Solar Photochemistry: Optimisation of the Photo Friedel-Crafts Acylation of Naphthoquinones †

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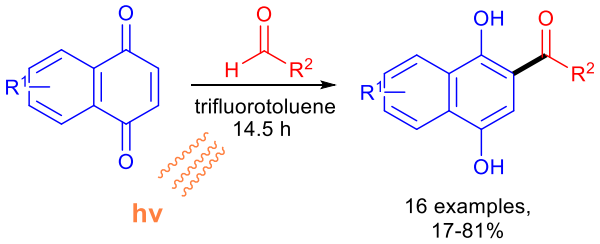

Abstract

A practical and robust photo Friedel-Crafts acylation of naphthoquinones is described. Although the reaction proceeds slowly in sunlight, the optimised conditions offer a substantial improvement to those already reported, by the utilisation of a more reliable and practical 'sun-mimicking' light source, a less hazardous solvent system (trifluorotoluene) and faster reaction times. Using these conditions, the reaction scope has been expanded to include functionalised aldehyde and naphthoquinone substrates, affording the desired photo-products in acceptable to excellent yields (17-81%). Factors influencing the regiochemistry of the photo Friedel-Crafts reaction on unsymmetrical naphthoquinones have also been investigated.

Introduction

Acylated quinones and their derivatives serve as valuable and versatile precursors for the construction of numerous biologically active natural products.[1-3] For example, several

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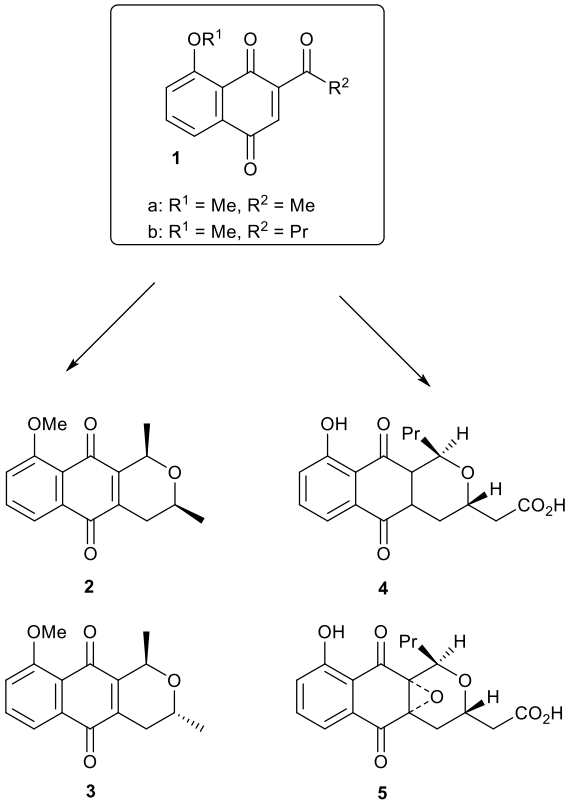
† Electronic supplementary information (ESI) available: copies of NMR spectra.

members of the pyranonaphthoquinone class of quinone natural products, are accessible from a common acylated core (Scheme 1).[1-3]

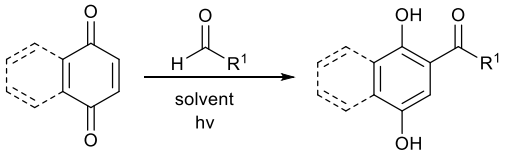


Scheme 1. Access to pyranonaphthoquinones elutherin **2**, isoelutherin **3**, deoxyfrenolicin **4** and frenolicin **5** from a common acylated quinone core **1**.

Various synthetic routes to such acyl naphthoquinone building blocks have been described. Common methods, such as the Friedel-Crafts acylation and the Fries rearrangement are often inefficient,[1,4] and require the use of corrosive reagents such as Lewis acids and acyl chlorides. Such methods also generate significant amounts of waste, further adding to the environmental burden of such procedures.

Recently, research has shifted towards the implementation of greener synthetic protocols throughout organic synthesis.[5,6] One such example is the photochemical reaction between a quinone and an aldehyde, often termed the 'photo Friedel-Crafts acylation' (Scheme 2), a reaction that can, in principle, be carried out in sunlight.[7-14]

However, in undertaking this reaction, the use of hazardous solvents (e.g. benzene) and impractical photochemical reactors is commonplace.[11-14] Whilst the use of supercritical carbon dioxide as an alternative reaction media has been reported,[15] such techniques also suffer from technical drawbacks (e.g. high pressure vessels). More recently, the use of room temperature ionic liquids as alternative reaction media has been reported.[16] Despite the noted improvement to the sustainability of the reaction, the use of such solvent systems led to the occurrence of photo-reduction side processes, low isolated yields, and furthermore, still required the use of specialised photochemical reactors.[16]



Scheme 2. The photo Friedel-Crafts acylation

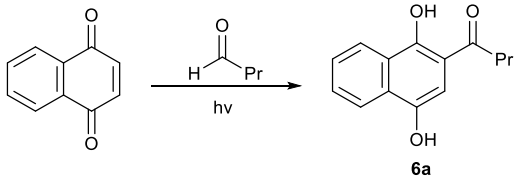
In a variation, Schiel and co-workers reported carrying out the reaction in a more environmentally benign solvent system (*t*-butanol/acetone) using sunlight as the light source.[9,10] However, the reaction set up was complex and impractical as it required the use of specialised equipment to both capture and concentrate sunlight. Successful examples of the reaction have recently been reported using the intense sunlight found in insolate regions of lower latitude,[7,8] although the reactions were carried out in benzene, greatly compromising the safety of the procedure.

With the aim of developing an efficient, greener and readily accessible photo Friedel-Crafts acylation suitable for widespread use in the laboratory, we considered that there was scope for further development, particularly in the use of more environmentally acceptable solvents, and of a simple experimental protocol that employed direct sunlight or a readily available sunlight-mimicking light source. Furthermore, to the best of our knowledge, there are very few examples of the photo Friedel-Crafts acylation on substituted quinone substrates.[7,9,11] Although heterocyclic,[8] aromatic[11] and aliphatic[13] aldehydes have previously been studied, there remains scope for further expansion in

this field. As quinones possessing additional functionalities are of direct interest within the field of natural products synthesis, there is also opportunity to apply the methodology to more complex substrates.

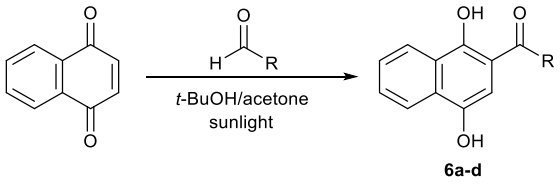
Results and Discussion

We began by considering the known photochemical reaction between 1,4-naphthoquinone and butyraldehyde to give 2-butanoyl-1,4-dihydroxynaphthalene **6a**, as carried out by Schiel and co-workers (Scheme 3).[9,10] The first objective of our research was to transfer these promising conditions into a more practical laboratory set-up.



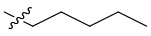
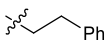
Scheme 3. Conditions: *t*-BuOH/acetone (3:1), sunlight, PROPHIS vessel, 5 days, 90%.

Initially the reaction was carried out in sunlight in a glass vessel placed on the window sill of the laboratory (latitude 52°56'31'' NE, 32 m above sea level) and left to stir for 3 months during autumn/winter. Under these conditions, little reaction was observed. When repeating these conditions in summer for a period of 5 days, we observed 45% conversion to product (36% isolated yield). Using the more desirable weather conditions to our advantage, the reaction was carried out with various other aliphatic aldehydes (Scheme 4, Table 1). Disappointingly, although product formation was observed in all cases, despite prolonged irradiation times, the reactions did not reach completion.



Scheme 4

Table 1. Variation of aldehyde

Entry	R	Product	Irradiation time (d)	Conversion (%)[a,b]
1	Pr	**6a**	5	45 (36)
2		**6b**	20	75
3		**6c**	20	61 (38)
4		**6d**	34	50

[a]Bracketed conversions represent isolated yields after purification by column chromatography; [b]Conversion as measured by ^{1}H NMR spectroscopy.

Given the obvious limitations of using sunlight as the photochemical source in regions of higher latitude, we decided to investigate artificial light sources as a reliable and predictable alternative. Whilst several of the light sources (Table 2) gave little or no conversion to product (Entries 1-2, 4), significant conversion was achieved with the UV sunlamp (Entry 3). Despite this, lack of current manufacture meant that the UV sunlamp was impractical for long-term use. A more promising result was achieved with the hydrargyrum quartz iodide (HQI) high intensity discharge (HID) lamp, which, owing to its wide spectral emittance when compared with conventional bulbs, is a commonly employed light source in commercial greenhouses. As a result, such bulbs can therefore be viewed as 'sunlight-mimicking' sources. Furthermore, they are economical and also readily accessed commercially, so are practical for use in the laboratory environment.

Table 2: Screening of artificial light sources in the reaction of 1,4-naphthoquinone with butyraldehyde

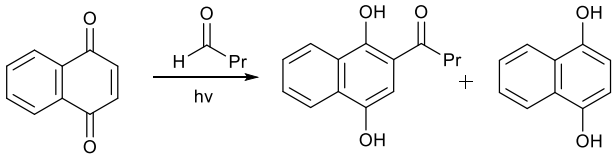
Entry	Light Source	Power (W)	Intensity (cd)[a]	Reaction time (h)	Conversion to **6a** (%)[b]
1	Energy saving LED bulb[c]	25	48	72	0
2	Energy saving halogen bulb[d]	55	50	72	0
3	UV Sunlamp[e]	300	1500	14.5	63 (55)
4	Halogen flood light[f]	400	1900	14.5	9 (6)
5	HQI-T HID greenhouse light[g]	400	6678	14.5	66 (72)

Reactions were carried out in borosilicate (pyrex) glass tubes which filters out 95% of radiation below 290 nm, at 0.08 M concentrations with 7.8 eq of aldehyde; Wavelength emission spectra were recorded for Entries 3-5 (see supplementary information). [a]Measured and calculated using readings from a LUX meter; [b]Conversion measured by ^{1}H NMR spectroscopy, bracketed conversions represent those carried out without the presence of acetone; [c]Philips myVision LED bulb 5 W (25 W eq); [d]General Electric GE halogen light bulb 55 W eq; [e]Philips MLU 300 UV lamp, last produced in 1968; [f]Defender security floodlight, 400 W halogen bulb; [g]Trac metal halide floodlight containing a 400 W Osram Powerstar HQI-T metal halide bulb.

We next focused on further optimisation of the reaction conditions by variation of the solvent. Whilst the initial study used a 3:1 mixture of *t*-butanol/acetone, the precise role of acetone in the reaction was unclear. Although acetone is a commonly employed photochemical sensitiser, its reported electronic transitions (n-π^*, λ_{max} = 275 nm, ε = 15)[17] compared to that of naphthoquinone (n-π^*, λ_{max} = 331 nm, ε = 5934) meant that this was unlikely to be the case.[18-20] Due to its unknown role, reactions were attempted both with and without acetone (Scheme 5, Table 3).

Whilst the use of *t*-butanol (Entry 1) gave promising conversion to product, despite prolonged irradiation, the reaction appeared to stall and no further product formation was observed. Furthermore, formation of the hydroquinone **7** was also observed in trace quantities. Additional attempts to develop this further by the use of alternative green alcoholic solvents such as 1- and 2-butanol also proved unsuccessful,[21] as the photo reduction process appeared to dominate in these cases (Entries 2-3). Interestingly, the use of acetone appeared to have little effect on the overall reaction outcome.

Due to the widespread use of benzene as a solvent, we considered that aromatic solvents might be beneficial.[8,11-14] However, the documented incompatibility of radical reactions with several 'greener' aromatic solvents such as toluene, xylene, cumene and mesitylene meant that there was little scope for further optimisation.[21,22] However, use of trifluorotoluene proved successful (Entry 5). Often viewed as a more sustainable and less hazardous alternative to many aromatic and chlorinated solvents, trifluorotoluene, although relatively unknown, is unarguably a green alternative to benzene, and as a result is often viewed as the solvent of choice for radical reactions.[23] Carrying out the reaction in trifluorotoluene led to acylated hydroquinone **6a** being formed with complete conversion in 14.5 hours and it was also successfully isolated in good yield (62%). These conditions are superior to those carried out in benzene (Entry 4), which gave lower conversion. Furthermore, product precipitation meant that no column chromatography was required.



6a **7**

Scheme 5. Conditions: solvent/acetone (3:1), HQI-T HID 400 W bulb, 14.5 h.

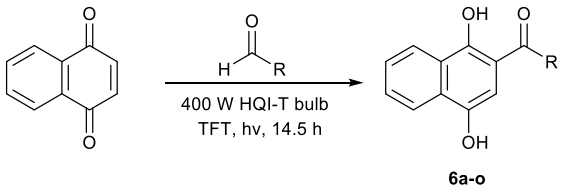
Table 3: Solvent optimisation

Entry	Solvent	Conversion to **6a** (%)[a-c]	Conversion to **7** (%)[a-c]
1	*t*-butanol[d]	66 (72)	8 (3)
2	2-butanol	19 (4)	81 (93)
3	1-butanol	20 (14)	78 (84)
4	benzene	81	0
5	trifluorotoluene	100[e] (62)[f]	0

All reactions were carried out in Pyrex tubes at 0.08 M concentrations; [a]Conversion measured by ^{1}H NMR spectroscopy; [b]Un-bracketed conversions represent those carried out in a 3:1 mixture of solvent: acetone; [c]Bracketed conversions represent those carried out without acetone; [d]Reaction mixture was irradiated for 30 h; [e]The same result was achieved without the presence of acetone and also by irradiating in direct sunlight for 5 d; [f]Isolated Yield.

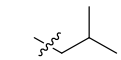
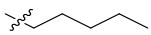
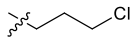
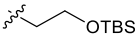
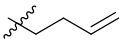
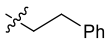
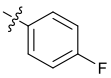
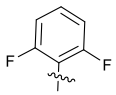
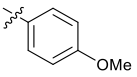
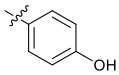
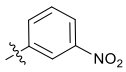
These optimised conditions were then applied to a range of aldehydes (Table 4). Pleasingly, in several cases (Entries 1-3), the isolated yields matched, or were superior to those previously reported.[13] Furthermore, they were achieved after shorter irradiation times under our more sustainable and practical laboratory conditions. With the aim of expanding the reaction scope, in addition to the literature examples, our optimised conditions were applied to a range of previously unexplored aliphatic aldehydes (Entries 4-9). In these cases, unfunctionalised aliphatic moieties (Entries 4-5) appear to be the

most successful and product precipitation meant that no further purification was required. Halides, ether, alkene and unconjugated aromatic functionalities in the aldehyde are also tolerated (Entries 6-9). Moderate success was achieved with the use of aromatic and heterocyclic aldehydes (Entries 10-15). However, in several of these cases (Entries 11-13) the reactions proceeded far more slowly and prolonged irradiation times were necessary. Furthermore, yields were often compromised by the formation of O-acylated hydroquinone monoesters (Entries 11 and 13), which despite prolonged irradiation, did not rearrange to the desired C-acylated hydroquinone.



Scheme 6

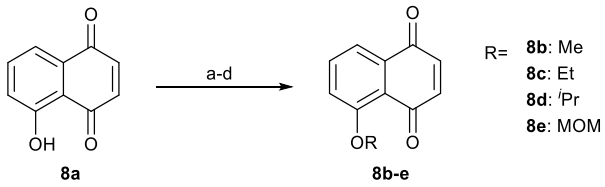
Table 4: Variation of the aldehyde

Entry	R	Product	Isolated Yield (%)
1	Me	**6e**	81 (75)[a]
2	Et	**6f**	73 (73)[a]
3	Pr	**6a**	62 (58)[a]
4		**6b**	61
5		**6c**	71
6		**6g**	30[b]
7		**6h**	28
8		**6i**	34
9		**6d**	55
10		**6j**	60[b,c]
11		**6k**	17[b-e]
12		**6l**	69[b,d]
13		**6m**	35[b-e]
14		**6n**	0
15		**6o**	0

All reactions were carried out in Pyrex tubes at 0.08 M concentrations in trifluorotoluene and were irradiated for 14.5 h using a 400 W Powerstar HQI-T bulb. [a]Bracketed yields represent those reported in the literature. **Literature Conditions**: RPR-3000 photochemical reactor, benzene, 23 h[13]; [b]Mixture was vigorously degassed with argon

prior to irradiation; [c]Based on recovered starting material; [d]Mixture was irradiated for 72 h; [e]Formation of the hydroquinone monoester was also observed.

After expansion of the reaction scope by variation of the aldehyde, the regiochemistry of the acylation was investigated with unsymmetrical quinone substrates. To the best of our knowledge, there exist only a few successful examples of the photo Friedel-Crafts acylation on 5-substituted naphthoquinones,[9,11] whilst the application of the methodology to 6-substituted substrates remains unexplored. As a number of biologically active quinone natural products, such as the pyranonaphthoquinones (Scheme 1) contain such functionalities, it was of interest to expand the breadth of our optimised conditions. The regiochemistry of the reaction was first investigated with 5-substituted naphthoquinones **8b-e** that were readily synthesised by alkylation reactions of commercially available juglone **8a** (Scheme 7).



8a 8b-e

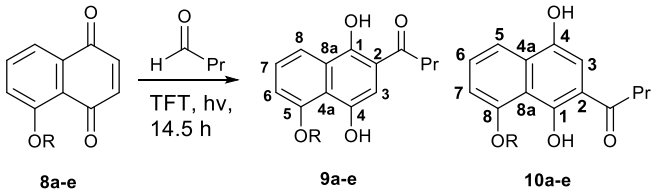
Scheme 7. Conditions: a) **8b**: MeI, Ag_2O, CH_2Cl_2, rt, 20 h, 90%; c) **8c**: EtI, Ag_2O, CH_2Cl_2, rt, 20 h, 90%; d) **8d**: 2-iodopropane, Ag_2O, CH_2Cl_2, rt, 20 h, quant.; e) **8e**: MOMCl, DIPEA, CH_2Cl_2, 16 h, 79%.

When carrying out the reaction on 5-substituted naphthoquinones, two regioisomeric hydroquinone products: 2,5-isomer **9** and 2,8-isomer **10**, are possible. It was anticipated that the regiochemical outcome may be influenced by the nature of the substituent in naphthoquinone substrates **8a-e** (Scheme 8, Table 5).

No reaction was observed with juglone **8a** itself (Entry 1), perhaps unsurprisingly, as there is literature precedent to suggest that such hydroxyquinones undergo a

phototautomerisation (intramolecular hydrogen transfer) process.[11,24-27] However, in the case of each successful reaction (Entries 2-5), the formation of 2,8-isomer **10** appeared to dominate over 2,5-isomer **9**. Pleasingly, the outcome of the photochemical reaction with methoxy naphthoquinone **8b** (Entry 2) is consistent with the results observed by Oelgemöller, [11] where 2,8-isomer **10** was isolated in a ratio of 1.7 to 1 relative to 2,5-isomer **9**.

However, in several cases (Entries 3-5), the isolated ratios of 2,5-isomer **9** and 2,8-isomer **10** did not match the ratio in the initial reaction mixture. Moreover, it was the 2,5-isomer **9** that was isolated as the major product. Whilst unexpected, reasons for this can be attributed to the difference in the ease of purification of the two regioisomers.



Scheme 8

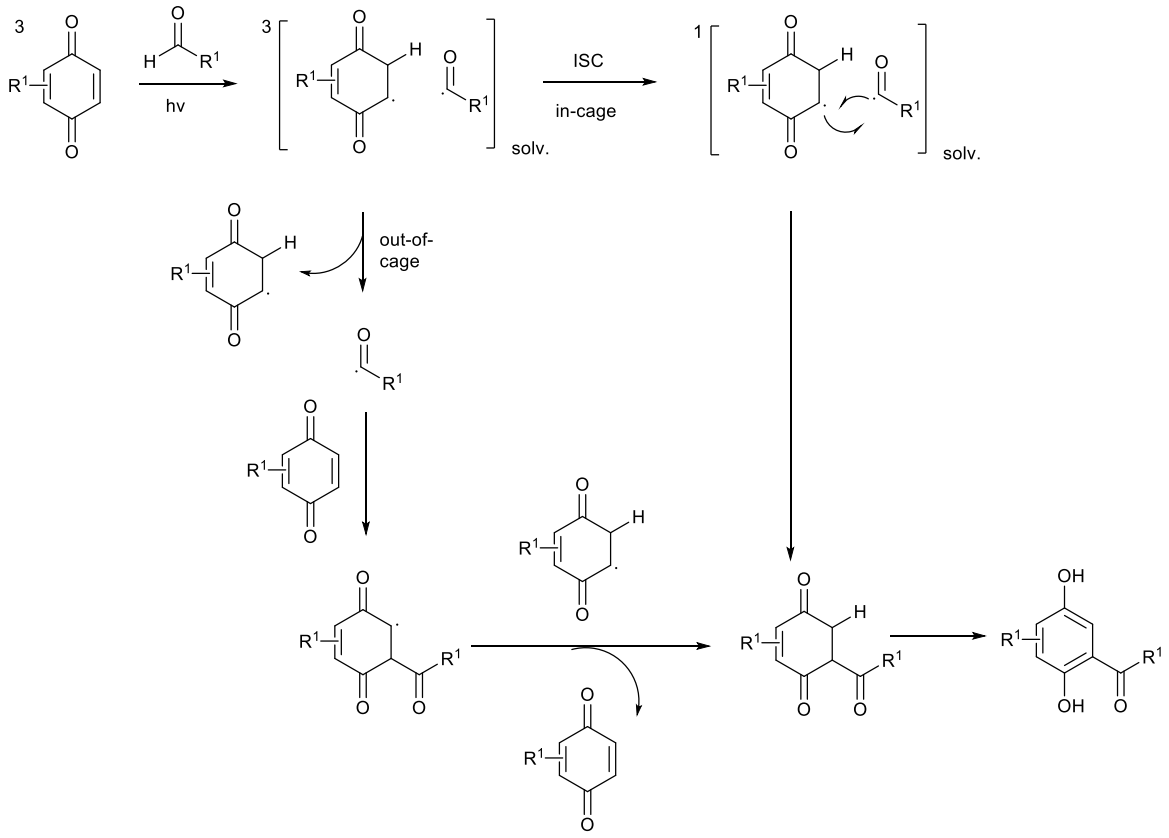
Table 5: Variation of 5-substituted naphthoquinone

Entry	R	Quinone	Products	Initial Ratio of **9**:**10**[a]	Isolated Yield of **9** (%)[b]	Isolated Yield of **10** (%)[b]
1	H	**8a**	**9a**/**10a**	0	0	0
2	Me	**8b**	**9b**/**10b**	1:1.3 (1:1.7)[c]	20 (23)[c]	39 (38)[c]
3	Et	**8c**	**9c**/**10c**	1:1.5	17	16[d]
4	^{i}Pr	**8d**	**9d**/**10d**	1:1.3	18	17[d]
5	MOM	**8e**	**9e**/**10e**	1:1.3	19	16[d]

[a]Crude ratios are calculated from ^{1}H NMR spectroscopic analysis of the crude reaction mixture before subsequent purification; [b]Yield after the crude reaction mixture is subjected to purification by column chromatography; [c]Yields/ratios reported by

Oelgemöller *et al*.[11] using the literature conditions: benzene, 5 d, high pressure mercury vapour lamp (125 W); [d]Recovered yield after rigorous chromatography/recrystallisation.

Mechanistically, two possible pathways have been proposed (Scheme 9). The 'in-cage' scenario, as first proposed by Schenck[28] and developed further by Maruyama,[29,30] suggests the formation of a 'caged' triplet biradical which directly combine to afford the acylated product. Conversely, the 'out-of-cage' scenario, as first proposed by Moore[31] and later reinforced by Bruce,[24,32,33] suggests dissociation of the triplet biradical and the reaction of the resultant acyl radical with the ground state quinone. Later research conducted by Maruyama on the acetylation of corresponding 1,2-naphthoquinones suggested the operation of both pathways, in a manner that is dependent on the specific conditions for each photo-acylation reaction.[34]



Scheme 9. Mechanistic scenarios for the photo Friedel-Crafts acylation

For 5-substituted naphthoquinones, the formation of 2,8-isomer **10** as the major product in all cases can be rationalised by consideration of the 'out-of-cage' scenario. Since acyl radicals are considered nucleophilic,[11,35] it is predicted that they will predominately attack the most electrophilic carbon atom on the quinone substrate. Preliminary AM1 calculations indicate that the C-3 position on quinone **8a** bears the larger LUMO coefficient and thus will be the preferential site of attack by nucleophiles. This would lead to the preferential formation of 2,8-isomer **10** as the major regioisomer, which is observed.[11,36]

The structures of the regioisomers were initially assigned by analysis of their 1D and 2D NMR spectra (Figure 1). Firstly, the protons on the aryl ring system can be assigned based on their multiplicities and interactions with C-5, in the case of 2,5-isomer **9** or C-8, in the case of 2,8-isomer **10** (interaction A). The 1-OH and 4-OH groups can be assigned with ease as significant differences in chemical shifts are observed in the ^{1}H spectra; the hydroxyl group positioned *ortho* and hydrogen bonded to the carbonyl is largely de-shielded compared to the other. From the information in the HMBC spectra, the carbons bound to OH-1 and 4 can be assigned (interactions B and C). Finally, further examination of the long-range interactions between C-1 and C-4 with the H-5 and H-8 on the aryl ring system using the HMBC spectra (interaction D) leads to the assignment of the regiochemistry. The structure of hydroquinones **9e** and **10c** were unambiguously confirmed by X-ray diffraction (Figure 2).

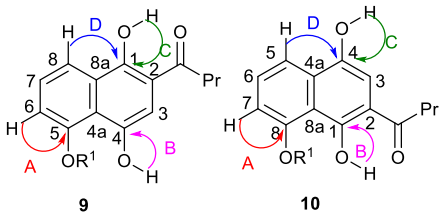


Figure 1. Assignment of 2,5-Regioisomer **9** and 2,8-Regioisomer **10**.

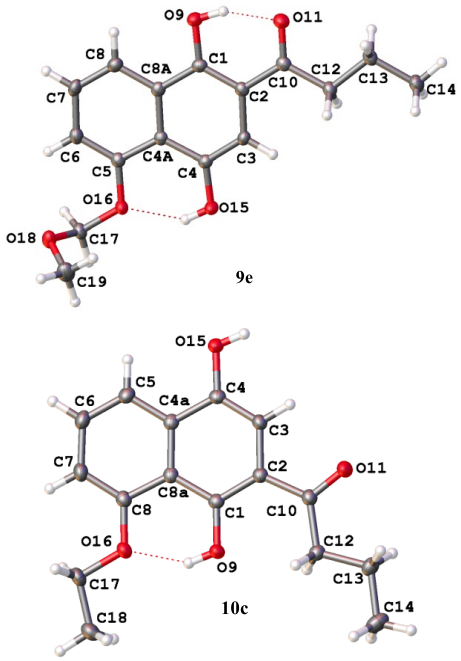
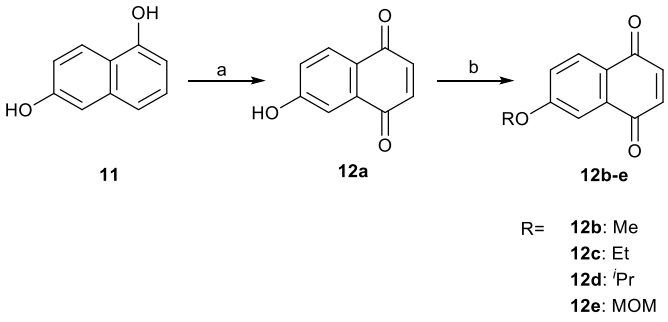


Figure 2. X-Ray crystal structures of acylated hydroquinones **9e** and **10c**

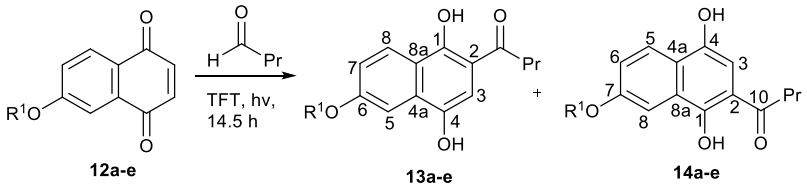
After investigation of the regiochemical outcome of the photo Friedel-Crafts acylation of unsymmetrical 5-substituted naphthoquinones, a corresponding series of 6-substituted naphthoquinones was studied. Unsymmetrical 6-substituted naphthoquinones **12b-e** were synthesised by functionalisation reactions of isojuglone **12a** which was prepared from the oxidation of commercially available 2,6-dihydroxynaphthalene **11** (Scheme 10).



Scheme 10. Conditions: a) O_2, salcomine, DMF, rt, 16 h, 46%; b) **12b**: MeI, Ag_2O, CH_2Cl_2, rt, 3 d, 100%; c) **12c**: EtI, Ag_2O, CH_2Cl_2, rt, 16 h, 76%; d) **12d**: 2-iodopropane, Ag_2O, CH_2Cl_2, rt, 20 h, quant.; e) **12e**: MOMCl, DIPEA, CH_2Cl_2, 16 h, 66%.

For the substituted 6-hydroxy-naphthoquinone substrates, the reverse regiochemical outcome was expected (Scheme 11, Table 6). As in this case, preliminary AM1 calculations indicated that the C-2 double bond position of the naphthoquinone substrate bears the larger LUMO coefficient, it was anticipated that 2,6-isomer **13** would be formed preferentially to 2,7-isomer **14**.

Pleasingly, this hypothesis was shown to be correct as in the case of each successful example (Entries 2-4), 2,6-isomer **13** was formed and subsequently isolated as the major regioisomer relative to 2,7-isomer **14**. Although the reaction with naphthoquinone **12e** was successful (Entry 5), both regioisomers co-eluted in all trialled solvent systems and as a result could not be successfully isolated. As with juglone **8a**, no reaction was observed with isojuglone **12a** (Entry 1).



Scheme 11

Table 6: Variation of the 6-Substituted Naphthoquinone Substrate

Entry	R^1	Quinone	Products	Crude Ratio of **13**:**14**[a]	Isolated Yield of **13** (%)[b]	Isolated Yield of **14** (%)[b]
1	H	**12a**	**13a**/**14a**	0	0	0
2	Me	**12b**	**13b**/**14b**	1.4:1 (1.5:1)[c]	30	20
3	Et	**12c**	**13c**/**14c**	1.2:1 (3:1)[c,d]	27	9
4	^{i}Pr	**12d**	**13d**/**14d**	1.3:1 (1.3:1)[c]	20	15
5	MOM[e]	**12e**	**13e**/**14e**	-	-	-

[a]Reference ratios are calculated from ^{1}H NMR analysis of the crude reaction mixture before subsequent purification; [b]Yield after the crude reaction mixture is subjected to

purification by column chromatography; [c]Actual (isolated) ratio of **13**:**14**; [d]Reasons for the inaccuracy of this ratio can be attributed to the challenging purification process; [e]Due to co-elution in all solvent systems trialled in our hands, the regioisomers could not be successfully isolated.

As before, the structures of the regioisomers were assigned by analysis of their 2D NMR spectra (Figure 3). By considering the HMBC interactions between hydroxyl protons 1 and 4, the carbon atoms bound to them could be assigned (Interactions A and B). By further analysis of the HMBC correlations between carbon atoms 1 and 4 and the protons 5 and 8 on the ring system (interactions C and D), regioisomers **13** and **14** could be assigned with certainty. The structure of hydroquinone **13b** was unambiguously confirmed by X-ray diffraction (Figure 4).

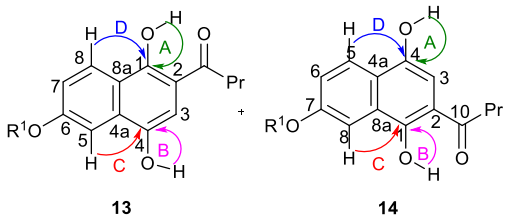


Figure 3. Assignment of 2,6-Regioisomer **13** and 2,7-Regioisomer **14**.

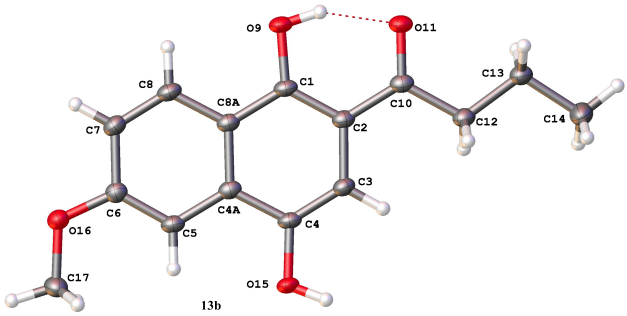


Figure 4. X-Ray Crystal structure of acylated hydroquinone **13b**

Conclusion

The photo Friedel-Crafts acylation offers an efficient method for the preparation of acylated hydroquinones. However, in order to transfer this promising reaction into a

more reliable and sustainable laboratory protocol, further development was required. By optimisation of the literature conditions, we have developed an improved procedure, that utilises a less hazardous solvent and a reliable commercially available 'sun-mimicking' light source. Moreover, we have expanded the scope of the reaction by its application to a wider range of aldehydes, including those with additional functionality (halide, ether, alkene), and investigated factors that influence the regiochemistry of the acylation of unsymmetrical naphthoquinone substrates.

Experimental Section

General Information

Starting materials were obtained from commercial suppliers and were used as purchased, except for aldehydes which were distilled immediately prior to use. Anhydrous solvents were used without further purification, except for the dichloromethane which was distilled from calcium hydride under nitrogen. Light petroleum refers to the fraction with bp 40-60 °C. Reactions were monitored by TLC using Merck Kieselgel 60GF_{254} aluminium-backed plates. The plates were visualised using UV light (254 nm) and/or chemical staining. Flash chromatography was carried out using using Devisil 35-70u 60 Å silica gel under medium pressure with the solvent system specified.

NMR spectra were recorded at 270 MHz on a Jeol EX270, 400 MHz on Bruker Avance III-400, Bruker Avance 400 or Bruker DPX 400 spectrometers or 500 MHz on a Bruker Avance III-500 spectrometer (corresponding ^{13}C frequencies are 68, 100 and 125 MHz respectively). NMR samples were analysed as dilute solutions with the solvent specified at 298 K. Chemical shifts are expressed in parts per million (ppm) downfield with the residual solvent peak as an internal standard ($CDCl_3$ δ_H 7.26, δ_C 77.16). Coupling constants (*J*) are reported in Hz and the multiplicities of each peak are quoted as follows: s singlet, d doublet, t triplet, q quartet, m multiplet and app. b. d. apparent broad doublet or combinations thereof. The signals were assigned by the analysis of

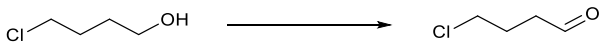
DEPT, COSY, NOESY, HMBC and HSQC experiments where appropriate. Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer as dilute chloroform solutions using NaCl cells. Low and high-resolution mass spectra were obtained for all compounds where possible. Electrospray ionisation (ESI) and high resolution mass spectrometric (HRMS) analyses were measured on a Bruker MicroTOF spectrometer. Electron ionization (EI) analyses were performed on the Waters Autospec or Bruker Apex IV instrument.

Melting points are uncorrected and were measured using Riechert-Kofler hot stage apparatus. CHN microanalysis was carried out using an Exeter Analytical CE-440 Elemental Analyser.

The wavelength output of the light source was measured using a compact CCD (Model: CCS150) spectrometer, produced by Thorlabs, or by a USB Miniature Fiber Optic Spectrometer, produced by Ocean Optics. Light intensities were measured using a digital light meter, produced by Sinometer (Model: MS6612), with an operating range of 20-200000 lux.

Preparation of Functionalised Aldehydes

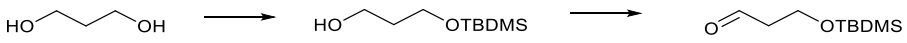
4-Chlorobutanal



The reaction was carried out according to the procedure in Snyder *et al*.[37] with minor modifications. To 4-chloro-1-butanol (2.80 mL, 28.2 mmol) in dichloromethane (100 mL) was added PCC (7.30 g, 33.9 mmol) and silica gel (7.30 g) and the reaction mixture was stirred at ambient temperature for 16 h. The resulting black slurry was filtered through a short column of florasil, washed with ether (3 × 100 mL) and concentrated *in vacuo*. The *title compound* (2.17 g, 73%) was isolated as a colourless oil which was used in the next

step without further purification; δ_H (400 MHz; $CDCl_3$) 9.79 (1 H, s, CH), 3.57 (2 H, t, *J* 6.50, CH_2Cl), 2.65 (2 H, td, *J* 7.0, 0.8, CH_2CO), 2.08 (2 H, pent, *J* 6.5, CH_2); δ_C (100 MHz; $CDCl_3$) 200.9 (CHO), 44.0 (CH_2), 40.8 (CH_2), 24.8 (CH_2). Data are consistent with those reported in the literature.[38]

3-(*t*-Butyldimethylsiloxy)propanal



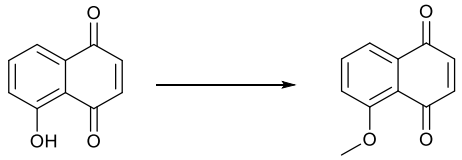
The reaction was carried out according to the procedure in McDougal *et al*.[39] with minor modifications. Sodium hydride (2.63 g, 65.7 mmol) was washed with pentane (3 × 10 mL) and dried under argon. THF (125 mL) was added followed by subsequent slow addition of the propane-1,3-diol (5.00 g, 65.7 mmol) and the reaction mixture was stirred at ambient temperature. After 45 min, TBDMS-Cl (9.90 g, 65.7 mmol) was added and the reaction mixture was stirred for a further 45 min. The reaction was diluted with ether (200 mL) and washed with sodium carbonate solution (200 mL), brine (200 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (light petroleum → 70:30 light petroleum/ethyl acetate) to afford product (10.6 g, 85%) as a colourless oil; δ_H (400 MHz; $CDCl_3$) 3.73 (1 H, td, *J* 6.1, 1.5, CH_2), 3.68 (1 H, td, *J* 5.8, 1.8, CH_2), 3.14 (1 H, s, OH), 1.69 (1 H, quint., *J* 5.6, CH_2), 0.83 (9 H, d, *J* 0.6, 3 × CH_3), 0.00 (6 H, d, *J* 1.6, 2 × CH_3); δ_C (100 MHz; $CDCl_3$) 62.0 (CH_2), 61.2 (CH_2), 34.4 (CH_2), 25.7 (CH_3), 18.0 (C), -5.67 (CH_3). Data are consistent with those reported in the literature.[39]

The next step was carried out according to the procedure by Grünanger *et al*.[40] Oxalyl chloride (1.04 mL, 12.2 mmol) in dichloromethane (27 mL) was cooled to -60 °C and DMSO (1.8 mL, 25.2 mmol) in dichloromethane (5 mL) was added and the reaction mixture stirred. After 5 min, 3-(*t*-butyldimethylsiloxy)propan-1-ol (2.00 g, 10.5 mmol) was added dropwise, followed by further dropwise addition of triethylamine (7.38 mL,

53.2 mmol). The reaction mixture was stirred whilst being gradually warmed to ambient temperature. After 1 h, water (50 mL) was added and the phases separated. The aqueous phase was back-extracted with further dichloromethane (50 mL) and the combined organic layers were washed with brine (100 mL), water (50 mL) and further brine (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was dissolved in ether, filtered through Celite and concentrated *in vacuo* to afford the *title compound* (1.69 g, 86%) as a colourless oil; δ_H (400 MHz; $CDCl_3$) 9.79 (1 H, t, *J* 2.3, CH), 3.98 (2 H, t, *J* 6.0, CH_2), 2.59 (2 H, td, *J* 6.0, 2.2, CH_2), 0.87 (9 H, s, 3 × CH_3), 0.05 (6 H, s, 2 × CH_3); δ_C (100 MHz; $CDCl_3$) 201.9 (CH), 57.4 (CH_2), 46.5 (CH_2), 25.8 (CH_3), 18.2 (C), -5.5 (CH_3). Data are consistent with those previously reported.[41]

Preparation of Functionalised Naphthoquinones

5-Methoxy-1,4-naphthoquinone 8b

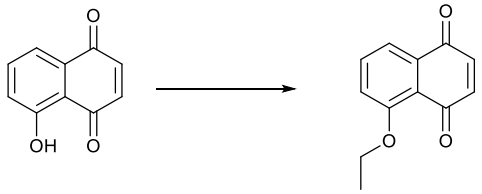


8a **8b**

The reaction was carried out according to the procedure in Tietze *et al*.,[42] with minor modifications. To 5-hydroxy-1,4-naphthoquinone **8a** (100 mg, 0.57 mmol) and silver(I) oxide (100 mg, 0.46 mmol) in dichloromethane (2 mL) was added iodomethane (0.07 mL, 1.12 mmol) and the mixture stirred at ambient temperature. After 20 h further iodomethane (0.03 mL, 0.46 mmol) and silver(I) oxide (100 mg, 0.46 mmol) were added and the reaction mixture stirred for a further 3 h. The reaction mixture was filtered through Celite, washed (dichloromethane) and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (light petroleum → 8:2 light petroleum: ethyl acetate) to give the *title compound* **8b** (96 mg, 90%) as fine orange crystals; mp 180-183 °C (lit.,[43] mp 180-185 °C); δ_H (400 MHz; $CDCl_3$) 7.72 (2 H, m,

ArH), 7.32 (1 H, dd, *J* 8.2, 1.0, ArH), 6.87 (2 H, app. br s, CH), 4.02 (3 H, s, OMe); δ_C (100 MHz; $CDCl_3$) 185.1 (C), 184.3 (C), 159.6 (C), 140.8 (CH), 136.1 (CH), 134.9 (CH), 134.0 (C), 119.6 (C), 119.1 (CH), 117.9 (CH), 56.4 (CH_3). Data are consistent with those reported in the literature.[42,43]

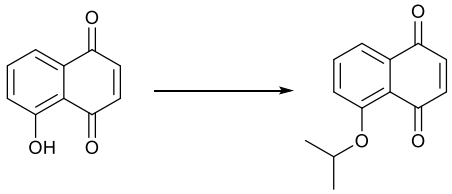
5-Ethoxy-1,4-naphthoquinone 8c



8a **8c**

To 5-hydroxy-1,4-naphthoquinone **8a** (100 mg, 0.57 mmol) and silver(I) oxide (100 mg, 0.46 mmol) in dichloromethane (2 mL) was added iodoethane (0.09 mL, 1.12 mmol) and the reaction mixture was stirred at ambient temperature. After 16 h further silver(I) oxide (100 mg, 0.46 mmol) and iodoethane (0.04 mL, 0.46 mmol) were added and the reaction mixture was stirred for a further 4 h. The reaction mixture was concentrated *in vacuo* and the product was crystallised from the minimum volume of hot toluene/light petroleum to yield the *title compound* **8c** (114 mg, 99%) as a brown solid; mp 78-79 °C; (Found: C, 71.28; H, 4.98; $C_{12}H_{10}O_3$ requires C, 71.32; H, 5.18 %); (Found: M+Na^+, 225.0521. $C_{12}H_{10}O_3Na^+$ requires 225.0522); λ_{max} (CH_2Cl_2)/nm 274 (log ε 5.71), 400 (4.37); ν_{max} ($CHCl_3$)/cm^{-1} 3686, 3012, 2415, 1521, 1239; δ_H (400 MHz; $CDCl_3$) 7.69 (1 H, dd, *J* 7.6, 1.4, ArH), 7.63 (1 H, app. br t, *J* 8.3, ArH), 7.27 (1 H, dd, *J* 8.3, 1.4, ArH), 6.83 (2 H, app. br s, CH), 4.20 (2 H, q, *J* 7.0, CH_2), 1.53 (3 H, t, *J* 7.0, CH_3); δ_C (100 MHz; $CDCl_3$) 185.3 (C), 184.2 (C), 159.0 (C), 140.9 (CH), 136.1 (CH), 134.8 (CH), 134.0 (C), 119.8 (C), 119.1 (CH), 119.0 (CH), 65.1 (CH_2), 14.6 (CH_3); *m/z* (ESI) 225 (M+Na^+, 100%), 103 (M+H^+, 5).

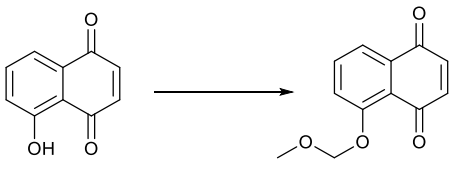
5-Isopropoxy-1,4-Naphthoquinone 8d



8a **8d**

To 5-hydroxy-1,4-naphthoquinone **8a** (200 mg, 1.15 mmol) and silver(I) oxide (220 mg, 0.96 mmol) in dichloromethane (2 mL) was added 2-iodopropane (0.12 mL, 2.29 mmol) and the reaction mixture was stirred at ambient temperature. After 16 h further silver(I) oxide (440 mg, 1.92 mmol) and 2-iodopropane (0.4 mL, 9.20 mmol) were added and the reaction mixture was stirred for a further 4 h. The reaction mixture was concentrated *in vacuo* to yield the *title compound* **8d** (248 mg, 100%) as a dark green solid; mp 89-90 °C; (Found: M+Na^+, 239.0669. $C_{13}H_{12}O_3Na^+$ requires 239.0679); λ_{max} (CH_2Cl_2)/nm 275 (log ε 4.40), 322 (2.91), 403 (3.46); ν_{max} (CH_2Cl_2)/cm^{-1} 2983, 1662, 1585, 1464, 1298, 1251; δ_H (400 MHz; $CDCl_3$) 7.70 (1 H, dd, *J* 7.6, 1.2, ArH), 7.63 (1 H, app. br t, *J* 8.3, ArH), 7.30 (1 H, app. br d, *J* 8.3, ArH), 6.85 (2 H, app. br s, CH), 4.69 (1 H, sept, *J* 6.2, CH), 1.45 (6 H, d, *J* 6.2, CH_3); δ_C (100 MHz; $CDCl_3$) 185.3 (C), 184.0 (C), 158.3 (C), 141.0 (CH), 136.0 (CH), 134.5 (CH), 134.2 (C), 121.3 (CH), 120.8 (C), 119.1 (CH), 72.3 (CH), 22.0 (CH_3); *m/z* (ESI) 239 (M+Na^+, 100%).

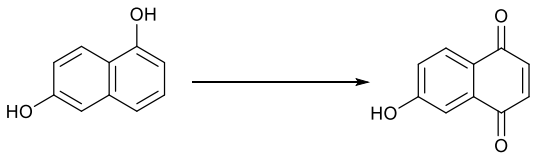
5-Methoxymethoxy-1,4-naphthoquinone 8e



8a **8e**

The reaction was carried out according to the procedure in Nandaluru *et al*.[44] with minor modifications. To 5-hydroxy-1,4-naphthoquinone **8a** (200 mg, 1.15 mmol) and MOM-Cl (0.23 mL, 2.87 mmol) in dichloromethane (3 mL) at 0 °C was added DIPEA (0.40 mL, 2.30 mmol) dropwise over 5 min and the reaction mixture was stirred at ambient temperature for 16 h. To the reaction mixture was added saturated ammonium chloride solution (50 mL) and the phases separated. The aqueous layer was washed with dichloromethane (50 mL), and the organic layers combined, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (4:1 light petroleum: ethyl acetate) to afford the *title compound* **8e** (179 mg, 79%) as an orange solid; mp 98-100 °C (lit.,[44] mp 98-101 °C); (Found: C, 66.00; H, 4.67; $C_{12}H_{10}O_4$ requires C, 66.05; H, 4.62 %); (Found: M+Na^+, 241.0467. $C_{12}H_{10}O_4Na^+$ requires 241.0471); λ_{max} (CH_2Cl_2)/nm 246 (log ε 5.16), 380 (4.28); ν_{max} ($CHCl_3$)/cm^{-1} 3012, 1663, 1587, 1335, 994; δ_H (400 MHz; $CDCl_3$) 7.75 (1 H, dd, *J* 7.5, 1.0, ArH), 7.63 (1 H, app. b. t, *J* 8.3, ArH), 7.51 (1 H, dd, *J* 8.3, 1.0, ArH), 6.85 (2 H, app. br. s, CH), 5.33 (2 H, s, CH_2), 3.52 (3 H, s, OCH_3); δ_C (100 MHz; $CDCl_3$) 184.8 (C), 184.0 (C), 157.0 (C), 140.6 (CH), 136.2 (CH), 134.6 (CH), 133.8 (C), 122.2 (CH), 120.5 (C), 120.3 (CH), 95.0 (CH_2), 56.5 (CH_3); *m/z* (ESI) 241 (M+Na^+, 100%).

6-Hydroxy-1,4-naphthoquinone 12a

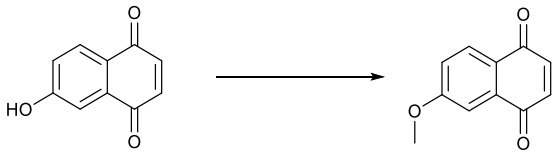


11 **12a**

A stirred solution of 1,6-dihydroxynapthalene **11** (5.00 g, 31.2 mmol) and salcomine (507 mg, 1.56 mmol) in DMF (33 mL) was bubbled rapidly with oxygen at ambient temperature. After 16 h, ether (200 mL) and brine (200 mL) were added and phases separated. The aqueous layer was back-extracted with further ether (10 × 200 mL) and

the organic layers combined, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel (7:3 light petroleum: ethyl acetate) to give the *title compound* **12a** (2.50 g, 46%) as a bright orange solid; mp 170-171 °C (decomp) (lit.,[45] mp 170 °C); (Found: C, 68.67; H, 3.42; $C_{10}H_6O_3$ requires C, 68.97; H, 3.47 %); (Found: M-H^+, 173.0238. $C_{10}H_5O_3^-$ requires 173.0244); λ_{max} (CH_2Cl_2)/nm 274 (log ε 5.26), 385 (3.26); ν_{max} ($CHCl_3$)/cm^{-1} 3689, 3607, 3045, 1602, 1523, 1240; δ_H (400 MHz; MeOD) 7.92 (1 H, d, *J* 8.5, ArH), 7.34 (1 H, d, *J* 2.6, ArH), 7.13 (1 H, dd, *J* 8.5, 2.6, ArH), 6.90 (2 H, d, *J* 2.1, CH); δ_C (100 MHz; MeOD) 186.7 (C), 185.6 (C), 164.6 (C), 140.3 (CH), 139.5 (CH), 135.6 (C), 130.2 (CH), 125.8 (C), 121.9 (CH), 113.2 (CH); *m/z* (ESI) 173 (M-H^+, 100%).

6-Methoxy-1,4-naphthoquinone 12b

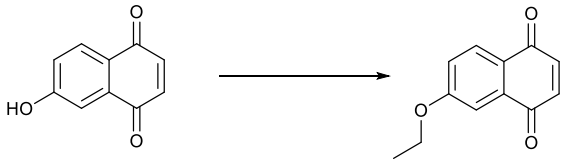


12a **12b**

To 6-hydroxy-1,4-naphthoquinone **12a** (100 mg, 0.57 mmol) and silver(I) oxide (200 mg, 0.92 mmol) in CH_2Cl_2 (2 mL) was added iodomethane (0.1 mL, 1.60 mmol) and the mixture stirred at ambient temperature for 3 d. The reaction mixture was filtered through Celite, washed with dichloromethane (50 mL) and concentrated *in vacuo* to afford the *title compound* **12b** (107 mg, 100%) as a fine yellow solid; mp 132–133 °C (lit.,[46] mp 133-135 °C); (Found: C, 69.82; H, 4.22; $C_{11}H_8O_3$ requires C, 70.21; H, 4.29 %); (Found: M+H^+, 189.0546. $C_{11}H_9O_3^+$ requires 189.0546); λ_{max} (CH_2Cl_2)/nm 261 (log ε 4.91), 382 (3.89); ν_{max} ($CHCl_3$)/cm^{-1}; 3012, 1667, 1593, 131, 1292; δ_H (400 MHz; $CDCl_3$) 8.02 (1 H, d, *J* 8.6, ArH), 7.50 (1 H, d, *J* 2.7, ArH), 7.21 (1 H, dd, *J* 8.6, 2.7, ArH), 6.92 (2 H, app br. s, CH), 3.95 (3 H, s, OCH_3); δ_C (100 MHz; $CDCl_3$) 185.2 (C),

184.1 (C), 164.1 (C), 139.0 (CH), 138.2 (CH), 133.9 (C), 128.9 (CH), 125.5 (C), 120.5 (CH), 109.6 (CH), 55.9 (CH_3); *m/z* (ESI) 399 ($2M+Na^+$, 100%), 211 ($M+Na^+$, 98), 189 ($M+H^+$, 47).

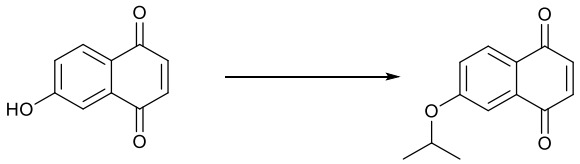
6-Ethoxy-1,4-naphthoquinone 12c



12a **12c**

To 6-hydroxy-1,4-naphthoquinone **12a** (50 mg, 0.29 mmol) and silver(I) oxide (106 mg, 0.46 mmol) in CH_2Cl_2 (1 mL) was added iodoethane (0.06 mL, 0.81 mmol) and the mixture stirred at ambient temperature for 16 h. The reaction mixture was filtered through Celite, washed with dichloromethane (50 mL) and concentrated *in vacuo* to afford the *title compound* **12c** (44 mg, 76%) as a fine yellow solid; mp 116-117 °C; (Found: C, 71.07; H, 4.99; $C_{13}H_{12}O_3$ requires C, 71.28; H, 4.98%); (Found: $M+Na^+$, 225.0522. $C_{12}H_{10}O_3Na^+$ requires 225.0522); λ_{max} (CH_2Cl_2)/nm 255 (log ε 4.37), 263 (4.39), 383 (3.27), 386 (3.20); ν_{max} ($CHCl_3$)/cm^{-1}; 3012, 2415, 1666, 1595, 1333, 1239, 965; δ_H (400 MHz; $CDCl_3$) 8.02 (1 H, d, *J* 8.6, ArH), 7.50 (1 H, d, *J* 2.7, ArH), 7.20 (1 H, dd, *J* 8.6, 2.7, ArH), 6.92 (2 H, app br. s, CH), 4.19 (2 H, q, *J* 6.9, CH_2), 1.48 (3 H, t, *J* 7.0, CH_3); δ_C (100 MHz; $CDCl_3$) 185.2 (C), 184.1 (C), 163.6 (C), 139.0 (CH), 138.2 (CH), 133.9 (C), 128.9 (CH), 125.3 (C), 120.8 (CH), 110.1 (CH), 64.4 (CH_2), 14.6 (CH_3); *m/z* (ESI) 225 ($M+Na^+$, 100%), 203 ($M+H^+$, 35).

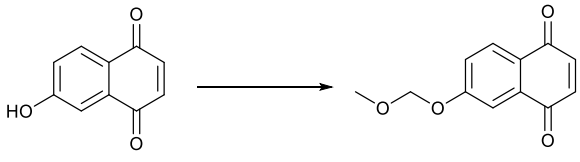
6-Isopropoxy-1,4-naphthoquinone 12d



12a 12d

To 6-hydroxy-1,4-naphthoquinone **12a** (100 mg, 0.57 mmol) and silver(I) oxide (110 mg, 0.48 mmol) in dichloromethane (1 mL) was added 2-iodopropane (0.1 mL, 1.12 mmol) and the mixture stirred at ambient temperature. After 16 h further silver(I) oxide (220 mg, 0.96 mmol) and 2-iodopropane (0.2 mL, 2.2 mmol) was added and the reaction mixture was stirred for a further 4 h. The reaction mixture was concentrated *in vacuo* to yield the *title compound* **12d** (123 mg, 100%) as a pale green solid; mp 111-113 °C; (Found: M+Na$^+$, 239.0671. $C_{13}H_{12}O_3Na^+$ requires 239.0679); λ_{max} (CH_2Cl_2)/nm 257 (log ε 4.54), 264 (4.56), 330 (2.96), 390 (3.54); ν_{max} ($CHCl_3$)/cm^{-1}; 2983, 1665, 1592, 1491, 1316, 1110, 1045, 961; δ_H (400 MHz; $CDCl_3$) 8.02 (1 H, d, *J* 8.6, ArH), 7.48 (1 H, d, *J* 2.6, ArH), 7.17 (1 H, dd, *J* 8.6, 2.7, ArH), 6.92 (2 H, app. br. s, CH), 4.76 (1 H, sept, *J* 6.0, CH), 1.40 (6 H, d, *J* 6.0, CH_3); δ_C (100 MHz; $CDCl_3$) 185.3 (C), 184.1 (C), 162.7 (C), 139.0 (CH), 138.2 (CH), 133.9 (C), 129.0 (CH), 125.0 (C), 121.7 (CH), 111.0 (CH), 70.8 (CH), 21.8 (CH_3); *m/z* (ESI) 239 (M+Na$^+$, 100%), 217 (M+H$^+$, 11).

6-Methoxymethoxy-1,4-naphthoquinone 12e



12a 12e

To 6-hydroxy-1,4-naphthoquinone **12a** (100 mg, 0.57 mmol) and MOM-Cl (0.12 mL, 1.44 mmol) in dichloromethane (2 mL) at 0 °C was added DIPEA (0.2 mL, 1.15 mmol) dropwise over 5 min and the reaction mixture was stirred at ambient temperature for 16 h. To the reaction mixture was added saturated ammonium chloride solution (50 mL)

and the phases separated. The aqueous layer was washed with dichloromethane (50 mL) and the organic layers combined, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (4:1 light petroleum: ethyl acetate) to afford the *title compound* **12e** (82 mg, 66%) as an orange solid; mp 110-112 °C; (Found: M+Na^+, 241.0468. $C_{12}H_{10}O_4Na^+$ requires 241.0471); λ_{max} (CH_2Cl_2)/nm 254 (log ε 4.69), 260 (4.69), 372 (3.69); ν_{max} ($CHCl_3$)/cm^{-1}; 3012, 1668, 1595, 1312, 988; δ_H (400 MHz; $CDCl_3$) 8.00 (1 H, d, *J* 8.6, ArH), 7.62 (1 H, d, *J* 2.6, ArH), 7.32 (1 H, dd, *J* 8.6, 2.6, ArH), 6.91 (2 H, app br. s, CH), 5.29 (2 H, s, CH_2), 3.48 (3 H, s, CH_3); δ_C (100 MHz; $CDCl_3$) 184.8 (C), 184.0 (C), 161.6 (C), 138.8 (CH), 138.3 (CH), 133.8 (C), 128.8 (CH), 126.1 (C), 121.5 (CH), 112.5 (CH), 94.1 (CH_2), 56.4 (CH_3); *m/z* (ESI) 241 (M+Na^+, 100%), 219 (M+H^+, 17).

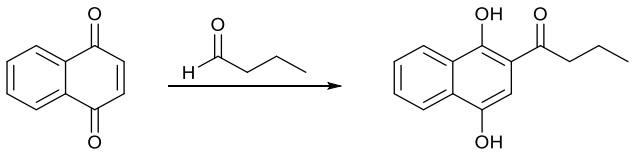
Photo Friedel-Crafts Acylation of 1,4-Naphthoquinones

Standard Procedure

Reaction mixtures were irradiated using a 400 W Trac metal halide floodlight containing a 400 W Osram Powerstar HQI-T metal halide bulb (λ_{max} 590 nm), at a distance of 29 cm from the reaction vessel (illuminance: 79405 lux). Reactions were carried out in 15 mL pyrex tubes, held from the rim and placed in front of the light source for a fixed and measured period of time. The temperature of the reaction vessels was between 25 and 35 °C.

To a stirred solution of the 1,4-naphthoquinone (50 mg) in trifluorotoluene (0.08 M) was added the aldehyde (7.8 eq) and the reaction mixture stirred and irradiated for 14.5 h. The products were obtained either by precipitation (light petroleum) or by column chromatography on silica gel (95:5 ethyl acetate:light petroleum).

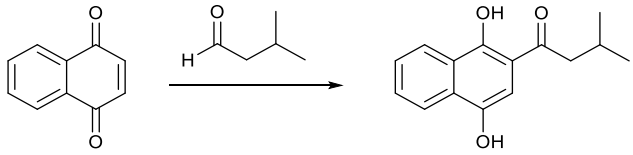
1-(1,4-Dihydroxy-2-naphthyl)-1-butanone 6a



6a

Standard procedure was used. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and butyraldehyde (0.18 mL, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6a** (45 mg, 62%) as a yellow solid; mp 145-146 °C (lit.,[9] mp 144-145 °C); (Found: M–H^+, 229.0881. $C_{14}H_{13}O_3^-$ requires 229.0870); λ_{max} (CH_2Cl_2)/nm 275 (log ε 4.18), 388 (3.22); ν_{max} ($CHCl_3$)/cm^{-1} 3600, 3012, 2967, 1629, 1467, 1396, 1193; δ_H (400 MHz; d_6-DMSO) 13.58 (1 H, s, OH), 9.81 (1 H, s, OH), 8.31 (1 H, app. br d, *J* 8.2, ArH), 8.13 (1 H, d, *J* 8.2, ArH), 7.71 (1 H, app. td, *J* 6.9, 1.3, ArH), 7.61 (1 H, app. td, *J* 6.9, 1.3, ArH), 7.14 (1 H, s, ArH), 3.05 (2 H, t, *J* 7.2, CH_2), 1.73 (2 H, sxt., *J* 7.3, CH_2), 1.00 (3 H, t, *J* 7.4, CH_3); δ_C (100 MHz; d_6-DMSO) 206.6 (C), 154.3 (C), 144.7 (C), 129.4 (C), 129.3 (CH), 126.4 (CH), 125.1 (C), 123.6 (CH), 122.1 (CH), 112.1 (C), 104.4 (CH), 39.9 (CH_2), 17.3 (CH_2), 13.6 (CH_3); *m/z* (ESI) 229 (M–H^+, 100%).

1-(1,4-Dihydroxy-2-naphthyl)-3-methyl-1-butanone 6b

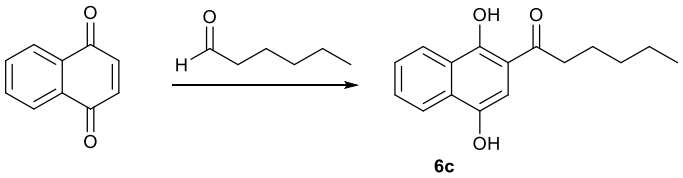


6b

Standard procedure was used. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and isovaleraldehyde (0.26 mL, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6b** (47 mg, 61%) as a yellow solid; mp 166–168 °C; (Found: M–H^+, 243.1030. $C_{15}H_{15}O_3^-$ requires 243.1027); λ_{max} ($CHCl_3$)/nm 276 (log ε 6.35), 398 (3.28); ν_{max} ($CHCl_3$)/cm^{-1} 3838, 3012, 2413, 1642, 1578, 1239, 929; δ_H (400 MHz; d_6-DMSO)

13.65 (1 H, s, OH), 9.79 (1 H, s, OH), 8.32 (1 H, app. b. d, *J* 8.2, ArH), 8.13 (1 H, d, *J* 8.2, ArH), 7.72 (1H, app. td, *J* 6.9, 1.3, ArH), 7.62 (1 H, app. td, *J* 6.9, 1.3, ArH), 7.16–7.12 (1 H, m, ArH), 2.92 (2 H, d, *J* 6.8, CH_2), 2.25 (1 H, hep., *J* 6.8, CH), 1.01 (6 H, d, *J* 6.8, CH_3); δ_C (100 MHz; d_6-DMSO) 206.3 (C), 154.6 (C), 144.6 (C), 129.4 (C), 129.3 (CH), 126.5 (CH), 125.1 (C), 123.7 (CH), 122.1 (CH), 112.3 (C), 104.5 (CH), 47.1 (CH_2), 15.0 (CH), 22.5 (CH_3); *m/z* (ESI) 243 ($M–H^+$, 100%).

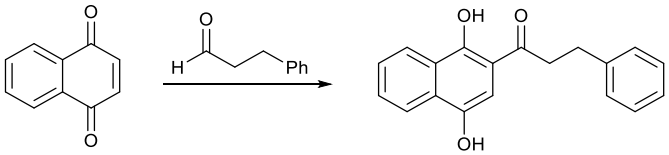
1-(1,4-Dihydroxy-2-naphthyl)-1-hexanone 6c



6c

Standard procedure was used. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and hexanal (0.3 mL, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6c** (58 mg, 71%) as a yellow solid; mp 166–167 °C; (Found: $M–H^+$, 257.1184. $C_{16}H_{17}O_3^-$ requires 257.1183); λ_{max} ($CHCl_3$)/nm 397 (log ε 3.57); ν_{max} ($CHCl_3$)/cm^{-1} 3438, 3012, 1631, 1397, 1273; δ_H (400 MHz; d_6-DMSO) 13.58 (1 H, s, OH), 9.80 (1 H, s, OH), 8.31 (1 H, app. b. d, *J* 8.2, ArH), 8.13 (1 H, d, *J* 8.2, ArH), 7.71 (1 H, app. td, *J* 6.9, 1.2, ArH), 7.61 (1 H, app. td, *J* 6.9, 1.2, ArH), 7.15–7.12 (1 H, m, ArH), 3.05 (2 H, t, *J* 7.4, CH_2), 1.75–1.60 (2 H, m, CH_2), 1.40–1.30 (4 H, m, CH_2), 0.95–0.85 (3 H, m, CH_3); δ_C (100 MHz; d_6-DMSO) 206.7 (C), 154.3 (C), 144.6 (C), 129.4 (C), 129.3 (CH), 126.4 (CH), 125.1 (C), 123.6 (CH), 122.0 (CH), 112.1 (C), 104.4 (CH), 38.2 (CH_2), 30.8 (CH_2), 23.6 (CH_2), 22.0 (CH_2), 13.8 (CH_3); *m/z* (ESI) 257 ($M–H^+$, 100%).

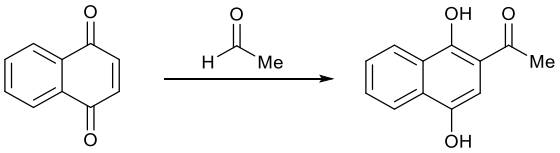
1-(1,4-Dihydroxynaphthalen-2-yl)-3-phenylpropan-1-one 6d



6d

Standard procedure was used. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and 3-phenylpropanal (0.3 mL, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6d** (51 mg, 55%) as a yellow solid; mp 137-138 °C; (Found: M-H^+, 291.1015. $C_{19}H_{15}O_3$ requires 291.1027); λ_{max} (MeOH)/nm 218 (log ε 4.40), 276 (4.24), 397 (3.68); ν_{max} ($CHCl_3$)/cm^{-1} 3852, 3066, 1629, 1397, 1190, 1066, 1016; δ_H (400 MHz; d_6-DMSO) 13.45 (1 H, s, OH), 9.77 (1 H, s, OH), 8.30 (1 H, d, *J* 8.2, ArH), 8.11 (1 H, d, *J* 8.2, ArH), 7.70 (1 H, app. b. t, *J* 7.3, ArH), 7.60 (1 H, app. b. t, *J* 7.3, ArH), 7.35-7.25 (4 H, m, ArH), 7.25-7.10 (2 H, m, ArH), 3.41 (2 H, t, *J* 7.2, CH_2), 3.02 (2 H, t, *J* 7.2, CH_2); δ_C (100 MHz; d_6-DMSO) 205.4 (C), 154.3 (C), 144.7 (C), 140.9 (C), 129.4 (C), 129.3 (CH), 128.3 (2 × CH), 126.5 (CH), 126.0 (CH), 125.1 (C), 123.7 (CH), 122.1 (CH), 112.1 (C), 104.3 (CH), 39.9 (CH_2), 29.5 (CH_2); *m/z* (ESI) 291 (M-H^+, 100).

1-(1,4-Dihydroxy-2-naphthyl)-1-ethanone 6e

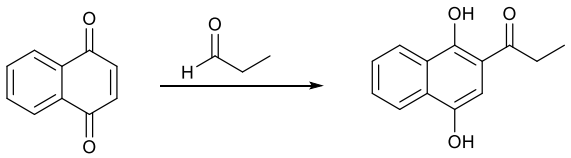


6e

Standard procedure was used. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and acetaldehyde (0.14 mL, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6e** (52 mg, 81%) as a yellow solid; mp 208–210 °C (lit.,[47] mp 205–207 °C); δ_H (400 MHz; d_6-DMSO) 13.50 (1 H, s, OH), 9.83 (1 H, s, OH), 8.30 (1 H, d, *J* 8.3, ArH), 8.12 (1 H, d, *J* 8.3, ArH), 7.70 (1 H, app. td, *J* 7.0, 1.2, ArH), 7.61 (1 H, app. td, *J* 7.0, 1.2, ArH), 7.12–7.08 (1 H, m, ArH), 2.66 (3 H, s, CH_3); δ_C (100 MHz; d_6-DMSO) 204.7

(C), 154.2 (C), 144.6 (C), 129.4 (C), 129.3 (CH), 126.4 (CH), 125.0 (C), 123.6 (CH), 122.1 (CH), 112.4 (C), 105.0 (CH), 27.1 (CH_3). Data are consistent with those reported in the literature.[47,48]

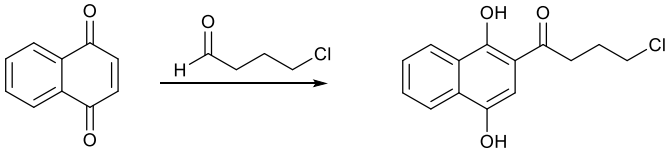
1-(1,4-Dihydroxy-2-naphthyl)-1-propanone 6f



6f

Standard procedure was used. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and propionaldehyde (0.18 mL, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6f** (50 mg, 73%) as a yellow solid; mp 164–166 °C; (lit.,[13] mp 164–166 °C); (Found: $M–H^+$, 215.0720. $C_{13}H_{11}O_3^-$ requires 215.0714); λ_{max} (CH_2Cl_2)/nm 274 (log ε 4.78), 382 (3.95); ν_{max} ($CHCl_3$)/cm^{-1} 3821, 3392, 3069, 2361, 1521; δ_H (400 MHz; d_6-DMSO) 13.52 (1 H, s, OH), 9.82 (1 H, s, OH), 8.30 (1 H, d, *J* 8.3, ArH), 8.12 (1 H, d, *J* 8.3, ArH), 7.70 (1 H, app. td, *J* 6.9, 1.2, ArH), 7.61 (1 H, app. td, *J* 6.9, 1.2, ArH), 7.14–7.10 (1 H, m, ArH), 3.10 (2 H, q, *J* 7.2, CH_2), 1.16 (3 H, t, *J* 7.2, CH_3); δ_C (100 MHz; d_6-DMSO) 207.0 (C), 154.1 (C), 144.7 (C), 129.3 (C), 129.2 (CH), 126.4 (CH), 125.1 (C), 123.6 (CH), 122.2 (CH), 112.0 (C), 104.3 (CH), 31.5 (CH_2), 8.1 (CH_3); *m/z* (ESI) 215 ($M–H^+$, 100%).

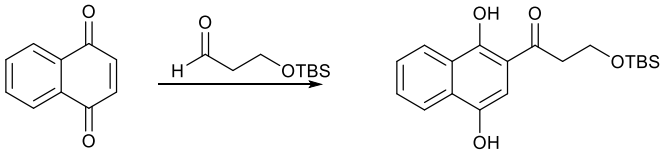
4-Chloro-1-(1,4-dihydroxynaphthalen-2-yl)butan-1-one 6g



6g

Standard procedure was used, and the reaction mixture was vigorously degassed with argon prior to irradiation. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and 4-chlorobutanal (261 mg, 2.47 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6g** (25 mg, 30%) as a yellow solid; mp 96-101 °C; (Found: M-H$^+$, 263.0435. $C_{14}H_{12}{}^{35}ClO_3$ requires 263.0553); λ_{max} (MeOH)/nm 399 (3.78); ν_{max} ($CHCl_3$)/cm^{-1} 3598, 3011, 1630, 1397, 1044, 827; δ_H (400 MHz; d_6-DMSO) 13.36 (1 H, s, OH), 9.82 (1 H, s, OH), 8.30 (1 H, app. b. d, *J* 8.3, ArH), 8.12 (1 H, d, *J* 8.0, ArH), 7.70 (1 H, td, *J* 7.6, 1.3, ArH), 7.61 (1 H, td, *J* 7.6, 1.3, ArH), 7.13 (1 H, s, ArH), 3.77 (2 H, t, J 6.6, CH_2), 3.25 (2 H, t, *J* 7.1, CH_2), 2.14 (2 H, pent, *J* 7.2, CH_2); δ_C (100 MHz; d_6-DMSO) 205.1 (C), 154.2 (C), 144.8 (C), 129.4 (C), 129.3 (CH), 126.5 (CH), 125.1 (C), 123.7 (CH), 122.2 (CH), 112.2 (C), 104.1 (CH), 44.8 (CH_2), 35.5 (CH_2), 26.5 (CH_2); *m/z* (ESI) 265/263 (M-H$^+$, 34/100).

3-(*t*-Butyldimethylsiloxy)-1-(1,4-dihydroxynaphthalen-2-yl)1-propanone 6h

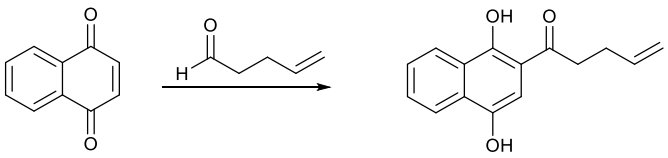


6h

Standard procedure was used. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and 3-(*t*-butyldimethylsiloxy)propanal (0.464 g, 2.47 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6h** (14 mg, 20%) as a gummy yellow solid; mp 128-131 °C; (Found: M$^-$, 346.1598. $C_{19}H_{26}O_4Si^-$ requires 346.1606); λ_{max} (CH_2Cl_2)/nm 276 (log ε 3.41), 391 (2.82); ν_{max} ($CHCl_3$)/cm^{-1} 3599, 3009, 1631, 1471, 1398, 1152; δ_H (400 MHz; $CDCl_3$) 13.68 (1 H, s, OH), 8.46 (1 H, app. br d, *J* 8.4, ArH), 8.12 (1 H, app. br d, J 8.2, ArH), 7.69 (1 H, app. t. d., *J* 7.0, 1.3, ArH), 7.59 (1 H, app t.d, *J* 7.0, 1.3, ArH), 7.04 (1 H, s, ArH), 4.11 (2 H, t, *J* 6.8, CH_2), 3.21 (2 H, t, J 6.8, CH_2), 0.88 (9 H, s, CH_3), 0.07 (6

H, s, CH_3); δ_H (100 MHz; $CDCl_3$) 204.2 (C), 157.5 (C), 142.9 (C), 129.8 (CH), 129.4 (C), 126.5 (CH), 126.1 (C), 124.6 (CH), 121.6 (CH), 112.2 (C), 105.7 (CH), 59.2 (CH_2), 41.7 (CH_2), 25.9 (CH_3), 18.3 (C), -5.39 (CH_3); *m/z* (ESI) 346/345 (M^-, 56/100).

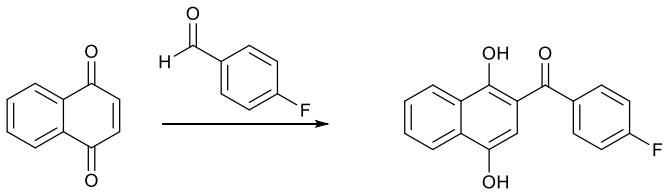
1-(1,4-Dihydroxynaphthalen-2-yl)pent-4-en-1-one 6i



6i

Standard procedure was used. The reaction mixture was irradiated for 28 h. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and pent-4-enal (0.24 mL, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6i** (26 mg, 34%) as a yellow solid; mp 125-129 °C; (Found: M-H^+, 241.0861. $C_{15}H_{13}O_3$ requires 241.0870); λ_{max} (MeOH)/nm 251 (log ε 4.11), 276 (4.21), 397 (3.65); ν_{max} ($CHCl_3$)/cm^{-1} 3600, 3009, 1630, 1468, 1397, 1066; δ_H (400 MHz; d_6-DMSO) 13.48 (1 H, s, OH), 9.82 (1 H, s, OH), 8.31 (1 H, d, *J* 8.3, ArH), 8.13 (1 H, d, *J* 8.3, ArH), 7.71 (1 H, app. b. t, *J* 7.4, ArH), 7.62 (1 H, app. b. t, *J* 7.4, ArH), 7.15 (1 H, s, ArH), 6.00-5.85 (1 H, m, CH), 5.15-5.00 (2 H, m, CH), 3.18 (2 H, t, *J* 7.2, CH_2), 2.46 (2 H, t, *J* 6.8, CH_2); δ_C (100 MHz; d_6-DMSO) 205.6 (C), 154.3 (C), 144.7 (C), 137.3 (CH), 129.4 (C), 129.3 (CH), 126.4 (CH), 125.1 (C), 123.7 (CH), 122.2 (CH), 115.4 (CH_2), 112.1 (C), 104.3 (CH), 37.3 (CH_2), 27.7 (CH_2); *m/z* (ESI) 241 (M-H^+, 100).

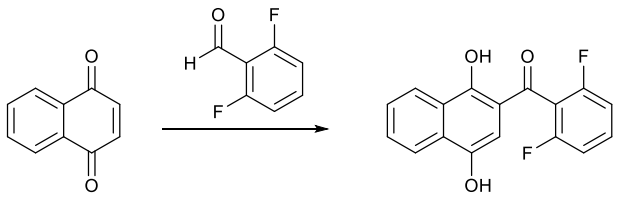
(1,4-Dihydroxynaphthalen-2-yl)(4-fluorophenyl)methanone 6j



6j

Standard procedure was used with minor modifications. The reaction mixture was degassed vigorously with argon prior to irradiation. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and 4-fluorobenzaldehyde (0.26 mL, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6j** (35 mg, 60% brsm) as a yellow solid; mp 170-173 °C; (Found: M-H$^+$, 281.0608. $C_{17}H_{10}FO_3$ requires 281.0619); λ_{max} (MeOH)/nm 221 (log ε 4.83), 269 (4.82), 419 (4.17); ν_{max} ($CHCl_3$)/cm^{-1} 3685, 3012, 2414, 1602, 1520, 1241; δ_H (400 MHz; d_6-acetone) 13.42 (1 H, s, OH), 8.65 (1 H, s, OH), 8.46 (1 H, d, *J* 8.4, ArH), 8.24 (1 H, d, *J* 8.3, ArH), 7.88-7.84 (2 H, m, ArH), 7.76 (1 H, td, *J* 7.6, 1.3, ArH), 7.66 (1 H, td, *J* 7.6, 1.3, ArH), 7.40-7.36 (2 H, m, ArH), 6.98 (1 H, s, ArH); δ_C (100 MHz; d_6-acetone) 200.6 (C), 165.6 (d, J_{FC} 250, C), 158.1 (C), 145.4 (C), 135.8 (C, d, J_{FC} 3.1), 132.7 (CH, d, J_{FC} 9.2), 130.9 (C), 130.7 (CH), 127.5 (CH), 126.9 (C), 125.0 (CH), 123.3 (CH), 116.3 (CH, d, J_{FC} 22), 112.8 (C), 107.8 (CH); δ_F (377 MHz, d^6-acetone) 109.4; *m/z* (ESI) 281 (M-H$^+$, 100).

(2,6-Difluorophenyl)(1,4-dihydroxynaphthalen-2-yl)methanone 6k

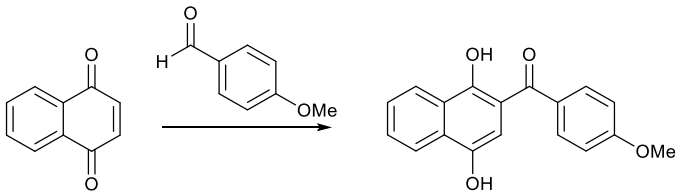


6k

Standard procedure A was used with minor modifications. The reaction mixture was degassed vigorously with argon prior to irradiation and the reaction was irradiated for 72 h. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and 2,6-difluorobenzaldehyde (349 mg,

2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6k** (16 mg, 17%) as a bright orange solid; mp 159-164 °C; (Found: M-H$^+$, 299.0516. $C_{17}H_9F_2O_3$ requires 299.0525); λ_{max} (MeOH)/nm 424 (log ε 3.84), 299 (3.85), 297 (3.96); ν_{max} ($CHCl_3$)/cm^{-1} 3684, 3045, 2415, 1637, 1241, 661; δ_H (400 MHz; d_6-acetone) 13.15 (1 H, s, OH), 8.73 (1 H, s, OH), 8.49 (1 H, d, *J* 8.4, ArH), 8.23 (1 H, d, *J* 8.4, ArH), 7.82-7.68 (3 H, m, ArH), 7.28 (2 H, t, *J* 7.8, ArH), 6.66 (1 H, s, ArH); δ_C (100 MHz; d_6-acetone) 194.3 (C=O), 161.4 (C, dd, J_{CF} 249), 158.3 (C), 146.3 (C), 134.0 (CH, t, J_{CF} 9.6), 131.6 (C), 131.5 (CH), 127.9 (CH), 126.5 (C), 125.2 (CH), 123.4 (CH), 114.3 (C), 113.12 (CH, d, J_{CF} 24.5), 113.11 (d, J_{CF} 15, C), 105.9 (CH); *m/z* (ESI) 299 (M-H$^+$, 100).

(1,4-Dihydroxynaphthalen-2-yl)(4-methoxyphenyl)methanone 6l

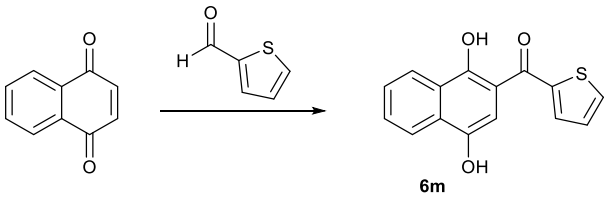


6l

Standard procedure was used with minor modifications. The reaction mixture was degassed vigorously with argon prior to irradiation and the reaction was irradiated for 72 h. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and *p*-anisaldehyde (335 mg, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6l** (64 mg, 69%) as a bright orange solid; mp 108-110 °C; (Found: M-H$^+$, 293.0805. $C_{18}H_{13}O_4$ requires 293.0819); λ_{max} (MeOH)/nm 416 (log ε 3.70), 299 (4.20), 297 (4.19); ν_{max} ($CHCl_3$)/cm^{-1} 3684, 3045, 2434, 1670, 1250, 821; δ_H (400 MHz; d_6-acetone) 13.52 (1 H, s, OH), 8.64 (1 H, s, OH), 8.45 (1 H, d, *J* 8.3, ArH), 8.24 (1 H, d, *J* 8.3, ArH), 7.29 (2 H, d, *J* 8.9, ArH), 7.74 (1 H, td, *J* 7.5, 1.2, ArH), 7.14 (2 H, d, *J* 8.9, ArH), 7.07 (1 H, s, ArH), 3.97 (3 H, s, OMe); δ_C (100 MHz; d_6-acetone) 200.7 (C), 163.8 (C), 157.7 (C), 145.2 (C), 132.5 (CH), 131.7

(C), 130.4 (CH), 127.3 (CH), 126.9 (C), 124.9 (CH), 123.3 (CH), 115.1 (C), 114.6 (CH), 113.0 (C), 108.2 (CH), 56.1 (CH_3); *m/z* (ESI) 293 ($M\text{-}H^+$, 100).

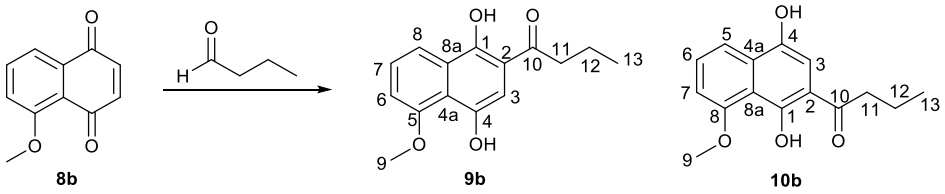
(1,4-dihydroxynaphthalen-2-yl)(thiophen-2-yl)methanone 6m



6m

Standard procedure was used with minor modifications. The reaction mixture was degassed vigorously with argon prior to irradiation and the reaction was irradiated for 72 h. 1,4-Naphthoquinone (50 mg, 0.316 mmol) and 2-thiophenecarboxaldehyde (0.23 mL, 2.46 mmol) in trifluorotoluene (4 mL) gave the *title compound* **6m** (30 mg, 35%) as a bright red solid; mp 136-138 °C; (Found: $M\text{-}H^+$, 269.0266. $C_{15}H_9O_3S$ requires 269.0278); λ_{max} (MeOH)/nm 431 (log ε 3.98), 302 (4.43), 298 (4.42); ν_{max} ($CHCl_3$)/cm^{-1} 3684, 3045, 2415, 1634, 1588, 1476, 1241; δ_H (400 MHz; d_6-acetone) 13.28 (1 H, s, OH), 8.78 (1 H, s, OH), 8.44 (1 H, d, J 8.3, ArH), 8.26 (1 H, d, *J* 8.5, ArH), 8.05 (1 H, d, *J* 5.0, ArH), 7.98 (1 H, d, *J* 3.7, ArH), 7.76 (1 H, app. t. d., *J* 7.2, ArH), 7.66 (1 H, app. b. t., *J* 7.4, ArH), 7.50 (1 H, s, ArH), 7.35 (1 H, t, *J* 4.3, ArH); δ_C (100 MHz; d_6-acetone) 190.4 (C), 156.7 (C), 144.9 (C), 142.4 (C), 134.4 (CH), 134.2 (CH), 129.6 (CH), 129.5 (C), 128.2 (CH), 126.5 (CH), 125.9 (C), 124.0 (CH), 111.8 (C), 105.9 (CH); *m/z* (ESI) 269 ($M\text{-}H^+$, 100).

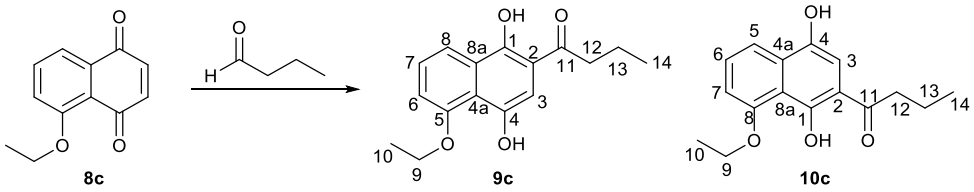
1-(1,4-Dihydroxy-5-methoxynaphthalen-2-yl)butan-1-one 9b and 1-(1,4-Dihydroxy-8-methoxynaphthalen-2-yl)butan-1-one 10b



Standard procedure was used. Reaction was carried out in duplicate and crude mixtures combined for purification. 1,4-Naphthoquinone **8b** (50 mg, 0.266 mmol) and butyraldehyde (0.19 mL, 2.07 mmol) in trifluorotoluene (3.4 mL) gave acylated hydroquinone **9b** (26 mg, 20%) as a bright yellow solid; mp 97-99 °C; (Found: $M–H^+$, 259.0975. $C_{15}H_{15}O_4^-$ requires 259.0976); λ_{max} (CH_2Cl_2)/nm 275 (log ε 5.94), 318 (3.66), 329 (3.70), 411 (3.94); ν_{max} ($CHCl_3$)/cm^{-1} 3607, 2961, 2933, 1781, 1723, 1464, 1329; δ_H (400 MHz; d_6-acetone) 13.50 (1 H, s, 1-OH), 8.86 (1 H, s, 4-OH), 8.00 (1 H, dd, *J* 8.6, 1.0, H-8), 7.49 (1 H, app. b. t, *J* 8.3, H-7), 7.23 (1 H, app. b. d, *J* 8.0, H-6), 7.06 (1 H, s, H-3), 4.15 (3 H, s, H-9), 3.09 (2 H, t, *J* 7.3, H-11), 1.78 (2 H, sxt, *J* 7.4, H-12), 1.04 (3 H, t, *J* 7.6, H-13); δ_C (100 MHz; d_6-acetone) 207.9 (C-10), 157.0 (C-5), 154.9 (C-1), 146.9 (C-4), 128.5 (C-8a), 127.4 (CH-7), 120.1 (C-2), 118.3 (CH-8), 114.4 (C-4a), 110.0 (CH-6), 107.2 (CH-3), 57.10 (CH_3-9), 41.2 (CH_2-11), 18.5 (CH_2-12), 14.1 (CH_3-13); *m/z* (ESI) 259 ($M–H^+$, 100%), 244 ($M–CH_5^+$, 47).

Also isolated regioisomer **10b** (49 mg, 39%) as dark orange solid; mp 179-182 °C; (Found: $M–H^+$, 259.0967. $C_{15}H_{15}O_4^-$ requires 259.0976); λ_{max} (CH_2Cl_2)/nm 275 (log ε 7.47), 314 (3.51), 326 (3.54), 401 (3.88); ν_{max} (CH_2Cl_2)/cm^{-1} 3708, 3009, 2961, 1780, 1723, 1277; δ_H (400 MHz; d_6-acetone) 13.50 (1 H, s, 1-OH), 8.86 (1 H, s, 4-OH), 7.80 (1 H, dd, *J* 8.3, 1.0, H-5), 7.56 (1 H, app. b. t., *J* 8.0, H-6), 7.23 (1 H, s, H-3), 7.07 (1 H, app. b. d., *J* 7.8, H-7), 4.04 (3 H, s, H-9), 3.03 (2 H, t, *J* 7.3, H-11), 1.75 (2 H, sxt., *J* 7.6, H-12), 1.00 (3 H, t, *J* 7.4, H-13); δ_C (100 MHz; d_6-acetone) 204.9 (C-10), 160.2 (C-8), 157.2 (C-1), 145.0 (C-4), 132.7 (C-8a), 130.3 (CH-6), 117.6 (C-4a), 115.7 (CH-5), 115.4 (C-2), 108.0 (CH-7), 107.4 (CH-3), 56.70 (CH_3-9), 43.2 (CH_2-11), 18.8 (CH_2-12), 14.2 (CH_3-13); *m/z* (ESI) 259 ($M–H^+$, 100%), 244 ($M–CH_5^+$, 2/16).

1-(5-Ethoxy-1,4-dihydroxynaphthalen-2-yl)butan-1-one 9c and 1-(8-Ethoxy-1,4-dihydroxynaphthalen-2-yl)butan-1-one 10c

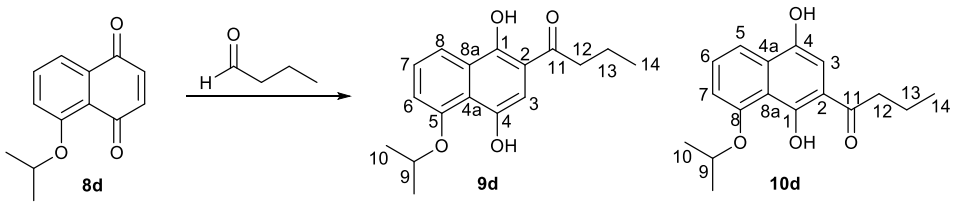


Standard procedure was used. 1,4-Naphthoquinone **8c** (50 mg, 0.247 mmol) and butyraldehyde (0.17 mL, 1.93 mmol) in trifluorotoluene (3.1 mL) gave acylated hydroquinone **9c** (12 mg, 17%) as a bright yellow solid; mp 96-97 °C; (Found: M–H^+, 273.1125. $C_{16}H_{17}O_4^-$ requires 273.1132); λ_{max} (CH_2Cl_2)/nm 275 (log ε 5.22), 329 (3.40), 412 (3.62); ν_{max} (CH_2Cl_2)/cm^{-1} 3418, 2931, 1724, 1611, 1469, 1396; δ_H (400 MHz; d_6-DMSO) 13.40 (1 H, s, 1-OH), 9.06 (1 H, s, 4-OH), 7.93 (1 H, dd, *J* 8.6, 0.9, H-8), 7.52 (1 H, app. b. t, *J* 8.2, H-7), 7.28 (1 H, app. b. d, *J* 7.8, H-6), 7.10 (1 H, s, H-3), 4.36 (2 H, q, *J* 7.0, H-9), 3.10 (2 H, t, *J* 7.3, H-12), 1.70 (2 H, sxt, *J* 7.3, H-13), 1.49 (3 H, t, *J* 7.0, H-10), 0.99 (3 H, t, *J* 7.3, H-14); δ_C (100 MHz; d_6-DMSO) 207.0 (C-11), 154.7 (C-5), 153.1 (C-1), 145.4 (C-4), 126.9 (C-8a), 128.9 (CH-7), 118.0 (C-2), 116.8 (CH-8), 113.1 (C-4a), 110.7 (CH-6) 106.2 (CH-3), 65.4 (CH_2-9), 39.5 (CH_2-12), 17.2 (CH_2-13), 14.3 (CH_3-10), 13.5 (CH_3-14); *m/z* (ESI) 273 (M–H^+, 100%), 245 (M-$C_2H_6^+$, 7), 244 (M-$C_2H_7^+$, 54).

Also isolated regioisomer **10c** (11 mg, 16%) as dark orange solid; mp 170-175 °C; (Found: M–H^+, 273.1129. $C_{16}H_{17}O_4^-$ requires 273.1132); λ_{max} (CH_2Cl_2)/nm 261 (log ε 4.09), 391 (3.44); ν_{max} ($CHCl_3$)/cm^{-1} 3010, 1604, 1421, 1389, 1239, 929; δ_H (400 MHz; d_6-DMSO) 12.59 (1 H, s, 1-OH), 9.66 (1 H, s, 4-OH), 7.69 (1 H, app. b. d, *J* 8.0, H-5), 7.54 (1 H, app. b. t, *J* 8.0, H-6), 7.12 (1 H, s, H-3), 7.08 (1 H, app. b. d, *J* 7.9, H-7), 4.27 (1 H, q, *J* 7.1, H-9), 3.03 (2 H, t, *J* 7.2, H-12), 1.69 (2 H, q, *J* 7.4, H-13), 1.47 (3 H, t, *J* 7.2, H-10), 0.97 (3 H, t, *J* 7.4, H-14); δ_C (100 MHz; d_6-DMSO) 203.6 (C-11), 157.6 (C-8), 154.2 (C-1), 144.2 (C-4), 131.1 (C-2), 129.3 (CH-6), 115.9 (C-4a), 114.8

(C-8a), 114.7 (CH-5), 108.2 (CH-7), 106.1 (CH-3), 64.9 (CH_2-9), 42.4 (CH_2-12), 17.6 (CH_2-13), 14.5 (CH_3-10), 13.7 (CH_3-14); *m/z* (ESI) 273 ($M\text{-}H^+$, 100%).

1-(1,4-Dihydroxy-5-isopropoxynaphthalen-2-yl)butan-1-one 9d and 1-(1,4-Dihydroxy-8-isopropoxynaphthalen-2-yl)butan-1-one 10d

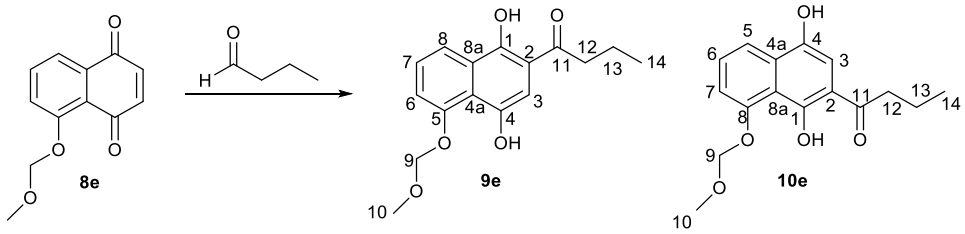


Standard procedure was used. 1,4-Naphthoquinone **8d** (50 mg, 0.231 mmol) and butyraldehyde (0.16 mL, 1.80 mmol) in trifluorotoluene (2.9 mL) gave acylated hydroquinone **9d** (12 mg, 18%) as a bright yellow solid; mp 58-63 °C; (Found: $M–H^+$, 287.1289. $C_{17}H_{19}O_4^-$ requires 287.1289); λ_{max} ($CHCl_3$) 252 (log ε 4.38), 331 (3.63), 412 (3.81); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3392, 3012, 1628, 1399; δ_H (400 MHz; d_6-acetone) 13.50 (1 H, s, 1-OH), 9.18 (1 H, s, 4-OH), 8.01 (1 H, dd, *J* 8.4, 0.8, H-8), 7.49 (1 H, app. b. t, *J* 8.2, H-7), 7.30 (1 H, app. b. d, *J* 7.9, H-6), 7.04 (1 H, d, *J* 2.7, H-3), 5.03 (1 H, sept, *J* 6.1, H-9), 3.09 (2 H, t, *J* 7.2, H-12), 1.78 (2 H, sxt, *J* 7.4, H-13), 1.51 (6 H, d, *J* 6.0, H-10), 1.04 (3 H, t, *J* 7.4, H-14); δ_C (100 MHz; d_6-acetone) 207.9 (C-11), 155.1 (C-5), 154.9 (C-1), 147.2 (C-4), 128.9 (C-8a), 127.4 (CH-7), 120.9 (C-2), 118.4 (CH-8), 114.3 (C-4a), 112.9 (CH-6), 106.8 (CH-3), 74.3 (CH-9), 41.2 (CH_2-12), 22.2 (CH_3-10), 18.5 (CH_2-13), 14.1 (CH_3-14); *m/z* (ESI) 287 ($M–H^+$, 100%).

Also isolated regioisomer **10d** (11 mg, 17%) as a dark yellow solid; mp 162-165 °C; (Found: $M–H^+$, 287.1277. $C_{17}H_{19}O_4^-$ requires 287.1289); λ_{max} ($CHCl_3$) 274 (log ε 4.27), 326 (3.62), 401 (3.76); ν_{max} (CH_2Cl_2)/cm^{-1} 3318, 3009, 1665, 1387, 1265, 1106; δ_H (400 MHz; d_6-acetone) 12.46 (1 H, s, 1-OH), 8.49 (1 H, s, 4-OH), 7.81 (1 H, dd, *J* 8.4, 0.9, H-5), 7.53 (1 H, t, *J* 8.3, H-6), 7.21 (1 H, s, H-3), 7.13 (1 H, d, H-7), 4.91 (1 H, sept, *J* 6.0, H-9), 3.04 (2 H, t, *J* 7.3, H-12), 1.75 (2 H, sxt, *J* 7.3, H-13), 1.48 (6 H, d, *J*

6.0, H-10), 0.99 (3 H, t, *J* 7.3, H-14); δ_C (100 MHz; d_6-acetone) 203.8 (C-11), 157.8 (C-8), 155.9 (C-1), 145.2 (C-4), 132.5 (C-2), 129.8 (CH-6), 118.4 (C-4a), 116.2 (C-8a), 116.18 (CH-5), 111.3 (CH-7), 107.5 (CH-3), 73.7 (CH-9), 44.1 (CH_2-12), 22.3 (CH_3-10), 18.8 (CH_2-13), 14.3 (CH_3-14); *m/z* (ESI) 287 ($M–H^+$, 100%).

1-(1,4-Dihydroxy-5-(methoxymethoxy)naphthalen-2-yl)butan-1-one 9e and 1-(1,4-Dihydroxy-8-(methoxymethoxy)naphthalen-2-yl)butan-1-one 10e

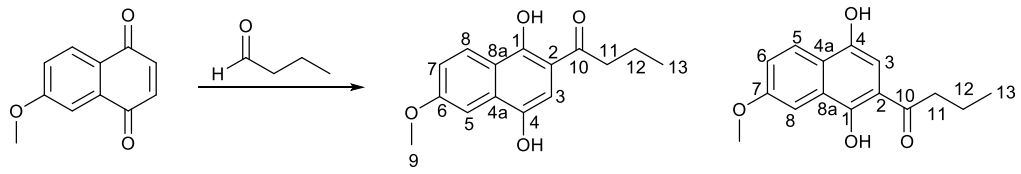


Standard procedure was used. 1,4-Naphthoquinone **8e** (50 mg, 0.229 mmol) and aldehyde (0.16 mL, 1.79 mmol) in trifluorotoluene (2.9 mL) gave acylated hydroquinone **9e** (13 mg, 19%) as a bright yellow solid; mp 100-103 °C; (Found: $M–H^+$, 289.1074. $C_{16}H_{17}O_5^-$ requires 289.1081); λ_{max} (CH_2Cl_2) 254 (log ε 4.77), 330 (3.87), 411 (4.22); ν_{max} (CH_2Cl_2)/cm^{-1} 3388, 3012, 1456, 1268; δ_H (400 MHz; d_6-acetone) 13.50 (1 H, s, OH-1), 8.90 (1 H, s, OH-4), 8.07 (1 H, dd, J 8.3, 1.1, H-8), 7.49 (1 H, t, J 8.0, H-7), 7.40 (1 H, dd, J 8.0, 1.1, H-6), 7.09 (1 H, s, H-3), 5.60 (2 H, s, H-9), 3.58 (3 H, s, H-10), 3.10 (2 H, t, J 7.2, H-12), 1.79 (2 H, sxt, J 7.2, H-13), 1.04 (3 H, t, J 7.4, H-14); δ_H (100 MHz; d_6-acetone) 207.9 (C-11), 155.1 (C-1), 154.5 (C-5), 146.8 (C-4), 128.7 (C-8a), 127.4 (CH-7), 120.5 (C-2), 119.3 (CH-8), 114.3 (C-4a), 113.7 (CH-6), 107.3 (CH-3), 96.8 (CH_2-9), 57.1 (CH_3-10), 41.2 (CH_2-12), 18.5 (CH_2-13), 14.1 (CH_3-14); *m/z* (ESI) 289 ($M-H^+$, 100%).

Also isolated regioisomer **10e** (11 mg, 16%) as a yellow oil; (Found: $M–H^+$, 289.1074. $C_{16}H_{17}O_5^-$ requires 289.1081); λ_{max} ($CHCl_3$); 250 (log ε 3.56), 393 (2.97); ν_{max} (CH_2Cl_2)/cm^{-1} 3377, 2966, 1664, 1392, 1156, 1031; δ_H (400 MHz; d_6-acetone) 13.52 (1

H, s, OH-4), 8.54 (1 H, s, OH-1), 7.89 (1 H, dd, *J* 8.3, 1.1, H-8), 7.56 (1 H, t, *J* 8.0, H-7), 7.24-7.20 (1 H, m, H-6, H-2), 5.39 (2 H, s, H-9), 3.56 (3 H, s, H-10), 3.03 (2 H, t, *J* 7.3, H-12), 1.77 (2 H, sxt, *J* 7.3, H-13), 1.01 (3 H, t, *J* 7.3, H-14); δ_C (100 MHz; d_6-acetone) 205.9 (C-11), 157.8 (C-4 or 5), 157.6 (C-4 or 5), 145.0 (C-1), 130.3 (CH-7), 129.9 (C-8a or 3), 129.1 (C-8a or 3), 117.1 (CH-8), 114.7 (C-4a), 113.6 (CH-6), 106.9 (CH-2), 96.9 (CH_2-9), 56.7 (CH_3-10), 42.5 (CH_2-12), 18.8 (CH_2-13), 14.2 (CH_3-14); *m/z* (ESI) 289 ($M\text{-}H^+$, 100%).

1-(1,4-Dihydroxy-6-methoxynaphthalen-2-yl)butan-1-one 13b and 1-(1,4-Dihydroxy-7-methoxynaphthalen-2-yl)butan-1-one 14b

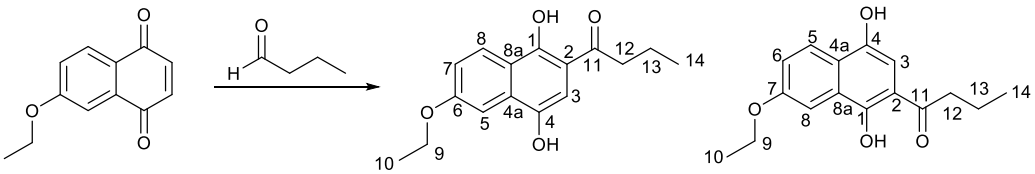


12b **13b** **14b**

Standard procedure A was used. Reaction was carried out in duplicate and crude mixtures combined for purification. 1,4-Naphthoquinone **12b** (50 mg, 0.266 mmol) and butyraldehyde (0.19 mL, 2.07 mmol) in trifluorotoluene (3.4 mL) gave acylated hydroquinone **13b** (34 mg, 30%) as a bright yellow solid; mp 157-161 °C; (Found: $M\text{–}H^+$, 259.0965. $C_{15}H_{15}O_4^-$ requires 259.0976); λ_{max} (CH_2Cl_2)/nm 276 (log ε 6.30), 383 (2.36); ν_{max} ($CHCl_3$)/cm^{-1} 3680, 3009, 1609, 1480, 1283; δ_H (400 MHz; d_6-acetone) 13.85 (1 H, s, 1-OH), 8.50 (1 H, s, 4-OH), 8.29 (1 H, app. b. d, *J* 9.2, H-8), 7.53 (1 H, app. br d, *J* 2.5, H-5), 7.20 (1 H, dd, *J* 9.2, 2.5, H-7), 7.17 (1 H, s, H-3), 3.97 (3 H, s, H-9), 2.98 (2 H, t, *J* 7.2, H-11), 1.77 (2 H, sxt, *J* 7.6, H-12), 1.02 (3 H, t, *J* 7.3, H-13); δ_C (100 MHz; d_6-acetone) 206.8 (C-10), 162.0 (C-6), 157.4 (C-1), 144.6 (C-4), 132.9 (C-2), 126.9 (CH-8), 121.4 (C-8a), 118.9 (CH-7), 111.7 (C-4a), 106.4 (CH-3), 102.3 (CH-5), 55.9 (CH_3-9), 41.0 (CH_2-11), 18.8 (CH_2-12), 14.2 (CH_3-13); *m/z* (ESI) 259 ($M\text{-}H^+$, 100%).

Also isolated regioisomer **14b** (24 mg, 20%) as dark orange solid; mp 149-156 °C; (Found: M–H^+, 259.0966. $C_{15}H_{15}O_4^-$ requires 259.0976); λ_{max} (CH_2Cl_2)/nm 232 (log ε 5.68), 257 (5.32), 287 (5.53), 401 (4.83); ν_{max} ($CHCl_3$)/cm^{-1} 3692, 3607, 3069, 1602, 1240; δ_H (400 MHz; d_6-acetone) 13.63 (1 H, s, OH-1), 8.53 (1 H, s, OH-4), 8.12 (1 H, app. b. d, *J* 9.2, H-5), 7.68 (1 H, t, *J* 2.4, H-8), 7.31 (1 H, dd, *J* 9.2, 2.7, H-6), 7.06 (1 H, d, *J* 2.6, H-3), 3.95 (3 H, s, H-9), 3.01 (2 H, t, *J* 7.4, H-11), 1.77 (2 H, sxt, *J* 7.5, H-12), 1.02 (3 H, t, *J* 7.3, H-13); δ_C (100 MHz; d_6-acetone) 207.6 (C-10), 159.4 (C-7), 155.7 (C-1), 145.8 (C-4), 128.2 (C-4a), 125.8 (C-2), 124.9 (CH-5), 122.0 (CH-6), 113.7 (C-8a), 103.5 (CH-3 and CH-8), 55.8 (CH_3-9), 41.2 (CH_2-11), 18.6 (CH_2-12), 14.1 (CH_3-13); *m/z* (ESI) 259 (M-H^+, 100).

1-(6-Ethoxy-1,4-dihydroxynaphthalen-2-yl)butan-1-one 13c and 1-(7-Ethoxy-1,4-dihydroxynaphthalen-2-yl)butan-1-one 14c



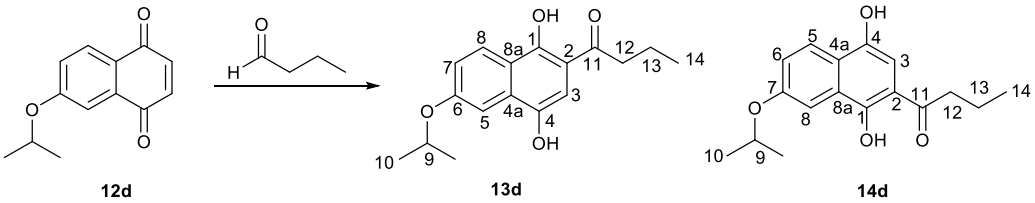
12c **13c** **14c**

Standard procedure A was used. Reaction was carried out in duplicate and crude mixtures combined for purification. 1,4-Naphthoquinone **12c** (50 mg, 0.247 mmol) and butyraldehyde (0.17 mL, 1.93 mmol) in trifluorotoluene (3.1 mL) gave acylated hydroquinone **13c** (37 mg, 27%) as a bright yellow solid; mp 136-137 °C; (Found M–H^+; 273.1132. $C_{16}H_{17}O_4^-$ requires 273.1132); λ_{max} (CH_2Cl_2)/nm 279 (log ε 4.78), 380 (3.92); ν_{max} ($CHCl_3$)/cm^{-1} 3599, 3043, 1607, 1485, 1414, 1293; δ_H (400 MHz; d_6-acetone) 13.86 (1 H, s, 1-OH), 8.47 (1 H, s, 4-OH), 8.28 (1 H, app. b. d, *J* 9.2, H-8), 7.52 (1 H, d, *J* 2.6, H-5), 7.20 (1 H, dd, *J* 9.2, 2.6, H-7), 7.17 (1 H, s, H-3), 4.23 (2 H, q, *J* 7.0, H-9), 2.98 (2 H, t, *J* 7.3, H-12), 1.77 (2 H, sxt., *J* 7.3, H-13), 1.46 (3 H, t, *J* 7.0, H-10), 1.02 (3 H, t, *J* 7.3, H-14); δ_C (100 MHz; d_6-acetone) 206.8 (C-11), 161.3 (C-

6), 157.5 (C-1), 144.6 (C-4), 132.9 (C-2), 126.9 (CH-8), 121.3 (C-4a), 119.2 (CH-7), 111.6 (C-8a), 106.4 (CH-3), 103.0 (CH-5), 64.5 (CH_2-9), 41.0 (CH_2-12), 18.8 (CH_2-13), 15.1 (CH_3-10), 14.2 (CH_3-14); *m/z* (ESI) 273 ($M\text{-}H^+$, 100%).

Also isolated regioisomer **14c** (12 mg, 9%) as yellow solid; mp 122-126 °C; (Found $M–H^+$; 273.1124. $C_{16}H_{17}O_4^-$ requires 273.1132); λ_{max} (CH_2Cl_2)/nm 276 (log ε 5.73), 403 (3.88); ν_{max} ($CHCl_3$)/cm^{-1} 3600, 3048, 1613, 1578, 1462, 1414, 1035; δ_H (400 MHz; d_6-acetone) 13.63 (1 H, s, 1-OH), 8.52 (1 H, s, 4-OH), 8.12 (1 H, app. b. d, *J* 9.1, H-5), 7.68 (1 H, d, *J* 2.6, H-8), 7.31 (1 H, dd, *J* 9.1, 2.6, H-6), 7.05 (1 H, s, H-3), 4.20 (2 H, 1, *J* 7.0, H-9), 3.00 (2 H, t, *J* 7.5, H-12), 1.78 (2 H, sxt., *J* 7.5, H-13), 1.45 (3 H, t, *J* 7.0, H-10), 1.02 (3 H, t, *J* 7.5, H-14); δ_C (100 MHz; d_6-acetone) 206.6 (C-11), 158.7 (C-7), 155.7 (C-1), 145.8 (C-4), 128.2 (C-4a), 125.7 (C-2), 124.9 (CH-5), 122.3 (CH-6), 113.7 (C-8a), 104.2 (CH-8), 103.4 (CH-3), 64.4 (CH_2-9), 41.2 (CH_2-12), 18.6 (CH_2-13), 15.1 (CH_3-10), 14.1 (CH_3-14); *m/z* (ESI) 273 ($M\text{-}H^+$, 100).

1-(1,4-Dihydroxy-6-isopropoxynaphthalen-2-yl)butan-1-one 13d and 1-(1,4-Dihydroxy-7-isopropoxynaphthalen-2-yl)butan-1-one 14d



12d 13d 14d

Standard procedure A was used. 1,4-Naphthoquinone **12d** (50 mg, 0.231 mmol) and butyraldehyde (0.16 mL, 1.80 mmol) in trifluorotoluene (2.9 mL) gave **13d** (14 mg, 20%) as a dark red solid; mp 93-95 °C; (Found: $M–H^+$, 287.1274. $C_{17}H_{19}O_4^-$ requires 287.1289); λ_{max} (CH_2Cl_2)/nm 276 (log ε 5.96), 381 (3.49); ν_{max} ($CHCl_3$)/cm^{-1} 3600, 3012, 1605, 1475, 1239; δ_H (400 MHz; d_6-acetone) 8.50 (1 H, s, 4-OH), 8.29 (1 H, app. b. d, *J* 9.1, H-8), 7.54 (1 H, d, *J* 2.5, H-5), 7.20 (1 H, dd, *J* 9.1, 2.5, H-7), 7.17 (1 H, s, H-3),

4.87 (1 H, sept, *J* 6.1, H-9), 2.99 (2 H, t, *J* 7.4, H-12), 1.78 (2 H, sxt, *J* 7.3, H-13), 1.41 (6 H, d, *J* 6.1, H-10), 1.03 (3 H, t, *J* 7.4, H-14); δ_C (100 MHz; d_6-acetone) 206.7 (C-11), 160.2 (C-6), 157.5 (C-1), 144.5 (C-4), 132.9 (C-2), 127.0 (CH-8), 121.1 (C-8a), 119.8 (CH-7), 111.5 (C-4a), 106.2 (CH-3), 104.2 (CH-5), 70.7 (CH-9), 40.9 (CH_2-12), 22.2 (CH_3-10), 18.8 (CH_2-13), 14.2 (CH_3-14); *m/z* (ESI) 287 ($M\text{-}H^+$, 100%).

Also isolated regioisomer **14d** (10 mg, 15%) as yellow solid; mp 128-130 °C; (Found: $M–H^+$, 287.1276. $C_{17}H_{19}O_4^-$ requires 287.1289); λ_{max} (CH_2Cl_2)/nm 276 (log ε 5.76), 404 (2.00); ν_{max} ($CHCl_3$)/cm^{-1} 3602, 3012, 1610, 1185, 821; δ_H (400 MHz; d_6-acetone) 13.64 (1 H, s, 1-OH), 8.52 (1 H, s, 4-OH), 8.11 (1 H, app. b. d, *J* 9.2, H-5), 7.70 (1 H, d, *J* 2.7, H-8), 7.30 (1 H, dd, *J* 9.2, 2.7, H-6), 7.05 (1 H, s, H-3), 4.82 (1 H, sept, *J* 6.2, H-9), 3.02 (2 H, t, *J* 7.4, H-12), 1.78 (2 H, sxt., *J* 7.4, H-13), 1.39 (6 H, d, *J* 6.2, H-10), 1.02 (3 H, t, *J* 7.4, H-14); δ_C (100 MHz; d_6-acetone) 207.6 (C-11), 157.5 (C-7), 155.7 (C-1), 145.8 (C-4), 128.3 (C-4a), 125.6 (C-2), 125.0 (CH-5), 123.0 (CH-6), 113.6 (C-8a), 105.9 (CH-8), 103.3 (CH-3), 70.7 (CH-9), 41.2 (CH_2-12), 22.2 (CH_3-10), 18.6 (CH_2-13), 14.1 (CH_3-14); *m/z* (ESI) 287 ($M\text{-}H^+$, 100).

X-Ray Crystallographic Studies

All data sets were collected either with a SuperNova Cu diffractometer or a GV1000 diffractometer. The crystal was kept at 120(2)K during data collection. Using Olex2, the structure was solved with the olex2.solve structure solution program using Charge Flipping and refined with the ShelXL refinement package using Least Squares minimisation. Crystal structure data and details are listed in Table 7.

Table 7. Crystal structure data

Compound		**9e**	**10c**	**13b**
CCDC		952123	952121	952122
Empirical formula		$C_{16}H_{18}O_5$	$C_{16}H_{18}O_4$	$C_{15}H_{16}O_4$
Formula weight		290.30	274.30	260.28
Crystal size/mm^3		0.51 × 0.0864 × 0.0426	0.126 × 0.1016 × 0.0629	0.1243 × 0.0791 × 0.0316
Crystal system		monoclinic	monoclinic	orthorhombic
Space group		$P2_1/c$	$P2_1/n$	Pbca
Unit cell dimensions	a/Å	15.7243(11)	7.7968(2)	12.8287(3)
	b/Å	5.0123(3)	21.1512(5)	7.9789(3)
	c/Å	18.5815(12)	9.1046(3)	24.2643(9)
	α/°	90	90	90
	β/°	107.285	114.189	90
	γ/°	90	90	90
Volume/Å^3		1398.35(17)	1369.64(7)	2483.67(15)
Z		4	4	8
Reflections collected		5181	12604	13106
Independent reflections		2731 [R(int) = 0.0207]	2766 [R(int) = 0.0207]	2494 [R(int) = 0.0371]
Final R indexes R [I>=2σ (I)]		R_1 = 0.0362, wR_2 = 0.0987	R_1 = 0.0329, wR_2 = 0.0900	R_1 = 0.0438, wR_2 = 0.1128
Final R indexes (all data)		R_1 = 0.0362, wR_2 = 0.0987	R_1 = 0.0378, wR_2 = 0.0941	R_1 = 0.0525 wR_2 = 0.1191

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