vacuo, the enol triflate was purified by flash chromatography on silica gel (petroleum ether) to give **26** (650 mg, 78% yield) as a colorless oil: $[\alpha]_D$ -2.47° (*c* 1.33, $CHCl_3$); IR (NaCl) 2965, 2860, 1682, 1473, 1415, 1252, 1212, 1145, 1024, 993, 876, 837, 776 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.67 (dd, *J* = 4.0, 4.0 Hz, 1 H), 3.66 (dd, *J* = 8.8, 3.2 Hz, 1 H), 2.26 (m, 1 H), 2.18 (m, 1 H), 1.74 (m, 2 H), 1.17 (s, 3 H), 1.12 (s, 3 H), 0.93 (s, 9 H), 0.10 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.2, 118.4 (q, $J_{^{13}C,^{19}F}$ = 319.6 Hz), 115.3, 75.5, 41.0, 26.4, 25.8 (3 C), 24.5, 20.9, 20.5, 18.1, -4.2, -5.0.

(-)-(*S*)-5-(*tert*-Butyldimethylsiloxy)-6,6-dimethyl-1-vinylcyclohexene (27). The general procedure of Stille was followed.[8] To a slurry of LiCl (320 mg, 6.5 mmol) and $Pd(PPh_3)_4$ (45 mg, 0.039 mmol) in anhydrous THF (25 mL) were added triflate **26** (500 mg, 1.3 mmol) in THF (5 mL) and tri-*n*-butylvinylstannane (410 mg, 1.3 mmol). The solution was refluxed for 18 h, cooled to room temperature, and diluted with petroleum ether (30 mL). The resultant solution was washed with 10% NH_4OH solution (15 mL), water (15 mL), and saturated NaCl solution (15 mL) and dried (Na_2SO_4). The solvent was removed in vacuo, and the residue was purified by flash chromatography on silica gel (petroleum ether) to give **27** (304 mg, 88% yield) as a colorless oil: $[\alpha]_D$ -15.0° (*c* 1.03, $CHCl_3$); IR (NaCl) 2957, 2931, 2886, 2858, 1616, 1472, 1361, 1256, 1122, 1092, 1044, 907, 889, 864, 836, 773 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.34 (dd, *J* = 17.1, 10.8 Hz, 1 H), 5.73 (dd, *J* = 3.7, 3.7 Hz, 1 H), 5.30 (dd, *J* = 17.1, 2.1 Hz, 1 H), 4.96 (dd, *J* = 10.8, 2.1 Hz, 1 H), 3.56 (dd, *J* = 6.7, 6.7 Hz, 1 H), 2.18 (m, 2 H), 1.70 (m, 2 H), 1.08 (s, 3 H), 1.04 (s, 3 H), 0.96 (s, 9 H), 0.10 (s, 3 H) 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.1, 136.8, 121.4, 113.2, 76.3, 39.1, 27.2, 25.9, 25.8 (3 C), 24.1, 21.7, 18.1, -4.0, -4.9; HRMS (EI, 70 eV) *m/z* 266.2030 (M^+, calcd for $C_{16}H_{30}OSi$ 266.2065).

Cycloaddition 1 with 27: (+)-(3*S*)-3-Hydroxytanshinone IIA *tert*-Butyldimethylsilyl Ether (28). A mixture of **1** (100 mg, 0.62 mmol), **27** (304 mg, 1.14 mmol), and anhydrous methanol (0.25 mL) was subjected to ultrasonication at 35 °C for 1 h. Excess diene **27** was recovered (162 mg, 88% recovery), and the crude cycloadducts were isolated and oxidized with DDQ (180 mg, 0.80 mmol) in refluxing benzene (35 mL, 12 h). After removal of the solvent in vacuo, flash chromatography on silica gel (CH_2Cl_2) gave a mixture of adducts **28** and **29** (191 mg, 73% yield, 30:1 **28**:**29** by ^1H NMR). Purification by recrystallization from petroleum ether and benzene yielded pure **28** as colorless crystals (165 mg, 65% yield): mp 185-186 °C; $[\alpha]_D$ +23.4° (*c* 0.05, $CHCl_3$); IR 3159, 2957, 2858, 1690, 1671, 1580, 1536, 1471, 1384, 1255, 1082, 891, 849, 773 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.63 (d, *J* = 8.3 Hz, 1 H), 7.57 (d, *J* = 8.3 Hz, 1 H), 7.23 (br s, 1 H), 3.70 (dd, *J* = 8.8, 2.3 Hz, 1 H), 3.34 (m, 1 H), 3.23 (m, 1 H), 2.26 (br s, 3 H), 1.90 (m, 2 H), 1.29 (s, 3 H), 1.26 (s, 3 H), 0.88 (s, 9 H), 0.12 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 183.5, 175.6, 161.7, 149.8, 143.3, 141.3, 133.7, 127.5, 125.8, 121.1, 120.5, 119.9, 74.6, 40.5, 29.5, 26.7, 26.6, 25.8 (3 C), 25.7, 18.1, 8.8, -4.0, -4.9; HRMS (EI, 70 eV) *m/z* 424.2068 (M^+, calcd for $C_{25}H_{32}O_4Si$ 424.2069).

(+)-(3*S*)-3-Hydroxytanshinone IIA (4).[3] Silyl ether **28** (30 mg, 0.07 mmol) was dissolved in a solution of 48% aqueous HF/THF (20 mL, 1:1, v/v) and stirred at room temperature for 2.5 h. Water (20 mL) was added, and the mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ (20 mL) and water (20 mL), dried (Na_2SO_4), and filtered. The solvent was removed in vacuo, and the residue was purified by flash chromatography on silica gel (CH_2Cl_2/ethyl acetate, 5:1). Recrystallization from $CHCl_3$/methanol yielded pure **4** as red crystals: mp 205-206 °C; $[\alpha]_D$ +22.2° (*c* 0.01, $CHCl_3$); IR (KBr) 3503, 3129, 2951, 2905, 1666, 1580, 1536, 1462, 1398, 1384, 1065, 995, 735 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.65 (d, *J* = 8.3 Hz, 1 H), 7.59 (d, *J* = 8.3 Hz, 1 H), 7.23 (q, *J* = 1.2 Hz, 1 H), 3.78 (dd, *J* = 8.0, 2.7 Hz, 1 H), 3.42 (ddd, *J* = 19.5, 6.5, 6.5 Hz, 1 H), 3.26 (ddd, *J* = 19.5, 7.0, 7.0 Hz, 1 H), 2.26 (d, *J* = 1.2 Hz, 3 H), 2.05 (m, 1 H), 1.94 (m, 1 H), 1.35 (s, 3 H), 1.33 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 183.4, 175.4, 161.5, 148.7, 142.8, 141.4, 133.7, 127.8, 125.9, 121.2, 120.7, 120.0, 74.0, 39.8, 29.3, 26.3, 26.1, 25.2, 8.8; HRMS (EI, 70 eV) *m/z* 310.1216 (M^+, calcd for $C_{19}H_{18}O_4$ 310.1205).

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Registry No. **1**, 113297-21-5; (+)-(*R*)-**2**, 127758-15-0; (-)-(*S*)-**2**, 18887-19-9; (+)-(3*R*,4*S*)-**3**, 96894-91-6; (-)-(3*S*,4*R*)-**3**, 97465-70-8; **4**, 127665-82-1; (+)-(*R*)-**5**, 127851-84-7; (-)-(*S*)-**5**, 17397-93-2; (-)-(*R*)-**6**, 89656-82-6; (+)-(*S*)-**6**, 89656-83-7; (+)-(*R*)-**7**, 127665-83-2; (-)-(*S*)-**7**, 127665-84-3; (+)-(*R*)-**8**, 127758-16-1; (-)-(*S*)-**8**, 127758-17-2; **9**, 127685-49-8; **10**, 127685-50-1; **11**, 33993-53-2; **12a**, 127759-63-1; **12b**, 127665-85-4; **13a**, 127758-18-3; **13b**, 127758-19-4; **14a**, 89576-08-9; **15**, 127851-85-8; *cis,cis*-**16**, 127665-86-5; *trans,cis*-**16**, 127665-87-6; **17**, 127665-88-7; **18**, 127665-89-8; **18** diol, 108392-44-5; **19**, 127758-20-7; **20**, 127758-21-8; **21**, 127758-22-9; **22**, 127758-23-0; **23**, 562-13-0; **24**, 87655-21-8; **25**, 106540-31-2; **26**, 127665-90-1; **27**, 127665-91-2; **28**, 127665-92-3; **29**, 127665-93-4; 2-methyl-1,3-cyclohexanedione, 1193-55-1.

Supplementary Material Available: ^1H and ^{13}C NMR spectra for new compounds described in this paper (17 pages). Ordering information is given on any current masthead page.

Synthesis of Miltirone by an Ultrasound-Promoted Cycloaddition

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The ultrasound-promoted cycloaddition of 3-isopropyl-*o*-benzoquinone, generated by the in situ silver oxide oxidation of the corresponding catechol, with 6,6-dimethyl-1-vinylcyclohexene has led to the synthesis of miltirone.

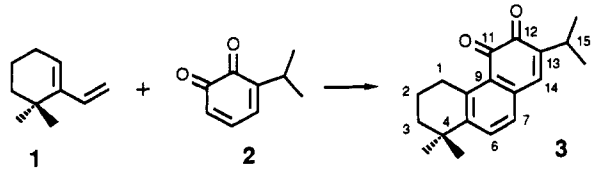
Introduction

The Chinese traditional medicine, Dan Shen, prepared from the roots of *Salvia miltiorrhiza*, has proven to be a rich source of abietane *o*-quinone diterpenoids. The synthesis of several of these natural products bearing the benzofuran-3,4-dione moiety was described in the preceding papers.[1] The Chinese species of sage, *S. miltiorrhiza*,[2] *S. przewalskii*,[3] and *S. trijuga*[4] are the best known

(1) (a) Lee, J.; Snyder, J. K. *J. Org. Chem.*, first paper in series in this issue. Haiza, M.; Lee, J.; Snyder, J. K. *J. Org. Chem.*, second paper in series in this issue. Preliminary report: (b) Lee, J.; Snyder, J. K. *J. Am. Chem. Soc.* **1989**, *111*, 1522.

0022-3263/90/1955-5013$02.50/0

Scheme I



species to produce the benzofuran unit.[5] The roots of these latter two species of *Salvia* have also been used to prepare Dan Shen.[6] The majority of abietanes isolated from other *Salvia* species retain the noncyclized isopropyl chain, often with the C ring in either the catechol or the *o*-quinone oxidation state. An example is miltirone (**3**) originally isolated from *S. miltiorrhiza*,[7a] but also found in other species.[8] The first reported synthesis of miltirone[9] followed a strategy that was reminiscent of Thomson's[2g] and Kakisawa's[10] approach to the tanshinones bearing the benzofuran unit. More recently, Knapp and Sharma reported a cycloaddition approach to **3**, utilizing 3-isopropyl-*o*-benzoquinone (**2**) as the dienophile (Scheme I).[11] Unfortunately, the instability of the *o*-quinone dienophile led to low yields of the cycloaddition (maximum of 30%), though the only regioisomer produced was the natural one. We now report that this cycloaddition route can indeed be used to prepare miltirone in yields exceeding 90% using ultrasound to promote the cycloaddition.

Results and Discussion

Model studies of the cycloaddition were performed with 1-vinylcyclohexene (**4**) as the diene system. Initial, exhaustive efforts to isolate **2** prior to the cycloaddition were abandoned for two reasons. First, **2** was very unstable, much more so than the isolable benzofuran-3,4-dione used in the previous work.[1] Second, efforts to separate **2** from unoxidized catechol were difficult, yet unoxidized catechol reacted with **2** to form dimers and higher oligomers if it was not removed prior to the cycloaddition. Even with ultrasound promotion, the highest yield of cycloadduct in the reaction of **4** with impure **2** (with 1 equiv of **2**) was only 45%, and the product mixture was heavily contaminated with oligomers, formed in the preparation and attempted isolation of **2**.

Given these difficulties, we then sought to generate **2** in situ via silver oxide oxidation with ultrasonication to promote the cycloaddition. Under these conditions, the aromatized cycloadduct, normiltirone (**8**), was formed in 81% yield with no trace of tetrahydroadduct **6** ($R_1 = R_2 = H$) or dihydroadduct **7** ($R_1 = R_2 = H$) detected (Scheme II). Presumably, **6** and **7** are dehydrogenated by **2**, regenerating the starting catechol which is subsequently recycled to **2** by the excess Ag_2O.[12] Furthermore, the cycloaddition was highly regioselective in favor of the natural regioisomer with only a possible trace of the unnatural regioisomer **9** detected in the ^1H NMR spectrum of the crude reaction mixture, analogous to the observations reported by Knapp in the synthesis of miltirone under thermal promotions.[11,13] In the absence of ultrasonication, cycloadduct **8** was obtained in only 46% yield after 72 h at ambient temperature, while thermal promotion (reflux in anhydrous ethanol) gave only 44% yield, with an increased amount of dimeric material from the reaction of **2** with the starting catechol. Similar results were observed with 6-methyl-1-vinylcyclohexene (**5**) to produce **10**, a tetrahydro derivative (A ring) of a natural product also found in *S. miltiorrhiza*,[7c] in good yield (76%).

With the conditions optimized, **3** was then prepared from 6,6-dimethyl-1-vinylcyclohexene (**1**) and **2** in 93% yield. Again the reaction was highly regioselective with only a possible trace of regioisomer **12** detected in the crude reaction mixture.[13] The spectroscopic properties (^1H NMR,[7a,11] ^{13}C NMR, MS IR, and UV[11]) and melting point[11] of synthetic **3** were identical with those reported in the literature. Under the same conditions (ambient temperature) without ultrasonication, **3** was obtained in only 53% yield after 96 h.

Analogous results were obtained with *o*-quinones **13** and **16**, though a slight increase in the amount of unnatural regioisomer **15** was obtained in the reaction with **13** so that

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(3) (a) Yang, B.; Qiang, M.; Qin, G.; Chen, Z. *Acta Pharm. Sin.* **1981**, *16*, 837. (b) Yang, B.; Huang, X.; Zhou, Q. *Acta Pharm. Sin.* **1984**, *19*, 274.

(4) Yang, B.-J.; Huang, T.-L.; Hu, Z.-B.; Chen, Z. X. *Yao Xue Tong Bao* **1982**, *17*, 242.

(5) Abietanoid *o*-quinones with the furan unit have also been reported in (a) *Rosmarinus officinalis*: Brieskorn, C. H.; Buchberger, L. *Planta Med.* **1973**, *24*, 190. (b) *S. drobovii, S. karabachensis, and S. trautvelteri*: Romanova, A. S.; Patadin, A. V.; Ban'kovskii, A. I. *Khim. Prir. Soedin.* **1977**, 414; *Chem. Abstr.* **1977**, *87*, 114654t. *S. sclarea*: Romanova, A. S.; Patadin, A. V.; Pervykh, L. N.; Zobenko, L. P. *Khim. Prir. Soedin.* **1978**, 515; *Chem. Abstr.* **1978**, *89*, 176374b.

(6) (a) In: *Zhong Cao Yao Xue*; Nanjing Yao Xue Yuan, "Zhong Cao Yao Xue" Bian Xie Zu, Jiangsu Ren Min Chu Ban She: Nanjing, 1976; Vol. 3, pp 947–951. (b) In: *Pharmacology and Applications of Chinese Materia Medica*; Chang, H. M., But, P. P. H., Eds.; World Scientific: Singapore, 1986; Vol. 1, pp 255–268.

(7) (a) Hayashi, T.; Kakisawa, H.; Hsu, H. Y.; Chen, Y. P. *J. Chem. Soc., Chem. Commun.* **1970**, 299. Other examples of abietanes from *S. miltiorrhiza* with a noncyclized isopropyl side chain: (b) Hayashi, T.; Handa, T.; Ohashi, M.; Kakisawa, H.; Hsu, H. Y.; Chen, Y. P. *J. Chem. Soc., Chem. Commun.* **1971**, 541. (c) Onitsuka, M.; Fujiu, M.; Shinma, N.; Maruyama, H. B. *Chem. Pharm. Bull.* **1983**, *31*, 1670. (d) Kusumi, T.; Ooi, T.; Hayashi, T.; Kakisawa, H. *Phytochemistry* **1985**, *24*, 2118. (e) Ginda, H.; Kusumi, T.; Ishituka, M. O.; Kakisawa, H.; Zhao, W.; Chen, J.; Tian, G. Y. *Tetrahedron Lett.* **1988**, *29*, 4603.

(8) Reference 5b, also: Houlihan, C. M.; Ho, C.-T.; Chang, S. S. *J. Am. Oil Chem. Soc.* **1985**, *62*, 96.

(9) Nasipuri, D.; Mitra, A. K. *J. Chem. Soc., Perk. Trans. 1* **1973**, 285.

(10) (a) Kakisawa, H.; Tateishi, M.; Kusumi, T. *Tetrahedron Lett.* **1968**, 3783. (b) Tateishi, M.; Kusumi, T.; Kakisawa, H. *Tetrahedron* **1971**, *27*, 231.

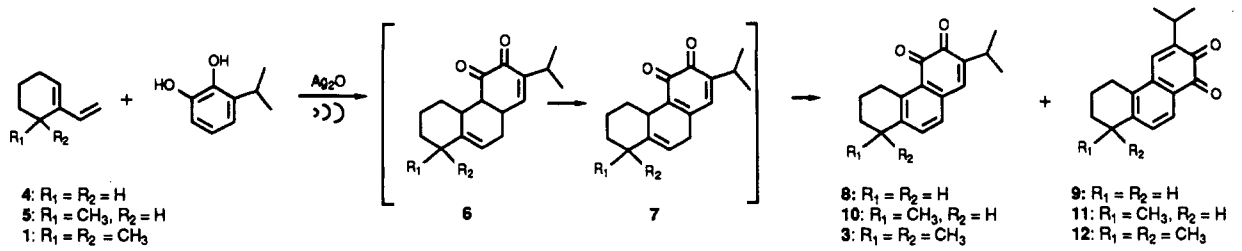
(11) Knapp, S.; Sharma, S. *J. Org. Chem.* **1985**, *50*, 4996. These workers referred to miltirone as rosmariquinone as it was termed upon isolation from rosemary leaves (ref 8) apparently unaware of the original isolation of this compound by Kakisawa and co-workers (ref 7a) from *S. miltiorrhiza*.

(12) In support of this suggestion, the cycloaddition of 1-acetoxybutadiene with benzofuran-3,4-dione as the dienophile (ref 1) produced the reduced catechol diacetate as a byproduct. The conclusion was that the *o*-quinone was functioning to dehydrogenate the initially formed cycloadduct, generating the catechol, which was subsequently acetylated by the excess 1-acetoxybutadiene. While the Ag_2O or another inorganic entity could also conceivably cause the dehydrogenation of the initially formed cycloadducts in this work, this could not be the case in the benzofuran-3,4-dione reaction since this *o*-quinone was isolated prior to the cycloaddition.

(13) Since a sufficient quantity of unnatural regioisomer for characterization was isolated in only one case (**15**), we could not rigorously prove the presence of the other regioisomers in the reaction mixtures, though the crude ^1H NMR spectra indicated that trace amounts may have been present.

(14) Reference 14 deleted in press.

Scheme II



4: $R_1 = R_2 = H$
5: $R_1 = CH_3$, $R_2 = H$
1: $R_1 = R_2 = CH_3$

8: $R_1 = R_2 = H$
10: $R_1 = CH_3$, $R_2 = H$
3: $R_1 = R_2 = CH_3$

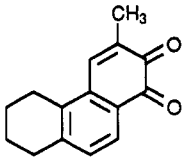
9: $R_1 = R_2 = H$
11: $R_1 = CH_3$, $R_2 = H$
12: $R_1 = R_2 = CH_3$

Table I. Cycloadditions of *o*-Quinones Generated in Situ with Vinylcyclohexenes

vinylcyclohexene	quinone[a]	conditions[b]	products	yield,[c] %
4	2	reflux, 3.5 h ambient temperature 72 h ultrasound, 24 °C, 3 h	8	45 46 81
5	2	ultrasound, 24 °C, 3 h	10	76
1	2	ambient temperature 96 h ultrasound, 24 °C, 3 h	3	53 93
4	13	ultrasound, 24 °C, 3 h	14	79
4	16	ultrasound, 24 °C, 3 h	17	66

[a] Generated in situ from the corresponding catechol. [b] All reactions were run in anhydrous ethanol. [c] Isolated yields.

a small amount (1 mg) could be isolated and characterized by ^1H NMR spectroscopy. A comparison of the results



15

obtained under both thermal and ultrasound promotion clearly shows the advantage of the in situ approach with ultrasound promotion of the cycloaddition (Table I).[15] The assignment of the regioisomers from the cycloaddition was based upon difference NOE studies as previously described.[1a] Thus, saturation of the *o*-quinone H-14 (**3**, **8**, **10**, and **14**) or 14-CH_3 (**17**) singlet of the natural regioisomers resulted in an enhancement of the aromatic doublet assigned to H-7. For **8**, **10**, and **14**, the NOE experiments were performed in benzene-d_6 in order to eliminate signal overlap between H-14 and H-6.

In conclusion, the ultrasound-promoted cycloaddition employing *o*-quinone **2** as a dienophile with vinylcyclohexene **1** has proven to be an expedient route to miltirone. The application of this approach with other diene systems should lend itself to the facile preparation of related abietane natural products.

Experimental Section

General. The NMR spectra were recorded on a Varian XL-400 spectrometer (93.93 kG, 400 MHz for ^1H, 100 MHz for ^{13}C) in $CDCl_3$. Residual $CHCl_3$ (δ 7.24 ppm) and $^{13}CDCl_3$ (δ 77.0 ppm) were used as internal references for ^1H and ^{13}C, respectively. All compounds were shown to be >95% pure by ^1H NMR spectroscopy. Mass spectra (medium and high resolution) were run on a Finnigan MAT-90 as indicated; IR were recorded on a Perkin-Elmer 1800 FTIR or a Perkin-Elmer 1300 IR spectrometer. Melting points are uncorrected. All solvents were purified and dried prior to use.[16] "Petroleum ether" refers to petroleum ether, bp 35–60 °C. 3-Isopropyl-1,2-dihydroxybenzene (ICN), 3-methyl-1,2-dihydroxybenzene (Aldrich), and 4-methyl-1,2-dihydroxybenzene (Aldrich) were commercially available, 1-vinylcyclohexene (**4**),[1a,17] 6-methyl-1-vinylcyclohexene (**5**),[1a] and 6,6-dimethyl-1-vinylcyclohexene (**1**)[11] were prepared according to literature procedures.

General Procedure: Ultrasound-Promoted Cycloadditions. The catechol, vinylcyclohexene, and Ag_2O were placed in a conical

(15) While these experiments do not rule out the possibility that the ultrasonication may function to enhance a slow catechol oxidation (a heterogeneous reaction) with a rapid, subsequent cycloaddition, this is considered unlikely in view of the results presented in the previous papers. Furthermore, as pointed out by a referee, the catechol oxidation should be rapid, far more rapid than is necessary to complete the reactions (3 h), suggesting that the slow step is the cycloaddition.

(16) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*, 2nd ed.; Pergamon Press: Oxford, 1980.
(17) Matsuo, K.; Tokoroyama, T.; Kubota, T. *Chem. Lett.* **1973**, 397.

vial containing anhydrous ethanol and subjected to ultrasonication at 24 °C until the reaction was complete by TLC. After completion of the reaction, the reaction mixture was filtered and the solvent was removed in vacuo. The *o*-quinone was isolated by flash chromatography on silica gel (CH_2Cl_2/petroleum ether, 1:1) to give the mixture of regioisomers. Final purification was accomplished by flash chromatography on silica gel, eluting with petroleum ether.

Cycloaddition of 2 with 4: Normiltirone (8). A mixture of 3-isopropyl-1,2-dihydroxybenzene (238 mg, 1.5 mmol), 1-vinylcyclohexene (**4**, 108 mg, 1 mmol), and Ag_2O (1.4 g, 6 mmol) in anhydrous ethanol (3 mL) was subjected to ultrasonication for 3 h at 24 °C. Purification of **8** gave red crystals (206 mg, 81% yield): mp 78–80 °C; IR (KBr) 2933, 2872, 1744, 1682, 1662, 1583, 1565, 1463, 1422, 1385, 1295, 1257, 914, 843, 812 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.30 (d, J = 7.6 Hz, 1 H), 7.09 (s, 1 H), 7.06 (d, J = 7.6 Hz, 1 H), 3.21 (t, J = 5.6 Hz, 2 H), 3.04 (sept, J = 7.0 Hz, 1 H), 2.82 (t, J = 5.8 Hz, 2 H), 1.80 (m, 4 H), 1.18 (d, J = 7.0 Hz, 6 H); ^1H NMR (benzene-d_6, 400 MHz) δ 6.74 (d, J = 7.5 Hz, 1 H), 6.60 (s, 1 H), 6.46 (d, J = 7.5 Hz, 1 H), 3.12 (t, J = 6.4 Hz, 2 H), 2.96 (sept, J = 6.9 Hz, 1 H), 2.36 (t, J = 6.1 Hz, 2 H), 1.46 (m, 2 H), 1.39 (m, 2 H), 1.02 (d, J = 6.9 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.1, 181.2, 145.0, 144.6, 140.8, 140.0, 135.9, 134.5, 128.0, 127.5, 30.4, 28.8, 26.8, 22.8, 21.9, 21.4 (2 C); LRMS (EI, 70 eV) m/z 254 (M^+, 6), 226 (96), 212 (29), 211 (100), 196 (10), 155 (10), 141 (14); HRMS (EI, 70 eV) m/z 254.1312 (M^+, calcd for $C_{17}H_{18}O_2$, 254.1307).

Cycloaddition of 2 with 5: *o*-Quinone 10. A mixture of 3-isopropyl-1,2-dihydroxybenzene (137 mg, 0.9 mmol), 6-methyl-1-vinylcyclohexene (**5**, 55 mg, 0.45 mmol), and Ag_2O (418 mg, 1.8 mmol) in anhydrous ethanol (2 mL) was subjected to ultrasonication for 3 h at 24 °C. Purification of **10** gave red crystals (92 mg, 76% yield): mp 87–89 °C; IR (KBr) 2953, 2869, 1680, 1652, 1631, 1581, 1465, 1422, 1392, 1257, 936, 830 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.42 (d, J = 7.8 Hz, 1 H), 7.08 (d, J = 7.8 Hz, 1 H), 7.07 (s, 1 H), 3.27 (m, 1 H), 3.10 (m, 1 H), 3.04 (m, 1 H), 2.96 (m, 1 H), 1.77–1.91 (m, 2 H), 1.76 (m, 1 H), 1.57 (m, 1 H), 1.31 (d, J = 7 Hz, 3 H), 1.18 (d, J = 6.8 Hz, 3 H), 1.17 (d, J = 6.9 Hz, 3 H); ^1H NMR (benzene-d_6, 400 MHz) δ 6.91 (d, J = 7.8 Hz, 1 H), 6.60 (s, 1 H), 6.50 (d, J = 7.8 Hz, 1 H), 3.2 (m, 1 H), 3.06 (m, 1 H), 2.97 (sept, J = 7.0 Hz, 1 H), 2.51 (m, 1 H), 1.53 (m, 1 H), 1.43 (m, 1 H), 1.34 (m, 1 H), 1.22 (m, 1 H), 1.02 (d, J = 7.0 Hz, 6 H), 1.01 (d, 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.3, 181.4, 145.9, 144.9, 144.8, 140.0, 135.2, 134.5, 128.0, 127.7, 33.2, 29.8, 29.1, 26.8, 22.9, 21.5, 21.4, 19.4; LRMS (EI, 70 eV) m/z 268 (M^+, 4), 241 (12), 240 (55), 226 (17), 225 (100), 210 (11), 165 (11); HRMS (EI, 70 eV) m/z 268.1442 (M^+, calcd for $C_{18}H_{20}O_2$, 268.1263).

Cycloaddition of 2 with 1: Miltirone (3). A mixture of 3-isopropyl-1,2-dihydroxybenzene (105 mg, 0.7 mmol), 6,6-methyl-1-vinylcyclohexene (**1**, 200 mg, 1.47 mmol), and Ag_2O (788 mg, 3.4 mmol) in anhydrous ethanol (1.5 mL) was subjected to ultrasonication for 3 h at 24 °C. Purification of **3** gave red crystals (184 mg, 93% yield): mp 94–96 °C; IR (KBr) 2962, 2938, 1667, 1657, 1632, 1579, 1563, 1385, 1257, 1230, 1141, 934, 923 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.56 (d, J = 7.8 Hz, 1 H), 7.08 (d, J = 7.8 Hz, 1 H), 7.05 (s, 1 H), 3.14 (t, J = 6.6 Hz, 2 H), 2.98 (sept, J = 6.9 Hz, 1 H), 1.75 (m, 2 H), 1.61 (m, 2 H), 1.26 (s, 6 H), 1.13 (d, J = 6.9 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.3, 181.4, 149.6, 144.9, 144.4, 139.9, 134.3, 133.7, 128.1, 127.9, 37.7, 34.4, 31.7 (2 C), 29.8, 26.8, 21.5 (2 C), 19.0; LRMS (EI, 70 eV) m/z 284 (M + 2, 35), 283 (M + 1, 30), 282 (M^+, 65), 269 (28), 254 (52), 252 (28), 240 (35), 239 (100), 237 (49), 225 (34), 165 (25); HRMS (EI, 70 eV) m/z 282.1617 (M^+, calcd for $C_{19}H_{22}O_2$, 282.1620).

Cycloaddition of 13 with 4: *o*-Quinones 14 and 15. A mixture of 3-methyl-1,2-dihydroxybenzene (251 mg, 2.0 mmol), 1-vinylcyclohexene (**4**, 167 mg, 1.3 mmol), and Ag_2O (1.56 g, 6.7 mmol) in anhydrous ethanol (3 mL) were subjected to ultrasonication for 3 h at 24 °C. Isolation of regioisomers **14** and **15** indicated a ratio of >30:1, **14**:**15**. Purification of **14** gave red crystals (241 mg, 79% yield): mp 84–86 °C; IR (KBr) 2931, 1696, 1684, 1653, 1635, 1617, 1559, 1457, 1384 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.26 (d, J = 7.7 Hz, 1 H), 7.12 (s, 1 H), 6.99 (d, J = 7.7 Hz, 1 H), 3.17 (m, 2 H), 2.80 (m, 2 H), 2.00 (s, 3 H), 1.76 (m, 4 H); ^1H NMR (benzene-d_6, 400 MHz) 6.73 (d, J = 7.6 Hz, 1 H), 6.40 (d, J = 7.6 Hz, 1 H), 6.33 (s, 1 H) 3.11, (dd, J = 6.2, 6.5 Hz, 2 H), 2.35 (dd, J = 6.1, 6.3 Hz, 2 H), 1.73 (s, 3 H), 1.45 (m, 2 H), 1.38 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.9, 181.7, 145.2, 143.2, 140.9, 135.9, 134.7, 134.5, 128.3, 127.2, 30.5, 28.8, 22.8, 21.9, 15.2; LRMS (EI, 70 eV) m/z 226 (M^+, 6), 225 (10), 199 (14), 198 (100), 183 (34), 158 (13), 155 (11), 128 (10), 115 (15); HRMS (EI, 70 eV) m/z 226.0989 (M^+, calcd for $C_{15}H_{14}O_2$, 226.0993). A small amount of **15** (~1 mg) was also isolated: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, J = 7.9 Hz, 1 H), 7.52 (s, 1 H), 7.10 (d, J = 7.9 Hz, 1 H), 2.87 (dd, J = 7.0, 6.1 Hz, 2 H), 2.81 (t, J = 6.1 Hz, 2 H), 2.06 (s, 3 H), 1.88 (m, 2 H), 1.80 (m, 2 H).

Cycloaddition of 16 with 4: *o*-Quinone 17. A mixture of 4-methyl-1,2-dihydroxybenzene (251 mg, 2.0 mmol), 1-vinylcyclohexene (**4**, 167 mg, 1.3 mmol), and Ag_2O (1.6 g, 6.7 mmol) in anhydrous ethanol (3 mL) was subjected to ultrasonication for 3 h at 24 °C. Purification of **17** gave red crystals (194 mg, 66% yield): mp 120–130 °C dec; IR (KBr) 2924, 2860, 2828, 1683, 1658, 1615, 1577, 1560, 1377, 1274, 1254, 865 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.26 (d, J_{AB} = 7.8 Hz, 1 H), 7.20 (d, J_{AB} = 7.8 Hz, 1 H), 6.24 (s, 1 H), 3.10 (m, 2 H), 2.75 (m, 2 H), 2.28 (s, 3 H), 1.67–1.74 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.6, 181.1, 154.9, 144.9, 142.2, 135.5, 134.7, 129.1, 126.2, 124.2, 30.5, 29.1, 22.9, 21.8, 21.2; LRMS (EI, 70 eV) m/z 226 (M^+, 21), 225 (41), 211 (13), 199 (16), 198 (100), 197 (13), 183 (55), 182 (10), 165 (15), 155 (12), 152 (12), 141 (11), 128 (10), 115 (13); HRMS (EI, 70 eV) m/z 226.1007 (M^+, calcd for $C_{15}H_{14}O_2$, 226.0994).

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Supplementary Material Available: ^1H and ^{13}C NMR spectra for new compounds described in this paper (11 pages). Ordering information is given on any current masthead page.