Total Synthesis of Discorhabdin C: A General Aza Spiro Dienone Formation from O-Silylated Phenol Derivatives Using a Hypervalent Iodine Reagent

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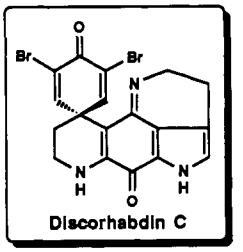
Abstract: Hypervalent iodine oxidation of O-silylated phenols bearing various types of aminoquinones at the para position in 2,2,2-trifluoroethanol gave azacarbocyclic spiro dienones in good yields. Using this method, the first total synthesis of discorhabdin C, which was isolated from the sponge of *Latrunculia* du Bocage in New Zealand, was achieved.

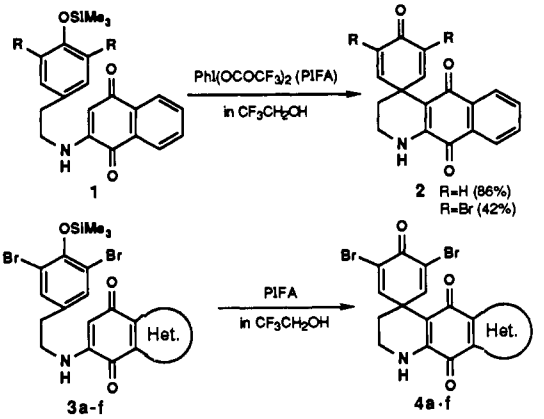
The discorhabdin alkaloids were isolated from the sponge of *Latrunculia* du Bocage in New Zealand[1,2] and the closely related prianosins from the Okinawan sponge *Prianos melanos*.[3] Discorhabdin C is the first of the discorhabdin alkaloids reported and exhibits extreme toxicity toward tumor cells (P388 and L1210 leukemia).[2] This novel molecule has a unique molecular skeleton incorporating an azacarbocyclic dibromospirocyclohexadienone system and a highly oxidized indole system in which the tryptamine side chain is cyclized onto an indoloquinone. Recently, much attention has been paid to the total synthesis of this challenging target.[4-6] As a part of our continuous studies on hypervalent iodine chemistry,[7] we have reported a general route to the spirocyclic quinones **2** by an oxidative coupling reaction of the O-silylated phenolic aminoquinone **1** using phenyliodine(III) bis(trifluoroacetate) (PIFA)[5] and applied this method to a general synthesis of azacarbocyclic spiro dienone systems (**4a-f**) from O-silylated phenol derivatives (**3a-f**) bearing both electron-poor and electron-rich aminoquinones at the para position,[8] as exemplified in eq 1.

We now report in detail the results of these investigations and the first total synthesis of discorhabdin C using this spiro annulation reaction.

Results and Discussion

A General Aza Spiro Dienone Formation from O-Silylated Phenol Derivatives Using a Hypervalent Iodine Reagent. Although intramolecular spirocyclization of phenols to carbocyclic dienones[9] by aryl participation of a neighboring phenoxy group,[10] decomposition of phenolic diazoketones,[11] oxidative phenol couplings,[12] or phenoxy-enoxy radical couplings[13] has been well-documented, effective synthesis of azacarbocyclic spiro dienone systems is quite rare.[14] We recently developed a novel route to azacarbocyclic spiro dienones (**2**) from O-silylated phenolic derivatives (**1**) bearing aminoquinones at the para position.[5] The significant points of this reaction are the protection of the phenolic OH group by a silyl group and the use of PIFA in 2,2,2-trifluoroethanol. This oxidative cyclization is useful for the preparation of various types of azacarbocyclic spiro dienones (**4a-f**).





eq 1

The starting O-silylated phenol derivatives (**3a-f**) were readily prepared by the reaction of tyramine with the corresponding quinone derivatives (**5a-f**), followed by the treatment of the para-substituted phenols (**6a-f**) with O-silylated ketene acetal[15]

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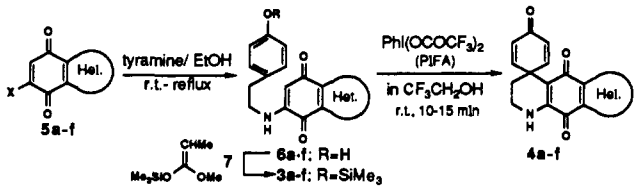
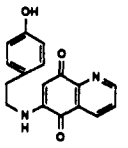
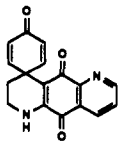
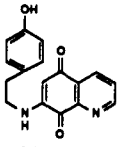
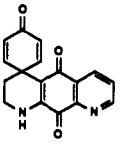
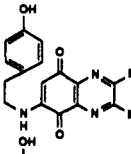
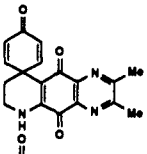
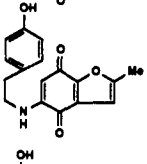
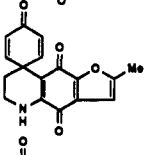
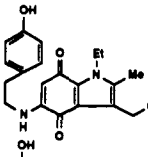
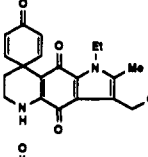
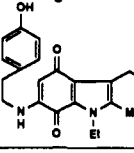
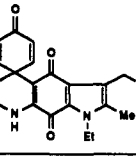
Table I. Syntheses of Azacarbocyclic Spiro Dienones



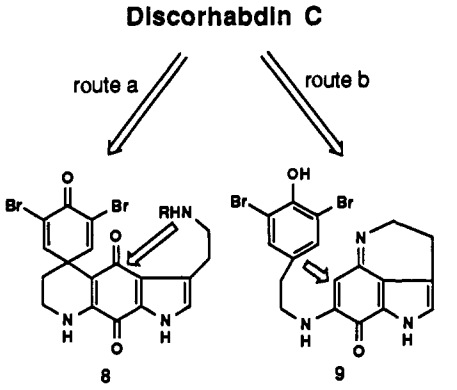
Run	Substrate	Product	Yield (%)
1	 6a	 4a	53
2	 6b	 4b	64
3	 6c	 4c	57
4	 6d	 4d	53
5	 6e	 4e	71
6	 6f	 4f	86

7 in CH_2Cl_2 under nitrogen, and were subsequently treated with PIFA to give the corresponding azacarbocyclic spiro dienones (**4a–f**) in 53–86% overall yields. The results are listed in Table I. Having achieved the success of the model study (run 6), our attention was finally focused on the total synthesis of discorhabdin C.

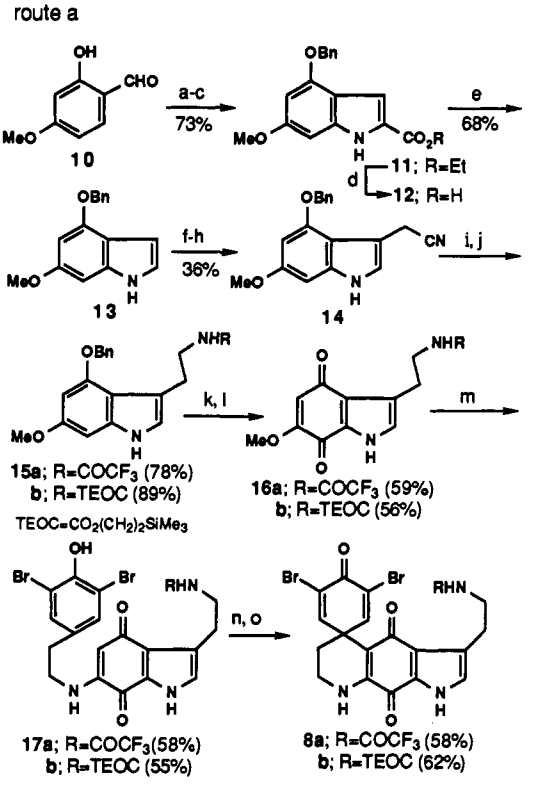
Total Synthesis of Discorhabdin C. The problems in the synthesis of discorhabdin C are the construction of highly fused ring systems and the formation of an acid-sensitive indoloquinone imine. Our approaches to the total synthesis of discorhabdin C are illustrated in Scheme I. One approach involves imine formation between the tryptamine nitrogen and the indoloquinone carbonyl as the final step of the synthesis (route a). Another approach involves the oxidative coupling of a preformed indoloquinone imine by PIFA as the final synthetic transformation (route b).

A reasonable starting material for the synthesis of **8** in route a is 2-hydroxy-4-methoxybenzaldehyde (**10**). Benzylation of **10** followed by condensation with ethyl azidoacetate in ethanolic sodium ethoxide gave the vinyl azide, which was decomposed in boiling xylene to give the 2-(ethoxycarbonyl)indole **11**.[16] Hydrolysis of the ester group of **11** gave the indolecarboxylic acid **12**, which was decarboxylated under thermal conditions to give the 2-unsubstituted indole **13**. Treatment of indole **13** with dimethyl(methylene)ammonium iodide[17] gave the 3-(dimethylamino)methyl derivative. The dimethylamino group was replaced by the cyano group with NaCN via the quaternary salt to yield the 3-(cyanomethyl)indole **14**. Catalytic hydrogenation of the cyano group of **14** followed by protection of the resulting amino group with the trifluoroacetyl and the [(trimethylsilyl)ethoxy]carbonyl (TEOC) groups afforded **15a** and **15b**, respectively. Debenzylation of **15a,b** followed by oxidation with Fremy's salt gave the corresponding quinones (**16a,b**). Treatment of **16a,b** with 3,5-dibromotyramine hydrobromide gave the phenol derivatives **17a,b**. Silylation of **17a,b** with **7** followed by oxidation with PIFA

Scheme I



Scheme II[a]



[a] Reagents: (a) $C_6H_5CH_2Br/K_2CO_3/EtOH$/reflux. (b) $N_3CH_2CO_2Et/NaOEt/EtOH$/−15 °C. (c) Xylene/reflux. (d) KOH/EtOH/reflux. (e) Copper chromite/quinoline/215 °C. (f) $CH_2{=}N^+Me_2I^-/CH_2Cl_2$/room temperature. (g) CH_3I/0 °C. (h) NaCN/H_2O/80 °C. (i) H_2/Raney Ni/NH_3/EtOH/3.3 atm. (j) $CF_3COSEt/NaOMe/MeOH$; p-$O_2NC_6H_4OCO_2(CH_2)_2SiMe_3$/NaOEt/EtOH/0 °C. (k) H_2/10% Pd–C/EtOH/3.3 atm. (l) Fremy's salt/KH_2PO_4/acetone–H_2O. (m) 3,5-Dibromotyramine HBr/Et_3N/EtOH/reflux. (n) $MeCH{=}C(OMe)(OSiMe_3)/CH_2Cl_2$/room temperature. (o) $PhI(OCOCF_3)_2$ (PIFA)/CF_3CH_2OH/room temperature.

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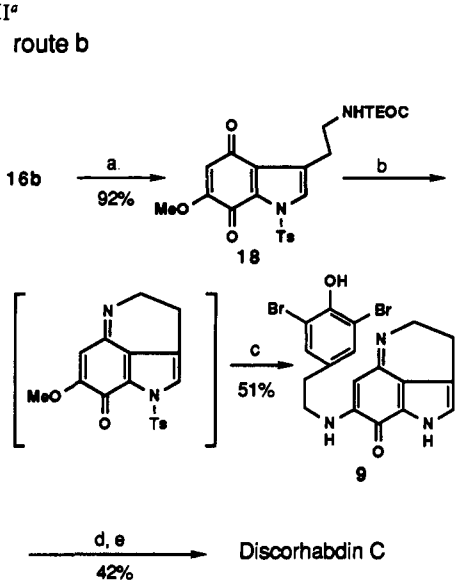
Scheme III[a]



[a] Reagents: (a) TsCl/*t*-BuOK/THF. (b) Anhydrous TsOH/CH_3CN. (c) 3,5-Dibromotyramine HBr/$NaHCO_3$/EtOH/reflux. (d) $MeCH{=}C(OMe)(OSiMe_3)/CH_2Cl_2$/room temperature. (e) $PhI(OCOCF_3)_2$ (PIFA)/CF_3CH_2OH/room temperature.

resulted in the desired intermediates **8a,b**. Unfortunately, all attempts to effect the final imine formation between the tryptamine nitrogen and the indoloquinone carbonyl in these types of intermediates (**8a,b**) were unsuccessful (Scheme II).[6,18]

An alternative approach (route b) in which phenolic coupling of the previously produced aminoindoloquinone imine **9** is employed in the final step accomplished the first total synthesis of discorhabdin C. This efficient route may be used for the synthesis of a wide variety of hitherto inaccessible sulfur-containing discorhabdin and prianosin alkaloids (Scheme III). Highlights include the following: (i) successful imine formation of an indoloquinone system by both protection of indoloquinone nitrogen with the electron-withdrawing (EWG) tosyl group and transformation of the 6-amino group into the methoxy group on the quinone moiety; (ii) simultaneous substitution of the 6-methoxy group by 3,5-dibromotyramine and clean deprotection of the *N*-tosyl group; and (iii) efficient oxidative coupling of phenolic aminoindoloquinone imine to the desired discorhabdin C.

Direct formation of the indoloquinone imine from **16b** by deprotection of the [2-(trimethylsilyl)ethoxy]carbonyl (TEOC) group followed by condensation under various acidic or basic dehydrative conditions failed. The synthesis of quinone imines (or quinone imine monoacetals) is, in general, complicated and has recently been achieved only by electrochemical[19] or hypervalent iodine oxidation of aniline derivatives.[20] After many unsuccessful trials,[18] the direct imine formation from indoloquinone was achieved by protection of the indoloquinone nitrogen with the tosyl group followed by an acidic dehydrative treatment. Treatment of **16b** with *p*-toluenesulfonyl chloride gave the *N*-tosylate (**18**). Deprotection of the TEOC group of **18** with *p*-toluenesulfonic acid in acetonitrile in the presence of 3A molecular sieves and sodium bicarbonate yielded an unstable indoloquinone imine, which was subjected to the following one-pot transformation without further purification. When treated with 3,5-dibromotyramine hydrobromide in ethanol, the indoloquinone imine underwent a facile substitution reaction at the C-6 position and subsequent detosylation to give the phenolic aminoindoloquinone imine **9**. Conversion of **9** into its corresponding silyl ether using **7** and a subsequent oxidative coupling reaction using PIFA gave rise to discorhabdin C, which was in all respects identical with a sample generously provided by Dr. N. B. Perry.

In summary, a reasonably concise total synthesis, considered as a presumed biogenetic route,[21] was achieved for the first time.

Experimental Section

All melting points were uncorrected. Infrared (IR) absorption spectra were recorded on a JASCO HPIR-102 spectrophotometer with $CHCl_3$ as a solvent. Proton nuclear magnetic resonance (^1H NMR) spectra were measured on JEOL JNM-FX90Q (90 MHz), JEOL JNM-EX270 (270 MHz), and JEOL JNM-GX500 (500 MHz) spectrometers with $CDCl_3$ as a solvent unless otherwise noted that tetramethylsilane was the internal standard. Mass spectra (MS) and high-resolution MS were obtained using ESCO EMD-05A and JEOL JMS-D300 mass spectrometers. UV spectra were taken on a SHIMADZU 2100 UV/VIS spectrometer. E. Merck silica gel 60 (70–230 mesh ASTM) was used for column chromatography, and E. Merck precoated TLC plates, silica gel F_{254}, was used for preparative thin-layer chromatography (prep. TLC). Organic layers were dried with anhydrous $MgSO_4$. PIFA is commercially available.

6-[2-(4-Hydroxyphenyl)ethylamino]quinoline-5,8-dione (6a). To a stirred suspension of quinoline-5,8-dione[22] (50 mg, 0.314 mmol) and nickel(II) chloride (40 mg, 0.314 mmol)[23] in ethanol (20 mL) was added tyramine (130 mg, 0.940 mmol) at room temperature. The mixture was stirred for 15 min under the same conditions and then evaporated. The residue was purified by column chromatography with ethyl acetate to give **6a** (67 mg, 72%), which was recrystallized from ethyl acetate to give a pure sample as red crystals: mp 228–231 °C; UV (MeOH) λ_{max} 229 (ϵ 17 500), 269 (9300) nm; IR (KBr) 3370, 3260, 2930, 2860, 1690, 1605, 1570, 1515 cm^{-1}; ^1H NMR (CD_3OD) δ 2.88 (t, 2 H, J = 7.3 Hz, $ArCH_2$), 3.47 (t, 2 H, J = 7.3 Hz, $ArCH_2CH_2$), 5.89 (s, 1 H, 7-CH), 6.72 (d, 2 H, J = 8.6 Hz, ArH), 7.09 (d, 2 H, J = 8.6 Hz, ArH), 7.71 (dd, 1 H, J = 4.9, 7.6 Hz, 3-CH), 8.43 (dd, 1 H, J = 1.5, 4 Hz, 4-CH), 8.90 (dd, 1 H, J = 1.5, 4 Hz, 2-CH). Anal. Calcd for $C_{17}H_{14}N_2O_3$: C, 69.37; H, 4.80; N, 9.52. Found: C, 69.32; H, 4.77; N, 9.52.

7-[2-(4-Hydroxyphenyl)ethylamino]quinoline-5,8-dione (6b). A suspension of quinoline-5,8-dione (20.0 mg, 0.126 mmol) and tyramine (17.2 mg, 0.126 mmol) in ethanol (2 mL) was stirred at room temperature for 15 min. The mixture was evaporated, and the residue was purified by column chromatography with ethyl acetate to give **6b** (14.8 mg, 40%) and **6a** (14.0 mg, 38%). **6b** was recrystallized from ethyl acetate to give a pure sample as red crystals: mp 272–274 °C; UV (MeOH) λ_{max} 227 (ϵ 16 800), 276 (8200) nm; IR (KBr) 3300, 2930, 2860, 1700, 1600, 1560, 1515 cm^{-1}; ^1H NMR (CD_3OD) δ 2.97 (t, 2 H, J = 7.3 Hz, $ArCH_2$), 3.71 (t, 2 H, J = 7.3 Hz, $ArCH_2CH_2$), 5.96 (s, 1 H, 6-CH), 6.72 (d, 2 H, J = 8.3 Hz, ArH), 7.09 (d, 2 H, J = 8.3 Hz, ArH), 7.69 (dd, 1 H, J = 4.6, 7.7 Hz, 3-CH), 8.36 (dd, 1 H, J = 1.6, 7.7 Hz, 4-CH), 8.84 (dd, 1 H, J = 1.6, 4.6 Hz, 2-CH). Anal. Calcd for $C_{17}H_{14}N_2O_3$: C, 69.37; H, 4.80; N, 9.52. Found: C, 69.29; H, 4.75; N, 9.43.

2,3-Dimethyl-6-[2-(4-hydroxyphenyl)ethylamino]quinoxaline-5,8-dione (6c). To a stirred solution of 2,3-dimethylquinoxaline-5,8-dione[24] (50.0 mg, 0.266 mmol) in ethanol (5 mL) was added tyramine (36.5 mg, 0.266 mmol) at room temperature. The mixture was stirred for 20 min under the same conditions and then evaporated. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **6c** (41.8 mg, 49%), which was recrystallized from ethanol to give a pure sample as orange crystals: mp 236–238 °C; UV (MeOH) λ_{max} 226 (ϵ 24 700), 304 (15 400) nm; IR 3380, 3030, 2850, 1690, 1605, 1515 cm^{-1}; ^1H NMR (CD_3OD) δ 2.68 (s, 3 H, CH_3), 2.70 (s, 3 H, CH_3), 2.87 (t, 2 H, J = 7 Hz, $ArCH_2$), 3.46 (t, 2 H, J = 7 Hz, $ArCH_2CH_2$), 5.84 (s, 1 H, 7-CH), 6.71 (d, 2 H, J = 9 Hz, ArH), 7.08 (d, 2 H, J = 9 Hz, ArH). Anal. Calcd for $C_{18}H_{17}N_3O_3$: C, 66.86; H, 5.30; N, 13.00. Found: C, 66.74; H, 5.27; N, 12.74.

5-[2-(4-Hydroxyphenyl)ethylamino]-2-methylbenzofuran-4,7-dione (6d). To a stirred suspension of tyramine (16.2 mg, 0.118 mmol) in ethanol was added 2-methylbenzofuran-4,7-dione[25] (6.4 mg, 0.0395 mmol) at room temperature. The mixture was stirred for 10 min under

(18) The failure of the imine formation of **8** may be due to the weak carbonyl character of indoloquinone, since the two electron-donating nitrogen groups are present at the β-position of the cyclohexadienone group. Attempts to protect these nitrogens with electron-withdrawing groups failed because of the instability of **8** under basic conditions such as lithium diisopropylamide and sodium hydride.

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the same conditions and then evaporated. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **6d** (6.2 mg, 53%), which was recrystallized from ethyl acetate–*n*-hexane to give a pure sample as purple crystals: mp 220–222 °C; UV (MeOH) λ_{max} 215 (ϵ 30700), 244 (19800), 336 (8500) nm; IR (CH_3CN) 3540, 2950, 1630, 1580 cm^{-1}; ^1H NMR (CD_3OD) δ 2.22 (s, 3 H, CH_3), 2.84 (t, 2 H, J = 7 Hz, $ArCH_2$), 3.39 (t, 2 H, J = 7 Hz, $ArCH_2CH_2$), 5.27 (s, 1 H, 6-CH), 6.73 (d, 2 H, J = 9 Hz, ArH), 7.07 (d, 2 H, J = 9 Hz, ArH), 7.53 (s, 1 H, 3-CH). Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.67; H, 5.08; N, 4.71. Found: C, 68.46; H, 4.98; N, 4.52.

3-(Acetoxymethyl)-1-ethyl-5-[2-(4-hydroxyphenyl)ethylamino]-2-methylindole-4,7-dione (6e). A suspension of 3-(acetoxymethyl)-1-ethyl-5-methoxy-2-methylindole-4,7-dione[26] (21.8 mg, 0.075 mmol) and tyramine (15.4 mg, 0.113 mmol) in ethanol (1.5 mL) was heated at reflux for 5 h. The reaction mixture was quenched with water and extracted with methylene chloride. The combined organic layers were washed with saturated aqueous sodium chloride, dried, and evaporated. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **6e** (22.3 mg, 75%), which was recrystallized from chloroform–*n*-hexane to give a pure sample as a red purple solid: mp 97–100 °C; UV (MeOH) λ_{max} 244 (ϵ 17900), 315 (10700) nm; IR (KBr) 3400–3300, 1735, 1660, 1590, 1500, 1470–1440, 1380, 1360 cm^{-1}; ^1H NMR δ 1.34 (t, 3 H, J = 7.3 Hz, CH_2CH_3), 2.05 (s, 3 H, $OCOCH_3$), 2.27 (s, 3 H, 2-CH_3), 2.86 (t, 2 H, J = 7.3 Hz, $ArCH_2$), 3.48 (q, 2 H, J = 7.3 Hz, $ArCH_2CH_2$), 4.40 (q, 2 H, J = 7.3 Hz, CH_2CH_3), 5.17 (s, 1 H, 6-CH), 5.22 (s, 2 H, CH_2OAc), 5.86 (br s, 1 H, NH), 6.80 (d, 2 H, J = 8.5 Hz, ArH), 7.07 (d, 2 H, J = 8.5 Hz, ArH). Anal. Calcd for $C_{22}H_{24}N_2O_5$: C, 66.65; H, 6.10; N, 7.07. Found: C, 66.49; H, 6.08; N, 7.03.

3-(Acetoxymethyl)-1-ethyl-6-[2-(4-hydroxyphenyl)ethylamino]-2-methylindole-4,7-dione (6f). A suspension of 3-(acetoxymethyl)-1-ethyl-6-methoxy-2-methylindole-4,7-dione (29.1 mg, 0.100 mmol) and tyramine (20.6 mg, 0.15 mmol) in ethanol (2 mL) was heated at reflux for 6.5 h. The reaction mixture was evaporated in vacuo, and the residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **6f** (21.6 mg, 55%), which was recrystallized from ethanol to give a pure sample as red prisms: mp 211–213 °C; UV (MeOH) λ_{max} 243 (ϵ 29700), 363 (14600) nm; IR (KBr) 3300, 1715, 1655, 1600, 1585, 1505, 1480, 1440 cm^{-1}; ^1H NMR δ 1.36 (t, 3 H, J = 7.3 Hz, CH_2CH_3), 2.08 (s, 3 H, $OCOCH_3$), 2.34 (s, 3 H, 2-CH_3), 2.90 (t, 2 H, J = 6.7 Hz, $ArCH_2$), 3.35 (t, 2 H, J = 6.7 Hz, $ArCH_2CH_2$), 4.35 (q, 2 H, J = 7.3 Hz, CH_2CH_3), 5.26 (s, 1 H, 5-CH), 5.35 (s, 2 H, CH_2OAc), 5.85 (br s, 1 H, NH), 6.83 (d, 2 H, J = 8.5 Hz, ArH), 7.10 (d, 2 H, J = 8.5 Hz, ArH). Anal. Calcd for $C_{22}H_{24}N_2O_5$: C, 66.65; H, 6.10; N, 7.07. Found: C, 66.62; H, 5.92; N, 7.05.

General Procedure for the Oxidation of O-Silylated Phenol Derivatives (6a–f) to Azacarbocyclic Spiro Dienones (4a–f). To a stirred suspension of phenol (**6**, 0.100 mmol) in CH_2Cl_2 (7.5 mL) was added dropwise *O*-trimethylsilyl ketene acetal **7** (0.500 mmol) at room temperature for 3 h under nitrogen. The mixture was concentrated in vacuo to give the O-silylated phenol **3**, which was dissolved in 2,2,2-trifluoroethanol (7.5 mL), and PIFA (0.100 mmol) was added to the mixture for 15 min under the same conditions. The reaction mixture was concentrated in vacuo, and the residue was purified by column chromatography to give the azacarbocyclic spiro dienone **4** in considerable yield.

5,6,7,8,9,10-Hexahydropyrido[2,3-*g*]quinoline-5,10-dione-9-spiro-4′-cyclohexa-2′,5′-dien-1′-one (4a). Reactants: **6a** (26.5 mg, 0.0900 mmol); **7** (75 mg, 0.469 mmol); CH_2Cl_2 (4 mL); PIFA (46.5 mg, 0.108 mmol); CF_3CH_2OH (5 mL). **4a** (14.0 mg, 53%): red crystals; mp 235–237 °C (from $CHCl_3$–*n*-hexane); UV (MeOH) λ_{max} 231 (ϵ 24400), 249 (21100), 464 (2640) nm; IR 3400, 2920, 2850, 1660, 1600, 1570, 1505 cm^{-1}; ^1H NMR δ 1.98 (t, 2 H, J = 6 Hz, CH_2CH_2NH), 3.60–3.68 (m, 2 H, CH_2NH), 6.33 (br s, 1 H, NH), 6.39 (d, 2 H, J = 10 Hz, 2′,6′-CH), 6.92 (d, 2 H, J = 10 Hz, 3′,5′-CH), 7.55 (m, 1 H, 3-CH), 8.34 (d, 1 H, J = 8 Hz, 4-CH), 8.97 (d, 1 H, J = 4 Hz, 2-CH). Anal. Calcd for $C_{17}H_{12}N_2O_3$: C, 69.85; H, 4.14; N, 9.59. Found: C, 69.57; H, 4.12; N, 9.52.

5,6,7,8,9,10-Hexahydropyrido[3,2-*g*]quinoline-5,10-dione-6-spiro-4′-cyclohexa-2′,5′-dien-1′-one (4b). Reactants: **6b** (6.3 mg, 0.0214 mmol); **7** (25 mg, 0.156 mmol); CH_2Cl_2 (0.8 mL); PIFA (11.0 mg, 0.0257 mmol); CF_3CH_2OH (0.8 mL). **4b** (4.0 mg, 64%): red crystals; mp 220 °C dec (from $CHCl_3$–*n*-hexane); UV (MeOH) λ_{max} 235 (ϵ 23300), 248 (23100), 298 (11300) nm; IR 3400, 2920, 2850, 1660, 1600, 1565, 1515 cm^{-1}; ^1H NMR δ 2.30 (t, 2 H, J = 6 Hz, CH_2CH_2NH), 3.62–3.66 (m, 2 H, CH_2NH), 6.42 (d, 2 H, J = 10 Hz, 2′,6′-CH), 6.54 (br s, 1 H, NH), 6.95 (d, 2 H, J = 10 Hz, 3′,5′-CH), 7.64 (dd, 1 H, J = 4, 8 Hz, 3-CH), 8.36 (dd, 1 H, J = 2, 8 Hz, 4-CH), 8.91 (dd, 1 H, J = 2, 4 Hz, 2-CH); HRMS calcd for $C_{17}H_{12}N_2O_3$ (M^+) 292.0848, found 292.0848.

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2,3-Dimethyl-9*H*-piperidino[3,2-*g*]quinoxaline-5,10-dione-6-spiro-4′-cyclohexa-2′,5′-dien-1′-one (4c). Reactants: **6c** (22.0 mg, 0.0680 mmol); **7** (55 mg, 0.344 mmol); CH_2Cl_2 (3 mL); PIFA (35.1 mg, 0.081 mmol); CF_3CH_2OH (3 mL). **4c** (12.4 mg, 57%): red plates; mp 254–257 °C (from $CHCl_3$); UV (MeOH) λ_{max} 219 (ϵ 19400), 249 (16900), 305 (11800) nm; IR 3400, 3010, 2940, 2870, 1690, 1660, 1590, 1550, 1540, 1520 cm^{-1}; ^1H NMR δ 1.99 (t, 2 H, J = 6 Hz, CH_2CH_2NH), 2.73 (s, 6 H, 2,3-CH_3), 3.60–3.68 (m, 2 H, CH_2NH), 6.39 (d, 2 H, J = 10 Hz, 2′,6′-CH), 6.50 (br s, 1 H, NH), 6.91 (d, 2 H, J = 10 Hz, 3′,5′-CH). Anal. Calcd for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.02; H, 4.71; N, 12.96.

2-Methyl-4,5,6,7,8,9-hexahydrofuro[2,3-*g*]quinoline-4,9-dione-8-spiro-4′-cyclohexa-2′,5′-dien-1′-one (4d). Reactants: **6d** (6.7 mg, 0.0225 mmol); **7** (20 mg, 0.125 mmol); CH_2Cl_2 (1.5 mL); PIFA (11.6 mg, 0.0270 mmol); CF_3CH_2OH (1.5 mL). **4d** (3.5 mg, 53%): purple crystals; mp 251–253 °C (from $CHCl_3$–*n*-hexane); UV (MeOH) λ_{max} 222 (ϵ 26600), 255 (29100), 337 (6800) nm; IR (CH_3CN) 3400, 3010, 2950, 2860, 1660, 1570, 1530, 1515 cm^{-1}; ^1H NMR (CD_3OD) δ 1.89 (t, 2 H, J = 6 Hz, CH_2CH_2NH), 2.23 (s, 3 H, 2-CH_3), 3.66 (t, 2 H, J = 6 Hz, CH_2NH), 6.25 (d, 2 H, J = 10 Hz, 2′,6′-CH), 7.11 (d, 2 H, J = 10 Hz, 3′,5′-CH), 7.50 (s, 1 H, 3-CH); HRMS calcd for $C_{17}H_{13}NO_4$ (M^+) 295.0832, found 295.0842.

3-(Acetoxymethyl)-1-ethyl-2-methyl-4,5,6,7,8,9-hexahydropyrrolo-[2,3-*g*]quinoline-8-spiro-4′-cyclohexa-2′,5′-dien-1′-one (4e). Reactants: **6e** (9.5 mg, 0.0240 mmol); **7** (28 mg, 0.175 mmol); CH_2Cl_2 (1 mL); PIFA (10.3 mg, 0.0240 mmol); CF_3CH_2OH (3 mL). **4e** (6.6 mg, 71%): purple prisms; mp 234–236 °C (from $CHCl_3$–*n*-hexane); UV (MeOH) λ_{max} 252 (ϵ 36000), 317 (16200), 356 (sh) nm; IR (KBr) 3350, 1720, 1655, 1615, 1580, 1505 cm^{-1}; ^1H NMR δ 1.27 (t, 3 H, J = 7.3 Hz, CH_2CH_3), 1.84–1.87 (m, 2 H, CH_2CH_2NH), 2.05 (s, 3 H, $OCOCH_3$), 2.25 (s, 3 H, 2-CH_3), 3.49–3.53 (m, 2 H, CH_2NH), 4.32 (q, 2 H, J = 7.3 Hz, CH_2CH_3), 5.22 (s, 2 H, CH_2OAc), 6.34 (d, 2 H, J = 10.0 Hz, 2′,6′-CH), 6.94 (d, 2 H, J = 10.0 Hz, 3′,5′-CH). Anal. Calcd for $C_{22}H_{22}N_2O_5$: C, 66.99; H, 5.62; N, 7.10. Found: C, 66.98; H, 5.58; N, 7.07.

3-(Acetoxymethyl)-1-ethyl-2-methyl-4,5,6,7,8,9-hexahydropyrrolo-[3,2-*g*]quinoline-5-spiro-4′-cyclohexa-2′,5′-dien-1′-one (4f). Reactants: **6f** (9.0 mg, 0.0230 mmol); **7** (28 mg, 0.175 mmol); CH_2Cl_2 (1 mL); PIFA (9.8 mg, 0.0230 mmol); CF_3CH_2OH (3 mL). **4f** (7.7 mg, 86%): purple needles; mp 200–201 °C (from $CHCl_3$–*n*-hexane); UV (MeOH) λ_{max} 246 (ϵ 50800), 320 (16000), 359 (19100) nm; IR 3330, 1735, 1655, 1615, 1575, 1540 cm^{-1}; ^1H NMR δ 1.35 (t, 3 H, J = 7.3 Hz, CH_2CH_3), 1.83–1.86 (m, 2 H, CH_2CH_2NH), 2.02 (s, 3 H, $OCOCH_3$), 2.29 (s, 3 H, 2-CH_3), 3.50–3.54 (m, 2 H, CH_2NH), 4.33 (q, 2 H, J = 7.3 Hz, CH_2CH_3), 5.27 (s, 2 H, CH_2OAc), 6.34 (d, 2 H, J = 10.0 Hz, 2′,6′-CH), 6.95 (d, 2 H, J = 10.0 Hz, 3′,5′-CH). Anal. Calcd for $C_{22}H_{22}N_2O_5$: C, 66.99; H, 5.62; N, 7.10. Found: C, 66.94; H, 5.53; N, 7.06.

Ethyl 4-(Benzyloxy)-6-methoxyindole-2-carboxylate (11). To a stirred solution of 2-hydroxy-4-methoxybenzaldehyde (**10**) (0.81 g, 5.30 mmol) and potassium carbonate (2.20 g, 15.9 mmol) in ethanol (100 mL) was added benzyl bromide (0.95 mL, 7.95 mmol) at room temperature. The mixture was then heated at reflux for 10 h. The mixture was concentrated in vacuo, and the residue was dissolved in ether and washed with saturated aqueous sodium chloride, 5% aqueous NaOH, and water. The organic layers were dried and evaporated to give the crude benzyl ether (1.28 g, quant). A solution of the benzyl ether (1.28 g, 5.3 mmol) and ethyl azidoacetate (4.19 g, 32.5 mmol) in THF (11 mL) was added dropwise to a cooled solution of sodium ethoxide obtained from sodium (0.748 g, 32.5 mmol) in ethanol (24 mL), while maintaining the temperature in the range of −20 to −10 °C. The mixture was stirred at −15 °C for 3 h and then at 4 °C for 12 h. The mixture was warmed to room temperature and evaporated. The residue was poured into a saturated ammonium chloride solution (100 mL) and extracted with ethyl acetate (4 × 200 mL). The organic layer was washed with water (2 × 300 mL), dried, and evaporated to give the crude vinyl azide ester as a red brownish solid. A suspension of the crude azido ester (2.84 g) in xylene (90 mL) was heated rapidly to reflux. After 3 h at reflux, the solution was cooled to room temperature and evaporated. The residue was purified by column chromatography to give **11** (1.06 g, 73%), which was recrystallized from ethyl acetate to give a pure sample as colorless plates: mp 164–165 °C; IR 3475, 3325, 3000, 2950, 1690, 1630, 1590, 1520 cm^{-1}; ^1H NMR δ 1.39 (t, 3 H, J = 7 Hz, $CO_2CH_2CH_3$), 3.83 (s, 3 H, OCH_3), 4.37 (q, 2 H, J = 7 Hz, $CO_2CH_2CH_3$), 5.16 (s, 2 H, OCH_2Ph), 6.26 (d, 1 H, J = 2 Hz, 7-CH), 6.44 (s, 1 H, 5-CH), 7.31–7.33 (m, 1 H, 3-CH), 7.34 (d, 1 H, J = 7 Hz, ArH), 7.40 (t, 2 H, J = 7 Hz, ArH), 7.48 (d, 2 H, J = 7 Hz, ArH), 8.80 (br s, 1 H, 1-NH). Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 69.91; H, 5.87; N, 4.27.

4-(Benzyloxy)-6-methoxyindole-2-carboxylic Acid (12). Compound **11** (2.00 g, 6.20 mmol) was heated at reflux for 1.5 h with ethanolic potassium hydroxide (720 mg, in 9 mL). The mixture was acidified with

10% hydrochloric acid and extracted with ethyl acetate (30 × 3 mL). The organic layer was washed with water (30 × 2 mL), dried, and evaporated. The residue was purified by column chromatography to give **12** (1.70 g, 93%), which was recrystallized from ethyl acetate to give a pure sample as colorless crystals: mp 196–197 °C; IR (KBr) 3400, 2875, 2820, 1665, 1625, 1585, 1525 cm^{-1}; ^1H NMR (in CD_3OD) δ 3.80 (s, 3 H, OCH_3), 5.16 (s, 2 H, OCH_2Ph), 6.24 (s, 1 H, 7-CH), 6.53 (s, 1 H, 5-CH), 7.20 (s, 1 H, 3-CH), 7.32 (d, 1 H, J = 7 Hz, ArH), 7.38 (t, 2 H, J = 7 Hz, ArH), 7.48 (d, 2 H, J = 7 Hz, ArH). Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.67; H, 5.08; N, 4.71. Found: C, 68.72; H, 5.07; N, 4.54.

4-(Benzyloxy)-6-methoxyindole (13). A suspension of 4-(benzyloxy)-6-methoxyindole-2-carboxylic acid (**12**) (4.00 g, 1.35 mmol) and copper chromite (270 mg) in quinoline (13.5 mL) was heated at 230 °C (bath temp) for 3 h. The mixture was poured into water and repeatedly extracted with methylene chloride. The organic layer was washed with 2 N hydrochloric acid, saturated sodium bicarbonate, and water, dried, and evaporated. The residue was purified by column chromatography to give **13** (2.50 g, 73%), which was recrystallized from ethyl acetate–*n*-hexane to give a pure sample as colorless crystals: mp 95–96 °C; IR 3490, 3010, 2960, 2950, 2910, 1625, 1590, 1510 cm^{-1}; ^1H NMR δ 3.80 (s, 3 H, OCH_3), 5.18 (s, 2 H, OCH_2Ph), 6.30 (d, 1 H, J = 2 Hz, 7-CH), 6.49 (s, 1 H, 5-CH), 6.61–6.63 (m, 1 H, 3-CH), 6.97–7.00 (m, 1 H, 2-CH), 7.32 (d, 1 H, J = 7 Hz, ArH), 7.38 (t, 2 H, J = 7 Hz, ArH), 7.49 (d, 2 H, J = 7 Hz, ArH), 8.01 (br s, 1 H, 1-NH). Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.51; H, 5.94; N, 5.39.

[4-(Benzyloxy)-6-methoxy-3-indolyl]acetonitrile (14). To a solution of **13** (868 mg, 3.43 mmol) in anhydrous methylene chloride at room temperature were added *N,N*-dimethylmethyleneammonium iodide (828 mg, 4.48 mmol) and acetic acid (8 mL). The mixture was stirred for 2 h under the same conditions and then evaporated. After dilution with water, the mixture was made strongly basic (pH > 11) with 4 N sodium hydroxide and cooling (ice–water). The mixture was extracted with methylene chloride, and the combined organic layers were washed with water, dried over potassium carbonate, and evaporated to give the crude 3-(dimethylamino)methyl compound. A solution of the 3-(dimethylamino)methyl compound in THF (12 mL) was added dropwise to a stirred solution of iodomethane (8.95 mL) in THF (6 mL) at 0 °C under nitrogen. The mixture was stirred for 10 h at 0 °C and then for 20 h at 4 °C. The volatiles were removed by evaporation in vacuo to give the corresponding crude quaternary salt. To a stirred solution of the quaternary salt in water (10 mL) was added sodium cyanide (185 mg, 3.77 mmol) at 80 °C (bath temp). The mixture was stirred for 3.5 h under the same conditions. After cooling to room temperature, the mixture was quenched with water and extracted with methylene chloride. The organic layers were dried over potassium carbonate and evaporated. The residue was purified by column chromatography with methylene chloride to give **14** (361 mg, 36%), which was recrystallized from ethyl acetate to give a pure sample as colorless needles: mp 110–111 °C; IR 3490, 3360, 3010, 2950, 2250, 1630, 1595, 1555, 1515, 1465, 1450, 1410 cm^{-1}; ^1H NMR δ 3.79 (s, 3 H, OCH_3), 3.94 (s, 2 H, CH_2CN), 5.12 (s, 2 H, OCH_2Ph), 6.27 (d, 1 H, J = 2 Hz, 7-CH), 6.42 (d, 1 H, J = 2 Hz, 5-CH), 6.95–6.97 (m, 1 H, 2-CH), 7.35 (d, 1 H, J = 7 Hz, ArH), 7.40 (t, 2 H, J = 7 Hz, ArH), 7.47 (d, 2 H, J = 7 Hz, ArH), 7.98 (br s, 1 H, 1-NH). Anal. Calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.66; H, 5.39; N, 9.46.

4-(Benzyloxy)-6-methoxy-3-[2-[(trifluoroacetyl)amino]ethyl]indole (15a). Compound **14** (95.9 mg, 0.330 mmol) was hydrogenated in ethanol (6 mL) (saturated with ammonia) over Raney nickel (excess) at room temperature for 2 days under 3.3 atm using the Parr equipment. After filtration, the filtrate was evaporated to give the corresponding amine. A solution of the amine in methanol (3 mL) was added dropwise to a cooled solution of sodium methoxide obtained from sodium (15.2 mg, 0.660 mmol) in methanol (5 mL) at 0 °C. The mixture was stirred for 1 h under the same conditions, and then *S*-ethyl trifluorothioacetate (0.18 mL, 1.32 mmol) was added to the mixture. The mixture was stirred at room temperature for 1.5 h and evaporated. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **15a** (100 mg, 78%), which was recrystallized from CH_2Cl_2–*n*-hexane to give a pure sample as colorless plates: mp 152–153 °C; IR 3495, 3425, 3040, 3010, 2950, 1720, 1630, 1590, 1550, 1510, 1465, 1450 cm^{-1}; ^1H NMR δ 3.01 (t, 2 H, J = 7 Hz, CH_2CH_2NH), 3.51 (q, 2 H, J = 7 Hz, CH_2NH), 3.82 (s, 3 H, OCH_3), 5.12 (s, 2 H, OCH_2Ph), 6.32 (s, 1 H, 7-CH), 6.48 (s, 1 H, 5-CH), 6.51 (br s, 1 H, $NHCOCF_3$), 6.78 (s, 1 H, 2-CH), 7.37 (d, 1 H, J = 7 Hz, ArH), 7.41 (t, 2 H, J = 7 Hz, ArH), 7.46 (d, 2 H, J = 7 Hz, ArH), 7.94 (br s, 1 H, 1-NH). Anal. Calcd for $C_{20}H_{19}N_2O_3F_3$: C, 61.22; H, 4.88; N, 7.14. Found: C, 61.57; H, 4.89; N, 7.27.

4-(Benzyloxy)-6-methoxy-3-[2-[[[2-(trimethylsilyl)ethoxy]carbonyl]amino]ethyl]indole (15b). Compound **14** (160 mg, 0.548 mmol) was hydrogenated in ethanol (8 mL) (saturated with ammonia) over Raney nickel (excess) at room temperature for 2 days under 3.3 atm using the Parr equipment. After filtration, the filtrate was evaporated to give the corresponding crude amine. A solution of the amine in ethanol (4.8 mL) was added dropwise to a cooled solution of sodium ethoxide obtained from sodium (18.9 mg, 0.82 mmol) in ethanol (1.5 mL) at 0 °C. The mixture was stirred for 1 h under the same conditions, and then 2-(trimethylsilyl)ethyl *p*-nitrophenyl carbonate (465.8 mg, 1.64 mmol) was added to the mixture. The mixture was stirred at room temperature for 3 h and evaporated. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **15b** (215 mg, 89%), which was recrystallized from ethyl acetate–*n*-hexane to give a pure sample as colorless needles: mp 109–110 °C; IR 3490, 3460, 3030, 2980, 1705, 1690, 1625, 1595, 1545, 1525, 1520, 1510 cm^{-1}; ^1H NMR δ 0.01 (s, 9 H, $SiMe_3$), 0.94 (t, 2 H, J = 8 Hz, CH_2SiMe_3), 2.95 (t, 2 H, J = 6 Hz, CH_2CH_2NH), 3.38 (t, 2 H, J = 6 Hz, CH_2NH), 3.80 (s, 3 H, OCH_3), 4.09 (t, 2 H, J = 8 Hz, $CH_2CH_2SiMe_3$), 4.61 (br s, 1 H, $NHCO_2$), 5.12 (s, 2 H, OCH_2Ph), 6.27 (s, 1 H, 7-CH), 6.44 (s, 1 H, 5-CH), 6.74 (s, 1 H, 2-CH), 7.35 (d, 1 H, J = 7 Hz, ArH), 7.40 (t, 2 H, J = 7 Hz, ArH), 7.46 (d, 2 H, J = 7 Hz, ArH), 8.00 (s, 1 H, 1-NH). Anal. Calcd for $C_{24}H_{32}N_2O_4Si$: C, 65.42; H, 7.32; N, 6.36. Found: C, 65.31; H, 7.39; N, 6.28.

6-Methoxy-3-[2-[(trifluoroacetyl)amino]ethyl]indole-4,7-dione (16a). Compound **15a** (19.6 mg, 0.05 mmol) was hydrogenated in ethanol (5 mL) over 10% Pd–C (11.0 mg) at room temperature for 2 days under 3.3 atm using the Parr equipment. After filtration, the filtrate was evaporated to give the crude debenzylated compound. A solution of the phenol in acetone (1.1 mL) was added to a buffered solution (KH_2PO_4/H_2O = 30 mg/4 mL) of Fremy's salt (53.7 mg, 0.200 mmol) at 0 °C. The resulting yellow-brown mixture was stirred for 1.5 h and then quenched with water and extracted with methylene chloride. The organic layer was washed with water, dried, and evaporated. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **16a** (9.30 mg, 59%), which was recrystallized from methanol to give a pure sample as orange plates: mp 283–285 °C; UV (MeOH) λ_{max} 221 (ϵ 22800), 283 (20100), 344 (6600) nm; IR (CH_3CN) 3625, 3550, 1720, 1670, 1635, 1600 cm^{-1}; ^1H NMR (CD_3OD) δ 2.97 (t, 2 H, J = 7 Hz, CH_2CH_2NH), 3.54 (t, 2 H, J = 7 Hz, CH_2NH), 3.82 (s, 3 H, OCH_3), 5.74 (s, 1 H, 5-CH), 6.99 (s, 1 H, 2-CH). Anal. Calcd for $C_{13}H_{11}N_2O_4F_3$: C, 49.37; H, 3.51; N, 8.86. Found: C, 49.46; H, 3.47; N, 8.87.

6-Methoxy-3-[2-[[[2-(trimethylsilyl)ethoxy]carbonyl]amino]ethyl]-indole-4,7-dione (16b). Compound **15b** (30.7 mg, 0.07 mmol) was hydrogenated in ethanol (5 mL) over 10% Pd–C (12.0 mg) at room temperature for 2 days under 3.3 atm using the Parr equipment. After filtration, the filtrate was evaporated to give the crude debenzylated compound. A solution of the phenol in acetone (1.3 mL) was added to a buffered solution (KH_2PO_4/H_2O = 36.0 mg/4.8 mL) of Fremy's salt (64.4 mg, 0.24 mmol) at 0 °C. The resulting yellow-brown mixture was stirred for 4 h and then quenched with water and extracted with methylene chloride. The organic layer was washed with water, dried, and evaporated. The residue was purified by column chromatography to give **16b** (14.2 mg, 56%), which was recrystallized from ethyl acetate to give a pure sample as orange crystals: mp 178–180 °C; UV (MeOH) λ_{max} 222 (ϵ 17400), 283 (16000), 350 (4300), IR 3450, 1705, 1660, 1640, 1600 cm^{-1}; ^1H NMR δ 0.02 (s, 9 H, $SiMe_3$), 0.95 (t, 2 H, J = 8 Hz, CH_2SiMe_3), 2.95 (t, 2 H, J = 6 Hz, CH_2CH_2NH), 3.45 (q, 2 H, J = 6 Hz, CH_2NH), 3.83 (s, 3 H, OCH_3), 4.12 (q, 2 H, J = 8 Hz, $CH_2CH_2SiMe_3$), 5.01 (br s, 1 H, $NHCO_2$), 5.71 (s, 1 H, 5-CH), 6.94 (s, 1 H, 2-CH); HRMS calcd for $C_{17}H_{24}N_2O_5Si$ (M^+) 364.1455, found 364.1460.

6-[[2-(3,5-Dibromo-4-hydroxyphenyl)ethyl]amino]-3-[2-[(trifluoroacetyl)amino]ethyl]indole-4,7-dione (17a). To a stirred suspension of 3,5-dibromotyramine hydrobromide (138.4 mg, 0.370 mmol) and triethylamine (0.056 mL, 0.370 mmol) in ethanol (1.5 mL) was added a solution of **16a** (38.9 mg, 0.120 mmol) in ethanol (3 mL) at room temperature, and then the mixture was heated at reflux for 2 days. The mixture was concentrated in vacuo. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **17a** (40.0 mg, 58%), which was recrystallized from ethanol to give a pure sample as red crystals: mp 208–210 °C; UV (MeOH) λ_{max} 239 (ϵ 32500), 293 (12300), 359 (11800) nm; IR (CH_3CN) 3550, 3350, 2925, 1720, 1665, 1620, 1600, 1550 cm^{-1}; ^1H NMR (CD_3OD) δ 2.81 (t, 2 H, J = 7 Hz, CH_2CH_2NHCO), 2.97 (t, 2 H, J = 6.5 Hz, $ArCH_2$), 3.35 (t, 2 H, J = 7 Hz, CH_2NHCO), 3.53 (t, 2 H, J = 6.5 Hz, $ArCH_2CH_2$), 5.19 (s, 1 H, 5-CH), 6.96 (s, 1 H, 2-CH), 7.38 (s, 2 H, ArH); HRMS calcd for $C_{20}H_{16}N_3O_4Br_2F_3$ (M^+) 576.9460, found 576.9492.

6-[[2-(3,5-Dibromo-4-hydroxyphenyl)ethyl]amino]-3-[2-[[[2-(trimethylsilyl)ethoxy]carbonyl]amino]ethyl]indole-4,7-dione (17b). To a stirred suspension of 3,5-dibromotyramine hydrobromide (24.8 mg,

0.0660 mmol) and diisopropylethylamine (0.012 mL, 0.0660 mmol) in ethanol (1 mL) was added a solution of **16b** (10.0 mg, 0.0270 mmol) in ethanol (3 mL) at room temperature. The mixture was heated at reflux for 2 days and concentrated in vacuo. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **17b** (9.30 mg, 55%), which was recrystallized from ethyl acetate to give a pure sample as red crystals: mp 189–191 °C; UV (MeOH) λ_{max} 239 (ϵ 50 200), 294 (19 800), 363 (18 600) nm; IR 3450, 3380, 2920, 1700, 1685, 1650, 1590 cm^{-1}; ^{1}H NMR (CD_3OD) δ 0.02 (s, 9 H, $SiMe_3$), 0.94 (t, 2 H, J = 8 Hz, CH_2SiMe_3), 2.80 (t, 2 H, J = 7 Hz, $ArCH_2$), 2.90 (t, 2 H, J = 6 Hz, $CH_2CH_2NHCO_2$), 3.29 (t, 2 H, J = 7 Hz, $ArCH_2CH_2$), 3.35 (t, 2 H, J = 6 Hz, CH_2NHCO_2), 4.09 (t, 2 H, J = 8 Hz, $CH_2CH_2SiMe_3$), 5.19 (s, 1 H, 5-CH), 6.98 (s, 1 H, 2-CH), 7.36 (s, 2 H, ArH); HRMS calcd for $C_{24}H_{29}N_3O_5Br_2Si$ (M^+) 625.0241, found 625.0239.

3-[2-[(Trifluoroacetyl)amino]ethyl]-4,5,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-*g*]quinoline-4,9-dione-5-spiro-4′-2′,6′-dibromocyclohexa-2′,5′-dien-1′-one (8a). To a stirred suspension of **17a** (9.80 mg, 0.0170 mmol) in anhydrous methylene chloride (1 mL) was added O-silylated ketene acetal **7** (25.0 mg, 0.156 mmol) at room temperature for 3 h under nitrogen. The mixture was concentrated in vacuo to give the O-silylated phenol, which was dissolved in 2,2,2-trifluoroethanol (2 mL). Then PIFA (8.7 mg, 0.0200 mmol) was added to the mixture and stirred for 15 min under the same conditions. The reaction mixture was quenched with water and extracted with methylene chloride. The organic layer was washed with saturated sodium chloride solution, dried, and evaporated. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **8a** (5.70 mg, 58%), which was recrystallized from CH_2Cl_2–*n*-hexane to give a pure sample as red crystals: mp 141–143 °C; UV (MeOH) λ_{max} 237 (ϵ 32 100), 313 (14 200), 363 (11 400) nm; IR (CH_3CN) 3630, 3550, 3350, 2950, 1720, 1670, 1620, 1585, 1550, 1510 cm^{-1}; ^{1}H NMR (CD_3OD) δ 1.97 (t, 2 H, J = 6 Hz, 6-CH_2), 2.91 (t, 2 H, J = 7 Hz, CH_2CH_2NHCO), 3.46 (t, 2 H, J = 7 Hz, CH_2NHCO), 3.53 (t, 2 H, J = 6 Hz, 7-CH_2), 6.98 (s, 1 H, 2-CH), 7.61 (s, 2 H, 3′,5′-CH); HRMS calcd for $C_{20}H_{14}N_3O_4Br_2F_3$ (M^{2+}) 576.9285, found 576.9295.

3-[2-[[[2-(Trimethylsilyl)ethoxy]carbonyl]amino]ethyl]-4,5,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-*g*]quinoline-4,9-dione-5-spiro-4′-2′,6′-dibromocyclohexa-2′,5′-dien-1′-one (8b). To a stirred suspension of **17b** (5.00 mg, 0.008 mmol) in anhydrous methylene chloride (1 mL) was added O-silylated ketene acetal **7** (25.0 mg, 0.156 mmol) at room temperature for 3 h under nitrogen. The mixture was concentrated in vacuo to give the O-silylated phenol, which was dissolved in 2,2,2-trifluoroethanol (1 mL). Then PIFA (3.80 mg, 0.0088 mmol) was added to the mixture and stirred for 15 min under the same conditions. The reaction mixture was quenched with water and extracted with methylene chloride. The organic layer was washed with saturated sodium chloride solution, dried, and evaporated. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **8b** (3.1 mg, 62%), which was recrystallized from CH_2Cl_2–*n*-hexane to give a pure sample as red purple crystals: mp 106–108 °C; UV (MeOH) λ_{max} 238 (ϵ 34 900), 314 (17 000), 359 (14 300) nm; IR 3650, 3400, 2950, 1710, 1665, 1585, 1505, 1405 cm^{-1}; ^{1}H NMR (CD_3OD) δ 0.02 (s, 9 H, $SiMe_3$), 0.95 (t, 2 H, J = 8 Hz, CH_2SiMe_3), 1.96 (t, 2 H, J = 6 Hz, 6-CH_2), 2.83 (t, 2 H, J = 7 Hz, $CH_2CH_2NHCO_2$), 3.26 (t, 2 H, J = 7 Hz, CH_2NHCO_2), 3.53 (t, 2 H, J = 6 Hz, 7-CH_2), 4.08 (t, 2 H, J = 8 Hz, $CH_2CH_2SiMe_3$), 6.97 (s, 1 H, 2-CH), 7.61 (s, 2 H, 3′,5′-CH); HRMS calcd for $C_{24}H_{27}N_3O_5Br_2Si$ (M^+) 623.0085, found 623.0082.

6-Methoxy-3-[2-[[[2-(trimethylsilyl)ethoxy]carbonyl]amino]ethyl]-1-(tolylsulfonyl)indole-4,7-dione (18). To a stirred suspension of potassium *tert*-butoxide (20.0 mg, 0.180 mmol) in THF (1.5 mL) was added dropwise a solution of **16b** (31.3 mg, 0.0860 mmol) in THF (2.5 mL) at 0 °C under nitrogen. The mixture was stirred for 1 h under the same conditions, and then *p*-toluenesulfonyl chloride (40.0 mg, 0.21 mmol) was added to the mixture. The mixture was stirred at room temperature for 3 h, quenched with water, and extracted with methylene chloride. The organic layers were dried and evaporated. The residue was purified by column chromatography with *n*-hexane–ethyl acetate to give **18** (41.0 mg, 92%), which was recrystallized from tetrachloromethane–*n*-hexane as yellow crystals: mp 62–64 °C; UV (MeOH) λ_{max} 224 (ϵ 29 300), 284 (20 400), 337 (7100) nm; IR 3025, 1700, 1680, 1645, 1610, 1495, 1330, 1185 cm^{-1}; ^{1}H NMR δ 0.01 (s, 9 H, $SiMe_3$), 0.96 (t, 2 H, J = 8 Hz, CH_2SiMe_3), 2.42 (s, 3 H, $C_6H_4(CH_3)$), 2.97 (t, 2 H, J = 7 Hz, $CH_2CH_2NHCO_2$), 3.43 (q, 2 H, J = 7 Hz, CH_2NHCO_2), 3.78 (s, 3 H, OCH_3), 4.13 (t, 2 H, J = 8 Hz, $CH_2CH_2SiMe_3$), 4.85 (br s, 1 H, $NHCO_2$), 5.71 (s, 1 H, 5-CH), 7.34 (d, 2 H, J = 8 Hz, ArH), 7.67 (s, 1 H, 2-CH), 8.05 (d, 2 H, J = 8 Hz, ArH); HRMS calcd for $C_{24}H_{30}N_2O_7SSi$ (M^+) 518.1542, found 518.1557.

7-[[2-(3,5-Dibromo-4-hydroxyphenyl)ethyl]amino]-1,3,4,8-tetrahydropyrrolo[4,3,2-*de*]quinolin-8-one (9). To a stirred solution of **18** (17.6 mg, 0.0340 mmol) in acetonitrile (2 mL) was added anhydrous *p*-toluenesulfonic acid (30.0 mg, 0.170 mmol) at room temperature under nitrogen. The mixture was stirred for 5 h. 3A molecular sieves and sodium bicarbonate were added to the mixture, which was concentrated in vacuo. The residue was dissolved in methylene chloride and filtered. The filtrate was evaporated to give the indoloquinone imine, which was dissolved in ethanol (3.3 mL), and the solution was added dropwise to a stirred solution of 3,5-dibromotyramine hydrobromide (18.0 mg, 0.048 mmol) and sodium bicarbonate (8.6 mg, 0.11 mmol) in ethanol (1.5 mL) at room temperature under nitrogen. The mixture was heated at reflux for 3 h and then evaporated. The residue was purified by column chromatography with methylene chloride–methanol–triethylamine to give **9** (8.10 mg, 51%), which was recrystallized from methanol to give a pure sample as red crystals: mp 152 °C dec; UV (MeOH) λ_{max} 246 (ϵ 12 100), 350 (5500) nm; IR (KBr) 3730, 2920, 1675, 1620, 1600, 1560 cm^{-1}; ^{1}H NMR (CD_3OD) δ 2.83 (t, 2 H, J = 7.1 Hz, $ArCH_2$), 2.95 (t, 2 H, J = 7.3 Hz, C=NCH_2CH_2), 3.53 (t, 2 H, J = 7.1 Hz, $ArCH_2CH_2$), 3.85 (t, 2 H, J = 7.3 Hz, C=NCH_2), 5.36 (s, 1 H, 8-CH), 7.15 (s, 1 H, 4′-CH), 7.34 (s, 2 H, ArH); HRMS calcd for $C_{18}H_{15}Br_2N_3O_2$ (M^+) 462.9531, found 462.9531.

Discorhabdin C. To a stirred suspension of **9** (4.80 mg, 0.0103 mmol) in anhydrous methylene chloride (1 mL) was added dropwise O-silylated *O*-trimethylsilyl ketene acetal **7** (25.0 mg, 0.156 mmol) at room temperature for 3 h under nitrogen, and then the mixture was concentrated in vacuo to give the O-silylated phenol, which was dissolved in 2,2,2-trifluoroethanol (1 mL). Then PIFA (4.50 mg, 0.0103 mmol) was added to the mixture and stirred for 20 min under the same conditions. The reaction mixture was concentrated in vacuo, and the residue was purified by column chromatography with methylene chloride–methanol to give discorhabdin C (2.00 mg, 42%), which was recrystallized from methanol–methylene chloride to give a pure sample as red crystals: mp >300 °C; UV (MeOH) λ_{max} 250 (ϵ 14 600), 355 (7700) nm; IR (KBr) 3630, 2925, 1670, 1655, 1600, 1540, 1385, 1325 cm^{-1}; ^{1}H NMR (CD_3OD) δ 2.10 (t, 2 H, J = 6.0 Hz, 7-CH_2), 2.89 (t, 2 H, J = 7.3 Hz, 16-CH_2), 3.70 (t, 2 H, J = 6.0 Hz, 8-CH_2), 3.78 (t, 2 H, J = 7.3 Hz, 17-CH_2), 7.19 (s, 1 H, 14-CH), 7.71 (s, 2 H, 1-CH and 5-CH); HRMS calcd for (M^+) $C_{18}H_{13}Br_2N_3O_2$ 460.9376, found 460.9376.

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Registry No. 4a, 134755-19-4; **4b**, 134755-29-6; **4c**, 134755-30-9; **4d**, 134755-31-0; **4e**, 131644-68-3; **4f**, 131644-65-0; **6a**, 134755-18-3; **6b**, 134755-26-3; **6c**, 134755-27-4; **6d**, 134755-28-5; **6e**, 131644-64-9; **6f**, 131644-67-2; **8a**, 134755-20-7; **8b**, 134755-36-5; **9**, 137022-91-4; **10**, 673-22-3; **10** (O-benzyl derivative), 32884-23-4; **11**, 134755-22-9; **12**, 138518-15-7; **13**, 138518-16-8; **14**, 134755-23-0; **15a**, 134755-24-1; **15b**, 134755-32-1; **16a**, 134755-25-2; **16b**, 134755-33-2; **17a**, 134755-21-8; **17b**, 134755-35-4; **18**, 138540-75-7; PIFA, 2712-78-9; discorhabdin C, 105372-81-4; tyramine, 51-67-2; 5,8-quinolinedione, 10470-83-4; 2,3-dimethylquinoxaline-5,8-dione, 2768-63-0; 2-methylbenzofuran-4,7-dione, 138518-17-9; 3-(acetoxymethyl)-1-ethyl-5-methoxy-2-methylindole-4,7-dione, 36131-99-4; 3-(acetoxymethyl)-1-ethyl-6-methoxy-2-methylindole-4,7-dione, 131644-63-8; 3,5-dibromotyramine hydrobromide, 73414-58-1; 3-(2-hydroxy-4-methoxyphenyl)-2-azido-2-propenoic acid ethyl ester, 138518-18-0; 6-methoxy-4-phenylmethoxy-*N*,*N*-dimethyl-3-(1*H*)-indolemethanamine, 138540-76-8; 6-methoxy-4-phenylmethoxy-*N*,*N*,*N*-trimethyl-1*H*-indole-3-methanaminium iodide, 138518-19-1.