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# The solar-chemical photo-Friedel–Crafts heteroacylation of 1,4-quinones

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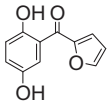
ABSTRACT

Photochemical reactions between 1,4-benzo- and 1,4-naphthoquinone and several heteroaromatic carbaldehydes were investigated under solar irradiation conditions. These reactions gave the corresponding heteroacylated hydroquinones in the range 71%–92% yield.



Acylated 1,4-quinones, easily prepared by oxidation of the corresponding acylhydroquinones, are valuable precursors of a variety of natural[1–4] and synthetic compounds endowed with a range of biological properties.[5–13] Acylhydroquinones are most commonly prepared via Friedel–Crafts acylation or Fries-rearrangement.[14–19] Although the yields are in general moderate to good, these classical methods involve the use of hazardous environmental substances and suffer of limitations regarding the use of precursor containing acid-labile functional groups because they are carried out under strong acid conditions.

Our continuous interest to extend the synthetic utility of acyl-1,4-benzoquinones to new biological active quinones[7–13] and precedents on photoacylation of 1,4-quinones with aldehydes,[20–29] in particular those reported by Klinger,[20] Oelgemöller and Mattay,[25–27] on the use of *green* photochemistry using natural sunlight to the Friedel–Crafts acylation of 1,4-quinones with carbocyclic aldehydes, led us to study the application of the solar chemistry to the synthesis of heteroacylhydroquinones from 1,4-benzo- and 1,4-naphthoquinones **1** and **2**, and various heteroaromatic aldehydes. It is important to point out that the synthesis of heteroacylhydroquinones has received relatively little attention and there is only one report on the preparation of some members such as **3** and **4**. The access to these compounds proceeds by acylation of hydroquinone dimethylether with the corresponding carboxylic acid induced with polyphosphoric acid. Further demethylation of the dimethoxyketones with boron tribromide followed by oxidation affords the corresponding heteroacylhydroquinones.[30,31]

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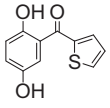


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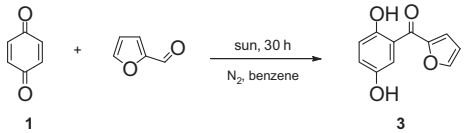
We firstly explored the photolysis of 1,4-benzoquinone **1** in the presence of 7.5 equiv of furan-2-carbaldehyde in order to inhibit competing photodimerizations of the quinone[26] in benzene solution, and also containing a catalytic amount of benzophenone to facilitate the eventual photoacylation.[32]

Solar irradiation was employed to induce the acylation and the reaction course was daily monitored by thin layer chromatography (light petroleum 40–60/ethyl acetate). After 30 h of light irradiation (six days) the reaction went to completion to give heteroacylhydroquinone **3** as the sole product in 88% isolated yield (Scheme 1).

Several trials of acylation reaction of benzoquinone **1** with furan-2-carbaldehyde were also carried out in the absence of




1 3

**Scheme 1.** Photoacylation of **1** with furan-2-carbaldehyde.

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benzophenone, which indicates that the use of this compound does not influence the yield of the phothoacylation.

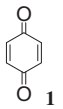
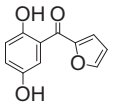
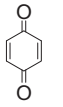
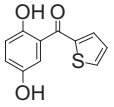
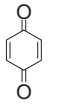
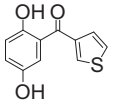
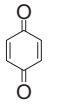
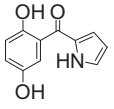
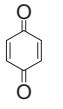
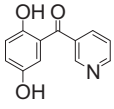
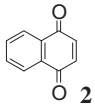
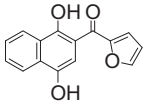
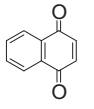
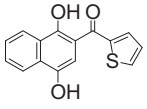
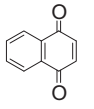
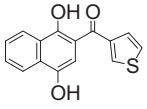
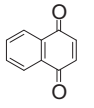
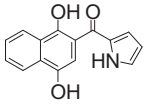
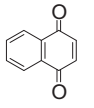
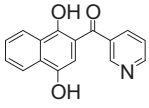
Encouraged by this result, we set out to study the scope of this photoacylation procedure for the synthesis of heteroacylhydroquinones **4**–**14** and the results are collected in Table 1. In all the examined cases the heteroacylhydroquinones were obtained in good to excellent yields. The structure of the new compounds **3**–**12** were deduced from IR, $^{1}H$ and $^{13}C$ NMR data.

All solar experiments reported here[33] were performed at the Canchones Experimental Center in Iquique/Chile (latitude 20°26′43.80″ S, 990 m above sea level), which is located in the Atacama desert, one of the most insolate regions of the world.

In order to evaluate the photoacylation of quinones employing an artificial irradiation source, the reactions of quinones **1** and **2** with furan-2-carbaldehyde were examined under the same conditions employed in the solar experiments.[33] Degassed reaction mixtures were irradiated by means of 130-W UV-fluorescent lamps and the progress of the reactions were monitored by TLC. The presence of the corresponding photoproducts **3** and **8**, as the unique products, were detected after 48 h of irradiation. However, partial conversion of quinone **1** and **2** (46% and 22%, respectively) to their photoproducts were observed after ten days of irradiation. Photoproducts **3** and **8** were isolated in 55% and 88% yields, respectively. As in the solar experiments, the presence of catalytic amounts of benzophenone did not improve the yields of the phothoacylation reactions. Although the above experiments demonstrate the feasibility of the photoacylation of quinones **1** and **2** with furan-2-carbaldehyde under artificial light, further experiments should be carried out to improve the photoacylation conversions and to know the scope of the reaction with heteroaldeydes.

In conclusion, we have described a facile, efficient, cheap and high-yielding procedure to prepare heteroacylhydroquinones. The reported method involves commercially available precursors and an efficient solar photoacylation of 1,4-benzo- and 1,4-naphthoquinone. Our work demonstrates that the use of *green* photochemistry with sunlight is achievable for the acylation of 1,4-quinones with heteroaromatic aldehydes. Further work is in progress to replace benzene by alternative solvents suitable for green chemistry.

**Table 1**
Solar photoacylation of 1,4-quinones with heteroaromatic carbaldehydes

| Quinone | Aldehyde | Photoproduct | No | Rend.[a] (%) |
|---|---|---|---|---|
|  **1** |  |  | **3** | 88 |
|  |  |  | **4** | 83 |
|  |  |  | **5** | 87 |
|  |  |  | **6** | 81 |
|  |  |  | **7** | 72 |
|  **2** |  |  | **8** | 89 |
|  |  |  | **9** | 85 |
|  |  |  | **10** | 92 |
|  |  |  | **11** | 71 |
|  |  |  | **12** | 80 |

[a] Isolated yield.

## Acknowledgement

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32. For the mechanism of the benzophenone-initiated photoadditions of acyl radicals to the quinone system see Refs. 23 and 24.
33. *General procedure for the synthesis of heteroaroylhydroquinones*: A 100 mL benzene solution of the required quinone (1 mmol) and aldehyde (7.5 mmol), was placed into the outer jacket of a Liebig condenser type. The solution was bubbled with nitrogen (2 min), sealed with a septum and then irradiated for six days (total illumination time of 30 h), under solar radiation conditions in the range 800–1100 Watts/$m^2$ (January–March) The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel (3:1 petroleum ether/ethyl acetate). The starting aldehyde and the solvent were recovered and employed in the next batches.
Data of selected examples: *(2,5-dihydroxyphenyl)(furan-2-yl)methanone* (**3**): orange solid mp, 125.5–126.5 °C. IR (KBr, $cm^{-1}$) $\nu_{max}$ 3330 (O–H), 1562 (C=O). $^1$H NMR (200 MHz, acetone-$d_6$): $\delta$ 11.45 (s, 1H, 2-OH), 8.21 (br s, 1H, 5-OH), 8.01 (dd, 1H, $J$ = 3.6, 2.7 Hz, 4′- or 5′-H), 7.79 (d, 1H, $J$ = 8.3 Hz, 3- or 4-H), 7.49 (m, 1H, 3′-H), 7.12 (d, 1H, $J$ = 8.3 Hz, 4- or 3-H), 6.80 (dd, 1H, $J$ = 3.6, 2.7 Hz, 5′- or 4′-H), 6.66 (s, 1H, 6-H). $^{13}$C NMR (50 MHz, acetone-$d_6$): $\delta$ 185.1, 157.2, 152.7, 150.2, 148.8, 125.3, 121.8, 119.4, 116.7, 116.5, 113.3. Anal. Calcd for $C_{11}H_8O_4$: C, 64.71; H, 3.95. Found: C, 64.80; H, 3.85.
*(2,5-Dihydroxyphenyl)(thiophen-3-yl)methanone* (**5**): orange solid mp, 135–136 °C. IR (KBr, $cm^{-1}$) $\nu_{max}$ 3334 (O–H), 1581 (C=O). $^1$H NMR (200 MHz, $CDCl_3$) 11.74 (s, 1H, 2-OH), 8.38 (s, 1H, 5-OH), 8.32 (s, 1H, 2′-H), 7.89 (m, 1H, 4′- or 5′-H), 7.85 (d, 1H, $J$ = 8.2 Hz, 3- or 4-H), 7.71 (d, 1H, $J$ = 8.2 Hz, 4- or 3-H), 7,49 (d, 1H, $J$ = 3.0 Hz, 5′- or 4′-H), 7.30 (s, 1H, 6-H). $^{13}$C NMR (50 MHz, $CDCl_3$) 193.6, 156.0, 148.7, 140.1, 132.1, 128.1, 125.9, 124.4, 122.1, 118.5, 116.9. Anal. Calcd for $C_{11}H_8O_3S$: C, 59.99; H, 3.66; S, 14.56. Found: C, 59.93; H, 3.65; S, 14.17.
*(1,4-Dihydroxynaphthalen-2-yl)(thiophen-3-yl)methanone* (**10**): dark orange solid mp, 159–160 °C. IR (KBr, $cm^{-1}$) $\nu_{max}$ 3317 (O–H), 1580 (C=O). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 13.08 (s, 1H, 1-OH), 9.87 (s, 1H, 4-OH), 8.34 (d, 1H, $J$ = 8.3 Hz, 5- or 8-H), 8.30 (br s, 1H, 2′-H), 8.14 (d, 1H, $J$ = 8.3 Hz, 8- or 5-H), 7.77 (m, 1H, 4′- or 5′-H), 7.71 (t, 1H, $J$ = 7.6 Hz, 6- or 7-H), 7.62 (t, 1H, $J$ = 7.6, Hz, 7- or 6-H), 7.56 (d, 1H, $J$ = 4.8 Hz, 5′- or 4′-H), 7.17 (s, 1H, 3-H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 193.6, 154.7, 144.8, 140.0, 133.3, 129.4, 129.2, 128.2, 127.3, 126.5, 125.3, 123.7, 122.2, 113.0, 106.2. Anal. Calcd for $C_{15}H_{10}O_3S$: C, 66.65; H, 3.73; O, 17.76; S, 11.86. Found: C, 66.78; H, 3.99; S, 11.64.
*(1,4-Dihydroxynaphthalen-2-yl)(1H-pyrrol-2-yl)methanone* (**11**): dark brown solid mp, 169–170 °C. IR (KBr, $cm^{-1}$) $\nu_{max}$ 3280 (O–H), 1579 (C=O). $^1$H NMR (400 MHz, DMSO-$d_6$+$CDCl_3$): $\delta$ 13.59 (s, 1H, 1-OH), 11.75 (br s, 1H, NH), 9.31 (s, 1H, 4-OH), 8.36 (d, 1H, $J$ = 8.4 Hz, 5- or 8-H), 8.17 (d, 1H, $J$ = 8.4 Hz, 8- or 5-H), 7.62 (dd, 1H, $J$ = 7.0, 8.0 Hz, 6- or 7-H), 7.58 (s, 1H, 4′- or 5′-H), 7.53 (dd, 1H, $J$ = 7.0, 8.0 Hz, 7- or 6-H), 7.21 (br s, 1H, 3′-H), 7.16 (br s, 1H, 5′- or 4′-H), 6.35 (s, 1H, 3-H). $^{13}$C NMR (100 MHz, DMSO-$d_6$+$CDCl_3$): $\delta$ 218.2, 185.5, 155.0, 144.2, 129.7, 128.6, 128.1, 125.3, 125.2, 123.2, 121.7, 118.7, 111.5, 110.2, 105.6. HRMS (M+): $m/z$ calcd for $C_{15}H_{11}O_3N$: 253.07389; found: 253.07249.