CHAPTER 4

CYCLOADDITION REACTIONS OF
3-METHYLENE-1,2,4-NAPHTHALENETRIONE
AND CAN MEDIATED OXIDATIVE ADDITION
OF 2-HYDROXY-1,4-NAPHTHOQUINONE

This chapter is divided into two sections. The first section deals with the generation and hetero Diels-Alder reactions of the quinone methide derived from 2-hydroxy-1,4-naphthoquinone. The second section gives an account of cerium(IV) ammonium nitrate (CAN) mediated oxidative addition of 2-hydroxy-1,4-naphthoquinone to dienes.

4.1. CYCLOADDITION REACTIONS OF 3-METHYLENE-1,2,4-NAPHTHALENETRIONE

4.1.1. INTRODUCTION

Naphthofurandiones, dihydronaphthofurandiones and dihydronaphthopyrandiones comprise an important group of heterocyclic quinones.\(^1\) Some representative examples of this class of compounds are given in Figure 1.
A number of these compounds exhibit wide range of pharmacological activities.\textsuperscript{1} For example, $\beta$-lapachone induces apoptosis in human prostate cancer cells \textit{in vitro}\textsuperscript{2,3} and several of its derivatives are cytotoxic agents.\textsuperscript{4,5}

The synthesis of these compounds is essentially dependent on the elaboration of lapachol \textsuperscript{2} and this has been the target of many synthetic efforts.\textsuperscript{6} Recently, a novel protocol for the synthesis of lapachol was reported by Frydman \textit{et al.} (Scheme 1).\textsuperscript{7}

\begin{equation}
\begin{align*}
1. & \text{ i) DMSO, -78 °C, LiH; ii) LiI, Me_2C=CHCH_2Br, 25 °C; iii) 45 °C, 5 h, H}^+ \\
2. & \text{ i) EtOAc, 5\% NaHCO}_3, \text{ HCl; ii) EtOAc, Et}_2\text{O, 2N NaOH, HCl}
\end{align*}
\end{equation}

\textbf{Scheme 1}

The acid catalyzed cyclization of lapachol by classical methods leads to the formation of lapachones (Scheme 2).\textsuperscript{8}
As part of our research program focused on the Diels-Alder and other cycloaddition reactions of quinonoid compounds, we became interested in the construction of dihydronaphthopyrandiones by hetero Diels-Alder reactions of 3-methylene-1,2,4-(3H)naphthalenetrione, the quinone methide generated from 2-hydroxy-1,4-naphthoquinone. The results of these investigations are presented here.

4.1.2. RESULTS AND DISCUSSION

The quinone methide 7 was generated by an uncatalyzed Knoevenagel condensation of 2-hydroxy-1,4-naphthoquinone 1 with paraformaldehyde (Scheme 3).
4.1.2.1. REACTION WITH CYCLIC DIENES

Our studies started with the reaction of cyclopentadiene with the quinone methide 7. When a mixture of 2-hydroxy-1,4-naphthoquinone 1 and paraformaldehyde was refluxed in dioxane in the presence of cyclopentadiene, the reaction proceeded smoothly to afford the cycloadduct 9 in 90% yield (Scheme 4).

\[
\text{Scheme 4}
\]

i. Dioxane, 100 °C, 3 h, 90%

The structure of the product was ascertained on the basis of spectroscopic data. The IR spectrum of the cycloadduct showed strong carbonyl absorption at 1676 cm\(^{-1}\). In the \(^1\)H NMR spectrum, the aromatic protons were seen as two multiplets centered at \(\delta 8.07\) and 7.65 integrating for two protons each. The olefinic protons were seen as a broad singlet at \(\delta 6.07\). The ring junction proton on the carbon adjacent to the pyran oxygen resonated to give a doublet at \(\delta 5.29\) (\(J = 5.2\) Hz) and the other ring junction proton displayed a multiplet centered at \(\delta 2.84\). In the \(^{13}\)C NMR spectrum, the signals due to the carbonyl groups were discernible at \(\delta 183.78\) (C-9) and 179.22 (C-10). The \(sp^3\) carbon adjacent to the pyran oxygen showed a signal at \(\delta 83.77\).

The regiochemistry of the cycloadduct was confirmed by 2D-\(^1\)H NMR spectroscopy. \(^1\)H-\(^1\)H Relayed COSY spectrum of the adduct showed through-bond connectivity between the two sets of hydrogen atoms. The ring junction proton on C-1 (\(\delta 5.29\), d, \(J = 5.2\) Hz) is connected to the olefinic proton on C-2.
(δ 6.07, brs) and the other ring junction proton on C-5 (δ 2.84, m) which in turn is connected to both the methylene moieties.

When a mixture of 2-hydroxy-1,4-naphthoquinone 1, α-phellandrene and paraformaldehyde was heated under reflux in dioxane for 6 h, two products, 11 and 12 were obtained in almost equal amounts (Scheme 5).

\[
\begin{align*}
\text{2-Hydroxy-1,4-naphthoquinone} & \quad \text{α-phellandrene} \\
\quad \text{paraformaldehyde} & \quad \text{Dioxane, 100 °C, 6 h, 62% (1:1)}
\end{align*}
\]

The products were separated by column chromatography and the structure of the products was assigned on the basis of spectroscopic data. The cycloadduct 11 showed the carbonyl absorption at 1679 cm\(^{-1}\) in the IR spectrum. The \(^1\)H NMR spectrum exhibited the olefinic protons as a multiplet centered at δ 5.74. The methylene protons of the pyran ring resonated to give double doublets at δ 2.68 (J = 18.7, 6.2 Hz, 1H) and 2.41 (J = 18.7, 7.8 Hz, 1H). The methyl group on the ring junction carbon appeared as a singlet at δ 1.55 and the methyl protons of the isopropyl moiety displayed doublets at δ 0.95 (J = 6.7 Hz,
3H) and 0.93 (J = 6.8 Hz, 3H). The signals due to the carbonyl groups were discernible in the $^{13}$C NMR spectrum at $\delta$ 184.20 and 180.10. The assigned structure was further confirmed by DEPT-135 spectrum. DEPT-135 spectrum of 11 ascertained that the $sp^3$ carbon adjacent to the pyran oxygen is a quaternary centre, which cannot be true in the other possible regioisomer.

The IR spectrum of 12 showed a sharp absorption at 1698 cm$^{-1}$. In the $^1$H NMR spectrum, the aromatic protons gave four separate signals at $\delta$ 8.05 (d, J = 6.7 Hz), 7.81 (d, J = 7.1 Hz), 7.61 (t, J = 7.5 Hz) and 7.49 (t, J = 7.5 Hz) integrating for one proton each. The signals due to the carbonyl groups were visible at $\delta$ 179.52 and 178.93 in the $^{13}$C NMR spectrum. The $^1$H and $^{13}$C NMR spectra displayed all the other characteristic peaks. Ultimately the structure assignment was confirmed by DEPT-135 NMR spectrum.

4.1.2.2. REACTION WITH ACYCLIC DIENES

Subsequently we turned our attention to the hetero Diels-Alder reaction of quinone methide 7 with acyclic dienes. Initially 2,4-dimethyl-1,3-pentadiene was treated with 2-hydroxy-1,4-naphthoquinone 1 and paraformaldehyde in refluxing dioxane. The reaction proceeded smoothly to afford 2,3-dihydro-2-methyl-2-(2-methylpropenyl)-4H-naphtho[2,3-b]pyran-5,10-dione 14 and 3,4-dihydro-2-methyl-2-(2-methylpropenyl)-2H-naphtho[1,2-b]-5,6-dione 15 in a total yield of 94% (Scheme 6).
As usual, the products were separated by column chromatography and the structure of the products was established by spectroscopic analysis. The IR spectrum of 14 exhibited the carbonyl absorption at 1678 cm\(^{-1}\). The \(^1\)H NMR spectrum showed the aromatic protons as two separate multiplets centered at \(\delta 8.06\) and 7.66. The signal due to the olefinic proton was visible as a singlet at \(\delta 5.10\). The absence of any other proton signal in the region \(\delta 7.00-3.00\) excluded the regioisomeric structure. The terminal methyl groups gave singlets at \(\delta 1.81\) and 1.68 and the methyl group at the quaternary center displayed a singlet at \(\delta 1.60\). The signals due to the carbonyl groups were observed at \(\delta 184.11\) and 179.47 in the \(^{13}\)C NMR spectrum.

The IR spectrum of 15 showed the carbonyl absorption band at 1698 cm\(^{-1}\). The four aromatic protons gave four separate signals in the region \(\delta 8.06-7.49\) in the \(^1\)H NMR spectrum. The singlet due to the olefinic proton was discernible at \(\delta 5.21\). The \(^{13}\)C NMR spectrum exhibited the carbonyl signals at \(\delta 179.64\) and 178.42.
Although the product distribution was found to vary from diene to diene, the reaction was found to be general. The results of these experiments are summarized in Table 1.

**Table 1.** Hetero Diels-Alder reaction of dienes with the quinone methide 7

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene</th>
<th>Product(s) (Yield %)^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Diene 1" /></td>
<td><img src="image2" alt="Product 16" /> <img src="image3" alt="Product 17" /> <img src="image4" alt="Product 18" /></td>
</tr>
<tr>
<td>2</td>
<td><img src="image5" alt="Diene 2" /></td>
<td><img src="image6" alt="Product 19" /> <img src="image7" alt="Product 20" /></td>
</tr>
<tr>
<td>3</td>
<td><img src="image8" alt="Diene 3" /></td>
<td><img src="image9" alt="Product 21" /> <img src="image10" alt="Product 22" /></td>
</tr>
</tbody>
</table>

Reaction conditions: Dioxane, 100 °C, 6 h, ^a Isolated yield

All these products showed characteristic carbonyl absorption in the IR spectrum and ^1H and ^13C signals in the NMR spectra.
4.1.2.3. **REACTION WITH VINYL ETHERS**

Subsequent to the above investigations, reaction of the quinone methide 7 with vinyl ethers was explored. When 2-hydroxy-1,4-naphthoquinone 1 was treated with ethyl vinyl ether and paraformaldehyde in refluxing dioxane, dihydronaphthopyran-5,10-dione 24 and dihydronaphthopyran-5,6-dione 25 were obtained in a total yield of 80% (Scheme 7).

```
\begin{center}
\begin{tikzpicture}
\node at (0,0) {1};
\node at (1.5,0) {6};
\node at (3,0) {23};
\node at (4.5,0) {i};
\node at (6,0) {24};
\node at (7.5,0) {25};
\draw (0,0) -- (1.5,0);
\draw (1.5,0) -- (3,0);
\draw (3,0) -- (4.5,0);
\draw (4.5,0) -- (6,0);
\draw (6,0) -- (7.5,0);
\end{tikzpicture}
\end{center}
```

\textit{i. Dioxane, 100 °C, 4 h, 80% (8:5)}

Scheme 7

The products were separated by chromatography and their structures ascertained by spectroscopic analysis. The carbonyl absorption peak was visible at 1676 cm\(^{-1}\) in the IR spectrum of 24. In the \(^1\)H NMR spectrum, the proton on the acetal carbon exhibited a singlet at \(\delta 5.47\). The methylene protons of the alkoxy moiety displayed two separate multiplets in the region \(\delta 3.97-3.91\) and 3.75-3.70 and the methyl protons appeared as a triplet at \(\delta 1.21\) (\(J = 7.0\) Hz). In the \(^{13}\)C NMR spectrum, the carbonyl signals were seen at \(\delta 183.95\) and 179.50. The signal due to the acetal carbon was observed at \(\delta 98.11\). All other \(^1\)H and \(^{13}\)C NMR signals were in agreement with the assigned structure.
The IR spectrum of 25 showed characteristic carbonyl absorption at 1698 cm\(^{-1}\). The \(^1\)H NMR spectrum displayed the acetal proton as a singlet at \(\delta 5.47\). The methylene protons of alkoxy group were discernible as multiplets in the regions \(\delta 4.00-3.92\) and \(3.78-3.70\). In the \(^{13}\)C NMR spectrum, the carbonyl signals were observed at \(\delta 179.19\) and \(178.45\) and the signal due to the acetal carbon was visible at \(\delta 99.75\).

Other vinyl ethers also underwent facile hetero Diels-Alder reaction with the quinone methide 7. The results of these experiments are summarized in Table 2.

**Table 2. Hetero Diels-Alder trapping of quinone methide 7 with vinyl ethers**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Vinyl ether</th>
<th>Time (h)</th>
<th>Product(s) (Yield%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph-OMe</td>
<td>9</td>
<td>26, 27 (75), 28 (20)</td>
</tr>
<tr>
<td>2</td>
<td>Me-OMe</td>
<td>6</td>
<td>29, 30 (60)</td>
</tr>
<tr>
<td>3</td>
<td>OC(_4)H(_9)</td>
<td>6</td>
<td>31, 32 (50)</td>
</tr>
</tbody>
</table>

Reaction conditions: Dioxane, 100 °C, *Isolated yield.
The products were isolated as usual and characterized by spectroscopic analysis. All these products showed characteristic IR absorptions and $^1$H and $^{13}$C NMR signals.

The foregoing results show that the above cycloaddition is always regioselective, *i.e.* in all the adducts, the allylic, more substituted or hetero atom substituted carbon of the dienophile bonds to the heterodiene oxygen. This is analogous to the regioselectivity observed in the [4+2] cycloaddition reactions of 1-oxa-1,3-butadienes. The [4+2] cycloaddition reactions of the latter are known to proceed with high regioselectivity with the preferential or exclusive formation of 2-substituted 3,4-dihydro-2H pyrans. Theoretical treatment of [4+2] cycloaddition reactions of 1-oxa-1,3-butadienes predicts the preferential formation of 2-substituted 3,4-dihydro-2H-pyrans and accommodates the preferred *endo* approach of the reactants in which the carbon-carbon bond formation is more advanced than carbon-oxygen bond formation. Such reactions proceed *via* a concerted but nonsynchronous mechanism.$^{10,11}$

4.1.2.4. THEORETICAL CALCULATIONS

In order to explain the observed reactivity and regioselectivity in the above reactions, we have carried out some theoretical calculations using PC SPARTAN Graphical Interface Package for Molecular Mechanics and Molecular Orbital Models.$^{12}$ The correlation diagram for the reaction of the quinone methide 7 with cyclopentadiene is provided as an illustrative example (Figure 2).
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Figure 2. The correlation diagram for the reaction between 7 and 8

From the correlation diagram in Figure 2, it is evident that NLUMO(7) - HOMO(8) interaction is the most favored one. The HOMO(7)-LUMO(8) interaction is unimportant due to the large energy gap. The very small coefficient at the reacting center in LUMO(7) indicates that the LUMO(7)-HOMO(8) interaction would not lead to effective overlap. Therefore the reaction is controlled by NLUMO(7)-HOMO(8) interaction and thus the reaction can be classified as an inverse electron demand Diels-Alder reaction. It is noteworthy that the observed regioselectivity and the preferential formation of 5,10-dione 9 over the corresponding 5,6-dione can be perfectly rationalized by the size and sign of the interacting orbitals.
In conclusion, we have shown that the generation of quinone methide from 2-hydroxynaphthoquinone as well as its hetero Diels-Alder reactions provide an efficient protocol for the one pot synthesis of dihydronaphthopyran derivatives.

4.1.3. EXPERIMENTAL DETAILS

For general information, see Section 2.3. in Chapter 2

General procedure for the reaction of hydroxyquinone

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and diene or vinyl ether (3 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere. On completion of the reaction, the solvent was removed \textit{in vacuo} and the residue was extracted into chloroform. The organic layer was washed with sodium carbonate solution and brine and dried over anhydrous sodium sulfate. The chloroform was evaporated off and the residue was subjected to chromatography on silica gel using ethyl acetate in hexane as eluent. All solid products were purified by recrystallization from CH$_2$Cl$_2$-hexane solvent system.

1,3a,11,11a-Tetrahydro-cyclopenta-4H-naphtho[2,3-b]pyran-5,10-dione 9

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and cyclopentadiene (0.264 g, 4 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere for 3 h. The usual work-up followed by chromatographic purification afforded the product 9 as a yellow solid (0.227 g, 90%). It was recrystallized from CH$_2$Cl$_2$-hexane, mp. 102-104 °C.

IR (KBr) $v(\text{max})$: 1676, 1626, 1589, 1384, 1203 cm$^{-1}$.

$^1$H NMR : $\delta$ 8.09-8.04 (m, 2H), 7.69-7.63 (m, 2H), 6.07 (brs, 2H), 5.29 (d, $J = 5.2$ Hz, 1H), 2.85-2.83 (m, 1H), 2.77-2.71 (m, 1H), 2.66-2.49 (m, 2H), 2.25 (dd, $J = 16.3, 2.8$ Hz, 1H).
Xanthenediones 11 and 12

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and R-α-phellandrene (0.408 g, 3 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere for 6 h. The usual work-up followed by chromatographic purification afforded 11 as a yellow solid (0.094 g, 30%) and 12 as a red solid (0.103 g, 32%).

2,4a,12,12a-Tetrahydro-4a-methyl-2-(1-methylethyl)-1H-benzo[b]xanthene-6,11-dione 11
Recrystallized from CH₂Cl₂-hexane, mp. 76-78 °C.
IR (KBr) ν(max): 1679, 1646, 1622, 1595, 1578, 1462, 1381, 1377, 1306, 1263, 1208, 1093 cm⁻¹.

¹H NMR : δ 8.08-8.03 (m, 2H), 7.68-7.63 (m, 2H), 5.75-5.73 (m, 2H), 2.68 (dd, J = 18.7, 6.2 Hz, 1H), 2.41 (dd, J = 18.7, 7.8 Hz, 1H), 2.15-2.10 (m, 2H), 1.78-1.63 (m, 3H), 1.55 (s, 3H), 0.95 (d, J = 6.7 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H).

¹³C NMR : δ 184.20, 180.10, 154.51, 133.67, 132.85, 132.80, 132.20, 131.19, 130.77, 126.29, 125.93, 120.04, 78.66, 38.57, 33.34, 31.79, 27.47, 27.35, 21.46, 20.01, 19.79.

7a,8,9,11a-Tetrahydro-11a-methyl-9-(1-methylethyl)-5H-benzo[c]xanthene-5,6(7H)-dione 12
Recrystallized from CH₂Cl₂-hexane, mp. 91-93 °C.
IR (KBr) ν(max): 1698, 1650, 1608, 1573, 1486, 1389, 1370, 1261, 1055 cm⁻¹.

¹H NMR : δ 8.05 (d, J = 6.7 Hz, 1H), 7.81 (d, J = 7.1 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 5.79-5.70 (m, 2H), 2.62 (dd, J = 17.5, 6.1 Hz, 1H), 2.37 (dd, J = 17.5, 7.8 Hz, 1H), 2.22-
2.19 (m, 2H), 1.78-1.66 (m, 3H), 1.57 (s, 3H), 0.95 (d, \( J = 6.7 \) Hz, 3H), 0.93 (d, \( J = 6.8 \) Hz, 3H).

\( ^{13} \text{C NMR} \) : \( \delta \) 179.52, 178.93, 157.12, 134.59, 133.72, 133.40, 132.53, 130.53, 130.33, 128.63, 124.03, 112.67, 78.28, 38.79, 33.48, 31.80, 27.58, 20.92, 20.07, 19.84.

Dihydronaphthopyrandonones 14 and 15

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and 2,4-dimethyl-1,3-pentadiene (0.288 g, 3 mmol) were refluxed (100 \( ^\circ \)C) in dioxane (6 mL) under argon atmosphere for 6 h. The usual work-up followed by chromatographic purification afforded 14 as a yellow crystalline solid (0.152 g, 54%) and 15 as a red semisolid (0.113 g, 40%).

2,3-Dihydro-2-methyl-2-(2-methylpropenyl)-4H-naphtho[2,3-b]pyran-5,10-dione 14
Recrystallized from \( \text{CH}_2\text{Cl}_2 \)-hexane, mp. 95-97\( ^\circ \)C.

IR (KBr) \( \nu_{(\text{max})} \): 1678, 1642, 1612, 1381, 1337, 1306, 1297, 1202, 1101, 959 \( \text{cm}^{-1} \).

\( ^1\text{H NMR} \) : \( \delta \) 8.08-8.04 (m, 2H), 7.68-7.65 (m, 2H), 5.10 (s, 1H), 2.72-2.62 (m, 1H), 2.55-2.44 (m, 1H), 2.05-1.97 (m, 1H), 1.81 (s, 3H), 1.76-1.70 (m, 1H), 1.68 (s, 3H), 1.60 (s, 3H).

\( ^{13} \text{C NMR} \) : \( \delta \) 184.11, 179.47, 154.39, 137.59, 133.60, 132.70, 132.14, 131.15, 126.70, 126.16, 125.90, 121.17, 79.47, 32.10, 27.15, 26.98, 18.86, 16.80.

HRMS calcd. for \( \text{C}_{18}\text{H}_{18}\text{O}_3 \): 282.1255. Found: 282.1246.

3,4-Dihydro-2-methyl-2-(2-methylpropenyl)-2H-naphtho[1,2-b]pyran-5,6-dione 15

IR (neat) \( \nu_{(\text{max})} \): 1698, 1644, 1603, 1572, 1450, 1389, 1306, 1327, 1179, 1074 \( \text{cm}^{-1} \).

\( ^1\text{H NMR} \) : \( \delta \) 8.06 (d, \( J = 7.3 \) Hz, 1H), 7.82 (d, \( J = 7.6 \) Hz, 1H), 7.63 (t, \( J = 7.0 \) Hz, 1H), 7.49 (t, \( J = 7.3 \) Hz, 1H), 5.21 (s, 1H), 2.63-2.58 (m,
2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and 1-phenyl-1,3-butadiene (0.260 g, 2 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere for 6 h. The usual work-up followed by chromatographic purification afforded the product 17 as a yellow solid (0.133 g, 42%) and 18 as a red semisolid (0.073 g, 23%).

**2,3-Dihydro-2-(2-phenylvinyl)-4H-naphtho[2,3-b]pyran-5,10-dione 17**

Recrystallized from 

\[
\text{IR (KBr) } \nu_{\text{max}}: \ 1672, 1647, 1616, 1578, 1390, 1342, 1300, 1261, 1203, 1150, 1066 \text{ cm}^{-1}.
\]

**H NMR**

\[
\delta 8.08-8.05 (m, 2H), 7.70-7.66 (m, 2H), 7.41-7.28 (m, 5H), 6.75 (d, \ J = 15.9 \text{ Hz}, 1H), 6.31 (dd, \ J = 15.9, 6.2 \text{ Hz}, 1H), 4.93-4.87 (m, 1H), 2.77-2.59 (m, 2H), 2.23-2.18 (m, 1H), 1.99-1.92 (m, 1H).
\]

**C NMR**

\[
\delta 184.23, 179.61, 154.97, 135.96, 133.97, 133.08, 132.03, 131.06, 128.64, 128.23, 126.73, 126.37, 126.30, 126.08, 121.44, 77.80, 26.01, 17.75.
\]

**3,4-Dihydro-2-(2-phenylvinyl)-2H-naphtho[1,2-b]pyran-5,6-dione 18**

IR (KBr) \(\nu_{\text{max}}\): 1694, 1651, 1574, 1494, 1450, 1263, 1204 cm\(^{-1}\).

**H NMR**

\[
\delta 8.08 (d, \ J = 7.0 \text{ Hz}, 1H), 7.85 (d, \ J = 7.5 \text{ Hz}, 1H), 7.65 (t, \ J = 7.3 \text{ Hz}, 1H), 7.52 (t, \ J = 7.2 \text{ Hz}, 1H), 7.43-7.28 (m, 5H), 6.75 (d, \ J = 15.8 \text{ Hz}, 1H), 6.34 (dd, \ J = 15.9, 6.6 \text{ Hz}, 1H), 4.93-4.91 (m, 1H), 2.77-2.69 (m, 1H), 2.61-2.44 (m, 1H), 2.27-2.22 (m, 1H), 2.02-1.90 (m, 1H).\]
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$\text{^13}C \text{ NMR} : \delta 179.23, 178.51, 162.25, 136.57, 135.76, 134.78, 133.39, 130.77, 130.20, 128.85, 128.78, 128.51, 126.77, 126.30, 124.09, 113.96, 78.90, 29.77, 18.01.$

HRMS calcd. for $\text{C}_{21}\text{H}_{16}\text{O}_3$: 316.1099. Found: 316.1090.

2,3-Dihydro-2-methyl-2-propenyl-4H-naphtho[2,3-b]pyran-5,10-dione 20

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and 2-methyl-1,3-pentadiene (0.246 g, 3 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere for 6 h. The usual work-up followed by chromatographic purification afforded the product 20 as a yellow solid (0.209 g, 78%). It was recrystallized from $\text{CH}_2\text{Cl}_2$-hexane, mp. 83-85 °C.

IR (KBr) $\nu_{(\text{max})}$: 1671, 1643, 1619, 1592, 1456, 1383, 1335, 1304, 1264, 1203, 1156, 1123, 1085 cm$^{-1}$.

$\text{^1}H \text{ NMR} : \delta 8.10-8.04 (m, 2H), 7.71-7.65 (m, 2H), 5.67-5.60 (m, 1H), 5.47 (dd, J = 15.5, 1.1 Hz, 1H), 2.70-2.60 (m, 1H), 2.48-2.37 (m, 1H), 2.00-1.92 (m, 1H), 1.82-1.72 (m, 1H), 1.68 (dd, J = 6.3, 1.1 Hz, 3H), 1.51 (s, 3H).

$\text{^13}C \text{ NMR} : \delta 184.14, 179.60, 154.48, 135.89, 134.53, 133.74, 132.85, 132.71, 127.91, 126.33, 126.02, 125.55, 121.93, 79.53, 35.52, 30.75, 17.62, 16.79.$

2,3-Dihydro-2,3-dimethyl-2-(4-methyl-1,3-pentadienyl)-4H-naphtho[2,3-b]pyran-5,10-dione 22

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and 2,6-dimethyl-2,4,6-octatriene (0.272 g, 2 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere for 6 h. The usual work-up followed by chromatographic purification afforded the product 22 as a yellow semisolid (0.094 g, 30%).

IR (neat) $\nu_{(\text{max})}$: 1679, 1647, 1618, 1454, 1378, 1337, 1261, 1205, 1108, 967 cm$^{-1}$. 
\[ ^1\text{H NMR} \quad \delta 8.10-8.03 \text{ (m, 2H)}, 7.71-7.65 \text{ (m, 2H)}, 6.45 \text{ (dd, } J = 13.7, 10.9 \text{ Hz, 1H)}, 5.78 \text{ (d, } J = 10.5 \text{ Hz, 1H)}, 5.58 \text{ (d, } J = 15.3 \text{ Hz, 1H)}, 2.69 \text{ (dd, } J = 18.7, 5.5 \text{ Hz, 1H)}, 2.31 \text{ (dd, } J = 18.7, 7.2 \text{ Hz, 1H)}, 2.02-1.93 \text{ (m, 1H)}, 1.76 \text{ (s, 3H)}, 1.72 \text{ (s, 3H)}, 1.42 \text{ (s, 3H)}, 1.03 \text{ (d, } J = 6.8 \text{ Hz, 3H)}. \]

\[ ^{13}\text{C NMR} \quad \delta 184.16, 179.43, 154.04, 136.71, 133.69, 132.83, 132.48, 132.22, 131.26, 126.69, 126.30, 126.01, 124.29, 120.28, 82.69, 33.54, 26.07, 25.09, 20.53, 18.48, 15.66. \]

**Dihydronaphthopyrandiones 24 and 25**

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and ethyl vinyl ether (0.288 g, 4 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere for 4 h. The usual work-up followed by chromatographic purification afforded the product 24 as a yellow solid (0.129 g, 50%) and the 5,6 dione 25 as a red semisolid (0.077 g, 30%).

**2,3-Dihydro-2-ethoxy-4H-naphtho[2,3-b]pyran-5,10-dione 24**

Recrystallized from CH\textsubscript{2}Cl\textsubscript{2}-hexane, mp. 124-126 °C.

IR (KBr) \( \nu_{\text{max}} \): 1676, 1620, 1340, 1191, 1041 cm\textsuperscript{-1}.

\[ ^1\text{H NMR} \quad \delta 8.09-8.04 \text{ (m, 2H)}, 7.72-7.64 \text{ (m, 2H)}, 5.47 \text{ (s, 1H)}, 3.97-3.91 \text{ (m, 2H)}, 3.75-3.70 \text{ (m, 1H)}, 2.71-2.51 \text{ (m, 2H)}, 2.13-2.11 \text{ (m, 1H)}, 1.90-1.75 \text{ (m, 1H)}, 1.21 \text{ (t, } J = 7.0 \text{ Hz, 3H)}. \]

\[ ^{13}\text{C NMR} \quad \delta 183.95, 179.50, 152.58, 133.77, 132.92, 131.98, 131.07, 126.23, 126.07, 122.65, 98.11, 64.80, 25.05, 15.05, 14.32. \]

Anal. calcd. for C\textsubscript{15}H\textsubscript{14}O\textsubscript{4}: C, 69.76; H, 5.49. Found: C, 70.00; H, 5.46.

**3,4-Dihydro-2-ethoxy-2H-naphtho[1,2-b]pyran-5,6-dione 25**

IR (KBr) \( \nu_{\text{max}} \): 1698, 1650, 1620, 1343, 1190, 1040 cm\textsuperscript{-1}.

\[ ^1\text{H NMR} \quad \delta 8.06 \text{ (d, } J = 7.5 \text{ Hz, 1H)}, 7.78 \text{ (d, } J = 7.6 \text{ Hz, 1H)}, 7.64 \text{ (t, } J = 7.5 \text{ Hz, 1H)}, 7.51 \text{ (t, } J = 7.4 \text{ Hz, 1H)}, 5.47 \text{ (s, 1H)}, 4.00-3.92 \text{ (m, 1H)}, 3.78-3.70 \text{ (m, 1H)}, 2.61-2.56 \text{ (m, 1H)}, 2.13-2.07 \text{ (m, 1H)}, 2.01-1.91 \text{ (m, 1H)}, 1.26 \text{ (t, } J = 7.0 \text{ Hz, 3H)}. \]


**Dihydronaphthopyrandiones 27 and 28**

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and β-methoxystyrene (0.268 g, 2 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere for 9 h. The usual work-up followed by chromatographic purification afforded the product 27 as a yellow solid (0.240 g, 75%) and the 5,6 dione 28 as a red semisolid (0.064 g, 20%).

2,3-Dihydro-2-methoxy-3-phenyl-4H-naphtho[2,3-b]pyran-5,10-dione 27

Recrystallized from CH$_2$Cl$_2$-hexane, mp. 160-162 °C.

IR (KBr) $\nu_{(\text{max})}$: 1673, 1628, 1327, 1189, 1111, 1053 cm$^{-1}$.

$^1$H NMR : $\delta$ 8.11-8.07 (m, 2H), 7.71-7.68 (m, 2H), 7.31-7.20 (m, 5H), 5.39 (d, $J = 3.1$ Hz, 1H), 3.59 (s, 3H), 3.38-3.35 (m, 1H), 3.03 (dd, $J = 18.9$, 6.6 Hz, 1H), 2.94 (dd, $J = 18.8$, 4.2 Hz, 1H).

$^{13}$C NMR : $\delta$ 184.16, 179.27, 152.61, 139.12, 134.08, 133.15, 131.50, 130.25, 128.89, 127.40, 126.44, 126.26, 122.12, 103.08, 56.94, 40.11, 22.01.

Anal. calcd. for C$_{20}$H$_{16}$O$_4$: C, 74.99; H, 5.03. Found: C, 74.52; H, 5.06.

3,4-Dihydro-2-methoxy-3-phenyl-2H-naphtho[1,2-b]pyran-5,6-dione 28

IR (KBr) $\nu_{(\text{max})}$: 1698, 1651, 1609, 1592, 1573, 1492, 1451, 1389, 1363, 1283, 1065 cm$^{-1}$.

$^1$H NMR : $\delta$ 8.09 (d, $J = 7.5$ Hz, 1H), 7.84 (d, $J = 7.7$ Hz, 1H), 7.67 (t, $J = 7.6$ Hz, 1H), 7.53 (t, $J = 7.7$ Hz, 1H), 7.36-7.19 (m, 5H), 5.40 (s, 1H), 3.50 (s, 3H), 3.19 (t, $J = 9.3$ Hz, 1H), 2.87 (d, $J = 9.6$ Hz, 2H).

$^{13}$C NMR : $\delta$ 179.09, 178.44, 159.12, 138.29, 134.94, 132.16, 130.77, 130.25, 129.08, 128.60, 128.49, 128.37, 127.57, 123.82, 115.51, 102.60, 57.00, 41.91, 20.46.
EIMS, m/z  : 320 (M⁺, 60), 289 (18), 231 (19), 158 (25), 134 (100), 102 (15), 91 (80), 76 (25).

2,3-Dihydro-2-methoxy-2-methyl-4H-naphtho[2,3-b]pyran-5,10-dione 30

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and methoxypropene (0.216 g, 3 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere for 6 h. The usual work-up followed by chromatographic purification afforded the product 30 as a yellow solid (0.155 g, 60%). It was recrystallized from CH₂Cl₂-hexane solvent system, mp. 100-102 °C.

IR (KBr) ν(max): 1673, 1644, 1620, 1591, 1383, 1342, 1303, 1266, 1211, 1197, 1169 cm⁻¹.

¹H NMR : δ 8.07-8.05 (m, 2H), 7.69-7.66 (m, 2H), 3.34 (s, 3H), 2.72-2.52 (m, 2H), 2.19-2.12 (m, 1H), 1.79-1.71 (m, 1H), 1.67 (s, 3H).

¹³C NMR : δ 184.07, 179.36, 152.68, 133.63, 132.83, 131.96, 131.11, 126.15, 125.97, 122.88, 100.52, 49.63, 30.76, 24.41, 15.84.

Anal. calcd. for C₁₅H₁₄O₄: C, 69.76; H, 5.49. Found: C, 70.02; H, 5.50.

2,3-Dihydro-2-butoxy-4H-naphtho[2,3-b]pyran-5,10-dione 32

2-Hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol), paraformaldehyde (0.240 g, 8 mmol) and butyl vinyl ether (0.300 g, 3 mmol) were refluxed (100 °C) in dioxane (6 mL) under argon atmosphere for 3 h. The usual work-up followed by chromatographic purification afforded the product 32 as a yellow oil (0.143 g, 50%).

IR (neat) ν(max): 1678, 1650, 1621, 1596, 1580, 1385, 1334, 1300, 1259, 1187, 1118, 1099, 1053 cm⁻¹.

¹H NMR : δ 8.10-8.05 (m, 2H), 7.71-7.64 (m, 2H), 5.46 (s, 1H), 3.92-3.84 (m, 1H), 3.68-3.61 (m, 1H), 2.69-2.57 (m, 2H), 2.14-2.10 (m, 1H), 1.88-1.82 (m, 1H), 1.59-1.50 (m, 2H), 1.35-1.26 (m, 2H), 0.87 (t, J = 7.3 Hz, 3H).

¹³C NMR : δ 184.01, 179.54, 152.65, 133.79, 132.94, 132.02, 131.12, 126.28, 126.12, 122.70, 98.30, 69.05, 31.52, 25.07, 19.17, 14.33, 13.79.
4.2. CAN MEDIATED OXIDATIVE ADDITION OF 
2-HYDROXY-1,4-NAPHTHOQUINONE

4.2.1. INTRODUCTION

4.2.1.1. GENERAL

In the previous section, we have dealt with the synthesis of dihydropyran 
derivatives by the hetero Diels-Alder reactions of quinone methide derived from 
2-hydroxy-1,4-naphthoquinone. As an extension of these studies we became 
interested in the synthesis of corresponding dihydrofuran derivatives by 
cerium(IV) ammonium nitrate (CAN) mediated oxidative addition of 2-
hydroxy-1,4-naphthoquinone to dienes. The following passages provide an 
account of these investigations.

Since an extensive review of cerium(IV) ammonium nitrate (CAN) 
mediated reactions is beyond the scope of this chapter, only a very brief 
introduction to the CAN mediated oxidative addition reactions is given below.

4.2.1.2. OXIDATIVE ADDITION REACTIONS MEDIATED BY CAN

Cerium(IV) ammonium nitrate [(NH₄)₂Ce(NO₃)₆], is a one electron 
oxidant, that has been utilized extensively for a variety of oxidative 
transformations.¹³ The pioneering work of Heiba and Dessau has shown that 
electrophilic carbon centered radicals generated by Ce(IV) reagents undergo 
addition to alkenes.¹⁴ The reaction between acetone and 1-octene is illustrative 
(Scheme 8).
Subsequently Baciocchi et al. made significant advance in this area by showing that a number of synthetic transformations can be performed in methanol or acetonitrile using CAN. They have studied the CAN mediated oxidative addition of 1,3-dicarbonyl compounds to activated alkenes (Scheme 9).\textsuperscript{15}

Studies in our own laboratory have shown that CAN mediated oxidative addition of active methylene compounds such as dimedone, acetyl acetone and ethyl acetoacetate to alkenes provides an excellent route to dihydrofuran derivatives.\textsuperscript{16} Similar reaction occurs with dienes also (Scheme 10).\textsuperscript{17}
An interesting and mechanistically fascinating reaction was observed in the oxidative addition of dimethyl malonate to styrene in the presence of CAN (Scheme 11)\textsuperscript{18}

\begin{equation}
\text{CAN, MeOH, 0 °C}
\end{equation}

Scheme 10

The CAN mediated radical addition of 2-hydroxy-1,4-naphthoquinone to alkenes was reported to result in the formation of \textit{p}-furoquinones and the corresponding \textit{o}-quinone derivatives (Scheme 12)\textsuperscript{19}

\begin{equation}
\text{CAN, MeOH, 20 °C}
\end{equation}

Scheme 11
Against this literature background and in the context of our general interest in the chemistry of quinonoid compounds,\textsuperscript{9} we have studied the oxidative addition reaction of 2-hydroxy-1,4-naphthoquinone to dienes. The results of these investigations are delineated below.

### 4.2.2. RESULTS AND DISCUSSION

#### 4.2.2.1. REACTION WITH CYCLIC DIENES

Our studies commenced with the reaction of 2-hydroxy-1,4-naphthoquinone 1 with cyclopentadiene. When a solution of 1 and cyclopentadiene in acetonitrile was treated with a solution of CAN in acetonitrile at 0°C, two products 54 and 55 were obtained (Scheme 13).
The structure of the products was assigned on the basis of spectroscopic analysis. The IR spectrum of 54 showed characteristic strong carbonyl absorption at 1676 cm$^{-1}$. In the $^1$H NMR spectrum, the proton on C-4 resonated as double triplet at $\delta$ 4.18 ($J = 2.2$, 8.5 Hz) and that on C-5 at $\delta$ 5.95 as a multiplet. The olefinic proton on C-6 and C-7 appeared as a doublet at $\delta$ 6.10 ($J = 8.9$ Hz) and as a triplet at $\delta$ 6.19 ($J = 2.6$ Hz), respectively. The characteristic peaks corresponding to the carbonyl carbons were observed in the $^{13}$C NMR spectrum at $\delta$ 182.43 (C-9) and 178.64 (C-10) and the signal due to the carbons C-2 and C-5 appeared at $\delta$ 158.51 and 96.09, respectively. The final proof for the structure was obtained from single crystal X-ray analysis (Figure 3).

The naphthofurandione 55 exhibited the carbonyl absorption peak at 1694 cm$^{-1}$ in the IR spectrum. The $^1$H NMR spectrum showed the proton on C-4 and C-5 as doublet of a triplet at $\delta$ 4.23 ($J = 8.2$, 2.2 Hz) and as a multiplet at $\delta$ 6.02, respectively. The signals due to the carbonyl carbons C-9 and C-10 were
observed in the $^{13}$C NMR spectrum at $\delta$ 180.73 and 174.94, respectively. The
signal due to C-2 appeared at $\delta$ 167.81 and C-5 showed a peak at $\delta$ 97.28.

Cyclohexadiene also showed similar reactivity towards 2-hydroxynaphthoquinone in the presence of CAN (Scheme 14).

\[ \text{Scheme 14} \]

The dihydrofuran 57 exhibited the carbonyl absorption peak at 1677 cm$^{-1}$. In the $^1$H NMR spectrum, the ring junction proton adjacent to the
pyran oxygen appeared as a multiplet around $\delta$ 5.15. The olefinic protons
displayed multiplets centered at $\delta$ 6.26 and 6.05. In the $^{13}$C NMR spectrum, the
signal due to the carbonyl groups were discernible at $\delta$ 182.42 and 178.40.
Additional evidence for the regiochemistry of the products was drawn from the
proton connectivity established by the 2D-COSY $^1$H NMR of 57. The ring
junction proton at $\delta$ 5.15 (m) is connected to the olefinic proton at $\delta$ 6.05 (m)
and the ring junction proton at $\delta$ 3.60 (m), which in turn is connected to the
methylenic protons at $\delta$ 2.15 (m).

The IR spectrum of 58 displayed the carbonyl absorption band at 1697

\[ \text{cm}^{-1} \]. The $^{13}$C NMR signals due to carbonyl groups were seen at $\delta$ 181.25 and
175.42. All $^1$H and $^{13}$C NMR signals were in agreement with the assigned
structure.
In another experiment, 2-hydroxy-1,4-naphthoquinone 1 was treated with \( \alpha \)-phellandrene in the presence of CAN. The reaction afforded the adducts 59 and 60 (Scheme 15).

\[
\begin{align*}
\text{O} & \quad \text{Me} \\
\text{OH} & \\
1 & + \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \\
10 & \quad \rightarrow \quad i \\
\text{Me} & \quad \text{Me} \\
59 & \quad + \\
\text{Me} & \quad \text{Me} \\
60 &
\end{align*}
\]

i. CAN, MeOH, 0 \( ^\circ \)C, 30 min, 76\% (5:2)

Scheme 15

The IR spectrum of 59 showed the carbonyl absorption peak at 1677 cm\(^{-1}\). In the \(^{13}\)C NMR spectrum, the signals due to the carbonyl groups were discernible at \( \delta \) 182.77 and 178.37. The assigned structure was further confirmed by DEPT-135 spectrum. The DEPT-135 spectrum of 59 clearly established that the \( sp^3 \) carbon adjacent to the furan oxygen is a quaternary center, which cannot be true in the other possible regioisomer.

The carbonyl groups of 60 exhibited the characteristic IR absorption at 1697 cm\(^{-1}\). The \(^{13}\)C NMR spectrum displayed signals due to the carbonyl groups at \( \delta \) 185.11 and 175.47.
4.2.2.2. REACTION WITH ACYCLIC DIENES

In the next phase of our investigations 2-hydroxy-1,4-naphthoquinone 1 was treated with 2,3-dimethylbutadiene. This reaction afforded the furan annulated naphthoquinone derivatives 61 and 62 (Scheme 16).

\[
\begin{align*}
\text{1} + \text{44} & \xrightarrow{i} \text{61} + \text{62} \\
\text{i, CAN, CH}_3\text{CN, 0}^\circ\text{C, 81\% (1:3)}
\end{align*}
\]

Scheme 16

As usual, the products were isolated by chromatography and characterized by spectroscopic analysis. The IR spectrum of the adduct 61 exhibited carbonyl absorption at 1680 cm\(^{-1}\). The \(^1\)H NMR spectrum displayed two singlets due to the olefinic protons at \(\delta\) 5.12 and 4.92. The methylene protons of the furan ring appeared as doublets at \(\delta\) 3.26 and 3.03 (\(J = 16.1\) Hz).

The IR spectrum of 62 exhibited the carbonyl absorption peak at 1708 cm\(^{-1}\). In the \(^1\)H NMR spectrum, the olefinic protons displayed singlets at \(\delta\) 5.11 and 4.95. The signals due to the carbonyl groups were discernible at \(\delta\) 181.14 and 175.57 in the \(^13\)C NMR spectrum.

Interestingly, when 1 was treated with other acyclic dienes, in each case the corresponding furan-4,9-dione was obtained as the only isolable product. Table 3 summarizes the results of these experiments.
Table 3. Oxidative addition of 2-hydroxy-1,4-naphthoquinone 1 to dienes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene</th>
<th>Product</th>
<th>Yield (%)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Diene 19" /></td>
<td><img src="image" alt="Product 63" /></td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Diene 13" /></td>
<td><img src="image" alt="Product 64" /></td>
<td>69</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="Diene 16" /></td>
<td><img src="image" alt="Product 65" /></td>
<td>50</td>
</tr>
</tbody>
</table>

Reaction conditions: CAN, CH$_3$CN, 0 °C, 30 min; $^a$ Isolated yield

4.2.2.3. MECHANISTIC RATIONALIZATION

A mechanistic rationalization for the formation of the above products can be conceived as follows. Oxidation of 1 by CAN would lead to the radical i, which can be trapped by cyclopentadiene 8 to yield the reactive intermediate ii. The latter is further oxidized by CAN to the cation iii, which in turn undergoes tautomerisation yielding iv and v. The cyclization of iv leads to 54 and v affords 55 (Scheme 17).
In conclusion, the present investigations offer a simple and rapid one step procedure for the synthesis of naphthofurandiones. It is noteworthy that there are a number of biologically active natural products, which contain both, linear and angular furanoquinone framework. The present protocol may be applicable to the synthesis of such compounds.

4.2.3. EXPERIMENTAL DETAILS

For general information, see Section 2.3. of Chapter 2

General procedure for the reaction of hydroxyquinone with dienes in the presence of CAN

A solution of CAN (1.260 g, 2.3 mmol) in distilled acetonitrile (20 mL) was added dropwise to an ice-cooled solution of 2-hydroxy-1,4-naphthoquinone
1 (0.174 g, 1 mmol) and diene (2 mmol) in acetonitrile (15 mL). The reaction mixture was stirred for 30 minutes and then it was diluted with water (20 mL) and extracted with dichloromethane (4x15 mL). The solvent was evaporated off and the crude product was then purified by column chromatography on silica gel (100-200 mesh) using mixtures of ethyl acetate and hexane as eluents. All solid products were purified by recrystallization from dichloromethane-hexane solvent system.

**Naphthofurandiones 54 and 55**

A solution of CAN (1.260 g, 2.3 mmol) in acetonitrile (20 mL) was added dropwise to an ice-cooled solution of 2-hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol) and cyclopentadiene (0.132 g, 2 mmol) in acetonitrile (15 mL). The reaction mixture was stirred for 20 minutes and then it was diluted with water (20 mL) and extracted with dichloromethane (4x15 mL). The solvent was evaporated off and the residue on silica gel column chromatography using 5% ethyl acetate in hexane afforded 54 (0.054 g, 23%) as a yellow solid and 55 (0.136 g, 57%) as a red solid.

**3a,10b-Dihydro-cyclopenta[2,3]naphtho[2,3-d]furan-5,10-dione 54**

Recrystallized from CH$_2$Cl$_2$-hexane, mp. 191-193°C.

**IR** (KBr) $\nu_{(\text{max})}$: 1676, 1639, 1613, 1587, 1449, 1385, 1365, 1244, 1195 cm$^{-1}$.

**$^1$H NMR**

$\delta$ 8.20-8.05 (m, 2H), 7.81-7.60 (m, 2H), 6.19 (t, $J = 2.6$ Hz, 1H), 6.10 (d, $J = 8.9$ Hz, 1H), 5.97-5.93 (m, 1H), 4.18 (dt, $J = 8.5, 2.2$ Hz, 1H), 2.99-2.89 (m, 2H).

**$^{13}$C NMR**

$\delta$ 182.43, 178.64, 158.51, 137.66, 134.23, 133.26, 132.99, 121.66, 127.84, 127.04, 126.31, 126.06, 96.09, 42.19, 38.32.

**HRMS** calcd. for C$_{15}$H$_{10}$O$_3$: 238.0632. Found: 238.0692.

**X-RAY** Crystal data: C$_{15}$H$_{10}$O$_3$. FW: 238.23. Crystal size: 0.40 x 0.40 x 0.20 mm$^3$, Monoclinic. Space group P2$_1$/c. Unit cell dimensions $a = 8.1663(2)$ Å, $\alpha = 90^\circ$; $b = 11.1884(2)$ Å, $\beta = 105.473(1)^\circ$; $c = 12.6039(2)$ Å, $\gamma = 90^\circ$. R indices (all data) R1 = 0.0821, wR2 = 0.1261. Volume, Z = 1109.85(4) Å$^3$, 4. D calc =
1.426 mg/m³. F (000) = 496. Absorption Coefficient = 0.100 mm⁻¹. Reflections collected = 2424. λ = 0.71073 Å. (Sheldrick, G. M., Siemens, Analytical X-ray Division, Madison, WI, 1995).

**6b,9a-Dihydrocyclopenta[8,9]naphtho[2,1-d]furan-5,6-dione 55**
Recrystallized from CH₂Cl₂-hexane, mp. 144-146 °C.

**IR (KBr) ν(max):** 1694, 1641, 1615, 1567, 1488, 1442, 1401, 1353, 1281, 1220, 1144, 1042 cm⁻¹.

**¹H NMR** : δ 8.10 (t, J = 9.0 Hz, 1H), 7.67-7.53 (m, 3H), 6.20-6.12 (m, 2H), 6.02 (m, 1H), 4.23 (dt, J = 8.2, 2.2 Hz, 1H), 2.94-2.83 (m, 1H), 2.74-2.64 (m, 1H).


**Naphthofurandiones 57 and 58**

A solution of CAN (1.260 g, 2.3 mmol) in acetonitrile (20 mL) was added dropwise to an ice-cooled solution of 2-hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol) and cyclohexadiene (0.160 g, 2 mmol) in acetonitrile. The aqueous work-up followed by chromatographic purification afforded 57 (0.123 g, 49%) as a yellow solid and 58 (0.116 g, 46%) as a red semisolid.

**1,2,4a,10b-Tetrahydrobenzo[b]naphtho[2,3-d]-furan-5,10-dione 57**
Recrystallized from CH₂Cl₂-hexane, mp. 145-147 °C.

**IR (KBr) ν(max):** 1677, 1637, 1612, 1584, 1390, 1366, 1227, 1190, 963 cm⁻¹.

**¹H NMR** : δ 8.09-8.05 (m, 2H), 7.76-7.64 (m, 2H), 6.29-6.24 (m, 1H), 6.09-6.03 (m, 1H), 5.19-5.17 (m, 1H), 3.60 (m, 1H), 2.25-2.11 (m, 2H), 2.06-1.98 (m, 1H), 1.66-1.53 (m, 1H).

**¹³C NMR** : δ 182.42, 178.40, 159.89, 135.24, 134.21, 133.24, 132.98, 131.60, 127.77, 126.33, 126.04, 122.63, 81.53, 38.84, 23.92, 22.76.

6b,7,8,10a-Tetrahydrobenzo[c]naphtho[2,1-d]furan-5,6-dione 58

IR (neat) \( \nu_{\text{max}} \): 1697, 1642, 1567, 1493, 1405, 1280, 1218, 1161, 1080 cm\(^{-1}\).

\(^1\)H NMR: \( \delta \) 8.05 (d, \( J = 7.1 \) Hz, 1H), 7.63-7.56 (m, 3H), 6.29 (brs, 1H),
6.06 (d, \( J = 9.9 \) Hz, 1H), 5.25 (d, \( J = 7.7 \) Hz, 1H), 8.55-3.47 (m, 1H),
2.20-2.14 (m, 2H), 1.99-1.93 (m, 1H), 1.60-1.53 (m, 1H).

\(^{13}\)C NMR: \( \delta \) 181.25, 175.42, 169.71, 135.95, 134.47, 131.85, 130.50,
129.29, 128.29, 124.58, 122.45, 119.56, 82.86, 37.78, 23.76,
22.59.

EIMS, \( m/z \): 253 (M\(^+\)+1, 4), 252 (M\(^+\), 15), 250 (25), 165 (28), 89 (25), 76
(45), 39 (44), 28 (80), 14 (100).

Naphthofurandiones 59 and 60

An ice cooled mixture of 2-hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol) and \( \alpha \)-phellandrene (0.272 g, 2 mmol) in methanol (10 mL) was treated with CAN (1.260 g, 2 mmol) in methanol (10 mL) for 30 minutes. The aqueous work-up followed by chromatographic purification afforded the compound 59 (0.166 g, 54%) as a yellow semisolid and 60 (0.068 g, 22%) was obtained as a red oil.

1,2,4a,10b-Tetrahydro-4a-methyl-2-(1-methylethyl)-benzo[b]naphtho[2,3-d]furan-5,10-dione 59

IR (neat) \( \nu_{\text{max}} \): 1677, 1649, 1614, 1595, 1387, 1367, 1270, 1206, 1085, 1040 cm\(^{-1}\).

\(^1\)H NMR: \( \delta \) 8.07-8.05 (m, 2H), 7.73-7.63 (m, 2H), 5.98 (d, \( J = 13.8 \) Hz,
1H), 5.72 (dd, \( J = 10.2, 1.5 \) Hz, 1H), 3.36-3.30 (m, 1H), 2.49-2.45 (m, 1H),
2.35-2.21 (m, 1H), 1.78 (m, 2H), 1.63 (s, 3H), 0.93
(d, \( J = 2.6 \) Hz, 6H).

\(^{13}\)C NMR: \( \delta \) 182.71, 178.37, 159.75, 136.24, 134.06, 133.50, 132.78,
131.00, 128.16, 125.88, 125.10, 90.65, 45.33, 37.00, 31.43,
30.90, 26.35, 25.65, 19.60.

HRMS calcd. for C\(_{20}\)H\(_{20}\)O\(_3\): 308.1412. Found: 308.1400
6b,7,8,10a-Tetrahydro-10a-methyl-8-(1-methylethyl)benzo[c]naphtho[2,1-d]furan-5,6-dione 60

IR (neat) $\nu_{(\text{max})}$: 1697, 1661, 1613, 1371, 1222, 1054 cm$^{-1}$.

$^1$H NMR: $\delta$ 8.04 (d, $J = 7.3$ Hz, 1H), 7.60-7.51 (m, 3H), 5.96 (d, $J = 10.2$ Hz, 1H), 5.67 (dd, $J = 10.1$, 2.0 Hz, 1H), 3.50 (q, $J = 4.4$ Hz, 1H), 2.50-2.46 (m, 1H), 1.67 (s, 3H), 1.64-1.57 (s, 3H), 0.90 (d, $J = 2.6$ Hz, 3H), 0.88 (d, $J = 2.5$ Hz, 3H).

$^{13}$C NMR: $\delta$ 181.11, 175.47, 169.12, 136.97, 134.15, 131.66, 129.69, 128.06, 124.41, 117.29, 109.29, 104.70, 92.35, 83.94, 31.29, 26.41, 25.38, 19.50, 19.33.

HRMS calcd. for C$_{20}$H$_{20}$O$_3$: 308.1412. Found: 308.1398.

2,3-Dihydronaphthofurandiones 61 and 62

A solution of CAN (1.260 g, 2.3 mmol) in acetonitrile (20 mL) was added dropwise to an ice-cooled solution of 2-hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol) and 2,3-dimethyl butadiene (0.164 g, 2 mmol) in acetonitrile (15 mL). The aqueous work-up followed by chromatographic purification afforded 61 (0.051 g, 20%) as a yellow solid and 62 (0.155 g, 61%) as a red solid.

2,3-Dihydro-2-methyl-2-(1-methylvinyl) naphtho [2,3-b] furan-4,9-dione 61

Recrystallized from CH$_2$Cl$_2$-hexane, mp. 103 -105 °C.

IR (KBr) $\nu_{(\text{max})}$: 1680, 1643, 1624, 1590, 1572, 1438, 1393, 1369, 1255, 1206, 1155 cm$^{-1}$.

$^1$H NMR: $\delta$ 8.08-8.05 (m, 2H), 7.72-7.67 (m, 2H), 5.12 (s, 1H), 4.92 (s, 1H), 3.26 (d, $J = 16.1$ Hz, 1H), 3.03 (d, $J = 16.1$ Hz, 1H), 1.85 (s, 3H), 1.66 (s, 3H).

$^{13}$C NMR: $\delta$ 182.45, 178.03, 158.92, 145.55, 134.11, 133.04, 132.92, 132.06, 126.30, 125.97, 123.37, 111.28, 94.57, 38.68, 26.23, 18.43.

HRMS calcd. for C$_{16}$H$_{14}$O$_3$: 254.0942. Found: 254.0949.
2,3-Dihydro-2-methyl-2-(1-methylvinyl)-naphtho[1,2-b]furan-4,5-dione 62
Recrystallized from CH$_2$Cl$_2$-hexane, mp. 112-114 °C.
IR (KBr) $\nu_{\text{max}}$: 1708, 1620, 1364, 1256 cm$^{-1}$.
$^1$H NMR : $\delta$ 8.10-8.08 (m, 1H), 7.69-7.59 (m, 3H), 5.11 (s, 1H), 4.95 (s, 1H), 3.16 (d, $J = 15.4$ Hz, 1H), 2.98 (d, $J = 15.4$ Hz, 1H), 1.85 (s, 3H), 1.68 (s, 3H).
$^{13}$C NMR : $\delta$ 181.14, 175.57, 168.70, 145.70, 134.58, 131.99, 130.85, 129.43, 127.69, 124.53, 114.88, 111.12, 96.24, 37.87, 26.28, 18.46.
HRMS calcd. for C$_{16}$H$_{14}$O$_3$: 254.0942. Found: 254.0949.

2,3-Dihydro-2-methyl-2-(2-methylpropenyl)naphtho[2,3-b]furan-4,9-dione 63

A solution of CAN (1.260 g, 2.3 mmol) in distilled acetonitrile (20 mL) was added dropwise to an ice-cooled solution of 2-hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol) and 2,4-dimethyl-1,3-pentadiene (0.192 g, 2 mmol) in acetonitrile. The aqueous work-up followed by chromatographic purification afforded the product 63 as a yellow solid (0.201 g, 75%). It was recrystallized from CH$_2$Cl$_2$-hexane, mp. 83-85 °C.
IR (KBr) $\nu_{\text{max}}$: 1682, 1651, 1620, 1370, 1264, 1201 cm$^{-1}$.
$^1$H NMR : $\delta$ 8.08-8.03 (m, 2H), 7.71-7.65 (m, 2H), 5.59 (s, 1H), 3.24 (d, $J = 16.9$ Hz, 1H), 3.18 (d, $J = 16.9$ Hz, 1H), 1.76 (s, 3H), 1.75 (s, 3H), 1.62 (s, 3H).
$^{13}$C NMR : $\delta$ 182.21, 177.90, 158.57, 136.44, 133.87, 133.15, 132.67, 131.64, 128.74, 126.18, 125.89, 123.22, 92.63, 41.17, 28.60, 26.52, 19.23.
HRMS calcd. for C$_{17}$H$_{16}$O$_3$: 268.1099. Found: 268.1094.

2,3-Dihydro-2-methyl-2-propenynaphtho[2,3-b]furan-4,9-dione 64

An ice cooled mixture of 2-hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol) and 2-methyl-1,3-pentadiene (0.164 g, 2 mmol) in acetonitrile was
treated with a solution of CAN (1.260 g, 2.3 mmol) in the same solvent. The aqueous work-up followed by chromatographic purification yielded 64 as a yellow solid (0.175 g, 69 %). It was recrystallized from CH₂Cl₂-hexane, mp. 79-81 °C.

IR (KBr) ν\(_{\text{max}}\) : 1681, 1634, 1384, 1249, 1202, 960 cm\(^{-1}\).

\(^1\)H NMR : δ 8.06-8.02 (m, 2H), 7.71-7.63 (m, 2H), 5.78 (m, 2H), 3.19 (d, \(J = 17.0\) Hz, 1H), 3.00 (d, \(J = 17.0\) Hz, 1H), 1.71 (d, \(J = 5.4\) Hz, 3H), 1.61 (s, 3H).

\(^{13}\)C NMR : δ 182.45, 178.15, 158.83, 134.07, 133.27, 132.85, 131.00, 126.26, 126.09, 125.95, 123.33, 92.50, 39.17, 26.79, 17.66.

Anal. calcd. for C\(_{16}\)H\(_{14}\)O\(_3\): C, 75.57; H, 5.55. Found: C, 75.71; H, 5.76.

2,3-Dihydro-2-(2-phenylvinyl)naphtho[2,3-b]furan-4,9-dione 65

An ice cooled mixture of 2-hydroxy-1,4-naphthoquinone 1 (0.174 g, 1 mmol) and 1-phenyl-1,3-butadiene (0.260 g, 2 mmol) in acetonitrile was treated with a solution of CAN (1.260 g, 2.3 mmol) in the same solvent. The aqueous work-up followed by chromatographic purification yielded 65 as a yellow solid (0.152 g, 50%). It was recrystallized from CH₂Cl₂-hexane, mp. 145-147 °C.

IR (KBr) ν\(_{\text{max}}\) : 1672, 1650, 1624, 1592, 1452, 1392, 1373, 1232, 1195 cm\(^{-1}\).

\(^1\)H NMR : δ 8.08 (brs, 2H), 7.75-7.65 (m, 2H), 7.40-7.30 (m, 5H), 6.74 (d, \(J = 15.8\) Hz, 1H), 6.32 (dd, \(J = 15.7, 7.2\) Hz, 1H), 5.61 (dd, \(J = 17.3, 7.9\) Hz, 1H), 3.47 (dd, \(J = 17.3, 7.9\) Hz, 1H).

\(^{13}\)C NMR : δ 182.05, 177.62, 159.81, 135.56, 134.11, 133.13, 132.96, 131.65, 128.73, 128.59, 126.90, 126.38, 126.11, 125.95, 123.87, 86.35, 33.53.

4.3. REFERENCES


12. AM1 calculations using PC SPARTAN Graphical Interface Package for Molecular Mechanics and Molecular Orbital Models by Wavefunction Inc. 18401. von Karman, suite 370, Irvine, California, USA.


