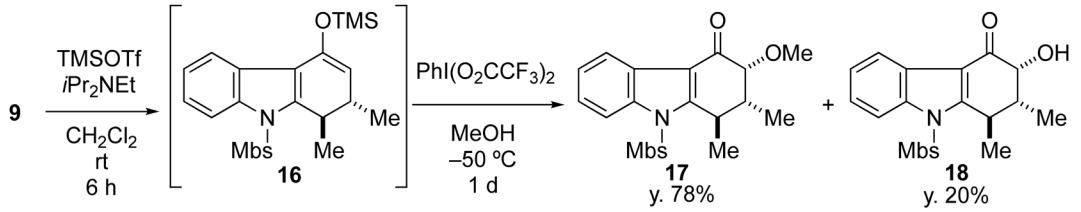

Chart 6. Introduction of a Methoxy Group *via* TMS Enol Ether **16**

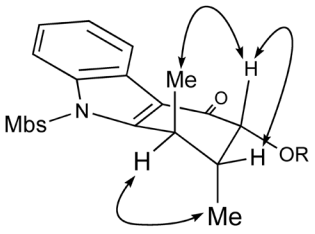

Chart 7. Key Correlations in NOESY Analyses of **17** and **18**

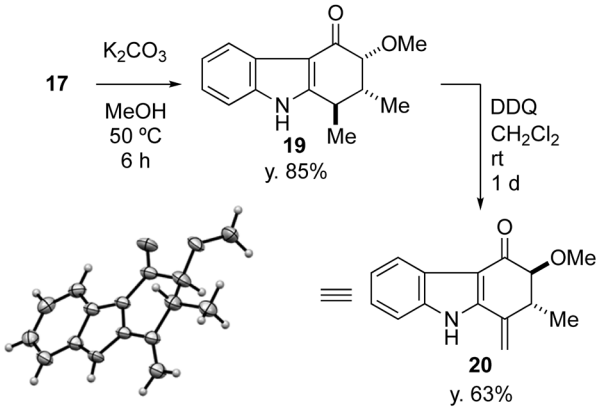

Chart 8. Unexpected Synthesis of Hydrocarbazolone **20** with Exocyclic Olefin

conditions described in Chart 5. This type of benzylic oxidation of carbazole derivative has been reported using potassium persulfate in the presence of copper sulfate.[35] A mechanistic study of our reaction is underway because compound **15** could be a potential synthetic intermediate for carbazole alkaloids with an oxygen functionality at C10, like compound **3**.

Next, we turned our attention to another synthetic route. We performed the methoxylation of hydrocarbazolone *via* trimethylsilyl (TMS) enol ether.[36] After the *in situ* generation of TMS enol ether **16**, we obtained the desired compound **17** in 78% yield along with hydroxy derivative **18** in 20% yield (Chart 6). The relative stereochemistries of **17** and **18** were determined by the key correlations in a nuclear Overhauser effect spectroscopy (NOESY) analysis (Chart 7).

Deprotection of the carbazole nitrogen was realized with potassium carbonate in methanol. However, a subsequent attempt at aromatization gave unexpected hydrocarbazolone **20** with an exocyclic olefin (Chart 8). During this transformation, the stereochemistry of the methoxy group was epimerized. To date, we have had no clear explanation on this epimerization,[37] but the structure was unambiguously determined by X-ray crystallographic analysis.[38] Compound **20** as well as **19** could not be converted to carbazomycin B under several conditions.

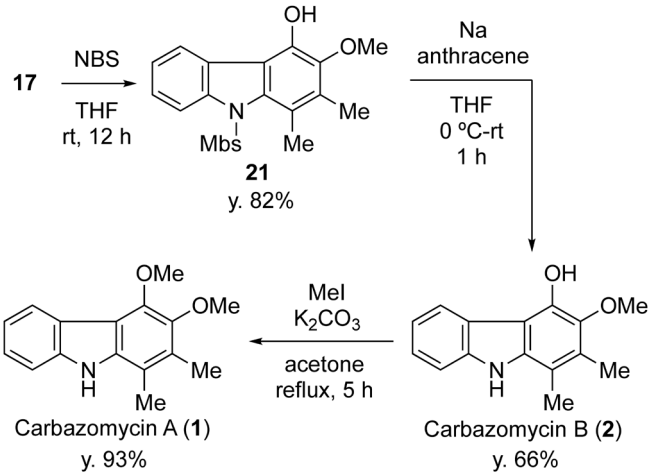

Chart 9. Total Synthesis of Carbazomycins A and B

Therefore, we aromatized **17** with *N*-bromosuccinimide (NBS) before deprotection to give carbazole **21** (Chart 9). Next, Mbs was removed with Na/anthracene to finally accomplish the total synthesis of carbazomycin B, which was converted to carbazomycin A by following Moody's method.[14]

Conclusion

We accomplished the total synthesis of carbazomycins A and B. The key point in our synthesis is that the hydrocarbazole skeleton was built in a single step by using our lanthanoid catalysis, which gave three-fourths of the substituents of carbazomycins A and B. Subsequent installation of a methoxy group and aromatization achieved the construction of a fully substituted benzene ring in the carbazomycin skeleton. Moreover, the application of this new oxidation method at the benzylic position of carbazole derivatives as well as the introduction of substituents to silyloxyvinylindole and the use of a variety of dienophiles opens the way to the construction of a library of carbazomycin derivatives. The biological activities of the synthetic intermediates will be screened in due course.

Experimental

General Information NMR spectra were recorded at 400 or 600 MHz for ^{1}H-NMR, and at 100 or 150 MHz for ^{13}C-NMR. Chemical shifts for proton are reported in parts per million downfield from tetramethylsilane, and are referenced to residual protium in the NMR solvent ($CDCl_3$ δ: 7.26 ppm). For ^{13}C-NMR, chemical shifts are reported relative to the NMR solvent ($CDCl_3$ δ: 77.0 ppm) as an internal reference. Infrared spectra were recorded on an attenuated total reflectance (ATR). Mass spectra were recorded using electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI) mode with a time of flight (TOF) analyzer. Reactions were

carried out in dry solvents under an argon atmosphere, unless otherwise noted. Solvents and reagents were purified by general methods. Flash column chromatography was performed on silica gel 60 μm particles, unless otherwise noted.

(±)-3-(9-((4-Methoxyphenyl)sulfonyl)-2-methyl-4-((triisopropylsilyl)oxy)-2,3,9,9a-tetrahydro-1*H*-carbazole-1-carbonyl)oxazolidin-2-one (6a) $Yb(OTf)_3$ (1.74 g, 2.8 mmol, 10 mol%) was placed in a 300 mL flask with a stirring bar and heated at 120°C under reduced pressure (<0.01 mmHg) for 30 min. After being cooled to room temperature, the flask was charged with dry argon, and CH_2Cl_2 (23 mL) were added. The reaction mixture was cooled to 0°C. A solution of dienophile **5a** (4.34 g, 28 mmol) in CH_2Cl_2 (25+5 mL to rinse) was added. A solution of diene **4** (16.3 g, 34 mmol, 1.2 equiv.) in CH_2Cl_2 (50+5 mL to rinse) was then added, and the mixture was stirred for 2 h under argon at room temperature. The reaction was quenched by the addition of H_2O and filtered through a pad of Celite. The water layer was extracted three times with CH_2Cl_2, and the combined organic layers was dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (CHROMATOREX-NH, 1/4=ethyl acetate/hexane) to give **6a** as a colorless foam (15 g, 84%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.06 (d, J=7.6 Hz, 9H), 1.07 (d, J=7.6 Hz, 9H), 1.09 (d, J=5.6 Hz, 3H), 1.19 (qq, J=7.6, 7.6 Hz, 3H), 2.11 (ddd, J=2.0, 8.0, 16.8 Hz, 1H), 2.28 (m, 1H), 2.46 (ddd, J=2.0, 5.6, 16.8 Hz, 1H), 3.78 (s, 3H), 4.09 (ddd, J=8.8, 8.8, 8.8 Hz, 1H), 4.30 (ddd, J=8.8, 8.8, 8.8 Hz, 1H), 4.34 (dd, J=8.0, 8.0 Hz, 1H), 4.42 (ddd, J=6.0, 8.8, 8.8 Hz, 1H), 4.49 (ddd, J=8.8, 8.8, 8.8 Hz, 1H), 4.75 (td, J=2.0, 8.0 Hz, 1H), 6.84 (d, J=8.8 Hz, 2H), 6.98 (dd, J=7.2, 8.0 Hz, 1H), 7.10 (dd, J=8.0, 8.0 Hz, 1H), 7.56 (d, J=7.2 Hz, 1H), 7.65 (d, J=8.8 Hz, 2H), 7.74 (d, J=8.0 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: 13.5, 17.9, 19.9, 32.5, 37.8, 43.0, 48.6, 55.4, 62.0, 65.4, 111.0, 114.0, 115.9, 123.4, 124.0, 126.9, 127.3, 129.0, 130.1, 144.1, 144.7, 153.7, 163.3, 175.0; high resolution (HR)-MS (ESI) *m/z* Calcd for $C_{33}H_{44}N_2Na_1O_7S_1Si_1$ $[M+Na]^+$ 663.2536. Found 663.2528; IR (neat): ν 2945, 2867, 1775, 1678, 1385, 1355, 1162, 1091, 1016 cm^{-1}.

(±)-3,3-Dibromo-9-((4-methoxyphenyl)sulfonyl)-1,2-dimethyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one (13) To a solution of **9** (38 mg, 0.1 mmol) in AcOEt (0.3 mL) was added $CuBr_2$ (132.5 mg, 0.6 mmol) at room temperature. Then the resulting mixture was heated to reflux and stirred for 1 d under argon. After being cooled to room temperature, H_2O was added to the reaction mixture. The organic layer was washed with water, dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 1/4=ethyl acetate/hexane) to give **13** as a colorless foam (49.7 mg, 92%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.75 (d, J=6.8 Hz, 3H), 1.77 (d, J=6.4 Hz, 3H), 2.38–2.41 (m, 1H), 3.47–3.51 (m, 1H), 3.74 (s, 3H), 6.72 (d, J=8.8 Hz, 2H), 7.32–7.34 (m, 2H), 7.56 (d, J=8.8 Hz, 2H), 8.00–8.02 (m, 1H), 8.11–8.13 (m, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ: 18.1, 22.7, 38.6, 52.5, 55.6, 75.9, 113.5, 114.3, 115.4, 122.0, 125.7, 126.1, 126.5, 128.2, 129.1, 137.9, 154.7, 164.1, 181.8; HR-MS (APCI) *m/z* Calcd for $C_{21}H_{19}Br_2N_1O_4S_1$ $[M+H]^+$ 539.9480. Found 539.9465; IR (neat): ν 2970, 1688, 1591, 1396, 1266, 1180, 1087 cm^{-1}.

3-Bromo-9-((4-methoxyphenyl)sulfonyl)-1,2-dimethyl-9*H*-carbazol-4-ol (11) To a solution of **13** (29 mg, 0.05 mmol) in *N*,*N*-dimethylformamide (DMF) (0.3 mL) was added K_2CO_3 (15 mg, 0.10 mmol, 2.0 equiv.) at room temperature. The mixture was stirred at room temperature for 8 h. The resulting mixture was diluted with CH_2Cl_2 and the organic phase was washed with water, dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 1/5=ethyl acetate/hexane) to give **11** as a yellow solid (19.2 mg, 78%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 2.54 (s, 3H), 3.70 (s, 3H), 3.67 (s, 3H), 5.94 (s, 1H), 6.49 (d, J=8.8 Hz, 2H), 6.98 (d, J=8.8 Hz, 2H), 7.25 (t, J=7.6 Hz, 1H), 7.34 (t, J=7.6 Hz, 1H), 7.84 (d, J=7.6 Hz, 1H), 8.09 (d, J=7.6 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ: 19.8, 20.8, 55.4, 111.6, 113.1, 117.0, 119.4, 122.6, 123.4, 125.9, 126.3, 126.4, 129.1, 129.3, 136.3, 141.4, 141.5, 145.1, 163.2; HR-MS (APCI) *m/z* Calcd for $C_{21}H_{17}Br_1N_1O_4S_1$ $[M-H]^-$ 458.0062. Found 458.0060; IR (neat): ν 2925, 1738, 1593, 1364, 1259, 1166 cm^{-1}.

3-Bromo-1-(methoxymethyl)-9-((4-methoxyphenyl)-sulfonyl)-2-methyl-9*H*-carbazol-4-ol (15) To a solution of **11** (17 mg, 0.036 mmol) in MeOH (0.4 mL) in sealed tube was added AcOEt/toluene (1/1, 0.2 mL), CuBr (10 mg, 0.07 mmol, 2 equiv.), NaOMe (25 mg, 0.36 mmol, 10 equiv.) at room temperature. Then the resulting mixture was heated to 80°C and stirred for 3 d under argon. After being cooled to room temperature, H_2O was added to the reaction mixture. The organic layer was washed with water, dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 1/3=ethyl acetate/hexane) to give **15** as a colorless solid (4.5 mg, 27%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 2.65 (s, 3H), 3.31 (s, 3H), 3.67 (s, 3H), 5.09 (s, 2H), 6.47 (d, J=8.8 Hz, 2H), 6.91 (d, J=8.8 Hz, 2H), 7.23 (t, J=7.6, 1H), 7.36 (t, J=7.6, 1H), 7.84 (d, J=7.6 Hz, 1H), 8.08 (d, J=7.6 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ: 21.1, 55.4, 57.8, 70.3, 112.7, 113.1, 116.5, 119.4, 122.7, 123.5, 125.9, 126.0, 126.5, 128.6, 129.4, 138.5, 141.2, 141.3, 146.5, 163.4; HR-MS (ESI) *m/z* Calcd for $C_{21}H_{20}Br_1N_1Na_1O_5S_1$ $[M+Na]^+$ 512.0143. Found 512.0137; IR (neat): ν 2924, 1726, 1366, 1167, 1087 cm^{-1}.

(±)-3-Methoxy-9-((4-methoxyphenyl)sulfonyl)-1,2-dimethyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one (17), and (±)-3-hydroxy-9-((4-methoxyphenyl)sulfonyl)-1,2-dimethyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one (18) Trimethylsilyl trifluoromethanesulfonate (TMSOTf) (0.75 mL, 4.2 mmol, 2 equiv.) was added dropwise to a solution of **9** (800 mg, 2.1 mmol) and *N*,*N*-diisopropylethylamine (DIEA) (1.4 mL, 8.4 mmol, 4 equiv.) in CH_2Cl_2 (11 mL) at 0°C under argon. The mixture was warmed up to room temperature and stirred for 6 h. Then the mixture was concentrated under reduced pressure. Volatile materials were further removed under reduced pressure (*ca.* 5 mmHg) for 6 h. Then, the residue was dissolved in MeOH and added $PhI(O_2CCF_3)_2$ (1.4 g, 3.2 mmol, 1.5 equiv.) at −50°C. The resulting mixture was stirred for 1 d at the same temperature. The mixture was diluted with CH_2Cl_2 and the organic layer was washed with water, dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (CHROMATOREX-NH, 1/2=ethyl acetate/hexane) to give **17** as a colorless form (676.5 mg, 78%) and **18** as a colorless foam (167.6 mg, 20%). For **17**, ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.91 (d, J=7.2 Hz, 3H), 1.71 (d, J=6.6 Hz, 3H), 2.46–2.79 (m, 1H), 3.65 (s, 3H), 3.73–3.77 (m, 1H), 3.79 (s, 3H), 4.29

(d, J=4.8 Hz, 1H), 6.86 (d, J=9.0 Hz, 2H), 7.33–7.37 (m, 2H), 7.71 (d, J=9.0 Hz, 2H), 8.12–8.14 (m, 1H), 8.18–8.20 (m, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ: 13.7, 20.8, 37.3, 41.5, 55.8, 59.1, 81.3, 114.5, 114.6, 116.3, 121.8, 125.2, 125.5, 125.8, 128.7, 129.5, 136.8, 153.3, 164.2, 193.1; HR-MS (ESI) *m/z* Calcd for $C_{22}H_{23}N_1Na_1O_5S_1$ $[M+Na]^+$ 436.1195. Found 436.1199; IR (neat): ν 2970, 2932, 1680, 1592, 1370, 1267, 1167, 1088 cm^{-1}. For **18**, ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.84 (d, J=6.6 Hz, 3H), 1.71 (d, J=6.6 Hz, 3H), 2.65–2.69 (m, 1H), 3.66 (br s, 1H), 3.78–3.81 (m, 1H), 3.80 (s, 3H), 4.76 (d, J=4.8 Hz, 1H), 6.87 (d, J=8.4 Hz, 2H), 7.33–7.39 (m, 2H), 7.72 (d, J=8.4 Hz, 2H), 8.13–8.17 (m, 2H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ: 13.1, 20.5, 37.1, 43.0, 55.8, 72.3, 114.7, 121.5, 125.3, 125.4, 125.6, 128.8, 129.6, 136.9, 155.0, 164.3, 194.6; HR-MS (ESI) *m/z* Calcd for $C_{21}H_{21}N_1Na_1O_5S_1$ $[M+Na]^+$ 422.1034. Found 422.1038; IR (neat): ν 3055, 2983, 1672, 1595, 1384, 1264, 1169, 731 cm^{-1}.

(±)-3-Methoxy-1,2-dimethyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one (19) To a solution of **17** (41.3 mg, 0.1 mmol) in MeOH (0.2 mL) was added K_2CO_3 (55 mg, 0.4 mmol, 4 equiv.) at room temperature. The mixture was stirred for 4 h at 50°C. The resulting mixture was cooled to room temperature and diluted with CH_2Cl_2. The organic layer was washed with water, dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 2/1=ethyl acetate/hexane) to give **19** as a white solid (20.7 mg, 85%). ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 1.27 (d, J=6.0 Hz, 3H), 1.51 (d, J=6.6 Hz, 3H), 2.15–2.17 (m, 1H), 2.90–2.93 (m, 1H), 3.63 (d, J=10.2 Hz, 1H), 3.68 (s, 3H), 7.24–7.27 (m, 2H), 7.34 (d, J=7.8 Hz, 1H), 8.22 (d, J=6.6 Hz, 1H), 8.35 (br s, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ : 16.0, 17.0, 35.6, 43.6, 59.6, 86.6, 110.8, 111.9, 121.8, 122.7, 123.6, 125.0, 136.2, 152.5, 192.5; HR-MS (ESI) *m/z* caled for $C_{15}H_{17}N_1Na_1O_2$ [M+Na]+ 266.1157. Found 266.1163; IR (neat): ν 3217, 2970, 1737, 1634, 1471, 1373, 1229, 1217 cm^{-1}.

(±)-3-Methoxy-2-methyl-1-methylene-1,2,3,9-tetrahydro-4*H*-carbazol-4-one (20) To a solution of **19** (8 mg, 0.03 mmol) in CH_2Cl_2 (0.2 mL) was added 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (30 mg, 0.13 mmol, 4 equiv.) at room temperature and the mixture was stirred for 1 d. The resulting mixture was taken up in CH_2Cl_2, and the organic phase was washed with water, dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 2/1=ethyl acetate/hexane) to give **20** as a colorless solid (5 mg, 62%). ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 1.31 (d, J=7.2 Hz, 3H), 3.16–3.19 (m, 1H), 3.55 (s, 3H), 3.62 (d, J=6.0 Hz, 1H), 5.47 (d, J=1.2 Hz, 1H), 5.63 (s, 1H), 7.26–7.30 (m, 2H), 7.38 (d, J=7.2 Hz, 1H), 8.22 (d, J=7.2 Hz, 1H), 8.62 (br s, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ: 16.9, 43.0, 58.8, 86.6, 111.1, 111.5, 111.8, 122.2, 122.9, 124.8, 125.1, 136.7, 137.8, 144.1, 191.6; HR-MS (ESI) *m/z* Calcd for $C_{15}H_{16}N_1Na_1O_2$ $[M+Na]^+$ 264.1001. Found 264.1002; IR (neat): ν 2970, 1738, 1726, 1367, 1228, 1217, 1029 cm^{-1}.

3-Methoxy-9-((4-methoxyphenyl)sulfonyl)-1,2-dimethyl-9*H*-carbazol-4-ol (21) To a solution of **17** (165 mg, 0.4 mmol) in tetrahydrofuran (THF) (4 mL) was added NBS (267 mg, 1.5 mmol, 4 equiv.) at room temperature. The mixture was stirred for 12 h. The resulting mixture was dissolved in CH_2Cl_2, and the organic layer was washed with water, dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 1/2=ethyl acetate/hexane) to give **21** as a yellow solid (135 mg, 82%). ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 2.37 (s, 3H), 2.62 (s, 3H), 3.67 (s, 3H), 3.81 (s, 3H), 5.85 (s, 1H), 6.47 (d, J=9.0 Hz, 2H), 6.96 (d, J=9.0 Hz, 2H), 7.24 (t, J=7.2 Hz, 1H), 7.31 (t, J=7.8 Hz, 1H), 7.81 (d, J=7.8 Hz, 1H), 8.07 (d, J=7.2 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ: 13.4, 18.5, 55.3, 61.3, 112.9, 116.8, 119.6, 122.3, 122.7, 125.7, 125.8, 126.3, 129.3, 129.8, 123.0, 137.9, 141.5, 141.5, 143.5, 163.1; HR-MS (ESI) *m/z* Calcd for $C_{22}H_{21}N_1Na_1O_5S_1$ $[M+Na]^+$ 434.1038. Found 434.1035; IR (neat): ν 2970, 2858, 1366, 1170, 1065, 908 cm^{-1}.

3-Methoxy-1,2-dimethyl-9*H*-carbazol-4-ol (2, Carbazomycin B) To a solution of anthracene (90 mg, 0.5 mmol, 5 equiv.) in THF (2 mL) was added Na (excess) at room temperature, and the mixture was stirred for 0.5 h. To this mixture, was added **21** (41.3 mg, 0.1 mmol) in THF (0.2 mL), and the whole mixture was stirred for 1 h. The supernatant was diluted with CH_2Cl_2, and to this mixture was added water. The organic layer was washed with water, dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 1/2=ethyl acetate/hexane) to give carbazomycin B (**2**) as a yellow solid (15.9 mg, 66%). ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 2.38 (s, 3H), 2.40 (s, 3H), 3.83 (s, 3H), 6.02 (s, 1H), 7.22 (t, J=7.2 Hz, 1H), 7.36 (t, J=7.2 Hz, 1H), 7.40 (d, J=7.8 Hz, 1H), 7.78 (br s, 1H), 8.24 (d, J=7.8 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ: 12.8, 13.2, 61.5, 109.3, 109.3, 110.0, 119.5, 122.6, 123.2, 124.8, 127.0, 136.7, 138.4, 139.2, 140.0; HR-MS (ESI) *m/z* Calcd for $C_{15}H_{16}N_1O_2$ $[M+H]^+$ 242.1183. Found 242.1181; IR (neat): ν 3426, 1454, 1411, 750 cm^{-1}.

3,4-Dimethoxy-1,2-dimethyl-9*H*-carbazole (1, Carbazomycin A) To a solution of **2** (6 mg, 0.025 mmol) in acetone (2 mL) was added K_2CO_3 (50 mg, 0.36 mmol, 14 equiv.) and methyl iodide (MeI) (0.3 mL) at room temperature. The mixture was heated under reflux for 5 h. The resulting mixture was diluted with CH_2Cl_2 and the organic layer was washed with water, dried over Na_2SO_4, filtered with a plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 1/10=ethyl acetate/hexane) to give carbazomycin A (**1**) as a pale yellow solid (6 mg, 93%). ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 2.38 (s, 3H), 2.40 (s, 3H), 3.83 (s, 3H), 6.02 (s, 1H), 7.22 (t, J=7.2 Hz, 1H), 7.36 (t, J=7.2 Hz, 1H), 7.40 (d, J=7.8 Hz, 1H), 7.78 (br s, 1H), 8.24 (d, J=7.8 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ: 12.7, 13.7, 60.6, 61.2, 110.3, 113.6, 114.5, 119.6, 122.6, 123.0, 125.1, 128.9, 136.5, 139.5, 144.6, 146.1; HR-MS (ESI) *m/z* Calcd for $C_{16}H_{18}N_1O_2$ $[M+H]^+$ 256.1338. Found 256.1337; IR (neat): ν 3428, 2926, 1454, 1292, 1013 cm^{-1}.

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Conflict of Interest The authors declare no conflict of interest.

Supplementary Materials The online version of this article contains supplementary materials.

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