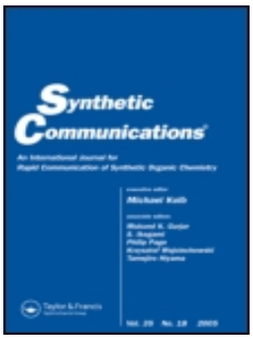

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# FACILE, ONE-POT, THREE-COMPONENT SYNTHESIS OF BENZO[*a*]NAPHTHACENE-8,13-DIONES

**Vakiti Srinivas and Vedula Rajeswar Rao**
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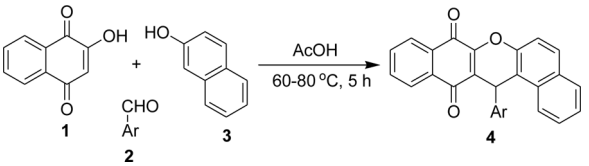
## GRAPHICAL ABSTRACT




**Abstract** *One-pot synthesis of 14-aryl-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-diones was developed by the reaction of 2-hydroxynaphthalene-1,4-dione, aromatic aldehydes, and 2-naphthol in the presence of acetic acid. The structures of these compounds were identified by elemental analyses, infrared,* $^1H$ *NMR, and mass.*

**Keywords** Benzo[*a*]naphthacene-8,13-diones; lawsone; 2-naphthol

## INTRODUCTION

The chemistry of quinones is of considerable interest, because this class of compounds includes many natural products and numerous important synthetic products.[1,2] Quinone derivatives may be toxic to cells by a number of mechanisms[3,4] including redox arylation, intercalation, induction of DNA strand breaks, generation of free radicals, and alkylation via quinone methide formation.[5] As a consequence, the molecular frameworks of a great number of pharmaceuticals and biologically important compounds contain a quinone moiety. Their importance in pharmocological activity is also attributed to the inhibition of special proteins, such as bacterial topoisomerase II-DNA gyrase (antibacterial),[6] mammalian topoisomerases I and II (antitumor),[7] and HIV-1 integrase and proteinase (antiviral).[8] Representative examples of this class of compounds are well-known anticancer drugs of the anthracycline series-doxorubicine and mitoxanthrone. The action of these compounds is believed to occur via topoisomerase II inhibition.[7]

Compounds containing the quinone group represent an important class of biologically active molecules that are widespread in nature.[9] However, to the best of

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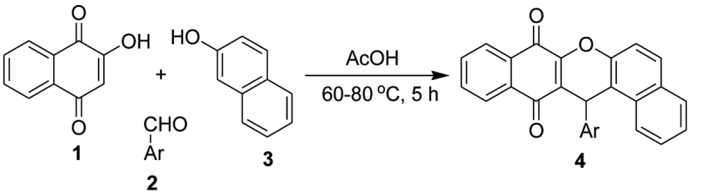
our knowledge, there are no reports on the synthesis of 14*H*-7-oxa-benzo [*a*]naphthacene-8,13-dione ring systems. The development of multicomponent reactions (MCRs) designed to produce elaborate biologically active compounds has become an important area of research in organic, combinatorial, and medicinal chemistry.[10–13] The MCR strategy offers significant advantages over conventional linear synthesis because of its flexible, convergent, and atom-efficient nature.[14,15] In continuation of our earlier work on the synthesis of heterocyclic quinones,[16,17] we report a one-pot synthesis of 14-aryl-14*H*-7-oxa-benzo [*a*]naphthacene-8,13-dione.

## RESULTS AND DISCUSSION

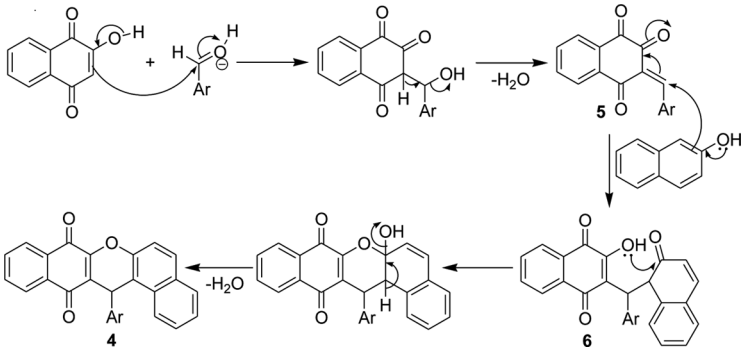
The one-pot, three-component reaction of lawsone **1** with various aromatic aldehydes **2** in the presence of 2-naphthol **3** proceeded rapidly in glacial acetic acid at 60–80 °C to afford 14-aryl-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione **4** in good yields (Scheme 1).

A plausible mechanism for the formation of products **4** is proposed in Scheme 2. Acid-catalyzed condensation between **1** and **2** will give an intermediate **5**. The intermediate **5** on reaction with **3** gave another intermediate **6**. The intermediate formed in situ **6** undergoes cyclization to give the final product **4**. The newly prepared compounds revealed the presence of 1,4-quinone moiety by the reduction and aerial oxidation test with Zn/AcOH. The structures of products **4** were established on the basis of their elemental analyses, infrared (IR), $^{1}$H and $^{13}$C NMR, and mass spectral data. The $^{1}$H NMR spectrum of **4a** exhibited one singlet for CH of pyranrine at δ 6.04 ppm and a multiplet observed at δ 7.52–8.28 ppm was assigned to aromatic protons. The proton decoupled $^{13}$C NMR spectrum of **4a** displayed 27 distinct resonance signals, in agreement with the proposed structure. The quinone carbonyls appeared downfield at 182.0 and 182.9 respectively. The mass spectrum of **4a** showed a molecular ion peak at $m/z$ 434 [M + H] (Table 1).




| 4 | Ar |
|---|---|
| a | m-Nitrophenyl |
| b | p-Chlorophenyl |
| c | p-Methylphenyl |
| d | p-Methoxyphenyl |
| e | o-Hydroxy-m-methoxyphenyl |
| f | m,m,p-Trimethoxyphenyl |
| g | N,N-Dimethylaminophenyl |
| h | Phenyl |
| i | 2-Naphthyl |

**Scheme 1.** One-pot, three-component reaction of 2-hydroxy-1,4-naphthoquinone, aromatic aldehyde, and 2-naphthol.



**Scheme 2.** Mechanism of the reaction.

**Table 1.** One-pot, three-component reaction of 2-hydroxy-1,4-naphthoquinone, aromatic aldehyde, and 2-naphthol

| Entry | Ar | Yield (%)[a] |
|---|---|---|
| **4a** | m-Nitrophenyl | 94 |
| **4b** | p-Chlorophenyl | 92 |
| **4c** | p-Methylphenyl | 95 |
| **4d** | p-Methoxyphenyl | 93 |
| **4e** | o-Hydroxy-m-methoxyphenyl | 91 |
| **4f** | m,m,p-Trimethoxyphenyl | 96 |
| **4g** | N,N-Dimethylaminophenyl | 90 |
| **4h** | Phenyl | 93 |
| **4i** | 2-Naphthyl | 96 |

[a]Isolated yields.

## CONCLUSION

In conclusion, we have carried out a three-component synthetic method for preparation of some benzo[*a*]naphthacene-8,13-diones. This method has several advantages such as readily available starting materials, easy workup, and good yields of the products.

## EXPERIMENTAL

Melting points were determined in open capillaries with a Cintex melting-point apparatus (Mumbai, India). Melting points are uncorrected, and CHNS analysis was done on a Carlo Erba EA 1108 automatic elemental analyzer. The purity of the compounds was checked by thin-layer chromatographic (TLC) plates (E. Merek, Mumbai, India), and IR spectra (KBr) were recorded on a Bruker WM-4(X) spectrometer (577 model). $^1$H NMR spectra were recorded on a Bruker WM 400-MHz spectrometer in $\delta$ ppm using tetramethylsilane (TMS) as internal standard. Mass spectra (EI-MS) were determined on a Perkin-Elmer (SCIEX API-2000, ESI) instrument at 12.5 eV.

### General Procedure for the Synthesis of 14-Aryl-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4)

A mixture of lawsone (1 mmol), aromatic aldehyde (1 mmol), and 2-naphthol (1 mmol) was stirred at 60–80 °C for 5 h. The progress of the reaction was monitored by TLC (20% methanol in chloroform). After completion of the reaction, the solid separated was filtered and washed with water. The crude product was purified by recrystallization from ethanol to give **4**.

### Data

**14-(3-Nitrophenyl)-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4a).** Yellow powder, mp > 300 °C; IR (KBr) ($\nu_{max}/cm^{-1}$): 3070 (C-H), 1698 (C=O), 1650 (C=O), 1527 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) (δ ppm): 6.04 (1H, s, CH of pyran ring), 7.52–8.28 (14H, m, ArH). Anal. calcd. for $C_{27}H_{15}NO_5$: C, 74.82; H, 3.49; N, 3.23%. Found: C, 72.77; H, 3.45; N, 3.19%.

**14-(4-Chlorophenyl)-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4b).** Yellow solid, mp > 300 °C; IR (KBr) ($\nu_{max}/cm^{-1}$): 2911 (C-H), 1703 (C=O), 1665 (C=O), 1576 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) (δ ppm): 5.83 (1H, s, CH of pyran ring), 7.26–8.27 (14H, m, ArH). Anal. calcd. for $C_{27}H_{15}ClO_3$: C, 76.69; H, 3.58%. Found: C, 76.61; H, 3.52%.

**14-(4-Methylphenyl)-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4c).** Orange powder, mp > 300 °C; IR (KBr) ($\nu_{max}/cm^{-1}$): 2914 (C-H), 1703 (C=O), 1665 (C=O), 1575 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) (δ ppm): 2.13 (3H, s, $CH_3$), 5.76 (1H, s, CH of pyran ring), 6.99–8.27 (14H, m, ArH). Anal. calcd. for $C_{28}H_{18}O_3$: C, 83.57; H, 4.51%. Found: C, 83.52; H, 4.48%.

**14-(4-Methoxylphenyl)-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4d).** Yellow powder, mp > 300 °C; IR (KBr) ($\nu_{max}/cm^{-1}$): 2931 (C-H), 1702 (C=O), 1666 (C=O), 1580 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) (δ ppm): 3.69 (3H, s, $OCH_3$), 5.97 (1H, s, CH of pyran ring), 6.75 (2H, d, $J = 8.8$ Hz, ArH), 7.13 (2H, d, $J = 8.8$ Hz, ArH), 7.75–7.98 (10H, m, ArH). Anal. calcd. for $C_{28}H_{18}O_4$: C, 80.37; H, 4.34%. Found: C, 80.31; H, 4.39%.

**14-(2-Hydroxy-3-methoxylphenyl)-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4e).** Yellow powder, mp > 300 °C; IR (KBr) ($\nu_{max}/cm^{-1}$): 2938 (C-H), 1683 (C=O), 1656 (C=O), 1575 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) (δ ppm): 3.88 (3H, s, $OCH_3$), 5.75 (1H, s, CH of pyran ring), 6.68–6.70 (1H, m, ArH), 6.96–7.07 (2H, m, ArH), 7.78–8.07 (10H, m, ArH). Anal. calcd. for $C_{28}H_{18}O_5$: C, 77.41; H, 4.18%. Found: C, 77.36; H, 4.39%.

**14-(3,3,4-Trimethoxylphenyl)-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4f).** Yellow powder, mp > 300 °C; IR (KBr) ($\nu_{max}/cm^{-1}$): 2937 (C-H), 1708 (C=O), 1673 (C=O), 1592 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) (δ ppm): 3.63 (9H, s, $OCH_3$), 5.98 (1H, s, CH of pyran ring), 6.52 (2H, s, ArH), 7.77–7.99 (10H, m, ArH). Anal. calcd. for $C_{30}H_{22}O_6$: C, 75.30; H, 4.63%. Found: C, 75.25; H, 4.69%.

**14-(4-N,N-Dimethylaminophenyl)-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4g).** Brown powder, mp > 300 °C; IR (KBr) ($\nu_{max}/cm^{-1}$): 3069 (C-H), 1693 (C=O), 1656 (C=O), 1587 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) (δ ppm): 2.50 (6H, s, N-$CH_3$), 3.95 (1H, s, CH of pyran ring), 6.78–8.10 (14H, m, ArH). Anal. calcd. for $C_{29}H_{21}NO_3$: C, 80.72; H, 4.91; N, 3.25%. Found: C, 80.65; H, 3.19; N, 3.20%.

**14-Phenyl-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4h).** Orange powder, mp > 300 °C; IR (KBr) ($\nu_{max}/cm^{-1}$): 3021 (C-H), 1697 (C=O), 1654 (C=O), 1571 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) (δ ppm): 5.81 (1H, s, CH of pyran ring), 7.08–8.28 (15H, m, ArH). Anal. calcd. for $C_{27}H_{16}O_3$: C, 83.49; H, 4.15%. Found: C, 83.41; H, 4.12%.

**14-(2-Naphthyl)-14*H*-7-oxa-benzo[*a*]naphthacene-8,13-dione (4i).** Orange powder, mp > 300 °C; IR (KBr) ($\nu_{max}/cm^{-1}$): 2918 (C-H), 1673 (C=O), 1636 (C=O), 1574 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) (δ ppm): 5.99 (1H, s, CH of pyran ring), 7.40–8.31 (17H, m, ArH). Anal. calcd. for $C_{31}H_{18}O_3$: C, 84.92; H, 4.14%. Found: C, 84.91; H, 4.10%.

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