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A novel one-pot synthesis of carbazole-1,4-quinones through Pd-catalyzed cyclocarbonylation, desilylation and oxidation processes from 3-iodo-2-propenylindoles

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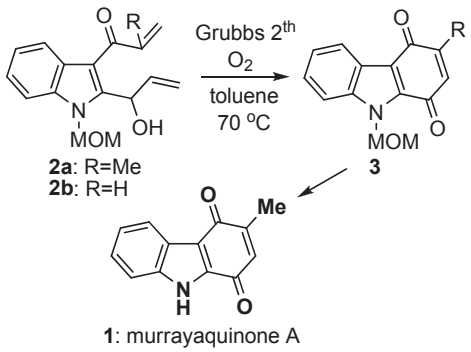
ABSTRACT

A novel one-pot synthesis of carbazole-1,4-quinone by consecutive Pd-catalyzed cyclocarbonylation, desilylation, and oxidation reactions is described. We propose a possible mechanism of the cyclocarbonylation reaction between 3-iodo-2-propenylindole and CO (1 atm) in the presence of a tributyl(vinyl)tin and Pd-catalyst and the resulting acylpalladium species was directly coupled with a terminal alkene to produce the carbazole-1,4-quinone. To our knowledge, this is the first example of this type of reaction. A new formal total synthesis of a carbazole-1,4-quinone alkaloid, murrayaquinone A was established using this reaction.

1. Introduction

Quinones are very important compounds in many biochemical functions. In addition, quinone moieties are essential fragments of a large number of pharmacologically active compounds, especially in the anticancer drugs.[1] Among quinones, the carbazolequinones exhibit a variety of biological activities, including cytotoxic activities.[2–4] Many biologically active carbazole alkaloids have been isolated from various natural sources.[4] The development of efficient methods to prepare a scaffold has been a major focus for synthetic organic chemists, and new strategies against functionalized carbazoles are in high demand.[4]

We are interested in the unique structure and biologic activity of the carbazolequinone, and have reported several total syntheses of carbazolequinone alkaloids (murrayaquinone A,[2,5] carbazomycin G,[6] carquinostatin A,[7] carbazoquinocins B–F,[8] calothrixins[9]) based on the allene-mediated electrocyclic reaction of the 6π-electron system as a key step. Furthermore, we recently reported a new efficient synthesis of carbazole-1,4-quinone **3** from allyl alcohol **2** using a tandem ring-closing metathesis (RCM) and dehydrogenation reaction with Grubbs second generation catalyst, and a total synthesis of murrayaquinone A (**1**)[5c] (Scheme 1). In our previous study, allyl alcohols **2** were synthesized in two steps by a three-component Pd-catalyzed cross-coupling reaction between 3-iodoindole-2-carbaldehyde, CO (1 atm), and alkenyl tributyltin under Fukuyama's conditions,[10] followed by the Grignard reaction of the resulting 3-acryroylindole-2-carbaldehydes with vinylmagnesium bromide. The yields of **2a** and **2b**, however, were only



Scheme 1. Our previous work.

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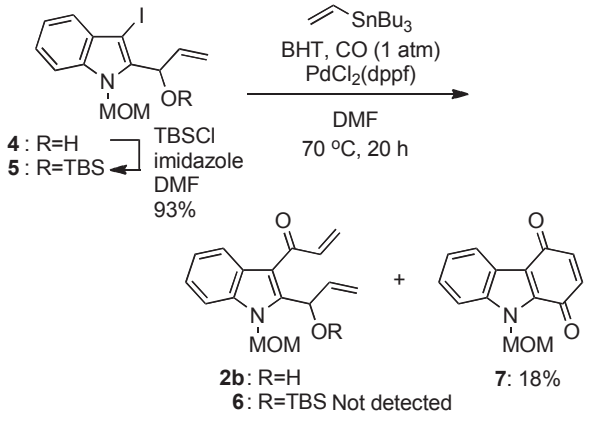
46% and 6%, respectively.[5c] The yield of the allyl alcohol **2b** was extremely low.

To obtain the carbazole-1,4-quinones **7** more efficiently, we attempted to improve the synthesis of the 3-acryloylindole **2b** using the 2-propenylindole **4**, as shown in Scheme 2.



Scheme 2. Synthesis of 3-acryloylindoles.

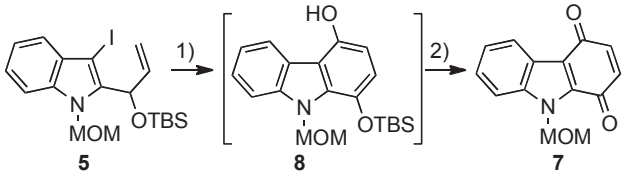
First, 3-iodo-2-propenylindole **4** was prepared by the Grignard reaction of 3-iodoindole-2-carbaldehyde with vinylmagnesium bromide. Next, we examined a three-component Pd-catalyzed cross-coupling reaction with 3-iodo-2-propenylindole **4** and tributyl(vinyl)tin in CO atmosphere, but the desired acryroylindole **2b** was not obtained. Therefore, the 3-acryroylindole **5**, protected with TBSCl, was subjected to a cross-coupling reaction between CO (1 atm) and alkenyl tributyltin in the presence of a $PdCl_2$(dppf) catalyst. The carbazole-1,4-quinone **7** was isolated as the sole product in 18% yield, but the expected 3-acryroylindole **6** was not detected at all.

Based on this result, we assumed that an initial cyclocarbonylation reaction was consecutively followed by desilylation and oxidation through treatment with aqueous KF in air. Some addition reactions of acylmetallates with α,β-unsaturated carbonyl compounds are known to undergo a similar process.[11] In addition, Negishi and co-workers reported that the cyclic acylpalladation reaction by *o*-iodo-*m*-tolyl 4-methylcyclohexen-1-yl ketone, CO (600 psi), and triethylamine in the presence of $Pd_2(dba)_3$ gave the anthraquinone derivative.[12] The cyclocarbonylation, in which an acylpalladium compound was coupled directly with a terminal alkene, has been reported in few examples.[13] To the best of our knowledge, however, this one-pot reaction is the first example. Herein, we wish to report a new cyclocarbonylation method for the synthesis of carbazole-1,4-quinone, including murrayaquinone A (**1**).[2,5]

2. Results and discussion

To optimize the cyclocarbonylation conditions, we used 3-iodo-2-(1-hydroxyprop-2-en-1-yl)indole **5** as a model substrate (Table 1). First, the effect of the amount of tributyl(vinyl)tin was studied in the model reaction, and the use of 3 equiv of tributyl(vinyl)tin afforded the carbazole-1,4-quinone **7** in 51% yield (runs 1–5). In particular, tributyl(vinyl)tin was found to be necessary to promote this reaction (run 2). The reaction also proceeded under the same conditions without BHT, but the yield decreased to 36% (run 7). In addition, the yield tended to decrease when the reaction temperature was lowered to 50 °C (run 8) or rised to 100 °C (run 9), or when the reaction time was extended (run 10). After a cyclocarbonylation occurred, treatment of the reactant with TBAF under oxygen atmosphere instead of aqueous KF solution in the air was an effective for increasing the yield to 60% (run 6). The effects of the catalyst and solvent were also examined in the model reaction. $PdCl_2$(dppf) produced the best results (Table 1, run 6), but the effects of other catalysts such as $Pd(OAc)_2$+dppf, $Pd(OAc)_2$+PPh_3, and $PdCl_2$(dppe) were also investigated (Table 2, runs 1–3). Among several solvents, such as DMF, DMA, toluene, THF and CH_3CN, DMF was found to be the most suitable solvent for these reaction conditions (Table 2, runs 3–7).

Table 1
Optimization of reaction conditions for the synthesis of carbazole-1,4-quinone



run	BHT	Vinyltin (equiv)	Temp (°C)	Time (h)	Yield (%) of **7**	
1	+	1.5	70	20	18	(18)[b]
2	+	0	70	20	—	(52)
3	+	0.5	70	20	15	(—)
4	+	3	70	20	51	(20)
5	+	5	70	20	40	(17)
6	+	3	70	20	60[a]	(10)
7	–	3	70	20	36	(—)
8	+	3	50	20	20	(20)
9	+	3	100	20	34	(34)
10	+	3	70	48	34	(34)

Reaction conditions: (1) **5**, tributyl(vinyl)tin, BHT (1.2 equiv), CO (1 atm), $PdCl_2$(dppf) (20 mol %), DMF (0.01 M). (2) KF aq in air.
[a] workup: TBAF, O_2, rt, 1 h.
[b] SM recovered (%).

Table 2
Effect of Pd-catalysts and solvents

run	Pd-catalysts[a]	Solvents	Yield (%) of **7**	
1	$Pd(OAc)_2$+dppf (1:2)	DMF	26	(62)[b]
2	$Pd(OAc)_2$+PPh_3 (1:2)	DMF	41	(16)
3	$PdCl_2$(dppe)	DMF	23	(16)
4	$PdCl_2$(dppf)	DMA	0	(—)
5	$PdCl_2$(dppf)	Toluene	0	(20)
6	$PdCl_2$(dppf)	THF	Trace	(33)
7	$PdCl_2$(dppf)	CH_3CN	Trace	(34)

[a] Reaction conditions: (1) **5**, tributyl(vinyl)tin, BHT (1.2 equiv), CO (1 atm), Pd-catalysts (20 mol %), solvents (0.01 M). (2) TBAF, O_2, rt, 1 h.
[b] SM recovered (%).

Next, we investigated additives other than tributyl(vinyl)tin (Table 3). The reaction was performed under the same conditions using other tin compounds, but the yield did not increase (runs 1–3). When 3 equiv of Bu_3SnH was used as an additive, the

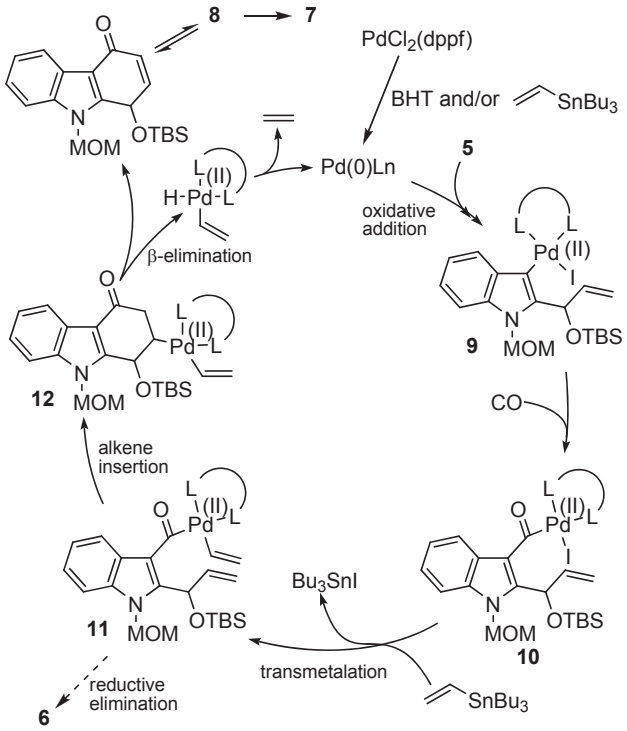
Table 3
Effects of reagents on cyclocarbonylation

Run	Reagents (equiv)[a]	Yield (%) of **7**	
1	Tributyl(isopropenyl)tin (3 equiv)	36	(17)[b]
2	Allyl(tributyl)tin (3 equiv)	26	(21)
3	Tributyl(phenyl)tin (3 equiv)	15	(21)
4	Bu_3SnH (3 equiv)	53	(8)
5	Bu_3SnH (1.5 equiv)	16	(10)
6	Bu_3SnH (5 equiv)	—	(12)
7	Vinylboronic acid pinacol ester (3 equiv)	—	(—)
8	$AlMe_3$ (3 equiv)	—	(10)
9	Et_3N (1.1 equiv)	—	(20)
10	*i*-Pr_2NEt (1.1 equiv)	—	(20)

[a] Reaction conditions: (1) **5**, reagents, BHT (1.2 equiv), CO (1 atm), $PdCl_2$(dppf) (20 mol %), DMF (0.01 M), 70 ∞C, 20 h. (2) TBAF, O_2 rt, 1 h.
[b] SM recovered (%).

carbazole-1,4-quinone **7** was obtained in 53% yield (run 4). Furthermore, changing the amount of Bu_3SnH to 1.5 equiv or 5 equiv did not improve the yield (runs 5 and 6). The reaction was then examined by using vinylboronic pinacol ester and trimethylaluminium instead of tributyl(vinyl)tin, but the desired product was not obtained (runs 7 and 8). In addition, when Et_3N and *i*-Pr_2NEt were used as a base (runs 9 and 10), this reaction gave no desired product **7**.

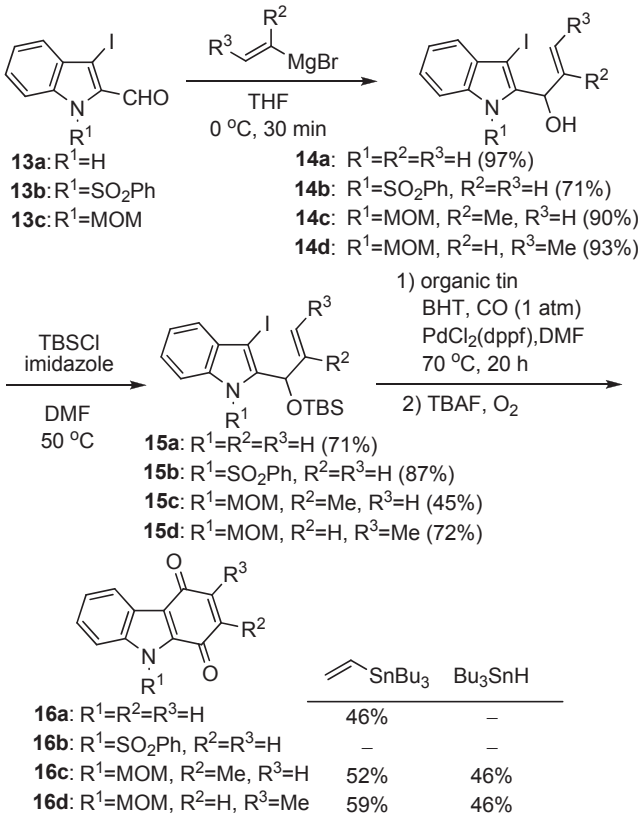
Based on the above-described results, a plausible mechanism for this reaction is illustrated in Scheme 3. At the beginning of the cycle, oxidative addition between the 3-iodoindole **5** and Pd^0 species should proceed to form **9**. Coordination insertion of CO would lead to Pd–CO species **10**. Subsequently, transmetallation would proceed between tributyl(vinyl)tin and Pd–CO species **10**. Next, the desired 3-acryloylindole **6** should be produced by reductive elimination of **11**, but the reaction did not undergo this process. Instead an alkenylpalladium intermediate **12** was generated by an alkene insertion reaction of the vinyl group into the Pd–CO bond. Finally, our unexpected carbazole product **7** was released by β-hydride elimination, and the resulting palladium(II) hydride was reduced to a Pd^0 species with a loss of ethylene. Although it is not clear why reductive elimination from the Ar–CO–Pd–vinyl species did not occur, we propose a possible reaction mechanism.



Scheme 3. Our plausible mechanism for this reaction $SnBu_3$.

To realize this reaction, we prepared important substrates **15a**–**d** for the synthesis of carbazole-1,4-quinones (Scheme 4). The Grignard reaction of 3-iodoindole-2-carbaldehydes **13a**–**c** with alkenylmagnesium bromide gave the 2-allyl alcohols **14a**–**d**, followed by treatment of 2-allyl alcohols **14a**–**d** with TBSCl in the presence of imidazole produced *O*-TBS ethers **15a**–**d**.

We examined the synthesis of carbazole-1,4-quinones by one-pot cyclocarbonylation using *O*-TBS ethers **15a**–**d**. The indole **15a** gave the carbazolequinone **16a** in 46% yield. The *N*-phenylsulfonylindole **15b**, however, did not give the desired carbazolequinone **16b**. The phenylsulfonyl group was not a suitable protecting group in this reaction. Thus, we established the novel



Scheme 4. One-pot synthesis of carbazole-1,4-quinones **16a**–**d**.

synthesis of the carbazole-1,4-quinones **16c**,**d** from 2-(2-methylprop-2-enyl)indole **15c** and 2-(but-2-enyl)indole **15d** under two conditions (tributyl(vinyl)tin and/or Bu_3SnH). These desired 2- and 3-methylcarbazolequinones **16c**,**d** were obtained in moderate yield by using tributyl(vinyl)tin. We synthesized the *N*-MOM-3-methylcarbazole-1,4-quinone **16d** in three steps from **13c**, and achieved the formal synthesis of murrayaquinone A (**1**).

3. Conclusion

We have developed a one-pot synthesis of carbazole-1,4-quinones by Pd-catalyzed cyclocarbonylation, followed by a desilylation and oxidation reaction under treatment with TBAF in O_2 atmosphere. The cyclocarbonylation reaction occurred between 3-iodo-2-propenylindole and CO (1 atm) in the presence of tributyl(vinyl)tin and Pd-catalyst. This is the first example, in which an acylpalladium compound was coupled directly with a terminal alkene. Thus carbazole-1,4-quinones **16a**,**c**,**d** were provided in three steps from **13** using this new method. Among them, carbazole-1,4-quinone **16d** was a synthetic precursor of murrayaquinone A (**1**),[5] and a new formal synthesis was achieved. Based on this result, we present an efficient method for synthetic studies of carbazole alkaloids and/or other natural products with a 1,4-quinone structure. Further studies of the synthesis of carbazolequinone alkaloids are ongoing.

4. Experimental section

4.1. General

All non-aqueous reactions were carried out under an atmosphere of nitrogen in dried glassware unless otherwise noted. Solvents were dried and distilled according to standard protocols.

Analytical thin-layer chromatography was performed with Silica gel 60PF_{254} (Merck). Silica gel column chromatography was performed with Silica gel 60 (70–230 mesh, Canto Co. Lit.). All melting points were determined on Yanagimoto micro melting point apparatus and are uncorrected. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a JEOL AL-300 at 300 MHz. Chemical shifts are reported relative to Me_4Si (δ 0.00). NMR spectra were measured with $CDCl_3$ unless otherwise noted. Multiplicity is indicated by one or more of the following: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); br (broad). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a JEOL AL-300 at 75 MHz. Chemical shifts are reported relative to $CDCl_3$ (δ 77.0) and DMSO-d_6 (δ 39.7). Infrared spectra were recorded with ATR method using a Shimadzu FTIR-8000 spectrophotometer and Technologies DuraScop. Low and High-resolution mass spectra were recorded on JEOL JMS-700 spectrometers by direct inlet system.

4.2. 2-(1-Hydroxyprop-2-en-1-yl)-3-iodo-*N*-(methoxymethyl) indole 4

A solution of vinylmagnesium bromide (1.0 M in THF, 3.16 mL, 3.16 mmol) was added dropwise to a solution of 3-iodoindole-2-carbaldehyde **3** (500 mg, 1.58 mmol) in THF (20 mL) under cooling with ice-water. After stirred at rt for 1 h, the reaction mixture was quenched with aqueous NH_4Cl solution (saturated), and then was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by column chromatography using EtOAc/hexane (1:9) as an eluent to give the alcohol **4** (463 mg, 92%). IR (ATR) ν: 3401 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.45 (1H, d, J=7.4 Hz), 7.41 (1H, d, J=7.7 Hz), 7.30 (1H, dt, J=7.7, 1.1 Hz), 7.23 (1H, dt, J=7.4, 1.1 Hz), 6.15 (1H, ddd, J=17.4, 10.3, 3.7 Hz), 5.79 (1H, dddd, J=7.0, 3.7, 2.3, 2.3 Hz), 5.72 (1H, d, J=11.0 Hz), 5.52 (1H, d, J=11.0 Hz), 5.47 (1H, ddd, J=17.4, 2.3, 1.3 Hz), 5.30 (1H, ddd, J=10.3, 2.3, 1.3 Hz), 3.36 (1H, d, J=7.0 Hz, disappeared with D_2O), 3.27 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 138.9, 138.4, 137.7, 129.8, 123.9, 121.9, 121.3, 115.5, 109.7, 74.7, 69.7, 63.3, 56.0. MS m/z: 343 (M^+). HRMS (EI) m/z: 343.0051 (M^+) (calcd for $C_{13}H_{14}INO_2$: 343.0069).

4.3. 2-(1-Hydroxyprop-2-en-1-yl)-3-iodoindole 14a

The same procedure as above was carried out using 3-iodoindole-2-carbaldehyde **13a** (400 mg, 1.48 mmol) to give the alcohol **14a** (429 mg, 97%). IR (ATR) ν: 3401, 3313 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.63 (1H, br s), 7.43 (1H, d, J=7.7 Hz), 7.33 (1H, d, J=7.7 Hz), 7.15–7.24 (2H, m), 6.05 (1H, ddd, J=17.2, 10.6, 5.5 Hz), 5.57–6.07 (1H, m), 5.49 (1H, ddd, J=17.2, 1.6, 1.4 Hz), 5.31 (1H, ddd, J=10.6, 1.6, 1.5 Hz), 2.21 (1H, d, J=2.7 Hz, disappeared with D_2O). ^{13}C NMR ($CDCl_3$) δ: 138.5, 136.8, 135.6, 130.5, 123.4, 120.9, 120.8, 116.6, 111.4, 69.6, 57.6. MS m/z: 298 (M^+). HRMS (EI) m/z: 298.9821 (M^+) (calcd for $C_{11}H_{10}INO$: 298.9807).

4.4. 2-(1-Hydroxyprop-2-en-1-yl)-3-iodo-*N*-(phenylsulfonyl) indole 14b

The same procedure as above was carried out using 3-iodoindole-2-carbaldehyde **13b** (500 mg, 1.12 mmol) to give the alcohol **14b** (379 mg, 71%). Mp 98–99 °C (EtOAc). IR (ATR) ν: 1645, 1616 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.96 (1H, d, J=7.0 Hz), 7.83–7.88 (2H, m), 7.50–7.56 (1H, m), 7.29–7.45 (5H, m), 6.34 (1H, ddd, J=17.2, 10.3, 5.1 Hz), 5.95–6.03 (1H, m), 5.35 (1H, d, J=17.2 Hz), 5.28 (1H, d, J=10.3 Hz), 4.11 (1H, d, J=11.0 Hz, disappeared with D_2O). ^{13}C NMR ($CDCl_3$) δ: 140.3, 137.9, 137.8, 136.7, 134.1, 131.6, 129.3, 126.8, 126.5, 124.6, 122.7, 116.8, 114.9, 71.4. MS m/z: 438 (M^+). HRMS (EI) m/z: 438.9736 (M^+) (calcd for $C_{17}H_{14}INO_3S$: 438.9739).

4.5. 2-(1-Hydroxy-2-methylprop-2-en-1-yl)-3-iodo-*N*-(methoxymethyl)indole 14c

The same procedure as above was carried out using 3-iodoindole-2-carbaldehyde **13c** (365 mg, 1.16 mmol) to give the alcohol **14c** (322 mg, 90%). IR (ATR) ν: 3421 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.46 (1H, d, J=7.4 Hz), 7.40 (1H, d, J=7.7 Hz), 7.31 (1H, dt, J=7.7, 1.3 Hz), 7.23 (1H, dt, J=7.4, 1.3 Hz), 5.73 (1H, d, J=11.0 Hz), 5.60 (1H, d, J=6.6 Hz), 5.43 (1H, d, J=11.0 Hz), 5.37 (1H, br s), 5.09–5.10 (1H, m), 3.64 (1H, d, J=7.9 Hz, disappeared with D_2O), 3.28 (3H, s), 1.64 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 144.8, 138.6, 138.5, 129.8, 124.0, 122.0, 121.3, 110.7, 109.6, 74.3, 71.8, 65.2, 56.0, 19.6. MS m/z: 357 (M^+). HRMS (EI) m/z: 357.0229 (M^+) (calcd for $C_{14}H_{16}INO_2$: 357.0226).

4.6. 2-(1-Hydroxybut-2-en-1-yl)-3-iodo-*N*-(methoxymethyl) indole 14d

The same procedure as above was carried out using 3-iodoindole-2-carbaldehyde **13c** (500 mg, 1.59 mmol) to give the alcohol **14d** (526 mg, 93%). IR (ATR) ν: 3398 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.38–7.46 (2H, m), 7.30 (1H, dt, J=7.0, 1.3 Hz), 7.22 (1H, dt, J=7.0, 1.3 Hz), 5.79–5.84 (2H, m), 5.72–5.76 (1H, m), 5.71 (1H, d, J=11.0 Hz), 5.57 (1H, d, J=11.0 Hz), 3.29 (3H, s), 3.12 (1H, d, J=6.0 Hz), 1.72–1.76 (3H, m). ^{13}C NMR ($CDCl_3$) δ: 140.1, 138.4, 130.2, 130.0, 128.3, 123.9, 121.9, 121.2, 109.9, 75.1, 66.2, 62.9, 56.1, 14.1. MS m/z: 357 (M^+). HRMS (EI) m/z: 357.0234 (M^+) (calcd for $C_{14}H_{16}INO_2$: 357.0226).

4.7. 2-[1-(*tert*-Butyldimethylsilyloxy)prop-2-en-1-yl]-3-iodo-*N*-(methoxymethyl)indole 5

A solution of *tert*-butyldimethylsilyl chloride (1.17 g, 7.77 mmol) in DMF (30 mL) was added to a solution of the alcohol **4** (891 mg, 2.59 mmol) and imidazole (881 mg, 13.0 mmol) at rt. After stirred at 50 °C for 12 h, the reaction mixture was quenched with H_2O, and then was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by column chromatography using EtOAc/hexane (1:9) as an eluent to give the silyl ether **5** (1.09 g, 93%). ^{1}H NMR ($CDCl_3$) δ: 7.48 (1H, d, J=7.9 Hz), 7.42 (1H, d, J=7.9 Hz), 7.27 (1H, dt, J=7.9, 1.1 Hz), 7.21 (1H, dt, J=7.9, 1.1 Hz), 6.08 (1H, ddd, J=17.1, 10.3, 3.9 Hz), 5.77 (1H, ddd, J=4.0, 1.8, 1.8 Hz), 5.73 (1H, d, J=10.3 Hz), 5.54 (1H, d, J=10.3 Hz), 5.44 (1H, ddd, J=17.1, 1.8, 1.8 Hz), 5.21 (1H, td, J=10.3, 1.8 Hz), 3.27 (3H, s), 0.91 (9H, s), 0.17 (3H, s), −0.05 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 139.3, 138.9, 138.2, 130.0, 123.5, 121.5, 121.1, 114.4, 111.1, 75.6, 70.8, 61.4, 55.8, 25.8, 18.2, −4.8, −4.9. MS m/z: 457 (M^+). HRMS (EI) m/z: 457.0912 (M^+) (calcd for $C_{19}H_{28}INO_2Si$: 457.0934).

4.8. 2-[1-(*tert*-Butyldimethylsilyloxy)prop-2-en-1-yl]-3-iodoindole 15a

The same procedure as above was carried out using the alcohol **14a** (400 mg, 1.34 mmol) to give the silyl ether **15a** (395 mg, 71%). IR (ATR) ν: 3463 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.53 (1H, br s), 7.42 (1H, dd, J=7.0, 1.1 Hz), 7.33 (1H, dd, J=7.0, 1.1 Hz), 7.22 (1H, dt, J=7.0, 1.1 Hz), 7.17 (1H, dt, J=7.0, 1.1 Hz), 5.93 (1H, ddd, J=16.9, 10.3, 4.8 Hz), 5.48 (1H, ddd, J=4.8, 1.8, 1.8 Hz), 5.40 (1H, ddd, J=16.9, 1.8, 1.8 Hz), 5.15 (1H, ddd, J=10.3, 1.8, 1.8 Hz), 0.91 (9H, s), 0.14 (3H, s), 0.02 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 139.7, 138.0, 135.6, 130.4, 123.0, 120.8, 120.5, 114.5, 111.2, 70.3, 56.3, 25.8, 18.3, −4.8, −5.0. MS m/z: 413 (M^+). HRMS (EI) m/z: 413.0684 (M^+) (calcd for $C_{17}H_{24}INOSi$: 413.0672).

4.9. 2-[1-(*tert*-Butyldimethylsilyloxy)prop-2-en-1-yl]-3-iodo-*N*-(phenylsulfonyl)indole 15b

The same procedure as above was carried out using the alcohol **14b** (571 mg, 1.30 mmol) to give the silyl ether **15b** (626 mg, 87%). IR (ATR) ν: 1645, 1616 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.13 (1H, d, J=7.7 Hz), 7.75 (2H, d, J=7.3 Hz), 7.50–7.55 (1H, m), 7.26–7.45 (5H, m), 6.10–6.28 (2H, m), 5.37 (1H, dd, J=17.3, 1.1 Hz), 5.16 (1H, dd, J=10.3, 1.1 Hz), 0.91 (9H, s), 0.12 (3H, s), -0.02 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 140.0, 138.7, 137.6, 136.4, 133.9, 132.5, 129.2, 126.5, 126.0, 124.3, 122.2, 116.0, 115.2, 69.1, 30.9, 26.0, 18.3, −4.6, −4.9. MS m/z: 553 (M^+). HRMS (EI) m/z: 553.0602 (M^+) (calcd for $C_{23}H_{28}INO_3SSi$: 553.0604).

4.10. 2-(1-*tert*-Butyldimethylsilyloxy-2-methylprop-2-en-1-yl)-3-iodo-*N*-(methoxymethyl)indole 15c

The same procedure as above was carried out using the alcohol **14c** (200 mg, 0.56 mmol) to give the silyl ether **15c** (120 mg, 45%). ^1H NMR ($CDCl_3$) δ: 7.48 (1H, d, J=7.2 Hz), 7.43 (1H, d, J=7.2 Hz), 7.27 (1H, dt, J=7.2, 1.1 Hz), 7.21 (1H, dt, J=7.2, 1.1 Hz), 5.67 (1H, d, J=10.3 Hz), 5.55–5.57 (1H, m), 5.51 (1H, d, J=10.3 Hz), 5.36–5.38 (1H, m), 5.00–5.01 (1H, m), 3.25 (3H, s), 1.61 (3H, s), 0.90 (9H, s), 0.16 (3H, s), −0.13 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 145.6, 138.7, 138.2, 130.0, 123.5, 121.5, 121.0, 111.3, 110.2, 75.5, 72.4, 63.2, 55.4, 25.8, 19.5, 18.2, −4.9, −5.1. MS m/z: 471 (M^+). HRMS (EI) m/z: 471.1100 (M^+) (calcd for $C_{20}H_{30}INO_2Si$: 471.1090).

4.11. 2-[(1-*tert*-Butyldimethylsilyloxy)but-2-en-1-yl]-3-iodo-*N*-(methoxymethyl)indole 15d

The same procedure as above was carried out using the alcohol **15c** (168 mg, 0.47 mmol) to give the silyl ether **15d** (159 mg, 72%). ^1H NMR ($CDCl_3$) δ: 7.47 (1H, dd, J=7.7, 1.1 Hz), 7.41 (1H, dd, J=7.7, 1.1 Hz), 7.27 (1H, dt, J=7.7, 1.5 Hz), 7.20 (1H, dt, J=7.7, 1.5 Hz), 5.99 (1H, d, J=8.4 Hz), 5.87–5.95 (1H, m), 5.92 (1H, d, J=10.3 Hz), 5.50–5.57(1H, m), 5.54 (1H, d, J=10.3 Hz), 3.34 (3H, s), 1.79 (3H, dd, J=7.3, 1.5 Hz), 0.88 (9H, s), 0.17 (3H, s), -0.03 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 140.9, 138.3, 131.8, 130.1, 126.0, 123.5, 121.5, 121.0, 110.7, 75.7, 67.0, 60.9, 55.9, 25.8, 18.1, 14.4, −4.7, −4.7. MS m/z: 471 (M^+). HRMS (EI) m/z: 471.1062 (M^+) (calcd for $C_{20}H_{30}INO_2Si$: 471.1090).

4.12. *N*-(Methoxymethyl)carbazole-1,4-quinone 7

Carbon monoxide was bubbled for 5 min to a mixture of the silyl ether (100 mg, 0.22 mmol), tributyl(vinyl)tin (210 mg, 0.66 mmol), BHT (58 mg, 0.26 mmol), and $PdCl_2$(dppf) (36 mg, 0.044 mmol) in DMF (22 mL) at rt. The resulting mixture was stirred at 70 °C for 20 h under a CO atmosphere. After cooling to ambient temperature, TBAF (1 M in THF, 0.33 mL, 0.33 mmol) was added to the mixture and then the mixture was stirred at the same temperature for 1 h under O_2 atmosphere. The mixture was quenched with water and then the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by column chromatography using EtOAc/hexane (1:9) as an eluent to give the carbazole-1,4-quinone **7** (32 mg, 60%). Mp 136–137 °C (EtOAc). IR (ATR) ν: 1739, 1647 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.31 (1H, dd, J=7.7, 1.1 Hz), 7.62 (1H, dd, J=7.7, 1.1 Hz), 7.48 (1H, dt, J=7.7, 1.1 Hz), 7.40 (1H, dt, J=7.7, 1.1 Hz), 6.71 (1H, d, J=10.3 Hz), 6.64 (1H, d, J=10.3 Hz), 6.03 (2H, s), 3.35 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 183.8, 180.9, 139.0, 137.7, 136.3, 133.3, 127.6, 125.0, 123.5, 123.2, 118.1, 111.9, 75.0, 56.5. MS m/z: 241 (M^+). HRMS (EI) m/z: 241.0729 (M^+) (calcd for $C_{14}H_{11}NO_3$: 241.0739).

4.13. Carbazole-1,4-quinone 16a

The same procedure as above was carried out using the silyl ether **15a** (100 mg, 0.24 mmol) to give the carbazole-1,4-quinone **16a** (22 mg, 46%). Mp 220–221 °C (EtOAc). IR (ATR) ν: 3181, 1812 cm^{-1}. ^1H NMR (DMSO-d_6) δ: 12.9 (1H, br s), 8.04 (1H, d, J=7.7 Hz), 7.55 (1H, d, J=7.7 Hz), 7.40 (1H, dt, J=7.7, 1.4 Hz), 7.31 (1H, dt, J=7.7, 1.4 Hz), 6.76 (2H, s). ^{13}C NMR (DMSO-d_6) δ: 183.3, 179.9, 138.8, 137.4, 135.5, 135.4, 126.5, 123.9, 123.3, 121.7, 115.4, 113.8. MS m/z: 197 (M^+). HRMS (EI) m/z: 197.0481 (M^+) (calcd for $C_{12}H_7NO_3$: 197.0477).

4.14. *N*-(Methoxymethyl)-2-methylcarbazole-1,4-quinone 16c

The same procedure as above was carried out using the silyl ether **15c** (50 mg, 0.11 mmol) to give the carbazole-1,4-quinone **16c** (14 mg, 52%). IR (ATR) ν: 1731, 1643 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.31 (1H, dd, J=8.0, 1.1 Hz), 7.60 (1H, dd, J=8.0, 1.1 Hz), 7.46 (1H, dt, J=8.0, 1.3 Hz), 7.39 (1H, dt, J=8.0, 1.3 Hz), 6.48 (1H, q, J=1.7 Hz), 6.01 (2H, s), 3.33 (3H, s), 2.16 (3H, d, J=1.7 Hz). ^{13}C NMR ($CDCl_3$) δ: 184.0, 181.2, 147.2, 139.0, 133.9, 132.9, 127.2, 124.8, 123.8, 123.1, 118.1, 111.9, 75.0, 56.4, 15.7. MS m/z: 255 (M^+). HRMS (EI) m/z: 255.0880 (M^+) (calcd for $C_{15}H_{13}NO_3$: 255.0895).

4.15. *N*-(Methoxymethyl)-3-methylcarbazole-1,4-quinone 16d

The same procedure as above was carried out using the silyl ether **15d** (50 mg, 0.11 mmol) to give the carbazole-1,4-quinone **16d** (16 mg, 59%). Mp 114–115 °C (EtOAc). IR (ATR) ν: 1645, 1616 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.31 (1H, d, J=8.0 Hz), 7.61 (1H, d, J=8.0 Hz), 7.46 (1H, dt, J=8.0, 1.1 Hz), 7.39 (1H, dt, J=8.0, 1.1 Hz), 6.48 (1H, q, J=1.5 Hz), 6.02 (2H, s), 3.33 (3H, s), 2.16 (3H, d, J=1.5 Hz). ^{13}C NMR ($CDCl_3$) δ: 184.0, 181.3, 147.2, 139.0, 133.9, 132.9, 127.2, 124.8, 123.8, 123.1, 118.1, 111.9, 75.0, 56.4, 15.7. MS m/z: 255 (M^+). HRMS (EI) m/z: 255.0893 (M^+) (calcd for $C_{15}H_{13}NO_3$: 255.0895).

Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.01.015. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. For recent reviews: biochemical roles of quinones, see: (a) Hargreaves, R. H. J.; Hartley, J. A.; Batler, J. *Front. Biosci.* **2000**, *5*, E172–E180; (b) Beall, H. D.; Winski, S. L. *Front. Biosci.* **2000**, *5*, D639–D648; (c) Sissi, C.; Palumbo, M. *Curr. Top. Med. Chem.* **2004**, *4*, 219–230; (d) Garuti, L.; Roberti, M.; Pizzirani, D. *Mini-Rev. Med. Chem.* **2007**, *7*, 481–489; (e) Walker, S. R.; Carter, E. J.; Huff, B. C.; Morris, J. C. *Chem. Rev.* **2009**, *109*, 3080–3098.
2. For isolation and biology of murrayaquinone A: see: (a) Furukawa, H.; Wu, T.-S.; Ohta, T.; Kuoh, C.-S. *Chem. Pharm. Bull.* **1985**, *33*, 4132–4138; (b) Takeya, K.; Itoigawa, M.; Furukawa, H. *Eur. J. Pharmacol.* **1989**, *169*, 137–145; (c) Itoigawa, M.; Kashiwada, Y.; Ito, C.; Furukawa, H.; Tachibana, Y.; Bastow, K.; Lee, K.-H. *J. Nat. Prod.* **2000**, *63*, 893–897.
3. Bernard, P. H.; Chai, C. L. L.; Heath, G. A.; Mahon, P. J.; Smith, G. D. *J. Med. Chem.* **2004**, *47*, 4958–4963.
4. For recent reviews: chemistry and biology of carbazoles, see: (a) Knölker, H.-J.; Reddy, K. R. *Chem. Rev.* **2002**, *102*, 4303–4428; (b) Chakraborty, D. P.; Roy, S. In *Progress in the Chemistry and Organic Natural Products*; Herz, W., Grisebach, H., Kirby, G. W., Steglich, W., Tamm, C., Eds.; Springer: Wien, Germany, 2003; Vol. 69, pp 128–230; (c) Knölker, H.-J.; Reddy, K. R. In *The Alkaloids*; Cordell, G. A., Ed.; Academic: Amsterdam, The Netherlands, 2008; Vol. 65, pp 1–430; (d) Schmidt, A. W.; Reddy, K. R.; Knölker, H.-J. *Chem. Rev.* **2012**, *112*, 3193–3328; (e) Bauer, I.; Knölker, H.-J. *Top. Curr. Chem.* **2012**, *309*, 203–254; (f) Roy, J.; Jana, A. K.; Mal, D. *Tetrahedron* **2012**, *68*, 6099–6121.
5. (a) Hagiwara, H.; Choshi, T.; Fujimoto, H.; Sugino, E.; Hibino, S. *Chem. Pharm. Bull.* **1998**, *46*, 1948–1949; (b) Hagiwara, H.; Choshi, T.; Nobuhiro, J.; Fujimoto, H.; Hibino, S. *Chem. Pharm. Bull.* **2001**, *49*, 881–886; (c) Nishiyama, T.; Choshi, T.; Kitano, K.; Hibino, S. *Tetrahedron Lett.* **2011**, *52*, 3876–3878.

6. Hagiwara, H.; Choshi, T.; Fujimoto, H.; Sugino, E.; Hibino, S. *Tetrahedron* **2000**, *56*, 5807–5811.
7. (a) Choshi, T.; Uchida, Y.; Kubota, Y.; Nobuhiro, J.; Takeshita, M.; Hatano, T.; Hibino, S. *Chem. Pharm. Bull.* **2007**, *55*, 1060–1064; (b) Hieda, Y.; Choshi, T.; Uchida, Y.; Fujioka, H.; Fujii, S.; Hibino, S. *Chem. Pharm. Bull.* **2012**, *60*, 1522–1530.
8. (a) Choshi, T.; Sada, T.; Fujimoto, H.; Nagayama, C.; Sugino, E.; Hibino, S. *J. Org. Chem.* **1997**, *62*, 2535–2543; (b) Choshi, T.; Sada, T.; Fujimoto, H.; Nagayama, C.; Sugino, E.; Hibino, S. *Tetrahedron Lett.* **1996**, *37*, 2593–2596.
9. (a) Tohyama, S.; Choshi, T.; Matsumoto, K.; Yamabuki, A.; Ikegata, K.; Nobuhiro, J.; Hibino, S. *Tetrahedron Lett.* **2005**, *46*, 5263–5264; (b) Yamabuki, A.; Fujinawa, H.; Choshi, T.; Tohyama, S.; Matsumoto, K.; Ohmura, K.; Nobuhiro, J.; Hibino, S. *Tetrahedron Lett.* **2006**, *47*, 5859–5861; (c) Tohyama, S.; Choshi, T.; Matsumoto, K.; Yamabuki, A.; Hieda, Y.; Nobuhiro, J.; Hibino, S. *Heterocycles* **2010**, *82*, 397–416; (d) Choshi, T.; Hibino, S. *Heterocycles* **2009**, *77*, 85–97.
10. Tokuyama, H.; Kaburagi, Y.; Chen, X.; Fukuyama, T. *Synthesis* **2000**, 429–434.
11. (a) Corey, E. J.; Hegedus, L. S. *J. Am. Chem. Soc.* **1969**, *91*, 4926–4928; (b) Gagnier, S. V.; Larock, R. C. *J. Am. Chem. Soc.* **2003**, *125*, 4804–4807; (c) Kandnikov, D. V.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3643–3646.
12. Negishi, E.; Tour, J. M. *Tetrahedron Lett.* **1986**, *27*, 4869–4872.
13. Wu, X.-F.; Neumann, H.; Beller, M. *Chem. Soc. Rev.* **2011**, *40*, 4986–5009.