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Hetero Diels-Alder Reaction of *o*-Benzoquinones with Tetracyclone: An Efficient Synthesis of Benzodioxinone Derivatives

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Abstract:

o-Benzoquinones undergo facile hetero Diels-Alder reaction with tetracyclone leading to cyclopenta[b][1,4]benzodioxinones.

Keywords: Quinone; Diels-Alder reactions; benzodioxins.

The chemistry of *o*-quinones, their cycloaddition reactions in particular, has invoked considerable interest.[1-6] Our own recent investigations[7-12] have uncovered novel reactivity patterns in the cycloaddition of *o*-quinones. Of special interest is the reaction of *o*-quinones with electron rich dienes leading to dioxins, either directly or *via* a two step process involving a hetero Diels-Alder reaction followed by a [3,3] sigmatropic rearrangement.[7] In continuation of our efforts in this area, it was of interest to examine the reactivity of *o*-quinones towards electron deficient dienes such as tetracyclone. It may be noted that tetracyclone is most frequently employed as a reactive diene in the Diels-Alder reaction[13] with a large number of vinylic and alkynic dienophiles, especially arynes.[14] Except for an isolated report[15] on the reaction of *o*-chloranil with tetracyclone leading to cyclopenta[b][1,4]benzodioxinone, there has been no work in this area. We have studied the cycloaddition of a variety of *o*-quinones with tetracyclone and our results are presented here.

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Results and Discussion.

The reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone **1a** and tetracyclone **2** afforded cyclopenta[b][1,4] benzodioxinone **3a** in quantitative yield (Table 1).

The structure of the adduct was established on the basis of spectral data. The IR spectrum exhibited carbonyl absorption at 1723 cm^{-1}, typical of cyclopentenones and ether absorption at 1312 and 1236 cm^{-1}. The ^{13}C NMR spectrum showed the carbonyl carbon at δ 198.66, characteristic of the α,β–unsaturated ketone. The carbon atoms adjacent to oxygen of benzodioxin appeared at δ 88.27 and 90.36, respectively. HRMS of **3a** gave a molecular ion peak at *m/z* 604.296. Final proof for the structure of **3a** was obtained by a single crystal X-ray analysis (Figure 1).

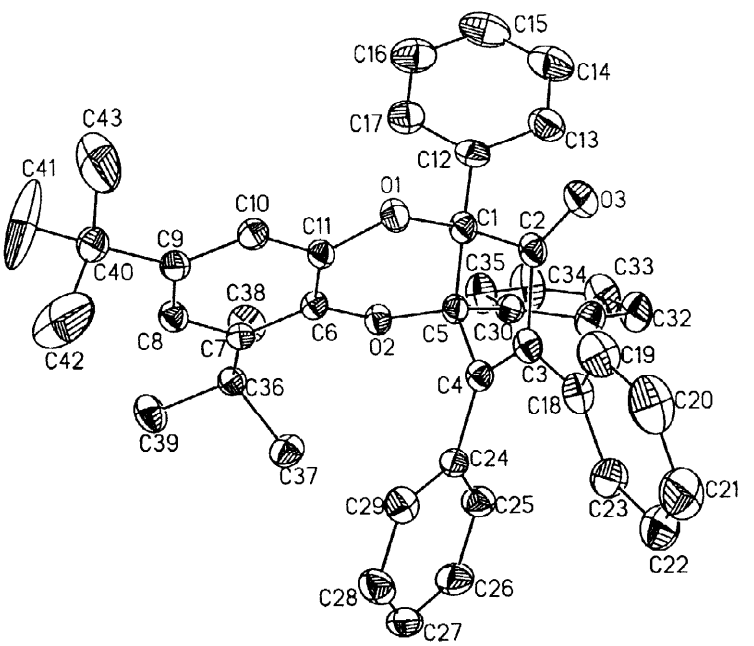
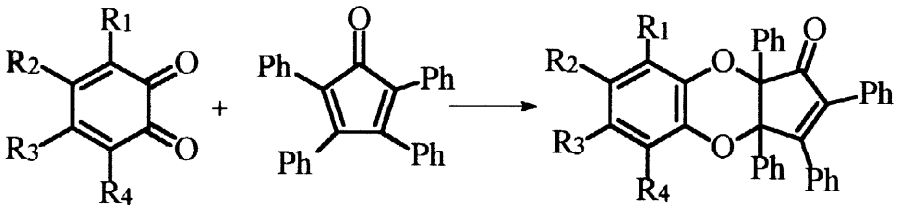


Figure **1**. X-ray structure of **3a**.

Similar reactivity pattern was observed with different substituted *o*-benzoquinones and the results obtained are summarized in Table 1.



1a-f **2** **3a-f**

Quinone	Substituents				Reaction Conditions	Products	Isomer Ratio[a]	Yield (%)[b]
	R^1	R^2	R^3	R^4				
1a	H	CMe_3	H	CMe_3	Benzene, S.T[d], 100 °C, 6 h	**3a**	-	100
1b	H	$HCPh_2$	H	$HCPh_2$	Benzene, S.T[d], 100 °C, 3 h	**3b**	-	92
1c	CMe_3	H	CMe_3	OMe	Toluene, S.T[d], 120 °C, 6 h	**3c**	1:1	50
1d	H	H	CMe_3	H	Benzene, S.T[d], 100 °C, 3 h	**3d**	3:2	95
1e[c]	H	H	H	OMe	Benzene, Reflux, 80 °C, 3 h	**3e**	1:1	72
1f[c]	H	H	Me	H	Benzene, Reflux, 80 °C, 3 h	**3f**	2:3	73

a. Regioisomeric ratio of the adducts was determined by ^1H NMR spectroscopy. b. Isolated yield.
c. Quinones **1e** and **1f** were prepared *in situ* by Ag_2CO_3 oxidation of the corresponding catechols . d. Sealed tube

Table 1

It may be noted that both 3d and 3f are mixtures of regioisomers in the ratio 3:2 and 2:3 respectively as shown in figure 2. It has not been possible to separate the mixtures. Their composition, however , can be ascertained from the interpretation of the ^{1}H NMR spectra as presented below.

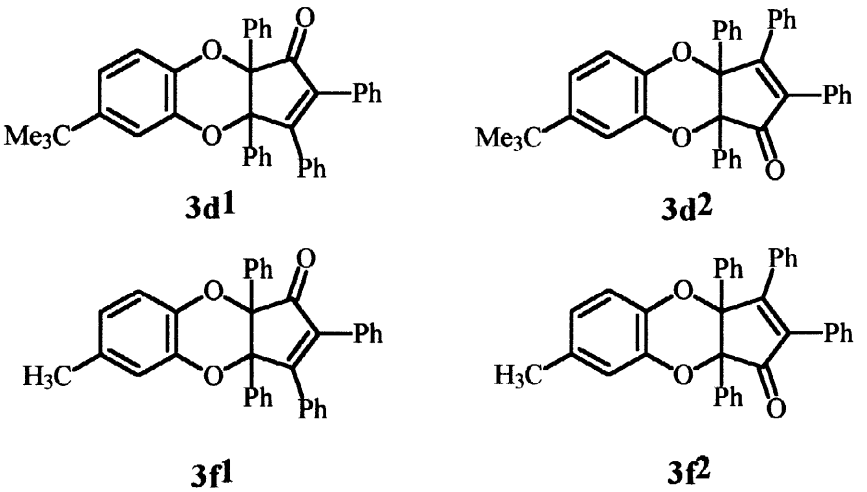
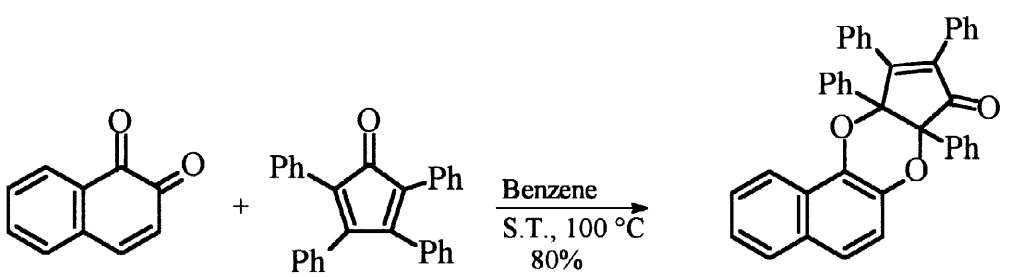


Figure 2

Examination of the molecular models reveals that the -CMe_3 group in $3d^1$ is close to two phenyl groups when compared to that in $3d^2$. Taking the deshielding effect in to account, the signal at δ 1.25 may be attributed to the -CMe_3 group in $3d^1$. The corresponding signal at δ 1.05 may be assigned to $3d^2$. Similarly -CH_3 group in $3f^1$ is more deshielded and therefore the signal at δ 2.25 may be attributed to $3f^1$ and the one at δ 2.1 may be assigned to $3f^2$. On the basis of this analysis the ratio of regioisomers in 3d is 3:2 and that in 3f is 2:3.

A similar reaction was also observed with 1,2-naphthoquinone which afforded cyclopenta[b][1,4]benzodioxinone derivative **5** regioselectively (Scheme 1).



Scheme 1

The correct regiochemistry of the cycloadduct **5** was assigned on the basis of single crystal X-ray analysis (Figure 3).

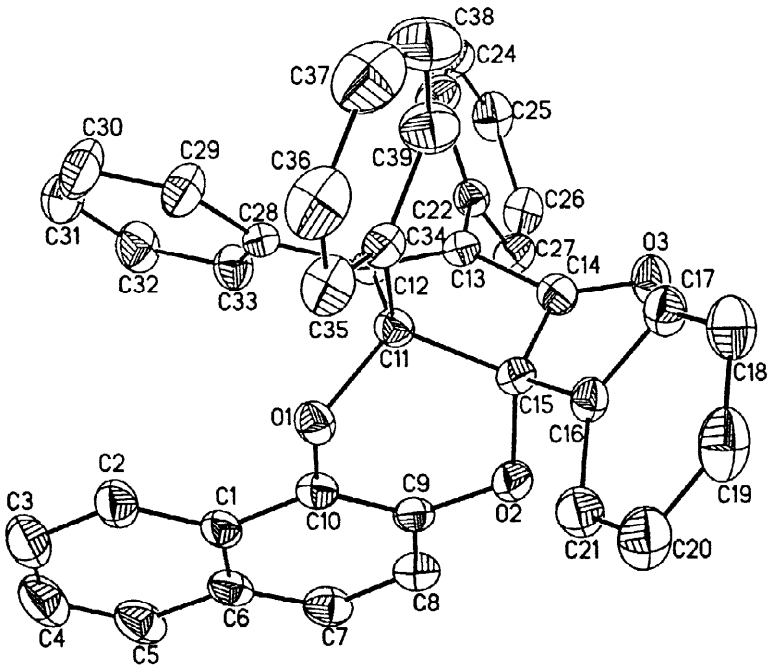


Figure **3**. X-ray structure of **5**

In conclusion, we have observed an interesting reactivity of *o*-benzoquinones with tetracyclone, leading to heavily substituted benzodioxinones. It is noteworthy that the potent biological activities associated with benzodioxins have drawn attention to the synthesis of compounds incorporating this heterocyclic system.[16]

Experimental Details.

All reactions were carried out in oven dried glassware. Analytical thin layer chromatography was performed on silicagel plates. Purification by gravity column chromatography was carried out using silica gel (100-200 mesh). Mixtures of ethyl acetate and petroleumether (60-80 °C) were used as eluents. IR spectra were recorded on a Perkin-Elmer model 882 spectrometer using KBr-pellets. NMR spectra were recorded on Hitachi-60, Jeol EX-90 and Bruker 300 spectrometers using chloroform-d as solvent. The chemical shifts are

given on the δ scale with tetramethylsilane as internal standard. The high resolution mass spectra were recorded on a Finnigan MAT model 8430.

(3a-cis)-2,3,3a,9a(tetraphenyl)-5,7-bis(1,1-dimethylethyl)-1,4-cyclopenta[b][1,4]benzodioxin-1-one (3a).

3,5-Di-*tert*-butyl-1,2-benzoquinone, **1a** (100 mg, 0.45 mmol) and tetracyclone, **2** (134 mg, 0.35 mmol) were dissolved in benzene (2 mL) in a Schlenk glass tube and heated at 100 °C for 6 h. The reaction could be followed by the slow decolourisation of the initially deep red solution. The solvent was removed *in vacuo* and the residue on silica gel column chromatography afforded the benzodioxinone derivative **3a** (210 mg, 100 %) as yellow crystalline solid, m.p. 218-220 °C.

IR (KBr): 2948, 1723, 1630, 1589, 1482, 1415, 1312, 1236, 1053, 973 cm^{-1}.

^1H NMR: δ 6.9-7.4 (m, 22 H), 1.3 (s, 9H), 1.2 (s, 9H).

^{13}C NMR: δ 198.66, 163.07, 144.72, 142.96, 141.02, 138.57, 137.83, 136.34, 132.58, 130.16, 129.86, 129.48, 128.76, 128.40, 127.98, 127.71, 127.57, 127.36, 117.18, 112.95, 90.36, 88.27, 34.87, 34.45, 31.41, 29.77.

HRMS: $C_{43}H_{40}O_3$: 604.29773; Found: 604.29691.

Anal. Calcd. for $C_{43}H_{40}O_3$: C, 85.43 %; H, 6.62 %; Found: C, 85.41 %; H, 6.64 %.

Crystal data for **3.** $C_{43}H_{40}O_3$, Fw 604.75, 0.52 x 040 x 0.33 mm, orthorombic, space group $P2_12_12_1$, unit cell dimensions:.a = 9.8576(7) Å, α = 90°; b = 17.8210(6) Å, β = 90°; c = 19.6029(9) Å, γ = 90 °. R indices(all data) R1 = 0.0559, wR2 = 0.1486. volume, Z = 3443.7(3) $Å^3$, 4. D calc = 1.166 Mg/m^3. F(000) = 1288. Absorption coefficient 0.558 mm^{-1}; reflections collected 3573 (Sheldrick, G. M., Siemens, Analytical X-ray Division, Madison, WI, 1995).

(3a-cis)-2,3,3a,9a(tetraphenyl)-5,7-bis(1,1-diphenylmethyl)-1,4-cyclopenta[b][1,4]benzodioxin-1-one (3b).

3,5-Bis(diphenylmethyl)-1,2-benzoquinone, **1b** (100 mg, 0.23 mmol) and tetracyclone, **2** (67 mg, 0.175 mmol) were dissolved in benzene (2 mL) in a Schlenk glass tube and heated at 100 °C for 3 h. The solvent was removed *in vacuo* and the residue on silica gel column chromatography afforded the benzodioxinone derivative **3b** (132 mg, 92 %) as yellow solid, m.p. 210-212 °C

IR (KBr): 3067, 3034, 2960, 1729, 1602, 1493, 1451, 1296, 1183, 1075, 967, 748, 697 cm^{-1}.

^1H NMR: δ 6.5-7.5 (m, 42H), 1.9-2.0 (s, 2H).

^{13}C NMR: δ 195.85, 161.72, 142.10, 141.82, 139.82, 137.65, 136.22,133.35, 129.96, 128.50, 127.80, 127.23, 126.85, 126.42, 125.78, 124.12, 120.01, 117.89, 91.37, 89.95, 51.35.

Anal. Calcd for $C_{61}H_{44}O_3$: C, 88.83 %; H, 5.34 %; Found: C, 88.78 %; H, 5.43 %.

(3a-cis)-2,3,3a,9a(tetraphenyl)-6,8-bis(1,1-dimethylethyl)-5-methoxy-1,4-cyclopenta[b][1,4]benzodioxin-1-one (3c).

4,6-Di-*tert*-butyl-3-methoxy-1,2-benzoquinone, **1c** (125 mg, 0.5 mmol) and tetracyclone, **2** (148 mg, 0.39 mmol) were dissolved in toluene (2 mL) in a Schlenk glass tube and heated at 120 °C for 6 h. The solvent was removed *in vacuo* and the residue on silica gel column chromatography afforded the benzodioxinone derivative **3c** (122 mg, 50 %) as yellow solid..

IR (KBr): 2968, 1728, 1616, 1493, 1450, 1418, 1367, 1313, 1233, 1092, 765 cm^{-1}.

^{1}H NMR: δ 6.7-7.3 (m, 42H), 3.6 (s, 3H), 3.5 (s, 3H), 1.1-1.5 (m, 36H).

^{13}C NMR: δ 195.32, 167.12, 149.20, 148.18, 147.29, 146.15, 142.42, 141.65, 139.89, 138.43, 136.70, 135.17, 134.93, 133.92, 132.43, 131.95, 131.38, 131.21, 130.64, 129.92, 129.53, 128.76,128.37, 128.19, 127.89, 127.57, 127.12, 126.85, 117.06, 116.91, 98.45, 89.79, 60.44, 60.32, 35.02, 34.78, 34.69, 30.60, 30.36, 30.15, 30.07, 29.95, 28.51, 26.96.

Anal. Calcd for $C_{44}H_{42}O_4$: C, 83.28 %; H, 6.62 %; Found : C, 83.16 %; H, 6.52 %.

(3a-cis)-2,3,3a,9a(tetraphenyl)-6-(1,1-dimethylethyl)-1,4-cyclopenta[b][1,4]benzodioxin-1-one (3d).

4-*tert*-Butyl-1,2-benzoquinone, **1d** (74 mg, 0.45 mmol) and tetracyclone, **2** (134 mg, 0.35 mmol) were dissolved in benzene (2 mL) in a Schlenk glass tube and heated at 100 °C for 3 h. The solvent was removed *in vacuo* and the residue on silica gel column chromatography afforded the benzodioxinone derivative **3d** (180 mg, 95 %) as yellow solid.

IR (KBr): 3053, 2960, 1720, 1596, 1496, 1447, 1273, 1130, 1081, 963, 783cm^{-1}.

^{1}H NMR: δ 6.7-7.8 (m, 46H), 1.25 (s, 11H), 1.05 (s, 7H).

^{13}C NMR: δ 196.27,163.73, 163.40, 162.23, 148.60, 144.30, 143.26, 141.11, 139.65, 137.80, 129.95, 129.42, 128.52, 127.86, 126.88, 123.57, 118.94, 117.42, 115.36, 115.04, 112.98, 96.12, 89.10, 34.63, 34.27, 34.12, 33.17, 31.77, 31.53, 29.92, 29.11.

Anal. Calcd for $C_{39}H_{32}O_3$: C, 85.40 %; H, 5.84 %; Found: C, 85.38 %; H, 5.75 %.

(3a-cis)-2,3,3a,9a(tetraphenyl)-5-methoxy-1,4-cyclopenta[b][1,4]benzodioxin-1-one Benzodioxinone (3e).

3-Methoxycatechol, **1e** (211 mg, 1.5 mmol) was dissolved in benzene (5 mL) and silver carbonate (828 mg, 3 mmol) was added followed by tetracyclone, **2** (192 mg, 0.5 mmol) and the mixture was refluxed in an oil bath at 80 °C for 3 h. The inorganic residue was then removed by filtering through celite and washed with dichloromethane. The solvent was removed *in vacuo* and the residue on column chromatography gave **3e** (189 mg, 72 % yield) as yellow solid.

IR (KBr): 3038, 2949, 1713, 1598, 1489, 1335, 1259, 1100, 1024, 756, 690 cm^{-1}.

^1H NMR: δ 7-7.6 (m, 46H), 3.85 (s, 3H), 3.65 (s, 3H).

^{13}C NMR: δ 195.18, 162.87, 162.09, 150.01, 148.94, 145.42, 142.43, 138.23, 138.08, 134.97, 134.80,132.44, 131.48, 131.19, 130.26, 129.99, 129.84, 129.51, 129.22, 128.80, 128.44, 128.26, 128.14, 127.90, 127.58, 127.13, 126.98, 122.71, 120.80, 110.99, 109.35, 107.44, 105.11, 90.28, 89.86, 89.66, 56.51, 55.70.

Anal. Calcd. for $C_{36}H_{26}O_4$: C, 82.75 %; H, 4.98 %; Found: C, 82.48 %; H, 5.09 %.

(3a-cis)-2,3,3a,9a(tetraphenyl)-6-methyl-1,4-cyclopenta[b][1,4]benzodioxin-1-one (3f).

4-Methylcatechol, **1f** (186 mg, 1.5 mmol) was dissolved in benzene (5 mL) and silvercarbonate (828 mg, 3 mmol) was added followed by the tetracyclone, **2** (192 mg, 0.5 mmol) and the mixture was refluxed in an oil bath at 80 °C for 3 h. The solvent was removed *in vacuo* and the residue on column chromatography gave **3f** (185 mg, 73 %) as yellow solid.

IR, KBr: 3059, 2923, 1719, 1497, 1281, 1219, 1025, 781, 690 cm^{-1}.

^1H NMR: δ 6.8-7.7 (m, 46H), 2.25 (s, 2.5H), 2.1 (s, 3.5H).

^{13}C NMR: δ 195.44, 163.55, 163.25, 162.62, 162.56, 157.67, 143.65,142.33, 141.89, 141.83, 139.47, 138.49, 138.40, 135.02, 134.96, 133.12, 131.56, 131.47, 131.41, 130.28, 130.04, 129.86, 129.80, 129.51, 128.85, 128.46, 128.25, 127.86, 127.57, 127.42, 127.33, 127.15, 126.91, 124.05, 122.40, 118.65, 117.93, 117.12, 116.50, 89.44, 88.96, 20.94, 20.58.

Anal. Calcd. for $C_{36}H_{26}O_3$: C, 85.37 %; H, 5.13 %; Found: C, 85.32 %; H, 5.10 %.

(3a-cis)-2,3,3a,11a(tetraphenyl)-naphtho[a] -1,4-cyclopenta[b][1,4]benzodioxin-1-one (5).

1,2-Naphthoquinone, **4** (100 mg, 0.63 mmol) and tetracyclone, **2** (187 mg, 0.48 mmol) were dissolved in benzene (2 mL) in a Schlenk glass tube and heated at 100 °C for 3 h. The solvent was removed *in vacuo* and the residue on silica gel column chromatography afforded the benzodioxinone derivative **5** (210 mg, 80 %) as yellow solid, m.p. 154-156°C.

IR (KBr): 3029, 2930, 1728, 1452, 1398, 1344, 1263, 1155, 1094, 1013, 798, 757 cm^{-1}

^1H NMR: δ 6.6 -7.5 (m, 26H)

^{13}C NMR: δ 194.89, 163.07, 142.15, 138.43, 134.62, 128.51, 127.96, 127.70, 127.27, 123.15, 117.47, 89.48, 88.97.

MS *m/z*: 543 (M^++1), 542 (M^+), 385, 159.

Anal. Calcd. for $C_{39}H_{26}O_3$: C, 86.35 %; H, 4.79 %; Found: C, 86.32 %; H, 4.72 %.

Crystal data for **3.** $C_{43}H_{40}O_3$, Fw 604.75, 0.52 x 040 x 0.33 mm, triclinic, space group $P\bar{1}$, unit cell dimensions:.a = 13.314(2) Å, α = 61.372(9)°; b = 16.080(3) Å, β = 67.225(9)°; c = 16.771(3) Å, γ = 73.736(10) °. R indices(all data) R1 = 0.1783, wR2 = 0.1274. volume, Z = 2885.7(8) $Å^3$, 4. D calc = 1.249 Mg/m^3. F(000) = 1136. Absorption coefficient 0.078 mm^{-1}; reflections collected 51713 (Sheldrick, G. M., Siemens, Analytical X-ray Division, Madison, WI, 1995).

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