# ADDITION OF UNSYMMETRICAL DIENES TO ACYL-1,4-BENZOQUINONES AND OXIDATION OF THE ADDUCTS WITH MANGANESE DIOXIDE: A REGIOSPECIFIC ROUTE TO MONO- AND DI-METHYL-1,4-NAPHTHOQUINONES

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## Abstract

Regioselective Diels-Alder reactions of acyl-1,4-benzoquinones **1** with, severally, isoprene, *trans*-piperylene,1-acetoxy-1,3-butadiene and 1-methoxy-1,3-butadiene gave the corresponding adducts **2** in high yield. Treatment of the adducts **2** with manganese dioxide gave regiospecifically the corresponding 1,4-naphthoquinones **3**. In several cases, the adducts of the acetylquinones afforded intermediates of type **4**, which subsequently gave the corresponding naphthoquinones by de-acetylation and aromatization.

## Introduction

Diels-Alder addition of electron-rich 1,3-dienes to unsymmetrically substituted 1,4-benzoquinones occurs preferentially at the ethene linkage with the lowest electron density, and almost exclusively at ethene linkage which carry strongly electron-accepting substituents [1]. The regiochemistry of addition of unsymmetrical 1,3-butadienes to this ethene linkage can be accounted for by both resonance and frontier orbital considerations [2], selection rules have been applied [3]. Lewis acids can catalyse the addition, and may control its regiochemistry [4]. These criteria have been utilised in the present work with substituted formyl- and acetyl-1,4-benzoquinones, the selectivity of the Diels-Alder additions being enhanced by use of the lowest practicable temperature, and by the presence of trifluoroacetic acid to protonate the carbonyl oxygen of the acyl group.

Literature reports on the application of active manganese dioxide as a selective dehydrogenating reagent are numerous [5,6]. Examples are the dehydrogenation of indolines to indoles [7], the oxidative dealkylation of 4-alkyl-1,4-dihydropyridines [8], the conversion of 2,3-dihydro-1,4-naphthoquinones to 1,4-naphthoquinone [6], and the dehydrogenation of the cycloadducts [9] of 1,4-naphthoquinones with 2-(hydroxymethyl)-1,3-butadiene.

**Keywords:** Regioselective addition; Acyl-1,4-benzoquinones; Diels-Alder adducts; Regiospecific synthesis; Alkyl-1,4-naphthoquinones; Manganese dioxide oxidation

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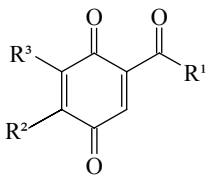
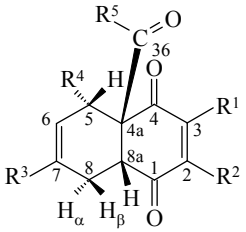


**1**

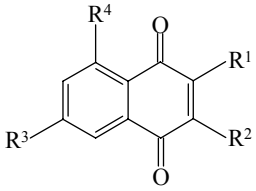


**2**

| | $R^1$ | $R^2$ | $R^5$ |
|---|---|---|---|
| **a** | H | H | H |
| **b** | H | Me | H |
| **c** | Me | H | H |
| **d** | H | H | Me |
| **e** | H | Me | Me |
| **f** | Me | H | Me |

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| **a** | H | H | Me | H | H |
| **b** | H | H | H | Me | H |
| **c** | H | H | H | OAc | H |
| **d** | H | H | H | OMe | H |
| **e** | H | Me | Me | H | H |
| **f** | H | Me | H | Me | H |
| **g** | Me | H | Me | H | H |
| **h** | Me | H | H | Me | H |

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| **i** | H | H | Me | H | Me |
| **j** | H | H | H | Me | Me |
| **k** | H | H | H | OAc | Me |
| **l** | H | H | H | OMe | Me |
| **m** | H | Me | Me | H | Me |
| **n** | H | Me | H | Me | Me |
| **o** | Me | H | Me | H | Me |
| **p** | Me | H | H | Me | Me |



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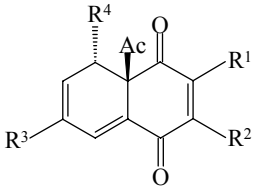


**4**

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **a** | H | H | Me | H |
| **b** | H | H | H | Me |
| **c** | H | H | H | H |
| **d** | H | H | H | OMe |

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **e** | H | Me | H | Me |
| **f** | Me | H | H | Me |
| **g** | H | Me | Me | H |
| **h** | Me | H | Me | H |

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **a** | H | H | H | Me |
| **b** | H | Me | H | Me |
| **c** | Me | H | H | Me |

It has been stated [10] that, because of the heterogenous nature of the reactions involved, elucidation of the mechanism [5,6] of oxidation by manganese dioxide is difficult.

The new work described in this paper extends the use of manganese dioxide to the regiospecific synthesis of substituted 1,4-naphthoquinones from the corresponding Diels-Alder adducts prepared from formyl- and acetyl-1,4-benzoquinones, and demonstrates the effectiveness of the reagent in removing these acyl functions from bridgehead positions; evidence relating to the stereochemistry of dehydrogenation is presented.

## Results and Discussion

### Preparation of the Adducts

Addition of isoprene and of *trans*-piperylene to formyl-1,4-benzoquinone **1a** and to its 5-methyl **1b** and 6-methyl **1c** homologues occurred smoothly in the presence of trifluoroacetic acid in dichloromethene at -76°C, and gave the corresponding adducts (**2a-h**, respectively*) in 91-98% yield. Acetyl-1,4-benzoquinone **1d** behaved analogously, affording the adducts (**2i, j**) in 90 and 98% yield, respectively.

In contrast to the situation with the extremely reactive formyl-1,4-benzoquinones, the presence of **5-1e** and **6-1f** methyl groups in the acetyl congener **1d** retarded the addition, possibly by steric inhibition of formation of the *endo* transition state, and a higher temperature (-20°C) was required: each of the Diels-Alder adducts **2m-p** was obtained in 97% yield.

Because of the sensitivity of 1-methoxy- and 1-acetoxy-1,3-butadiene to proton acids, addition of these particularly reactive dienes to formyl- and acetyl-1,4-benzoquinone was effected in benzene alone, at room temperature. The adducts **2c, d** and **2k, l** were isolated in yields of 87-94%.

* Compounds described in this paper were racemic, only one enantiomer is depicted.

**Manganese Dioxide Oxidation of the Adducts**

Treatment of the adducts **2a** or **2i** with manganese dioxide in dry benzene at room temperature gave 6-methyl-1,4-naphthoquinone **3a** in both cases, in 90 and 86% yield, respectively.

Treatment of the formyl-1,4-benzoquinone adduct **2b** with manganese dioxide at room temperature gave 5-methyl-1,4-naphthoquinone **3b** in 92% yield, but treatment of the corresponding acetyl adduct **2j** with manganese dioxide at room temperature gave a mixture of 5-methyl-1,4-naphthoquinone **3b** and 4a-acetyl-4a,5-dihydro-5-methyl-1,4-naphthoquinone **4a** in 53 and 37% yield respectively. Refluxing of the dihydro-compound **4a** with manganese dioxide in benzene gave only 5-methyl-1,4-naphthoquinone **3b**.

Treatment of the formyl adduct **2b** with manganese dioxide (neutral, basic and acidic) in dry benzene at room temperature gave a mixture of 1,4-naphthoquinone **3c** and 5-methoxy-1,4-naphthoquinone **3d**, but oxidation of the acetyl adduct **2k** gave only 1,4-naphthoquinone **3c**.

Oxidation of the formyl adduct **2f** with manganese dioxide in dry benzene at room temperature gave 2,5-dimethyl-1,4-naphthoquinone **3e** in 73% yield, but treatment of the analogous acetyl adduct **2n** with manganese dioxide in refluxing benzene for 1.5 h gave a mixture of 2,5-dimethyl-1,4-naphthoquinone **3e** and 4a-acetyl-4a,5-dihydro-2,5-dimethyl-1,4-naphthoquinone **4b** in 41 and 36% yield, respectively. Treatment of the dihydro-compound **4b** with an excess of manganese dioxide in refluxing benzene for 7 h gave only 2,5-dimethyl-1,4-naphthoquinone **3e**.

Treatment of the formyl adduct **2h** with manganese dioxide at room temperature gave 2,8-dimethyl-1,4-naphthoquinone **3f** in 76% yield, but refluxing of the corresponding acetyl adduct **2p** with manganese dioxide in dry benzene for 2 h gave a mixture of 2,8-dimethyl-1,4-naphthoquinone **3f** and 4a-acetyl-4a,5-dihydro-3,5-dimethyl-1,4-naphthoquinone **4c** in 30 and 41% yield, respectively.

Reaction of either the formyl adduct **2e** at room temperature or the acetyl analogue **2m** under reflux with manganese dioxide in dry benzene gave 2,7-dimethyl-1,4-naphthoquinone **3g** in each case, in 83 and 77% yield, respectively.

Finally, reaction of the formyl adduct **2g** at room temperature and the acetyl adduct **2o** under reflux with manganese dioxide in dry benzene gave 2,6-dimethyl-1,4-naphthoquinone **3h**, in 77 and 70% yield, respectively.

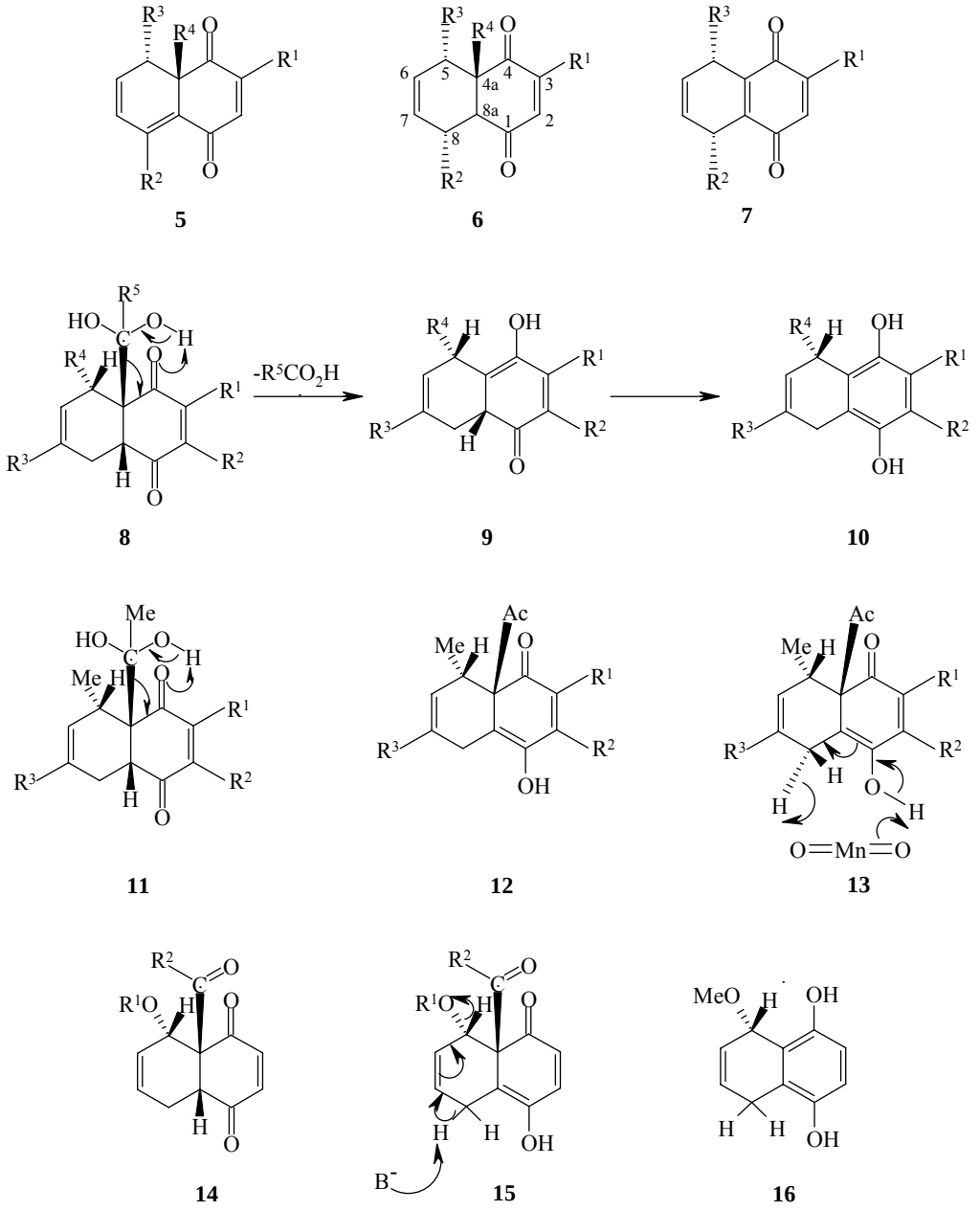
**Mechanisms of Oxidation**

All of the formyl adducts prepared in the present work gave the corresponding naphthoquinones on treatment with manganese dioxide under mild conditions (20°C), but the acetyl adducts, especially those from piperylene, gave the corresponding naphthaquinones only on refluxing in benzene. The piperylene adducts of the acetylquinones first gave dehydro-intermediates of type **4a-c**, which then afforded the corresponding naphthoquinones by de-acetylation and aromatization, on prolonged or on more drastic (refluxing in benzene) conditions. The combination of a 5-methyl group and a bridgehead, 4a, acetyl group thus hinders the complete dehydrogenation, allowing the isolation of intermediates of type **4**, where dehydrogenation has occurred only at the 8, 8a positions.

The adduct **5**; ($R^1$=H, $R^2$=$R^3$=Me, $R^4$=Ac) did not give an intermediate of type **6**; ($R^1$=H, $R^2$=$R^3$=Me, $R^4$=Ac), but instead gave the de-acetylated compound **7**; ($R^1$=H, $R^2$=$R^3$=Me) as an intermediate; this finally gave the corresponding naphthoquinone by dehydrogenation. The presence of the methyl group in the 8-position appears to be responsible for this difference, since the adduct **5**; ($R^1$=$R^2$=$R^4$=Me, $R^3$=H) [11] remained unchanged on treatment with manganese dioxide in benzene at room temperature or even at reflux; the corresponding dehydro-compound **6** was not formed.

Mechanisms which account for these observations can be based on initiation by traces of water adsorbed on the manganese dioxide. Thus for adducts **2a-h**, hydration of the formyl group would give the corresponding hydrates (**8**; $R^5$=H), all $\beta$-ketols, which may fragment (as **8**, arrows) to yield formic acid and the enols **9**, further enolisation of which would give the hydroquinones **10**; oxidation of these, which is already precedent [12,13], would give the corresponding 5,8-dihydro-1,4-naphthoquinones (as **7**), which would be further oxidized to the naphthoquinones **3**.

A parallel mechanism would apply for the 4a-acetyl adducts **2i-p**, although the equilibrium hydration of the acetyl group would be less favourable than that for the formyl analogue. This, together with the steric effects resulting from the more bulky hydrate and the added effect of a methyl group at the 5$\alpha$-position (**2j**, **n** and **p**) would disfavour both formation and fragmentation (as **11**) of the hydrates to give the enols (**9**; $R^4$=Me), and, in consequence, would allow an alternative mechanism to predominate, providing an explanation for the formation of the 8, 8a-bisdehydro compounds **4** when $R^4$=Me. Thus competing enolisation of the 1-carbonyl system, giving **12**, renders the 8-methylene hydrogens doubly allylic: hydride transfer to the oxidant and proton loss (as **13**) from the substrates, presumably adsorbed on the manganese dioxide, are then favoured. Removal of the hydrated 4a-acetyl functions follows, as depicted in **11**. The immediate inorganic product from the oxidation shown in **13** is the base $Mn(OH)_2$, which may dehydrate, thus releasing water for the deacylation of



further substrates.

However, the process depicted in **13** is prevented by the presence of an $\alpha$-methyl group at C-8, as evidenced by the adduct **5**; ($R^1$=H, $R^2$=$R^3$=Me, $R^4$=Ac) which, at the first stage of dehydrogenation, yields the corresponding 5,8-dihydro-1,4-naphthoquinone, suggesting either that 8,8a-bisdehydrogenation is precluded by the steric effect of the 8$\alpha$-methyl group, or, rather strikingly, that it is the $\delta\alpha$-hydrogen which is removed, exclusively, in this dehydrogenation as depicted in **13**.

An alternative mechanism for the formation of the 5,8-dihydro-1,4-naphthoquinone **7**; ($R^1$=H, $R^2$=$R^3$=Me) is therefore required. A sequence analogous to that shown above for **8**; ($R^5$=Me), giving the corresponding cyclohexadienolone (as **9**), followed by enolisation to the hydroquinone and subsequent oxidation of this provides an explanation.

Dehydrogenation of the adduct **2k**; (≡**14**, $R^1$=Ac, $R^2$=Me) leads exclusively to 1,4-naphthoquinone. This may be explained by enolisation of the 1-carbonyl system to give **15**; ($R^1$=Ac, $R^2$=Me), in which base-induced homo-allylic loss of acetate, as **15**, is particularly favourable. Subsequent removal of the 4a-acetyl group, as in **8**, would then afford 1,4-

naphthohydroquinone, which would be oxidized to 1,4-naphthoquinone. For **2d**; (≡**14**, $R^1$=Me, $R^2$=H), initial loss of the formyl group (as in **8**) would lead to the hydroquinone **16**, which may undergo further aromatization via competitive homo-allylic loss of methanol to give 1,4-naphthohydroquinone, or, because methoxide is a poorer leaving group than acetate, competitive dehydrogenation to yield 5-methoxy-1,4-naphthohydroquinone. Subsequent oxidation of these hydroquinones would then give the corresponding quinones, both of which were formed.

## Conclusion

Each of the foregoing reactions proceeds in high yield. Collectively, they provide for regioselective synthesis of alkyl-4a-acyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinones and regiospecific synthesis of the corresponding alkyl-1,4-naphthoquinones. In principle these reactions can be extended to the synthesis of homologues and congeners of these compounds. The use of this strategy in the synthesis of 9,10-anthraquinones has been described elsewhere [14].

## Experimental Section

Infrared spectra were recorded on Perkin-Elmer 237 and 257 instruments. (NMR) spectra, referenced to internal tetramethylsilane, were recorded using Perkin-Elmer R2A and R12B (60 MHz), Perkin-Elmer R32 (90 MHz) and Varian SC 300 (300 MHz) instruments. Mass spectra were determined with AEI MS 12 and MS 30 instruments.

All solvents, liquid reagents and starting materials were distilled prior to use. All solid reagents and starting materials were sublimed and/or recrystallised prior to use. Manganese dioxide was freshly prepared [15].

All experiments involving 1,4-benzoquinones and their Diels-Alder adducts were carried out in vessels covered in aluminum foil to avoid light exposure.

### Preparation of the Adducts (2a-p): General Procedure

A solution of the quinone (1 mmol) in a mixture of dry dichloromethane (15 ml) and redistilled trifluoroacetic acid (1.05 mmol) was stirred and cooled to -76°C (acetone-solid $CO_2$), and freshly distilled diene (1.1 mmol) in dry dichloromethane (4 ml) was added. The solution was stirred at -76°C for 1 h, while the initial orange colour faded to very pale yellow during this time. The solution was left to warm up to room temperature, and the solvent was removed to give a pale yellow oil or solid. Distillation or recrystallisation of the residue produced the adduct in the form of a pale yellow oil or crystal.

After stirring for 1 h at -76°C, the colour of the solution had remained unchanged, therefore it was then stirred for 1 h at -20°C to synthesize **2m-p**. The colour subsequently faded from orange to light yellow.

For of the adducts **2c**, **d**, **k**, **l**, benzene was used as solvent and the reaction was carried out at room temperature (10 min) in the absence of trifluoroacetic acid.

The yields, melting points, boiling points, elemental analyses and $^1$H NMR spectra of the adducts are presented in Tables 1 and 2.

### Preparation of Bisdehydro-Compounds (4a-c): General Procedure

Each of the adducts **2j**, **2n** and **2p** (0.2 mmol) in dry benzene (10 ml) was treated with freshly prepared [15] manganese dioxide (0.5 g) at room temperature or at reflux. Filtration through celite, and removal of the solvent gave a yellow oil, which showed two spots on TLC (Thin Layer Chromatography). Separation of the mixtures by silica gel PLC (Preparative Thin Layer Chromatography) using 3:1 toluene-ether gave the corresponding 1,4-naphthoquinones **3b**, **3e** and **3f** as the first band and the corresponding dihydro-compounds **4a**, **4b** and **4c** as the second band, respectively.

The yields, melting points, elemental analyses and $^1$H NMR spectra of the dihydro-compounds are listed in Tables 3 and 4.

### Preparation of 1,4-Naphthoquinones (3a-h): General Procedure

The adducts (0.2 mmol) in dry benzene (10 ml) was treated with freshly prepared [15] manganese dioxide (0.5 g). The mixture was stirred at room temperature for the formyl adducts, and refluxed for the acetyl adducts. Filtration through celite and removal of the solvent gave the corresponding 1,4-naphthoquinones as yellow needles.

Treatment of the adduct **2d** with freshly made manganese dioxide [16] and following the course of the reaction by TLC gave a mixture of **3c** and **3d** in a ratio of 3:2, respectively ($^1$H NMR spectrum). The reaction was repeated using manganese dioxide prepared by the "basic" method [15], but again it gave a mixture of **3c** and **3d**, in the ratio of 7:5, respectively. Using acidic manganese dioxide (prepared by the method of Attenburrow [15], and then stirred on the steam bath with 3% sulphuric acid, filtered, washed with water, and dried at 130°C for 36 h) again gave the mixture of **3c** and **3d** but in the ratio of 4:1, respectively.

Treatment of the adducts **2c** and **2k** with manganese dioxide at both room temperature and refluxing conditions gave only **3c**.

The yields, melting points, and $^1$H NMR spectra of the 1,4-naphthoquinones are presented in Table 5.

**Table 1.** Physical and analytical data for the adducts **2a-p**

| Product | Yield (%)* | m.p./b.p. (°C) | Molecular formula | Found (C, H%) C | H | $M^+$ | Required (C, H%) C | H | M |
|---|---|---|---|---|---|---|---|---|---|
| **2a** | 97 | 85-90/0.1 mmHg | $C^{12}H^{12}O^3$ | 70.3 | 5.9 | 204.0785 | 70.6 | 5.9 | 204.0786 |
| **2b** | 97 | Oil (decomposed on distillation) | $C^{12}H^{12}O^3$ | 70.3 | 5.9 | 204.0785 | 70.6 | 5.9 | 204.0786 |
| **2c** | 91 | 99-100 | $C^{13}H^{12}O^5$ | 62.7 | 5.0 | 248.0683 | 62.9 | 4.8 | 248.0685 |
| **2d** | 94 | 76-77 | $C^{12}H^{12}O^4$ | 65.4 | 5.5 | 220.0733 | 65.5 | 5.5 | 220.0736 |
| **2e** | 95 | 53-56 | $C^{13}H^{14}O^3$ | 71.7 | 6.3 | 218.0941 | 71.6 | 6.4 | 218.0943 |
| **2f** | 97 | 60-62 | $C^{13}H^{14}O^3$ | 71.3 | 6.4 | 218.0941 | 71.6 | 6.4 | 218.0943 |
| **2g** | 98 | Oil | $C^{13}H^{14}O^3$ | 71.3 | 6.6 | 218.0941 | 71.6 | 6.4 | 218.0943 |
| **2h** | 94 | 44-46 | $C^{13}H^{14}O^3$ | 71.4 | 6.5 | 218.0946 | 71.6 | 6.4 | 218.0943 |
| **2i** | 90 | 72-73 | $C^{13}H^{14}O^3$ | 71.7 | 6.6 | 218.0946 | 71.6 | 6.4 | 218.0943 |
| **2j** | 93 | 101-102 | $C^{13}H^{14}O^3$ | 71.3 | 6.6 | 218.0941 | 71.6 | 6.4 | 218.0943 |
| **2k** | 87 | 125-126 | $C^{14}H^{14}O^5$ | 64.4 | 5.2 | 262.0838 | 64.1 | 5.3 | 262.0841 |
| **2l** | 89 | 91 | $C^{13}H^{14}O^4$ | 66.3 | 6.1 | 234.0890 | 66.7 | 6.0 | 234.0982 |
| **2m** | 97 | 105-110/0.1 mmHg | $C^{14}H^{16}O^3$ | 72.5 | 6.8 | 232.1095 | 72.4 | 6.9 | 232.1099 |
| **2n** | 92 | 52-54 | $C^{14}H^{16}O^3$ | 72.8 | 7.1 | 232.1099 | 72.4 | 6.9 | 232.1099 |
| **2o** | 97 | 106-110/0.1 mmHg | $C^{14}H^{16}O^3$ | 72.3 | 6.9 | 232.1096 | 72.4 | 6.9 | 232.1099 |
| **2p** | 93 | 47-48 | $C^{14}H^{16}O^3$ | 72.5 | 7.0 | 232.1097 | 72.4 | 6.9 | 232.1099 |

* The yields are of recrystallised (from light petroleum, b.p. 40-60°C) or distilled (bulb-to-bulb) materials.

**Table 2.** $^1$H NMR spectra of the adducts **2a-p**

| Compound | Signal $\delta$(ppm) | Assignment | Compound | Signal $\delta$(ppm) | Assignment |
|---|---|---|---|---|---|
| **2a** | $\delta$($CDCl_3$, 90MHz) 9.52(s, 1H) | CHO | **2d** | $\delta$($CDCl_3$, 300MHz) 9.73(s, 1H) | CHO |
| | 6.74(d, J =11Hz, 1H) | H-2 or H-3 | | 6.85(d, J =10.2Hz, 1H) | H-2 or H-3 |
| | 6.54((d, J =11Hz, 1H) | H-3 or H-2 | | 6.60(d, J =10.2Hz, 1H) | H-3 or H-2 |
| | 5.36(bs, 1H) | H-6 | | 6.01(bd, J =9.4Hz, 1H) | H-6 or H-7 |
| | 3.52(dd, $J_1$=6.5Hz, $J_2$=4.5Hz, 1H) | H-8a | | 5.96(bd, J =9.4Hz, 1H) | H-7 or H-6 |
| | 2.75-2.30(m, 3H) | 2×H-5+1×H-8 | | 4.34(d, J =3.6Hz, 1H) | H-5 |
| | 2.02(bd, $J_1$=17Hz, $J_2$=6.5Hz, 1H) | 1×H-8 | | 3.59(d, J =8Hz, 1H) | H-8a |
| | 1.65(bs, 3H) | 7-Me | | 3.18(s, 3H) | OMe |
| | | | | 3.08(d, J =19.6Hz, 1H) | H-8$\alpha$ |
| | | | | 2.05(dd, $J_1$=19.6Hz, $J_2$=8Hz, 1H) | H-8$\beta$ |
| **2b** | $\delta$($CDCl_3$, 90MHz) 9.65(s, 1H) | CHO | **2e** | $\delta$($CDCl_3$, 90MHz) 9.55(s, 1H) | CHO |
| | 6.87(d, J =10Hz, 1H) | H-2 or H-3 | | 6.44(q, J =1.5 Hz, 1H) | H-3 |
| | 6.60(d, J =10Hz, 1H) | H-3 or H-2 | | 5.37(bS, 1H) | H-6 |
| | 5.77(bd, J =11Hz, 1H) | H-6 or H-7 | | 3.51(dd, $J_1$=7Hz, $J_2$=4Hz, 1H) | H-8a |
| | 5.54(bd, J =11Hz, 1H) | H-7 or H-6 | | 2.70-2.30(m, 3H) | 2×H-5+1×H-8 |
| | 3.71(dd, $J_1$=8Hz, $J_2$=2Hz, 1H) | H-8a | | 2.30-1.85(m, 1H) | 1×H-8 |
| | 3.01(m, 1H) | H-5 | | 2.03(d, J =1.5Hz, 3H) | 2-Me |
| | 2.98(d, J =18Hz, 1H) | H-8$\alpha$ | | 1.67(bs, 3H) | 7-Me |
| | 2.06(dd, $J_1$=18Hz, $J_2$=8Hz, 1H) | H-8$\beta$ | | | |
| | 0.96(s, 3H) | 5-Me | | | |
| **2c** | $\delta$($C_6D_6$, 300MHz) 9.42(s, 1H) | CHO | **2f** | $\delta$($CDCl_3$, 90MHz) 9.65(s, 1H) | CHO |
| | 6.27(d, J =10Hz, 1H) | H-2 or H-3 | | 6.45(q, J =12Hz, 1H) | H-3 |
| | 6.01(d, J =10Hz, 1H) | H-3 or H-2 | | 5.74(bd, J =12Hz, 1H) | H-6 or H-7 |
| | 5.82(m, 2H) | H-6 + H-7 | | 5.57(bd, J =12Hz, 1H) | H-7 or H-6 |
| | 5.56(m, 1H) | H-5 | | 3.66(dd, $J_1$=8Hz, $J_2$=1Hz, 1H) | H-8a |
| | 3.22(d, J =8.2Hz, 1H) | H-8a | | 3.00(m, 1H) | H-5 |
| | 2.98(dd, $J_1$=19.4Hz, $J_2$=3.6Hz, 1H) | H-8$\alpha$ | | 2.98(bd, J =18Hz, 1H) | H-8$\alpha$ |
| | 1.77(dd, $J_1$=19.4Hz, $J_2$=8.2Hz, 1H) | H-8$\beta$ | | 2.07(d, J =1.5Hz, 3H) | 2-Me |
| | 1.39(s, 3H) | OAc | | 2.05(dd, $J_1$=18Hz, $J_2$=8Hz, 1H) | H-8$\beta$ |
| | | | | 0.91(d, J =7Hz, 3H) | 5-Me |

**Table 2.** Continued

| Compound | Signal $\delta$(ppm) | Assignment | Compound | Signal $\delta$(ppm) | Assignment |
|---|---|---|---|---|---|
| **2g** | $\delta$($C_6D_6$, 90MHz) 9.26(s6, 1H) | CHO | **2l** | $\delta$($CDCl_3$, 300MHz) 6.85(d, J = | |
| | 6.04(q, J =1.5Hz, 1H) | H-2 | | 11Hz, 1H) | H-2 or H-3 |
| | 4.99(m, 1H) | H-6 | | 6.61(d, J =11Hz, 1H) | H-3 or H-2 |
| | 3.08(dd, $J_1$=7Hz, $J_2$=4Hz, 1H) | H-8a | | 6.04(bd, J =11.5Hz, 1H) | H-6 or H-7 |
| | 2.45(bd, J =18Hz, 1H) | H-8$\alpha$ | | 5.91(bd, J =11.5Hz, 1H) | H-7 or H-6 |
| | 2.10(bs, 2H) | 2×H-5 | | 4.32(d, J =5.1Hz, 1H) | H-5 |
| | 1.77(dd, $J_1$=18Hz, $J_2$=7Hz, 1H) | H-8$\beta$ | | 3.74(d, J =7.8Hz, 1H) | H-8a |
| | 1.44(d, J =1.5Hz, 3H) | 3-Me | | 3.15(s, 3H) | OMe |
| | 1.39(bs, 3H) | 7-Me | | 3.05(bd, J =19Hz, 1H) | H-8$\alpha$ |
| | | | | 2.35(s, 3H) | Ac |
| | | | | 1.95(dd, $J_1$=19Hz, $J_2$=7.8Hz, 1H) | H-8$\beta$ |
| **2h** | $\delta$($CDCl_3$, 90MHz) 9.63(s, 1H) | CHO | **2m** | $\delta$($CDCl_3$, 90MHz) 6.44(q, J = | |
| | 6.70(q, J =1.5Hz, 1H) | H-2 | | 1.5Hz, 1H) | H-3 |
| | 5.70(bd, J =12Hz, 1H) | H-6 or H-7 | | 5.39(bs, 1H) | H-6 |
| | 5.55(bd, J =12Hz, 1H) | H-7 or H-6 | | 3.46(t, J =7.5Hz, 1H) | H-8a |
| | 3.65(dd, $J_1$=9Hz, $J_2$=1Hz, 1H) | H-8a | | 3.02(bd, J =18Hz, 1H) | H-8$\alpha$ |
| | 2.96(m, 1H) | H-5 | | 2.45-1.96(mm, 3H) | 2×H-5+H-8$\beta$ |
| | 2.93(bd, J =18Hz, 1H) | H-8$\alpha$ | | 2.16(s, 3H) | Ac |
| | 2.01(dd, $J_1$=18Hz, $J_2$=9Hz, 1H) | H-8$\beta$ | | 2.01(d, J =1.5Hz, 3H) | 2-Me |
| | 1.97(d, J =1.5Hz, 3H) | 3-Me | | 1.64(bs, 3H) | 7-Me |
| | 0.89(d, J =7Hz, 3H) | 5-Me | | | |
| **2i** | $\delta$($CDCl_3$, 90MHz) 6.70(d, J = | | **2n** | $\delta$($CDCl_3$, 90MHz) 6.48(q, J = | |
| | 10.5Hz, 1H) | H-2 or H-3 | | 1.5Hz, 1H) | H-3 |
| | 6.54(d, J =10.5Hz, 1H) | H-3 or H-2 | | 5.64(bt, J =12.5Hz, 2H) | H-6+H-7 |
| | 5.42(bs, 1H) | H-6 | | 3.81(dd, $J_1$=8Hz, $J_2$=2.5Hz, 1H) | H-8a |
| | 3.50(t, J =7.5Hz, 1H) | H-8a | | 3.25-2.95(m, 1H) | H-5 |
| | 3.01(bd, J =18Hz, 1H) | 1×H-8 | | 2.88(bd, J =18Hz, 1H) | H-8$\alpha$ |
| | 2.45-2.10(m, 3H) | 2×H-5+1×H-8 | | 2.38(s, 3H) | Ac |
| | 2.18(s, 3H) | Ac | | 2.05(d, J =1.5Hz, 3H) | 2-Me |
| | 1.67(bs, 3H) | 7-Me | | 1.95(dd, $J_1$=18Hz, $J_2$=8Hz, 1H) | H-8$\beta$ |
| | | | | 0.86(d, J =7Hz, 3H) | 5-Me |
| **2j** | $\delta$($CDCl_3$, 300MHz) 6.86(d, J = | | **2o** | $\delta$($CDCl_3$, 90MHz) 6.49(q, J = | |
| | 10.2Hz, 1H) | H-2 or H-3 | | 1.5Hz, 1H) | H-2 |
| | 6.68(d, J =10.2Hz, 1H) | H-3 or H-2 | | 5.48(bs, 1H) | H-6 |
| | 5.74(bd, J =10.8Hz, 1H) | H-6 or H-7 | | 3.48(t, J =7.5Hz, 1H) | H-8a |
| | 5.61(bd, J =10.8Hz, 1H) | H-7 or H-6 | | 2.94(bd, J =18Hz, 1H) | H-8$\alpha$ |
| | 3.87(dd, $J_1$=8.4Hz, $J_2$=2.5Hz, 1H) | H-8a | | 2.40-2.05(mm, covered with a | Ac+2×H-5+ |
| | 3.06(m, 1H) | H-5 | | singlet at $\delta$2.15, 6H) | H-8$\beta$ |
| | 2.85(bd, J =19Hz, 1H) | H-8$\alpha$ | | 1.97(d, J =1.5Hz, 3H) | 3-Me |
| | 2.38(s, 3H) | Ac | | 1.65(bs, 3H) | 7-Me |
| | 1.99(dd, $J_1$=19Hz, $J_2$=8Hz, 1H) | H-8$\beta$ | | | |
| | 0.93(J =7.2Hz, 1H) | 5-Me | | | |
| **2k** | $\delta$($CDCl_3$, 300MHz) 6.93(d, J = | | **2p** | $\delta$($CDCl_3$, 90MHz) 6.62(q, J = | |
| | 10.5Hz, 1H) | H-2 or H-3 | | 1.5Hz, 1H) | H-2 |
| | 6.64(d, J =10.5Hz, 1H) | H-3 or H-2 | | 5.63(bt, J =12.5Hz, 2H) | H-6+H-7 |
| | 5.98(m, 2H) | H-6+H-7 | | 3.75(dd, $J_1$=8Hz, $J_2$=4Hz, 1H) | H-8a |
| | 5.75(d, J =4.8Hz, 1H) | H-5 | | 3.15-2.80(m, 1H) | H-5 |
| | 3.92(d, J =7.8Hz, 1H) | H-8a | | 2.78(bd, J =18Hz, 1H) | H-8$\alpha$ |
| | 3.08(bd, J =20.4Hz, 1H) | H-8$\alpha$ | | 2.35(s, 3H) | Ac |
| | 2.41(s, 3H) | OAc | | 2.02(dd, $J_1$=18Hz, $J_2$=8Hz, 1H) | H-8$\beta$ |
| | 2.02(dd, $J_1$=20.4Hz, $J_2$=7.8Hz, 1H) | H-8$\beta$ | | 2.00(d, J =1.5Hz, 3H) | 3-Me |
| | 1.82(s, 3H) | Ac | | 0.94(d, J =7Hz, 3H) | 5-Me |

**Table 3.** Physical and analytical data for the bisdehydro-compounds **4a-c**

| Product | Yield | m.p. | Molecular | Found (C, H%) | | | Required (C, H%) | | |
|---|---|---|---|---|---|---|---|---|---|
| | (%)* | (°C) | Formula | C | H | $M^+$ | C | H | M |
| **4a** | 37(53) | 47-49 | $C^{13}H^{12}O^3$ | 72.5 | 5.8 | 216.0784 | 72.2 | 5.6 | 216.0786 |
| **4b** | 36(41) | 100-102 | $C^{14}H^{14}O^3$ | 72.8 | 6.2 | 230.0943 | 73.0 | 6.1 | 230.0943 |
| **4c** | 41(30) | 105-107 | $C^{14}H^{14}O^3$ | 72.9 | 6.3 | 230.0941 | 73.0 | 6.1 | 230.0943 |

* The yields in parentheses are related to 1,4-naphthoquinones, separated as first fractions.

Table **4.** $^1$H NMR spectra of bisdehydro-compounds **4a-c**

| Compound | Signal $\delta$(ppm) | Assignment |
|---|---|---|
| **4a** | $\delta$($CCl_4$, 90MHz) 7.11(dd, $J_1$=4.5Hz, $J_2$=1.5Hz, 1H) | H-8 |
| | 6.92(d, J =11Hz, 1H) | H-2 or H-3 |
| | 6.63(d, J =11Hz, 1H) | H-3 or H-2 |
| | 6.34(dd, $J_1$=9.5Hz, $J_2$=6Hz, 1H) | H-6 |
| | 6.06(dd, $J_1$=9.5Hz, $J_2$=4.5Hz, 1H) | H-7 |
| | 3.64(quitet, J =6Hz, 1H) | H-5 |
| | 2.13(s, 3H) | Ac |
| | 0.89(d, J =7Hz, 3H) | 5-Me |
| **4b** | $\delta$($CCl_4$, 90MHz) 7.10(dd, $J_1$=5.5Hz, $J_2$=1Hz, 1H) | H-8 |
| | 6.52(q, J =1.5Hz, 1H) | H-3 |
| | 6.30(dd, $J_1$=9.5Hz, $J_2$=6Hz, 1H) | H-6 |
| | 6.04(dd, $J_1$=9.5Hz, $J_2$=5.5Hz, 1H) | H-7 |
| | 3.60(heptet, J =7Hz, 1H) | H-5 |
| | 2.14(s, 3H) | Ac |
| | 2.11(d, J =1.5Hz, 3H) | 2-Me |
| | 0.86(d, J =7Hz, 3H) | 5-Me |
| **4c** | $\delta$($CCl_4$, 90MHz) 7.10(dd, $J_1$=5Hz, $J_2$=1Hz, 1H) | H-8 |
| | 6.82(q, J =1.5Hz, 1H) | H-2 |
| | 6.32(dd, $J_1$=9Hz, $J_2$=6Hz, 1H) | H-6 |
| | 6.05(dd, $J_1$=9Hz, $J_2$=5Hz, 1H) | H-7 |
| | 3.82-3.50(m, 1H) | H-5 |
| | 2.10(s, 3H) | Ac |
| | 2.02(d, J =1.5Hz, 3H) | 3-Me |
| | 0.86(d, J =7Hz, 3H) | 5-Me |

**Table 5.** Physical and $^1$H NMR data for 1,4-naphthoquinones **3a-h**

| Compound | Yield (%)* | | m.p. (°C) | Signal $\delta$(ppm) | Assignment |
|---|---|---|---|---|---|
| | fa | aa | | | |
| **3a** | 90 | 86 | 91-92<br>(lit [17], 91) | $\delta$($CDCl_3$, 60MHz) 7.98(d, J =8Hz, 1H)<br>7.9(bs, 1H)<br>7.55(bd, J =8Hz, 1H)<br>6.93(s, 2H)<br>2.50(s, 3H) | H-8<br>H-5<br>H-7<br>H-2+ H-3<br>6-Me |
| **3b** | 92 | 83 | 122-123<br>(lit [18], 122.5-123 | Identical with authentic sample | |
| **3c** | 89 | 81 | 124-125<br>(lit [19], 124-125) | Identical with authentic sample | |

* fa and aa are the yields of 1,4-naphthoquinones obtained from oxidation of formyl adducts and acetyl adducts, respectively.

**Table 5.** Continued

| Compound | Yield (%)* | | m.p. (°C) | Signal $\delta$(ppm) | Assignment |
|---|---|---|---|---|---|
| | fa | aa | | | |
| **3d** | 31 | – | 187-188<br>(lit [20], 189) | $\delta$($CDCl_3$, 60MHz) 7.81-7.51(m, 2H)<br>7.42-7.20(m, 2H)<br>6.83(s, 2H)<br>3.99(s, 3H) | H-8+ H-8 or H--7+ H-8<br>H-6 or H-7<br>H-2+ H-3<br>OMe |
| **3e** | 73 | 68 | 92-93<br>(lit [20], 94) | $\delta$($CDCl_3$, 60MHz) 8.03(dd, $J_1$=6Hz, $J_2$=3.5Hz, 1H)<br>7.72-7.40(m, 2H)<br>6.75(q, J=1.5Hz, 1H)<br>2.73(s, 3H)<br>2.15(d, J=1.5Hz, 3H) | H-8<br>H-6+ H-7<br>H-3<br>5-Me<br>2-Me |
| **3f** | 76 | 68 | 133-134<br>(lit [21], 135-135.5) | $\delta$($CDCl_3$, 60MHz) 8.02(dd, $J_1$=7Hz, $J_2$=3.5Hz, 1H)<br>7.75-7.47(m, 2H)<br>6.8(q, J=1.5Hz, 1H)<br>2.75(s, 3H)<br>2.17(d, J=1.5Hz, 3H) | H-5<br>H-6+ H-7<br>H-3<br>8-Me<br>2-Me |
| **3g** | 83 | 77 | 112-113<br>(lit [22], 114-115) | $\delta$($CDCl_3$, 60MHz) 7.9(d, J=8Hz, 1H)<br>7.84(bs, 1H)<br>7.46(bd, J=8, 1H)<br>6.76(q, J=1.5Hz, 1H)<br>2.48(s, 3H)<br>2.17(d, J=1.5Hz, 3H) | H-5<br>H-8<br>H-6<br>H-3<br>7-Me<br>2-Me |
| **3h** | 77 | 70 | 133-135<br>(lit [22], 136-137) | $\delta$($CDCl_3$, 60MHz) 8.0(d, J=8Hz, 1H)<br>7.87(bs, 1H)<br>7.51(bd, J=8Hz, 1H)<br>6.79(q, J=1.5Hz, 1H)<br>2.49(s, 3H)<br>2.18(d, J=1.5Hz, 3H) | H-8<br>H-5<br>H-7<br>H-3<br>6-Me<br>2-Me |

* fa and aa are the yields of 1,4-naphthoquinones obtained from oxidation of formyl adducts and acetyl adducts, respectively.

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