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Studies on the Reactivity of Phenyliodonium Ylide of 2-Hydroxy-1,4-Naphthoquinone: Reactions with Indole Derivatives and Other *C*-Nucleophiles

Sofia Koulouri, Elizabeth Malamidou-Xenikaki, Spyros Spyroudis,* and Maria Tsanakopoulou

Laboratory of Organic Chemistry, Department of Chemistry, University of Thessaloniki, Thessaloniki 54124, Greece

sspyr@chem.auth.gr

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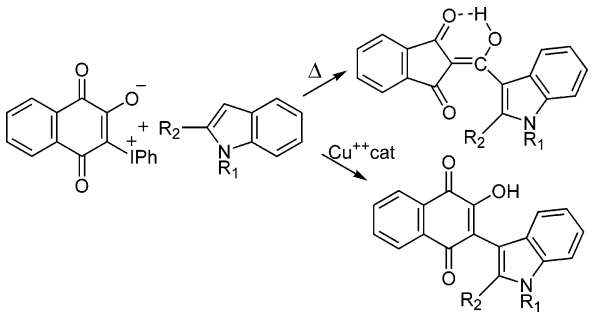

Thermal decomposition of phenyliodonium ylide of 2-hydroxy-1,4-naphthoquinone (lawsone) in the presence of indole derivatives affords 3-acylated indoles existing in their enol forms, through a ring contraction and α,α′-dioxoketene formation reaction. The same reactants afford 3-(3-indolyl)-2-hydroxy-1,4-naphthoquinones in a copper-catalyzed reaction. Enamines, among other *C*-nucleophiles tested, give analogous results.

Introduction

Hydroxyquinones, quinones bearing a hydroxy group on the quinone ring, are an important class of the naturally occurring quinones with diverse biological activity.[1] The synthesis and reactivity of hydroxyquinones have recently been reviewed.[2]

An interesting feature of hydroxyquinone chemistry is the easy formation of 2-oxido-3-aryliodonio-1,4-quinones or aryliodonium ylides of hydroxyquinones (**1**). These ylides are labile compounds and give rise to interesting derivatives.[2] Two main reactivity patterns are observed: Thermal decomposition, especially in moist CH_3CN, leads to α,α′-dioxoketene **2** formation with cyclopentenediones **3** as final products.[3] The second pathway involves the aryliodonio group replacement by a nucleophile at room temperature, in the presence of catalytic amounts of Cu^{2+}, Pd^{2+}, or Pd^0 or photochemically, as illustrated in Scheme 1.[4]

In a recent publication, we reported[5] the thermal and copper-catalyzed reactions of aryliodonium ylides of lawsone **5** with amines. In refluxing dichloromethane ylides **5** afforded good yields of 1,3-indanedione 2-carboxamides **6**. The latter exist in solution exclusively in an enol form that is unusual for amides but here are stabilized by two intramolecular hydrogen bonds (Scheme 2). The copper-catalyzed reaction followed an interesting pathway: Instead of the expected hydroxyaminoquinones analogues to **4** (Nu = NHR), arylated amines **7** were the isolated products along with iodohydroxyquinone **8**, which was surprisingly isolated under its *o*-quinonic form.

The same type of reactivity was observed with other amino compounds such as amino acids and their esters,

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(2) Spyroudis, S. *Molecules* **2000**, *5*, 1291.
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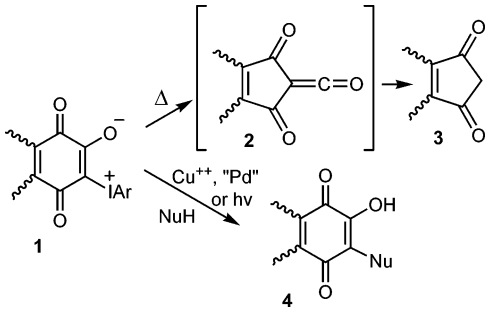
SCHEME 1



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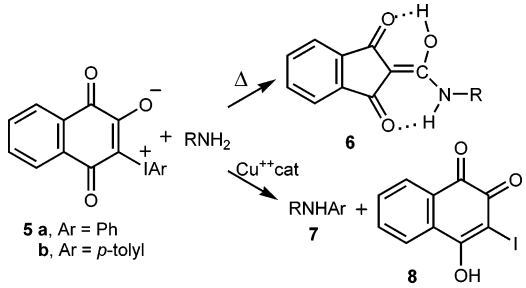

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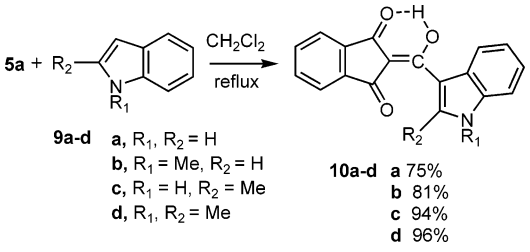


aminophenols, amino alcohols, and ureas.[6] The convenient isolation of compounds of type **6** suggests that α,α′-dioxoketenes **2** might find application in the preparation of the enol forms of other carboxylic acid derivatives.

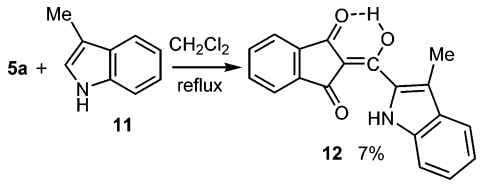
This interesting reactivity of aryliodonium ylides of hydroxyquinones with amino derivatives, acting as strong *N*-nucleophiles, prompted us to extend our studies and to investigate the reactivity of the former with *C*-nucleophiles.

Results and Discussion

Indole and its methyl derivatives **9a**−**d** were selected as appropriate *C*-nucleophiles. A suspension of equimolecular amounts of ylide **5a** and the proper indole derivative in CH_2Cl_2 was refluxed for 4−7 h to afford very good yields of acylated indoles **10a**−**d** in a clean reaction (Scheme 3). Indole derivatives **10** were isolated from the reaction solution simply by crystallization, as the other main product was iodobenzene. Alternatively, the same compounds can be isolated by column chromatography, usually in higher yields than in the former case, as reported in Scheme 3.

As was suggested previously,[5] the reaction proceeds through expulsion of iodobenzene, carbene formation, and

SCHEME 4



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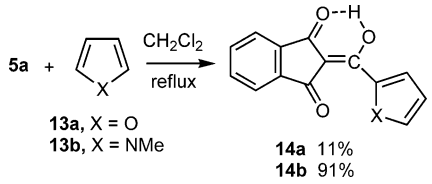

Wolff rearrangement of the latter to an α,α′-dioxoketene of type **2.** This ketene reacts with indole derivatives to afford compounds **10**, which exist in solution exclusively in their enol form. Indeed, indoylindanedione derivatives **10** are stabilized by the hydrogen bond formed between the enolic hydrogen and the carbonyl of the indanedione ring. In $CDCl_3$, the enolic hydrogen resonates as a broad 1H signal, exchangeable with D_2O, at 15−16 δ. In ^{13}C NMR, the enolic carbon appears at 170−176 δ and there are two carbonyl peaks, one at 177−179 δ for the hydrogen-bonded carbonyl and one at 197−199 δ for the free one. These data are consistent with those of analogous enol−amide structures **6**.[5] It must be noted that N-unsubstituted compounds **10a** and **10c** are not soluble in $CDCl_3$ and their spectra are recorded in $CDCl_3$−DMSO-d_6. In this case, the two carbonyl peaks are hardly seen in ^{13}C NMR, possibly due to some interaction with the solvent.

Another interesting feature in the ^1H NMR spectra is the downfield shift of the indole ring 2-H in compounds **10a** and **10b** (δ 9.86 and 9.89, respectively). An analogous downfield shift (δ 9.45−9.54) has been reported for indoles coupled through a methylidene bridge to barbituric acid derivatives, which possess structures similar to compounds **10**.[7] This shift was attributed to the possible formation of a weak hydrogen bond between the 2-H and a carbonyl group.

In case the more electron-rich position 3 in the indole ring is substituted, as in 3-methylindole (**11**), the reaction takes place from position 2, but the yield of the corresponding derivative **12** is very low (7%) (Scheme 4).

N-Tosylindole failed to give any products with **5a** under the same conditions, suggesting that electron-withdrawing groups diminish the nucleophilicity of the indole ring considerably and the addition does not take place.

The thermal reaction of **5a** with other aromatic *C*-nucleophiles such as 1,3-dimethoxybenzene and 2,5-dimethylfuran did not afford products analogous to **10**. Only furan (**13a**) and 1-methylpyrrole (**13b)** afforded the expected acylation products **14a** and **14b**, the latter in considerably higher yield (Scheme 5). Both **14a** and **14b** exhibit spectroscopic data consistent with the enol structure.

The reaction of **5a** with furan was repeated at room temperature with the addition of a catalytic amount of

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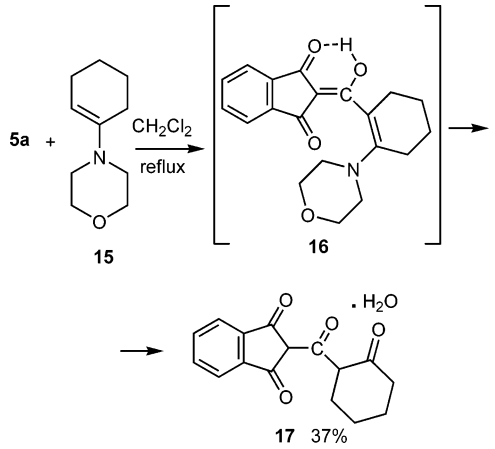
SCHEME 6



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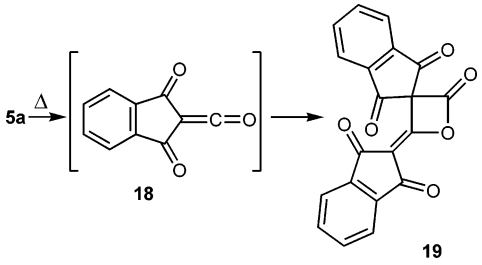

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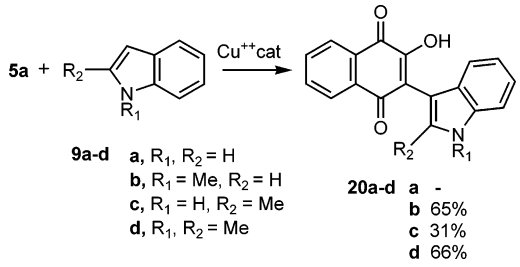

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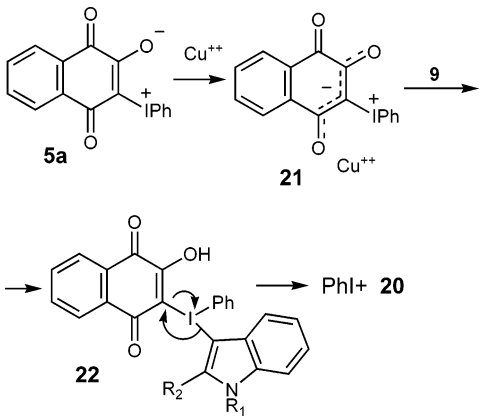


$Rh_2(OAc)_4$. The same as in the thermal decomposition derivative **14a** was isolated in 12% yield, suggesting that the catalyst facilitates the fission of the C−I bond and the formation of α,α′-dioxoketene. Under the same conditions (Rh^{2+} catalysis, room temperature), *N*-methylindole (**9b**) afforded the acylated derivative **10b** (in 45% yield), in all respects identical to that isolated from the thermal reaction.

Finally, the thermal reaction of ylide **5a** with nonaromatic *C*-nucleophiles, such as dimedone or indanedione, did not afford any acylated products. On the contrary, the reaction with 4-(1-cyclohexen-1-yl)morpholine (**15**) afforded the acylated cyclohexanone **17**, crystallized with one molecule of water, in 37% yield. It is most probable that the reaction proceeds through the acylated enamino compound **16**, which hydrolyzes during the isolation procedure to **17** (Scheme 6).

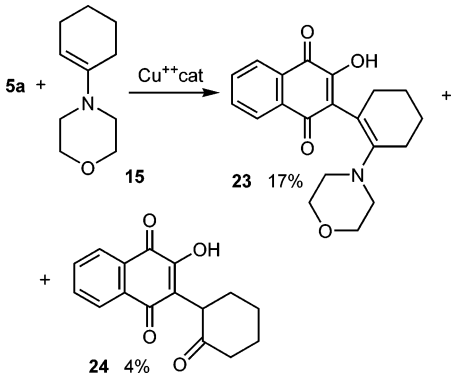
Spectral data indicate the absence of enolic form. The ^{13}C NMR spectrum exhibits a total of six peaks for carbonyls, two at δ 209.7 and 209.0, and four at δ 194.7−190.8, as well as 11 peaks at δ 138.6−108.5. These data, in addition to the absence of peaks in the enolic region (∼δ 170−176), indicate possibly that water forms mixtures of acetal derivatives of tetraketone **17**.

As was previously mentioned, all the above products arise from the electrophilic attack of the in situ formed α,α′-dioxoketene **18** on the proper position of indole or other *C*-nucleophile. In the absence of such a nucleophile, ketene **18** affords a dimerization product in yields varying between 37 and 48% in different experiments, along with small amounts of indanedione and its self-condensation derivative. Spectroscopic evidence indicates that this product has the tetraoxo-oxetanone structure **19** (Scheme 7). This dimerization derivative, which crystallizes out of the dichloromethane solution of the thermal reaction, is a labile compound and slowly decomposes on air. It must be noted that varying amounts of oxetanone **19** are isolated from thermal reactions of **5a** with less reactive nucleophiles, such as 1,3-dimethoxybenzene, 2,5-dimethylfuran, and 1,3-indanedione, which failed to afford acylated products. The same oxetanone **19** was obtained in 40% yield when a suspension of ylide **5a** was stirred for 3 days at room temperature and in the presence of a catalytic amount of $Pd(OAc)_2$.

Whereas the thermal reaction of ylide **5a** with indole derivatives affords acylated indoles, the corresponding Cu^{2+}-catalyzed reaction leads to the insertion of indole to the hydroxyquinone ring in a substitution reaction (Scheme 8). Indeed, a suspension of equimolecular amounts of ylide **5a** and the corresponding indole **9a**−**d** in CH_2Cl_2, in the presence of a catalytic amount of $Cu(CF_3SO_3)_2$, after overnight stirring at room temperature afforded as main product the corresponding 3-indolyl-2-hydroxy-1,4-naphthoquinones (**20b**−**d**) (Scheme 8).

Regarding the catalytic role of copper in the reaction, it is believed that copper ions form with ylide **5a** enolates of type **21**, increasing thus the electrophilic character of iodine and accelerating the nucleophilic attack of indole to iodine to form iodanes **22** (Scheme 9), a reaction pathway proposed for the analogous reaction of **5a** with amines and amino compounds.[5,6] Iodane **22**, through an internal nucleophilic attack and expulsion of iodobenzene, is transformed to the isolated products **20**. The reaction did not proceed with indole (**9a**), and this could be attributed to the complexation of copper ions to N−H bond, although the corresponding 2-methylindole (**9c**) afforded the expected **20c**, in moderate yield (31%). This difference between **9a** and **9c** can be explained by terms of the greater steric hindrance to nitrogen−copper complexation of the latter.

SCHEME 10



In no case was substitution reaction observed at the indole nitrogen atom, even when the reaction was repeated with 2,3-dimethylindole. Also, it must be noted that the reaction of ylide **5a** with furan in the presence of a catalytic amount of Cu^{2+} afforded only decomposition products of the ylide, along with polymeric material.

Finally, 4-(1-cyclohexen-1-yl)morpholine (**15**) in a copper-catalyzed reaction with **5a** afforded the enamino-substituted hydroxyquinone **23** in low yield (17%) accompanied by a small amount (4% yield) of the hydrolyzed (probably on column) derivative **24** (Scheme 10).

In conclusion, dioxoketene **18**, produced during the thermal decomposition of phenyliodonium ylide of lawsone, reacts with indole derivatives from the most reactive position 3 to afford high yields of the acylated products. The latter exist in solution in their enolic forms. Pyrrole, furan, and enamines exhibit the same reactivity, although yields are low for the latter two. In the absence of a suitable nucleophile, dioxoketene **18** dimerizes to oxetanone **19**.

The copper-catalyzed analogous reaction leads to the direct insertion of indolyl group into the hydroxyquinone ring, in medium yields. As indolylhydroxyquinones generally represent a class of compounds with interesting biological activity,[2] this might be a useful reaction for the preparation of such derivatives.

Experimental Section

General Procedure for the Thermal Reaction of 5a with Indole Derivatives. A suspension of 2-oxido-3-phenyliodonio-1,4-naphthoquinone (**5a**)[3a] (1 mmol) and the corresponding indole **9** (1 mmol) in CH_2Cl_2 (15 mL) was refluxed for 4−7 h, until a clear solution resulted and TLC showed the disappearance of ylide **5a**. The solution was concentrated in a vacuum until a small volume (∼3 mL) of the precipitated yellow solid was filtered and washed repeatedly with hexanes. The isolated derivatives **10** were pure enough, but analytical samples were obtained by recrystallization from CH_2Cl_2−hexanes. This procedure is convenient but yields range between 60 and 70%; alternatively, the concentrated reaction solution was subjected to column chromatography (silica gel, hexanes−ethyl acetate) to afford the higher yields reported below.

2-[Hydroxy(1*H*-indol-3-yl)methylene]-1*H*-indene-1,3(2*H*)-dione (10a): Yield 75%; mp 260−262 °C; ^{1}H NMR ($CDCl_3$ + DMSO-d_6, 300 MHz) δ 15.72 (s, br, 1H, OH), 12.59 (s, br, 1H, NH), 9.86 (s, 1H), 8.25 (s, br, 1H), 7.72−7.63 (m, 4H), 7.57 (s, br, 1H), 7.28−7.20 (m, 2H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 75 MHz) δ 176.1, 139.2, 136.5, 133.6 (br), 125.7, 123.3, 122.5, 121.2, 112.5, 109.1, 103.9; MS *m/z* (%) 290 (M^+ + 1, 95), 289 (M^+, 81) 173 (17), 145 (32), 118 (100), 117 (81). Anal. Calcd for $C_{18}H_{11}NO_3$: C, 74.73; H, 3.72; N, 4.84. Found: C, 74.35; H, 3.94; N, 4.95.

2-[Hydroxy(1-methyl-1*H*-indol-3-yl)methylene]-1*H*-indene-1,3(2*H*)-dione (10b): Yield 81%; mp 219−223 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 15.6 (s, br, 1H, OH), 9.89 (s, 1H), 8.39 (m, 1H), 7.78−7.71 (m, 2H), 7.68−7.58 (m, 2H), 7.41−7.33 (m, 3H), 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 198.7, 188.1, 176.4, 142.3, 139.6, 137.6, 137.4, 134.0, 133.1, 127.0, 123.8, 123.7, 123.3, 121.8, 121.4, 110.1, 109.3, 104.7, 34.0; MS *m/z* (%) 303 (M^+, 100), 173 (30), 131 (98). Anal. Calcd for $C_{19}H_{13}NO_3$: C, 75.24; H, 4.32; N, 4.62. Found: C, 74.92; H, 4.40; N, 4.65.

2-[Hydroxy(2-methyl-1*H*-indol-3-yl)methylene]-1*H*-indene-1,3(2*H*)-dione (10c): Yield 94%; mp 199−200 °C; ^{1}H NMR ($CDCl_3$ + DMSO-d_6, 300 MHz) δ 12.00 (s, br, 1H), 7.95−7.68 (m, 6H), 7.40 (d, J = 7.0 Hz, 1H), 7.23−7.09 (m, 2H), 2.51 (s, 3H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 75 MHz) δ 174.3, 145.5, 138.2, 134.8, 133.1, 125.9, 121.9, 121.5, 120.4, 119.9, 110.6, 106.1, 105.9, 14.0; MS *m/z* (%) 304 (M^+ + 1, 24), 303 (M^+, 14), 173 (37), 131 (84), 104 (100). Anal. Calcd for $C_{19}H_{13}NO_3$: C, 75.24; H, 4.32; N, 4.62. Found: C, 75.16; H, 4.32; N, 4.60.

2-[Hydroxy(1,2-dimethyl-1*H*-indol-3-yl)methylene]-1*H*-indene-1,3(2*H*)-dione (10d): Yield 96%; mp 174−176 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 14.20 (br, 1H, OH), 7.91−7.58 (two overlapping multiplets, 6H), 7.36−7.17 (m, 2H), 3.72 (s, 3H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.9, 186.7, 175.5, 145.9, 140.3, 138.3, 137.0, 134.2, 133.3, 126.3, 122.6, 122.2, 121.9, 121.8, 121.1, 109.3, 107.2, 30.0, 13.8; MS *m/z* (%) 317 (M^+, 39), 172 (70), 146 (100), 144 (33). Anal. Calcd for $C_{20}H_{15}NO_3$: C, 75.70; H, 4.76; N, 4.41. Found: C, 75.58; H, 4.85; N, 4.23.

2-[Hydroxy(3-methyl-1*H*-indol-2-yl)methylene]-1*H*-indene-1,3(2*H*)-dione (12): Yield 7%; oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 15.42 (s, 1H, OH), 13.30 (s, br, 1H, NH), 7.89−7.68 (m, 5H), 7.52 (d, J = 8.9 Hz, 1H), 7.39 (t, J = 7.4 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 198.8, 190.1, 173.0, 139.4, 138.5, 137.8, 134.8, 134.3, 127.8, 122.8, 122.1, 121.0, 120.5, 113.0, 12.1; MS *m/z* (%) 304 (M^+ + 1, 64), 303 (M^+, 37), 274 (10), 247 (10), 131 (100). ESI−HRMS *m/z* calcd for $C_{19}H_{13}NO_3$ + Na (MNa^+) 326.07897, found 326.07883.

Reaction of 5a with Furan (13a). Furan (3 mL) was added to a suspension of ylide **5a** (1 mmol) in CH_2Cl_2 (15 mL), and the mixture was refluxed for 5 h, until TLC showed the disappearance of ylide **5a**. In another experiment, a catalytic amount of $Rh_2(OAc)_4$ (20 mg) was added to the same mixture of furan and ylide **5a** in CH_2Cl_2, and the resulting suspension was stirred overnight at room temperature. After concentration and column chromatography (silica gel, hexanes−ethyl acetate), both reactions afforded **2-[2-furyl(hydroxy)methylene]-1*H*-indene-1,3(2*H*)-dione (14a)**, in 11 and 12% yields, respectively. mp 287−290 °C; ^{1}H NMR ($CDCl_3$ + DMSO-d_6, 300 MHz) δ 8.04 (br, 1H), 7.70−7.44 (m, 5H), 6.53 (br, 1H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 75 MHz) δ 191.2, 173.3, 152.4 (br), 144.0, 138.3, 131.4, 119.6, 117.8, 110.9, 107.8; MS *m/z* (%) 240 (M^+, 28), 146 (35), 68 (100). ESI−HRMS *m/z* calcd for $C_{14}H_8O_4$ + Na (MNa^+) 263.03148, found 263.03179.

Reaction with 1-Methylpyrrole (13b). The reaction was run under the same conditions as those used for indoles. Column chromatography afforded **2-[hydroxy(1-methyl-1*H*-pyrrol-2-yl)methylene]-1*H*-indene-1,3(2*H*)-dione (14b):** Yield 91%; mp 140−144 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 15.96 (br, 1H, OH), 8.44 (dd, J_1 = 1.5 Hz, J_2 = 6.5 Hz, 1H), 7.82−7.73 (m, 2H), 7.69−7.58 (m, 2H), 7.03−6.97 (m, 1H), 6.32 (dd, J_1 = 2.5 Hz, J_2 = 6.5 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 199.3, 186.7, 171.0, 139.6, 137.6, 134.5, 134.4, 133.2, 126.4, 124.5, 122.3, 121.5, 110.1, 104.2, 39.0; MS *m/z* (%) 254 (M^+ + 1, 47), 253 (M^+, 49), 173 (38), 80 (100). Anal. Calcd for $C_{15}H_{11}NO_3$: C, 71.14; H, 4.38; N, 5.53. Found: C, 70.85; H, 4.47; N, 5.13.

Reaction with 4-(1-Cyclohexen-1-yl)morpholine (15). A suspension of equimolecular quantities of ylide **5a** and enamine **15** (1 mmol) in CH_2Cl_2 (15 mL) was refluxed for 5 h. Upon column chromatography, **2-[(2-oxocyclohexyl)carbonyl]-1*H*-indene-1,3(2*H*)-dione (17)**, crystallized with one molecule of water, was isolated in 37% yield: mp >320 °C; ^{1}H NMR ($CDCl_3$ + DMSO-d_6, 300 MHz) δ 7.70−7.45 (m, 4H), 4.71−4.53 (m, 1H), 3.10−2.85 (m, 2H), 2.67−2.44 (m, 2H), 2.11−1.93 (m, 3H), 1.93−1.62 (m, 2H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 75 MHz) δ 209.7, 209.0, 194.7, 192.1, 191.1, 190.8, 138.6, 138.4, 138.1, 132.5, 131.7, 120.8, 120.7, 120.3, 120.0, 108.9, 108.5, 58.9, 58.5, 42.2, 42.0, 29.4, 29.1, 27.0, 26.9, 24.9, 23.5, 23.4; MS *m/z* (%) 288 ($M^+ + H_2O$, 3), 270 (M^+, 5), 252 (72), 146 (100). Anal. Calcd for $C_{16}H_{14}O_4 \cdot H_2O$: C, 66.66; H, 5.59. Found: C, 66.21; H, 5.38.

Dimerization Reaction. A suspension of ylide **5a** (1 mmol) in CH_2Cl_2 (15 mL) was refluxed for 5 h, until a clear solution resulted and TLC showed the disappearance of ylide **5a**. The solution was concentrated in a vacuum until half its volume and the precipitated yellow solid were filtered and washed repeatedly with hexanes. A second crop can be obtained from the filtrate upon gradual addition of hexanes. The yield of spiro dioxetanone derivative, **4′-(1,3-Dioxo-1,3-dihydro-2*H*-inden-2-ylidene)spiro[indene-2,3′-oxetane]-1,2′,3-trione (19)**, ranges between 37 and 48%. mp 177−182 °C, dec; IR (KBr) 1771, 1673, 1650, 1592, 1396 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.27−8.18 (m, 2H), 7.94−7.89 (m, 1H), 7.87−7.82 (m, 2H), 7.77−7.73 (m, 1H), 7.73−7.66 (m, 2H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 75 MHz) δ 195.7, 179.8, 141.8, 139.2, 134.1, 131.9, 128.9, 124.1, 121.8, 121.4, 43.7; MS *m/z* (%) 344 (M^+, 30), 316 (55), 288 (48), 172 (88), 105 (100). Anal. Calcd for $C_{20}H_8O_6$: C, 69.77; H, 2.34. Found: C, 69.45; H, 2.48.

Copper-Catalyzed Reactions of Ylide 5a with Indole Derivatives. A suspension of 2-oxido-3-phenyliodonio-1,4-naphthoquinone (**5a**) (1 mmol), the corresponding indole derivative **9** (1 mmol), and a catalytic amount of $Cu(CF_3SO_3)_2$ (20 mg, 0.055 mmol) in CH_2Cl_2 (15 mL) was stirred overnight at room temperature. The resulting reaction mixture was concentrated and chromatographed on column (silica gel, hexanes−ethyl acetate, 10:1, gradually increasing to pure ethyl acetate for the elution of **20**) to afford in order of eluance iodobenzene, a small amount of 3-iodo-2-phenoxynaphthoquinone[5] (3−5%), and finally indolylhydroxyquinones **20**, as purple solids.

2-Hydroxy-3-(1-methyl-1*H*-indol-3-yl)-1,4-naphthoquinone (20b): Yield 65%; mp 236−240 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.68 (s, br, 1H, OH), 8.11−8.04 (m, 2H), 7.83−7.72 (m, 2H), 7.57 (s, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H), 7.18 (t, J = 7.3 Hz, 1H), 7.05 (t, J = 7.3 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 183.7, 180.6, 152.9, 136.1, 133.8, 132.6, 132.3, 130.0, 126.7, 125.9, 125.1, 121.9, 121.0, 118.9, 117.8, 109.1, 104.2, 32.5; MS *m/z* (%) 303 (M^+, 55), 275 (35), 246 (46), 218 (59), 131 (40), 91 (100). Anal. Calcd for $C_{19}H_{13}NO_3$: C, 75.24; H, 4.32; N, 4.62. Found: C, 74.98; H, 4.37; N, 4.41.

2-Hydroxy-3-(2-methyl-1*H*-indol-3-yl)-1,4-naphthoquinone (20c): Yield 31%; mp 255−257 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.27−8.12 (m, 3H), 7.87−7.70 (m, 2H), 7.53 (s, br, 1H), 7.37−7.22 (m, 2H), 7.18−7.06 (m, 2H), 2.39 (s, 3H), in $CDCl_3$ + DMSO-d_6 two broad singlets at 10.51 and 10.00 (each 1H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 75 MHz) δ 182.8, 180.4, 153.5, 135.2, 134.6, 133.1, 131.7, 129.3, 127.3, 125.4, 124.7, 119.3, 118.7, 117.8, 109.6, 101.8, 12.56 (most of the peaks are broad, indicating possibly some restriction in the rotation of the 2-methylindolyl group); MS *m/z* (%) 303 (M^+, 9), 302 (100), 245 (30), 131 (53). ESI−HRMS *m/z* calcd for $C_{19}H_{13}NO_3$ + Na (MNa^+) 326.07876, found 326.07836.

2-Hydroxy-3-(1,2-dimethyl-1*H*-indol-3-yl)-1,4-naphthoquinone (20d): Yield 66%; mp 240−243 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.20 (d, J = 7.9 Hz, 1H), 8.16 (d, J = 7.9 Hz, 1H), 7.82−7.69 (m, 2H), 7.54 (s, 1H, OH), 7.33−7.27 (m, 2H), 7.18, (t, J = 7.6 Hz, 1H), 7.09 (t, J = 7.3 Hz, 1H), 3.73 (s, 3H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 75 MHz) δ 182.8, 180.4, 153.8, 136.0, 135.7, 133.2, 131.7, 129.4, 126.2, 125.4, 124.7, 119.5, 118.8, 118.2, 117.4, 107.8, 101.8, 28.6, 11.3; MS *m/z* (%) 317 (M^+, 15), 316 (24), 144 (100). Anal. Calcd for $C_{20}H_{15}NO_3$: C, 75.70; H, 4.76; N, 4.41. Found: C, 75.38; H, 4.74; N, 4.17.

Copper-Catalyzed Reaction of Ylide 5a with 4-(1-Cyclohexen-1-yl)morpholine (15). The reaction was run under the same conditions as those previously used with equimolecular amounts of reactants. Column chromatography afforded **2-hydroxy-3[2-(4-morpholinyl)-1-cyclohexene-1-yl]-1,4-naphthoquinone (23)**, as red-orange crystals: Yield 17%; mp 168−170 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (two d appearing as t, J = 6.7 Hz, 2H), 7.78 (dd, appearing as t, J = 7.4 Hz, 1H), 7.66 (dd, appearing as t, J = 7.7 Hz, 1H), 7.58 (s, br, 1H), 3.72 (ddd, appearing as d, J = 9.6 Hz, 2H), 3.53 (ddd, appearing as t, J = 11.2 Hz, 2H), 2.85 (ddd, appearing as d, J = 11.5 Hz, 2H), 2.34 (ddd, appearing as t, J = 10.3 Hz, 2H), 2.18−1.92 (m, 5H), 1.85−1.76 (m, 1H), 1.71−1.62 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 184.9, 182.2, 155.7, 135.3, 133.0, 132.8, 129.3, 127.0, 126.1, 119.9, 67.8, 51.6, 33.3 (br), 27.7, 26.9; MS *m/z* (%) 339 (M^+, 61), 252 (34), 167 (20), 86 (100). ESI−HRMS *m/z* calcd for $C_{20}H_{21}NO_4$ + Na (MNa^+) 362.13677, found 362.13677. Also afforded was **2-hydroxy-3-(2-oxocyclohexyl)-1,4-naphthoquinone (24):** Yield 5%; mp 144−147 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.19−8.01 (m, 2H), 7.79−7.63 (m, 2H), 5.90 (s, 1H, OH), 4.72 (dd, J_1 = 5.4 Hz, J_2 = 10.6 Hz, 1H), 3.78−3.61 (m, 1H), 2.69−2.58 (m, 1H), 2.56−2.35 (m, 2H), 2.20−1.97 (m, 2H), 1.90−1.72 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 203.8, 185.0, 180.0, 158.4, 134.2, 133.4, 133.0, 127.1, 126.8, 126.1, 111.8, 81.1, 40.8, 33.9, 27.2, 23.3; MS *m/z* (%) 270 (M^+, 20), 252 (32), 174 (38), 105 (100). ESI−HRMS *m/z* calcd for $C_{16}H_{14}O_4$ + Na (MNa^+) 293.07843, found 293.07817.

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