organics

MDPI

Article

Photochemical Acylation of 1,4-Naphthoquinone with Aldehydes Under Continuous-Flow Conditions

Madyan A. Yaseen [1,2] and Michael Oelgemöller [1,3,*]

[1] College of Science and Engineering, James Cook University, Townsville, QLD 4811, Australia; madyan.yaseen@uosamarra.edu.iq
[2] College of Education, University of Samarra, Samarra 34010, Salah Al-Deen, Iraq
[3] Faculty of Chemistry and Biology, Hochschule Fresenius gGmbH—University of Applied Science, 65510 Idstein, Germany
* Correspondence: michael.oelgemoeller@jcu.edu.au

Abstract: A series of photoacylations of 1,4-naphthoquinone with various aldehydes and using Pyrex-filtered UVB light was conducted under continuous-flow conditions. Acetone served as a triplet photosensitizer and convenient solvent that kept all materials in solution and could be easily removed. The corresponding acylated 1,4-naphthohydroquinone photoproducts were obtained in acceptable to excellent yields of 30–90% with residence times of just 70 min. The photoacylation process was successfully coupled with in-line oxidation to obtain acylated 1,4-naphthoquinones.

Keywords: photoacylation; naphthoquinone; acylated naphthohydroquinones; flow-photochemistry; tandem photochemical–thermal flow reaction

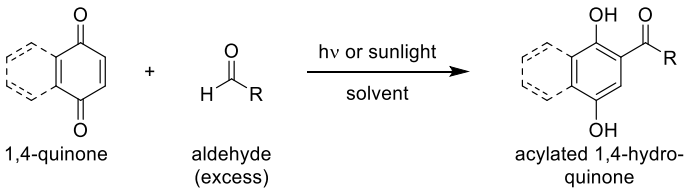
Academic Editor: Edward Lee-Ruff

Received: 4 January 2025
Revised: 21 January 2025
Accepted: 12 February 2025
Published: 14 February 2025

Citation: Yaseen, M.A.; Oelgemöller, M. Photochemical Acylation of 1,4-Naphthoquinone with Aldehydes Under Continuous-Flow Conditions. *Organics* **2025**, *6*, 9. https://doi.org/10.3390/org6010009

1. Introduction

Naphthoquinones and their derivatives are important natural products, synthesis intermediates, and biologically active compounds of interest to the chemical industry [1–4]. Due to their favorable photophysical properties, the photochemistry of quinones has also been intensively studied, and a variety of photochemical transformations have consequently been developed [5–9]. The photoacylation of 1,4-quinones with aldehydes, for example, represents a straightforward access to acylated 1,4-hydroquinones from readily available starting materials (Scheme 1) [10–12]. Due to its easy reaction protocol, the transformation has been used as a key step in the synthesis of a variety of biologically active compounds [13–16]. However, the strong absorption of the photoproducts typically causes a significant decrease in light usability (noticeable in a drop in quantum yield [17]), which necessitates exhaustive irradiation times and can lead to photodecomposition or secondary acylation [18,19]. An excess amount of aldehyde is also used to suppress dimerization of the quinones [20].



Scheme 1. Photoacylation of 1,4-quinones with aldehydes.

Most of the experimental procedures are performed using conventional batch or chamber reactors equipped with mercury lamps [21,22]. These traditional conditions commonly

demand prolonged irradiation times due to poor light penetration and mixing or cause decomposition of light-sensitive photoproducts due to over-irradiation [23,24]. Recently, continuous flow chemistry has been developed as a new process technology for the on-site and on-demand synthesis of chemical products [25–27]. Flow operation inside narrow inner structures has proven especially beneficial for preparative photochemistry [28–32]. As a result, photochemical transformations are now routinely performed under continuous-flow conditions even on larger scales [33]. Despite this, only three flow-photochemical studies involving quinones have been reported so far [34–36]. Of these, photoacylations were conducted in a machined microchip [35] or in an improvised solar trough reactor [36]. This study thus investigated photoacylations of 1,4-naphthoquinone in a simple capillary reactor, of which some transformations were furthermore coupled with in-series oxidation.

2. Materials and Methods

2.1. General Information

All solvents and reagents were commercially available (Merck Life Science Pty Ltd., Bayswater, VIC, Australia, or Thermo Fisher Scientific Australia Pty Ltd., Scoresby, VIC, Australia) and were used without purification. 1,4-Naphthoquinone was purified by sublimation prior to use. Aldehydes were stored under nitrogen to prevent autooxidation [37].

Continuous-flow irradiations were conducted in an in-house reactor system equipped with a single UVB fluorescent tube (G8T5E, Ushio Inc., Tokyo, Japan) [38]. Tandem photoacylation–oxidations were performed in a modified version of this reactor. The plunger cartridge was loosely filled with a mixture of freshly prepared Ag_2O (10 g) [39] and anhydrous sodium sulfate (10 g). Additional information and pictures of the reactors can be found in the Supplementary Materials.

Column chromatography was carried out in Pyrex glass columns using Scharlau silica gel 60 (particle size 0.06–0.2 nm) and 70–230 mesh ASTM as a stationary phase. Mixtures of cyclohexane and ethyl acetate (4:1) were used as the mobile phase.

Melting points were measured in open capillaries using a Tathastu or Gallenkamp melting point apparatus and are uncorrected.

NMR spectra were recorded on a Bruker 400 Ascend^{TM} (^{1}H: 400 MHz and ^{13}C: 100 MHz) equipped with an auto-sampler. NMR spectra were processed using the MestReNova software (Version 6.0.2-5475, Mestrelab Research S.L., Santiago de Compostela, Spain) and the residual solvent peak as an internal standard. Samples were prepared in $CDCl_3$ (δ = 7.26/77.3 ppm ppm), DMSO-d_6 (δ = 2.50/39.5 ppm) and acetone-d_6 (δ = 2.09/30.6 ppm). NMR-spectra of all photoacylation products can be found in the Supplementary Materials.

Mass spectra were recorded using direct injection on a Shimadzu LCMS-2020 equipped with a DUIS ion source. Ions were subsequently detected in positive mode and/or negative mode within a mass range of m/z 100–500. The mobile phases were aqueous solutions of HPLC-grade methanol or acetonitrile with 0.1% formic acid added. All experimental event sequences were controlled, and processing was performed using LabSolutions for LCMS-2020 software. Alternatively, MS spectra were recorded on a Finnigan MAT 312 (EI, 70 eV) with an SS 300 data system.

Infrared spectra were recorded on a Perkin Elmer Spectrum One FT-IR Spectrometer as thin films. Spectra were recorded in the range of 600–4000 cm^{-1}.

2.2. General Procedure for Photoacylations Under Continuous-Flow Conditions

The cooling fans and fluorescent tube of the in-house flow reactor were started, and the capillary tube was flushed with acetone. A solution of 1,4-naphthoquinone (0.5 mmol) and aldehyde (2.5 mmol) in acetone (25 mL) was degassed with nitrogen for 5 min, drawn

into a precision syringe, and pumped at a flow rate of 0.071 mL/min through the reactor tube. The capillary tube was subsequently flushed with approx. 15 mL of acetone. The reaction mixture and wash acetone portions were collected in an amber round-bottom flask. The solvent was removed by evaporation, and the residues were subjected to repeated trituration using cyclohexane and sonication or to column chromatography.

2.3. General Procedure for Tandem Photoacylation–Oxidation Reactions

Following the same general procedure as described above, a previously degassed solution of 1,4-naphthoquinone (0.5 mmol) and aldehyde (2.5 mmol) in acetone (25 mL) was pumped through the tandem reactor at a flow rate of 0.071 mL/min. The reaction mixture and all acetone washings were evaporated to dryness, and the residues were subjected to repeated trituration using cold diethyl ether or to column chromatography.

2.4. Spectroscopic Details

All photoacylation and oxidation products are known, and their spectroscopic details matched previously described data.

1-(1,4-Dihydroxynaphthalen-2-yl) butan-1-one (3a) [40]**.** Yellow solid. M.p.: 144–145 °C (Lit. 145–146 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 13.78 (s, 1H, OH), 8.46 (d, J = 8 Hz, 1H, CH_{arom}), 8.10 (d, J = 8.2, 1H, CH_{arom}), 7.68 (ddd, J = 8.3, 1.4 Hz, 1H, CH_{arom}), 7.58 (ddd, J = 8.2, 1.3 Hz, 1H, CH_{arom}), 7.03 (s, 1H, CH_{arom}), 5.07 (br s, 1H, OH), 2.96 (t, J = 7.4 Hz, 2H, CH_2), 1.82 (sxt, J = 7.4 Hz, 2H, CH_2), 1.05 (t, J = 7.4 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 206.0, 157.6, 143.0, 129.8, 129.5, 126.7, 126.3, 124.8, 121.7, 111.9, 105.6, 40.8, 18.2, 14.0. MS (DUIS): m/z = 231 [M^++H]. MS (EI): m/z = 230 [M^+], 213, 187 (100%), 172, 157, 131, 116, 102, 77, 51. IR (neat): $\tilde{\upsilon}$ = 3325, 2878–2965, 1632, 1588, 1464, 1378, 1325, 1293, 1201, 1136, 1070, 1041, 868, 818, 763.

1-(1,4-Dihydroxynaphthalen-2-yl) propan-1-one (3b) [10]. Yellow solid. M.p.: 175–177 °C (Lit. 178–179 °C). ^{1}H-NMR (400 MHz, acetone-d_6): δ = 13.68 (s, 1H, OH), 8.64 (br s, 1H, OH), 8.39 (d, J = 8.3 Hz, 1H, CH_{arom}), 8.21 (dd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.70 (ddd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.60 (ddd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.20 (s, 1H, CH_{arom}), 3.10 (q, J = 7.3 Hz, 2H, CH_2), 1.22 (t, J = 7.3 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 206.3, 157.4, 143.0, 129.8, 129.4, 126.7, 126.4, 124.8, 121.6, 111.7, 105.5, 32.1, 8.5. MS (DUIS): m/z = 217 [M^++H]. MS (EI): m/z = 216 [M^+, 100%], 202, 187, 159, 131, 103, 77, 51. IR (neat): $\tilde{\upsilon}$ = 3396, 3356, 2980, 2915, 1635, 1590, 1472, 1380, 1304, 1207, 1073, 802, 760.

1-(1,4-Dihydroxynaphthalen-2-yl) heptan-1-one (3c) [41]**.** Yellow solid. M.p.: 133–134 °C (Lit. 135–136 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 13.77 (s, 1H, OH), 8.45 (d, J = 8.3 Hz, 1H, CH_{arom}), 8.09 (d, J = 8.3 Hz, 1H, CH_{arom}), 7.67 (ddd, J = 8.3, 1.4 Hz, 1H, CH_{arom}), 7.57 (ddd, J = 8.3, 1.4 Hz, 1H, CH_{arom}), 7.02 (s, 1H, CH_{arom}), 5.15 (br s, 1H, OH), 2.96 (t, J = 7.4 Hz, 2H, CH_2), 1.77 (quin, J = 7.4 Hz, 2H, CH_2), 1.46–1.24 (br m, 6H, 3 × CH_2), 0.90 (t, J = 6.9 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 206.2, 157.5, 143.1, 129.8, 129.5, 126.6, 126.3, 124.7, 121.7, 111.9, 105.9, 38.9, 31.8, 29.2, 24.7, 22.7, 14.2. MS (DUIS): m/z = 271 [M^+-H]. MS (EI): m/z = 272 [M^+, 100%], 254, 225, 202, 187, 172, 158, 131, 103, 77, 55. IR (neat): $\tilde{\upsilon}$ = 3425, 3348, 2860–2952, 1635, 1590, 1467, 1375, 1296, 1191, 1138, 1070, 1023, 876, 760.

1-(1,4-Dihydroxynaphthalen-2-yl) dodecan-1-one (3d) [36]**.** Yellow solid. M.p.: 105–106 °C (Lit. 130–133 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 13.78 (s, 1H, OH), 8.46 (d, J = 8.4 Hz, 1H, CH_{arom}), 8.10 (d, J = 8.4 Hz, 1H, CH_{arom}), 7.67 (ddd, J = 8.4, 1.3 Hz, 1H, CH_{arom}), 7.57 (ddd, J = 8.4, 1.2 Hz, 1H, CH_{arom}), 7.02 (s, 1H, CH_{arom}), 5.16 (br s, 1H, OH), 2.95 (t, J = 7.5 Hz, 2H, CH_2), 1.77 (quin, J = 7.5 Hz, 2H, CH_2), 1.45–1.20 (br m, 16H, 8 × CH_2), 0.88 (t, J = 6.8 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 206.2, 157.6, 143.0, 129.8, 129.5, 126.7, 126.4, 124.8, 121.6, 111.8, 105.7, 38.9, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4,

24.8, 22.8, 14.3. MS (DUIS): m/z = 341 [M^+-H]. MS (EI): m/z = 342 [M^+, 100%], 324, 239, 225, 202, 187, 172, 157, 131, 103, 77, 55. IR (neat): $\tilde{\upsilon}$ = 3338, 2957, 2917, 2849, 1635, 1588, 1401, 1293, 1075, 763.

1-(1,4-Dihydroxynaphthalen-2-yl) buten-1-one (3e) [36]**.** Reddish solid. M.p.: 169–170 °C (Lit. 164–165 °C). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 14.13 (s, 1H, OH), 9.76 (s, 1H, OH), 8.31 (d, J = 8.3 Hz, 1H, CH_{arom}), 8.13 (d, J = 8.3 Hz, 1H, CH_{arom}), 7.72 (ddd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.61 (ddd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.20 (s, 1H, CH_{arom}), 7.18–7.15 (m, 2H, 2 × CH=), 2.05 (d, J = 4.1 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, acetone-d_6): δ = 194.3, 158.7, 146.5, 145.5, 130.9, 130.3, 127.2, 126.9, 126.7, 124.8, 123.1, 113.0, 105.3, 18.7. MS (DUIS): m/z = 229 [M^++H]. IR (neat): $\tilde{\upsilon}$ = 3302, 1630, 1578, 1514, 1474, 1441, 1390, 1299, 1221, 1140, 1076, 1062, 959, 893, 810, 762.

(1,4-Dihydroxynaphthalen-2-yl)(4-methylphenyl)methanone (3f) [36]**.** Orange-brown solid. M.p.: 154–155 °C (Lit. 167–169 °C). ^{1}H-NMR (400 MHz, acetone-d_6): δ = 13.55 (s, 1H, OH), 8.66 (br s, 1H, OH), 8.45 (d, J = 8.4 Hz, 1H, CH_{arom}), 8.23 (d, J = 8.4 Hz, 1H, CH_{arom}), 7.74 (ddd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.69–7.62 (m, 3H, CH_{arom}), 7.42 (d, J = 7.8 Hz, 2H, CH_{arom}), 7.02 (s, 1H, CH_{arom}), 2.47 (s, 3H, CH_3). ^{13}C-NMR (100 MHz, acetone-d_6): δ = 201.8, 158.0, 145.2, 143.1, 136.6, 130.5, 130.0, 129.8, 127.3, 126.8, 124.9, 123.2, 112.9, 108.0, 21.5. MS (DUIS): m/z = 279 [M^++H]. MS (EI): m/z = 278 (M^+), 263, 187, 186 (100%), 158, 139, 131, 130, 119, 105, 102, 91, 76. IR (neat): $\tilde{\upsilon}$ = 3293, 1632, 1580, 1551, 1393, 1286, 1249, 1073, 828, 755.

(1,4-Dihydroxy-2-naphthalenyl)bis(*p*-tolylmethanone) (5) [36]**.** Orange solid. M.p.: 169–170 °C (Lit. 169–170 °C). ^{1}H-NMR (400 MHz, acetone-d_6): δ = 12.26 (s, 2H, OH), 8.52 (m, 2H, CH_{arom}), 7.03 (m, 2H, CH_{arom}), 2.37 (s, 6H, 2 × CH_3). ^{13}C-NMR (100 MHz, acetone-d_6): δ = 198.7, 154.2, 144.0, 138.3, 131.2, 129.7, 129.5, 129.4, 125.2, 112.6, 21.5. MS (DUIS): m/z = 397 [M^++H]. IR (neat): $\tilde{\upsilon}$ = 3330, 2969–2919, 1738, 1658, 1592, 1495, 1454, 1372, 1281, 1229, 1216, 1117, 1034, 996, 901, 814, 749.

(1,4-Dihydroxynaphthalen-2-yl)(4-chlorophenyl)methanone (3g) [36]**.** Brownish solid. M.p.: 207–208 °C (Lit. 189–190 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 13.43 (s, 1H, OH), 9.98 (s, 1H, OH), 8.13 (d, J = 8.3 Hz, 1H, CH_{arom}), 8.03 (d, J = 8.6 Hz, 1H, CH_{arom}), 7.72 (ddd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.66 (d, J = 8.6 Hz, 2H, CH_{arom}), 7.62 (ddd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.50 (d, J = 8.6 Hz, 2H, CH_{arom}), 7.45 (d, J = 8.6 Hz, 1H, CH_{arom}), 6.82 (s, 1H, CH_{arom}). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 199.5, 159.1, 142.9, 138.2, 136.7, 131.7, 130.5, 130.4, 129.7, 129.1, 128.9, 126.9, 126.3, 124.9, 121.9, 111.4, 107.7. MS (DUIS): m/z = 299 [M^++H]. IR (neat): $\tilde{\upsilon}$ = 3295, 2554, 1677, 1633, 1580, 1545, 1425, 1398, 1294, 1200, 1110, 1076, 998, 843, 757.

(1,4-Dihydroxynaphthalen-2-yl)(furan-2-yl)methanone (3h) [11]**.** Orange solid. M.p.: 188–189 °C (Lit. 188.5–189 °C). ^{1}H-NMR (400 MHz, acetone-d_6): δ = 13.87 (s, 1H, OH), 8.82 (broad s, 1H, OH), 8.44 (d, J = 7.8 Hz, 1H, CH_{arom}), 8.24 (d, J = 8.3 Hz, 1H, CH_{arom}), 8.02 (m, 1H, CH_{arom}), 7.81 (s, 1H, CH_{arom}), 7.75 (ddd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.64 (ddd, J = 8.3, 1.3 Hz, 1H, CH_{arom}), 7.56 (m, 1H, CH_{arom}), 6.82 (m, 1H, CH_{arom}). ^{13}C-NMR (100 MHz, acetone-d_6): δ = 185.1, 159.0, 153.2, 148.6, 145.7, 139.9, 130.6, 127.3, 126.8, 124.9, 123.1, 121.6, 113.5, 112.2, 106.2. IR (neat): $\tilde{\upsilon}$ = 3299, 3132, 2852, 1634, 1560, 1459, 1387, 1301, 1275, 1197, 1123, 1076, 1030, 914, 886, 751.

2-Butanoyl-1,4-naphthoquinone (6a) [19]**.** Orange-brownish solid. M.p.: 66–67 °C (Lit. 64–66 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.10 (dd, J = 8.9 Hz, 1H, CH_{arom}), 7.83–7.75 (m, 3H, CH_{arom}), 7.07 (s, 1H, CH_{quin}), 2.92 (t, J = 7.3 Hz, 2H, CH_2), 1.72 (sxt, J = 7.3 Hz, 2H, CH_2), 0.99 (t, J = 7.3 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 200.9, 185.1, 183.5, 146.2, 136.7, 134.6, 134.5, 131.9, 127.0, 126.4, 45.5, 17.2, 13.8. MS (EI): m/z = 229 (M^{+1}), 210, 200, 185, 157 (100%), 129, 101, 76, 50, 39. IR (neat): $\tilde{\upsilon}$ = 3041, 2965, 2933, 2875, 1664, 1588, 1454, 1346, 1293, 1251, 1225, 1041, 931, 868, 776, 713.

2-Propanoyl-1,4-naphthoquinone (6b) [19]**.** Orange-brown solid. M.p.: decomposition >50 °C (Lit. 84–85 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.10 (dd, J = 9.0 Hz, 1H, CH_{arom}), 7.84–7.73 (m, 3H, CH_{arom}), 7.09 (s, 1H, CH_{quin}), 2.97 (q, J = 7.2 Hz, 2H, CH_2), 1.19 (t, J = 7.2 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 200.2, 184.1, 182.5, 145.3, 136.2, 134.1, 134.0, 131.3, 126.5, 126.0, 37.4, 8.4. MS (EI): *m*/*z* = 215 (M^{+1}), 196, 187, 168, 157 (100%), 129, 101, 76, 50, 39. IR (neat): ῡ = 2978, 2936, 1661, 1588, 1341, 1296, 1251, 1220, 941, 773.

2-Dodecanoyl-1,4-naphthoquinone (6d) [42]**.** Yellow solid. M.p.: 62–64 °C (Lit. 65–66 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.10 (m, 2H, 2 × CH_{arom}), 7.81 (m, 2H, 2 × CH_{arom}), 7.08 (s, 1H, CH_{quin}), 2.93 (t, J = 7.2 Hz, 2H, CH_2), 1.68 (q, J = 7.2 Hz, 2H, CH_2), 1.20–1.40 (br m, 16H, 8 × CH_2), 0.88 (t, J = 6.8 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 201.2, 185.1, 183.5, 146.2, 136.7, 134.7, 134.5, 131.9, 131.9, 127.0, 126.5, 43.7, 32.1, 29.8, 29.7, 29.6, 29.5, 29.2, 23.7, 22.8, 14.3. IR (neat): ῡ = 2959, 2917, 282, 1693, 1667, 1590, 1296, 1249, 786, 715.

2-Crotonyl-1,4-naphthoquinone (6e) [43]**.** Brownish oily solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.15–8.06 (m, 2H, 2 × CH_{arom}), 7.82–7.77 (m, 2H, 2 × CH_{arom}) 7.01 (s, 1H, CH_{arom}), 7.00–6.91 (m, 1H, CH=), 6.53 (dd, J = 15.7 Hz, 1H, CH=), 2.05 (dd, J = 6.9 Hz, 3H, CH_3).

3. Results and Discussion

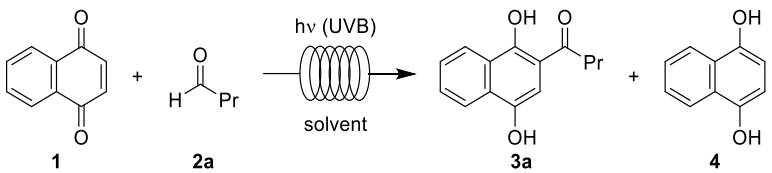
3.1. Photoacylations Under Continuous-Flow Conditions

3.1.1. In-House Capillary Reactor

The reactor setup has been described in detail earlier [38]. The device consisted of a fluorinated ethylene propylene (FEP, λ ≥ 240 nm [44]) capillary tightly wrapped around a Pyrex (λ ≥ 300 nm [21]) cylinder with a single 8 W fluorescence tube in its center. The reaction mixture was transferred through the capillary tubing with a syringe pump and collected in an amber flask.

3.1.2. Optimization Study

The photoacylation of 1,4-naphthoquinone (**1**) in the presence of butyraldehyde (**2a**) was selected as a model reaction (Scheme 2) for process optimization. Irradiations were initially conducted under direct excitation conditions of **1** with UVB light (λ = 300 ± 25 nm) to shorten the reaction time [45]. Previously degassed solutions of the starting materials (0.5 mmol of **1** and 2.5 mmol of **2a** in 25 mL of solvent) were pumped through the flow reactor, and the conversion rates of the crude product mixtures were determined by ^{1}H-NMR analysis (Table 1). Most of the batch laboratory procedures reported use benzene [11,40] or trifluorotoluene (TFT) [10,46] as a reaction medium from which the polar acylated naphthohydroquinone products commonly precipitate during irradiation. While this feature minimizes photodegradation of the desired products, it may cause clogging, pressure buildup, and rupture of the flow reactor tube or fittings [47]. The polar aprotic acetonitrile was thus initially chosen as the solvent to determine the best residence time for high conversions.



Scheme 2. Photoacylation of 1,4-naphthoquinone with butyraldehyde as a model system for process optimization.

Table 1. Experimental results of the optimization study with Pyrex-filtered UVB light.

Entry	Solvent	Residence Time (min)	Conversion (%) [1]	Yield of 3a (%) [2]
1	acetonitrile	25	82	70
2	acetonitrile	50	87	78
3	acetonitrile	70	90	86
4	acetonitrile	100	92	90
5	acetone	70	96	88
6	chloroform	70	95	90
7	tert-butyl alcohol	70	92 (22 [3])	55
8	ethyl acetate	70	91 (16 [3])	53

[1] Determined by ^{1}H-NMR analysis (±3%). [2] After trituration with cyclohexane. [3] Amount of photoreduction product **4** in crude product mixture.

In acetonitrile, all reactions proceeded cleanly and selectively with acceptable losses during workup [48]. Residence times of 25, 50, and 70 min already achieved good to high conversion rates of 82, 87, and 90% and isolated yields for **3a** of 70, 78, and 86% (entries 1–3), respectively. A further increase to 100 min only marginally increased the conversion to 92% and subsequently the yield to 90% (entry 4). Additional experiments in other solvents were thus conducted with a fixed residence time of 70 min. The reaction proceeded with excellent conversions of 96 and 95% and subsequently yields of 88 and 90% in acetone and chloroform (entries 5 and 6). Despite high conversions of >90%, photoreduction of **1** to 1,4-naphthohydroquinone (**4**) by hydrogen-abstraction from the solvent became competitive in tert-butyl alcohol [49] (entry 7) and ethyl acetate [50] (entry 8). Acetone was subsequently chosen for further studies due to its low toxicity, excellent solvation properties, and ease of removal [51]. In contrast to all other solvents, acetone also acted as a triplet sensitizer (T_1 = 332 kJ/mol vs. **1**: T_1 = 241 kJ/mol [52]) [53], as similarly demonstrated with benzophenone [54].

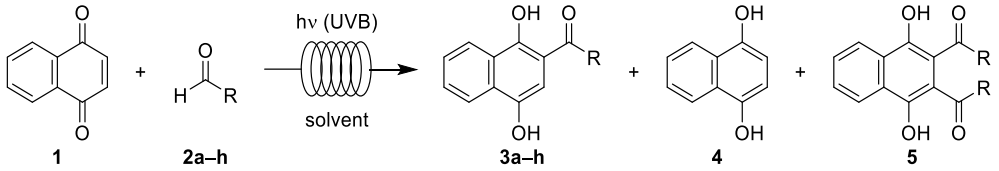
3.1.3. Photoacylations with Other Aldehydes

The photoacylation in acetone was subsequently conducted with a series of aliphatic, unsaturated, aromatic, and heteroaromatic aldehydes **2a**–**h** (Scheme 3). Using a general residence time of 70 min, acceptable to high yields of the photoproducts **3a**–**h** of 30–90% were achieved in all cases without any undesired photoreduction to **4** (Table 2).

Table 2. Experimental results of photoacylations with various aldehydes (residence time of 70 min).

Entry	R	Yield of 3 (%)
1	C_3H_7	90 (**a**) [1]
2	C_2H_5	71 (**b**) [1]
3	C_6H_{13}	75 (**c**) [1]
4	$C_{11}H_{23}$	34 (**d**) [2]/64 [3]
5	*E*-CH_3CH=CH	72 (**e**) [1]
6	*p*-MeC_6H_4	66 (**f**) [2]/12 (**5**) [2,4]
7	*p*-ClC_6H_4	80 (**g**) [1]
8		30 (**h**) [2]

[1] After trituration with cyclohexane. [2] After column chromatography. [3] Conversion of **1** as determined by ^{1}H-NMR analysis (±3%). [4] Amount of bisacylation product **5**.

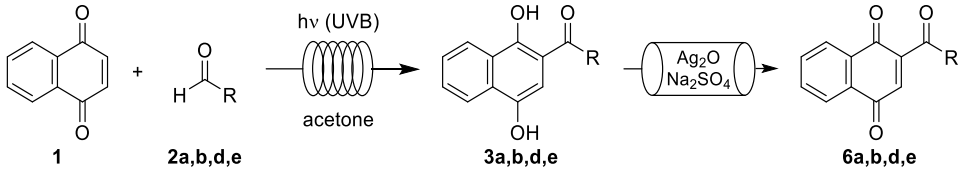


Scheme 3. Photoacylation of 1,4-naphthoquinone with various aldehydes.

Short-chain aliphatic aldehydes furnished the desired acylated naphthohydroquinones **3a–c** after simple evaporation, drying, and trituration with cyclohexane (entries 1–3). In the case of the non-volatile and oily dodecylaldehyde, the reaction achieved an incomplete conversion of 64%, from which the desired photoproduct **3d** could be isolated in 34% yield (53% based on conversion) by column chromatography (entry 4) [48]. The photoacylation of crotonaldehyde readily furnished product **3e** again in a yield of 72% without isomerization of the double bond (entry 5) [55]. In the case of *p*-tolualdehyde, the diacylated product **5** was additionally obtained in a yield of 12%, along with the mono-acylated compound **3f** in 66% (entry 6). While bisacylation products have been previously reported, the mechanism of their formation remains largely unknown [12,19]. In contrast, *p*-chlorobenzaldehyde selectively furnished the corresponding mono-acylated product **3g** in a high yield of 80% (entry 7). The heteroaromatic furfural achieved a somewhat lower yield of **3h** of 30% due to the need for chromatographic purification (entry 8) [48]. In their ^{1}H-NMR spectra, all photoproducts **3a–h** showed a characteristic sharp singlet peak between 13.5 and 14.2 ppm for the newly formed hydroxy group at C-1, which is locked in an intramolecular hydrogen bond with the acyl-carbonyl group. For the bisacylation product **5**, steric hindrance caused a distortion of this hydrogen bond, which subsequently shifted to 12.26 ppm instead.

3.2. Tandem Photoacylation–Oxidation Reactions Under Continuous-Flow Conditions

Individual continuous-flow processes can be easily combined in series through telescoping [56]. The photoacylation was thus coupled with a thermal oxidation step using silver (I) oxide to obtain the corresponding acylated 1,4-naphthoquinone derivatives (Scheme 4) [57]. Both processes have been separately conducted in flow in the past [35,36,58].



Scheme 4. Tandem photoacylation–oxidation to acylated 1,4-naphthoquinones.

3.2.1. In-House Tandem Capillary Reactor

The capillary reactor was modified to allow for in-flow oxidation (Figure 1). The effluent stream of the photoreactor module entered a plunger cartridge against gravity from the bottom. All connecting tubes were masked with black shrinking tube. The cartridge was loosely loaded with solid Ag_2O and anhydrous sodium sulfate, and the product solution was collected externally in an amber flask.

3.2.2. Tandem Photoacylation–Oxidation Reactions with Selected Aldehydes

Maintaining the advantageous residence time for light exposure of 70 min, previously degassed solutions of 1,4-naphthoquinone (**1**; 0.5 mmol) and selected aldehydes (**2a**,**b**,**d**,**e**; 2.5 mmol) in acetone (25 mL) were pumped through the tandem reactor. The desired acylated naphthoquinones **6a**,**b**,**d**,**e** were subsequently obtained as colorful solids and in

yields of 15–94% after a total residence time of under 2 h each (Table 3). Due to their known sensitivity towards spontaneous thermal reduction [46], the dried acylated naphthoquinones were stored in the dark and under nitrogen. The identity of the compounds was confirmed by the presence of three carbonyl singlet peaks between 180 and 205 ppm in their respective ^{13}C-NMR spectra.

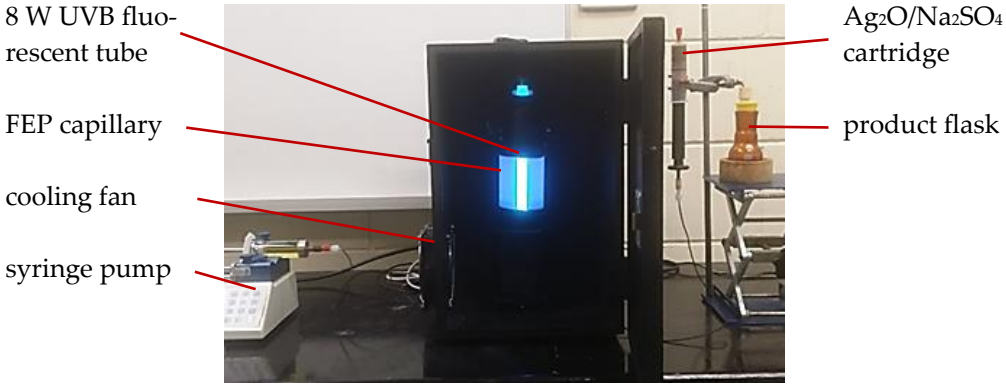


Figure 1. In-house tandem photochemical–thermal continuous-flow reactor during operation.

Table 3. Experimental results of tandem photoacylation–oxidations with selected aldehydes (total residence time of under 2 h).

Entry	R	Yield of 6 (%)
1	C_3H_7	94 (**a**) [1]
2	C_2H_5	76 (**b**) [1]
3	$C_{11}H_{23}$	15 (**d**) [1]/61 [2]
4	*E*-CH_3CH=CH	75 (**e**) [1]

[1] After trituration with cold diethyl ether. [2] Conversion of **1** as determined by ^{1}H-NMR analysis (±3%).

In line with the decoupled flow-photoacylation, butyraldehyde and propionaldehyde achieved complete conversions of **1** and furnished the desired acylated naphthoquinones **6a** and **b** in high yields of 94 and 76% (entries 1 and 2), respectively. Likewise, the long-chained dodecylaldehyde only accomplished an incomplete consumption of **1** of 61%, which resulted in a low yield of **6d** of 15% (25% based on conversion) due to significant losses during workup and isolation (entry 3) [48]. For crotonaldehyde, near-complete consumption of **1** was again noted, and the tandem process produced compound **6e** in 75% yield.

Despite its improvised design, the flow device showed excellent performance for stand-alone or coupled operation. The narrow FEP tubing with an inner diameter of just 0.8 mm enabled superior light penetration for photoacylation. Although the capillary coil only covered approximately $^1/_3$ of the arc length of the central fluorescent tube, its inside–out irradiation design permitted efficient light utilization. The flow reactor is easily constructed from readily available components and only utilizes a single 8 W fluorescent tube. In comparison, the corresponding batch protocols demand prolonged reaction times of several hours to achieve similar conversions or yields [10–12,40,46].

4. Conclusions

In conclusion, a series of photoacylations of 1,4-naphthoquinone with various aldehydes was successfully realized under continuous-flow conditions in an in-house reactor. The simple procedure furnished the corresponding acylated 1,4-naphthohydroquinones in acceptable to high yields with residence times of just 70 min. In-series coupling with thermal oxidation in a tandem reactor enabled the direct synthesis of acylated 1,4-naphthoquinones

in reasonable to excellent yields and total residence times of under 2 h. The easy reaction protocols of both processes may be readily scaled up [59] or conducted more efficiently in a purpose-designed flow module [60].

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/org6010009/s1: Experimental details, procedures, and NMR spectra. Figure S1: In-house continuous-flow capillary reactor during operation. Figure S2: In-house tandem photochemical–thermal continuous-flow reactor during operation.

Author Contributions: M.A.Y. conducted the research and collected the data; M.O. secured the funding, supervised the research, and wrote the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the College of Science and Engineering at James Cook University through a Competitive Research Training Grant.

Data Availability Statement: All data are available upon request from the corresponding author.

Acknowledgments: M.A.Y. thanks the Ministry of Higher Education and Scientific Research of Iraq for a Ph.D. Scholarship.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Jha, R.K.; Kumar, S. Direct Functionalization of *para*-Quinones: A Historical Review and New Perspectives. *Eur. J. Org. Chem.* **2024**, *27*, e202400535. [CrossRef]
2. Mone, N.S.; Bhagwat, S.A.; Sharma, D.; Chaskar, M.; Patil, R.H.; Zamboni, P.; Nawani, N.N.; Satpute, S.K. Naphthoquinones and Their Derivatives: Emerging Trends in Combating Microbial Pathogens. *Coatings* **2021**, *11*, 434. [CrossRef]
3. Ahmadi, E.S.; Tajbakhsh, A.; Iranshahy, M.; Asili, J.; Kretschmer, N.; Shakeri, A.; Sahebkar, A. Naphthoquinone Derivatives Isolated from Plants: Recent Advances in Biological Activity. *Mini-Rev. Med. Chem.* **2020**, *20*, 2019–2035. [CrossRef]
4. López, L.I.; Leyva, E.; García de la Cruz, R.F. Naphthoquinones: More than Natural Pigments. *Rev. Mex. Cienc. Farm.* **2011**, *42*, 6–17.
5. Jang, J.; Lee, G.; Cho, E.J. Visible Light Induced Reactions of Quinones. *Bull. Korean Chem. Soc.* **2024**, *45*, 966–976. [CrossRef]
6. Ando, Y.; Suzuki, K. Photoredox Reactions of Quinones. *Chem. Eur. J.* **2018**, *24*, 15955–15964. [CrossRef] [PubMed]
7. de Lucas, N.C.; Ferreira, A.B.B.; Netto-Ferreira, J.C. Fotoquímica de Naftoquinonas. *Rev. Virtual Quim.* **2015**, *7*, 403–463. [CrossRef]
8. Mukherjee, T. Photo and Radiation Chemistry of Quinones. In *Proceedings of Indian National Science Academy A*; Sapre, A.V., Mukherjee, T., Mittal, J.P., Eds.; Indian National Science Academy: New Delhi, India, 2000; Volume 66, pp. 239–265.
9. Maruyama, K.; Osuka, A. Recent Advances in the Photochemistry of Quinones. In *The Chemistry of Quinonoid Compounds*; Patai, S., Rappaport, Z., Eds.; John Wiley & Sons Ltd.: New York, NY, USA, 1988; Volume 2, Part 1, Chapter 13, pp. 759–878. [CrossRef]
10. Mitchell, L.J.; Lewis, W.; Moody, C.J. Solar Photochemistry: Optimisation of the Photo Friedel–Crafts Acylation of Naphthoquinones. *Green Chem.* **2013**, *15*, 2830–2842. [CrossRef]
11. Benites, J.; Rios, D.; Díaz, P.; Valderrama, J.A. The Solar-chemical Photo-Friedel–Crafts Heteroacylation of 1,4-Quinones. *Tetrahedron Lett.* **2011**, *52*, 609–611. [CrossRef]
12. Oelgemöller, M.; Mattay, J. The "Photochemical Friedel-Crafts Acylation" of Quinones: From the Beginnings of Organic Photochemistry to Modern Solar Chemical Applications. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; Horspool, W.M., Lenci, F., Eds.; CRC Press: Boca Raton, FL, USA, 2004; Chapter 88, pp. 1–45. [CrossRef]
13. Benites, J.; Valderrama, J.A.; Contreras, Á.; Enríquez, C.; Pino-Rios, R.; Yáñez, O.; Calderon, P.B. Discovery of New 2-Phenylamino-3-acyl-1,4-naphthoquinones as Inhibitors of Cancer Cells Proliferation: Searching for Intra-Cellular Targets Playing a Role in Cancer Cells Survival. *Molecules* **2023**, *28*, 4323. [CrossRef]
14. Araya, G.; Benites, J.; Reyes, J.S.; Marcoleta, A.E.; Valderrama, J.A.; Lagos, R.; Monasterio, O. Inhibition of *Escherichia coli* and *Bacillus subtilis* FtsZ Polymerization and *Bacillus subtilis* Growth by Dihydroxynaphtyl Aryl Ketones. *Front. Microbiol.* **2019**, *10*, 1225. [CrossRef] [PubMed]
15. Xia, L.; Idhayadhulla, A.; Lee, Y.R.; Wee, Y.-J.; Kim, S.H. Anti-tyrosinase, Antioxidant, and Antibacterial Activities of Novel 5-Hydroxy-4-acetyl-2,3-dihydronaphtho[1,2-b]furans. *Eur. J. Med. Chem.* **2014**, *86*, 605–612. [CrossRef] [PubMed]
16. Pedroza, D.A.; De Leon, F.; Varela-Ramirez, A.; Lema, C.; Aguilera, R.J.; Mito, S. The cytotoxic Effect of 2-Acylated-1,4-naphthohydroquinones on Leukemia/Lymphoma Cells. *Bioorg. Med. Chem.* **2014**, *22*, 842–847. [CrossRef]

17. Maruyama, K.; Miyagi, Y. Photo-induced Condensation Reaction of p-Quinones with Aldehydes. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 1303–1304. [CrossRef]
18. Albini, A. Norrish' Type I and II Reactions and their Role in the Building of Photochemical Science. *Photochem. Photobiol. Sci.* **2021**, *20*, 161–181. [CrossRef]
19. Oelgemöller, M.; Schiel, C.; Fröhlich, R.; Mattay, J. The "Photo-Friedel-Crafts Acylation" of 1,4-Naphthoquinones. *Eur. J. Org. Chem.* **2002**, *2002*, 2465–2474. [CrossRef]
20. Dekker, J.; van Vuuren, P.J.; Venter, D.P. Photodimerization. I. The *syn* and *anti*-Photodimers of 1,4-Naphthoquinone. *J. Org. Chem.* **1968**, *33*, 464–466. [CrossRef]
21. Protti, S.; Ravelli, D.; Fagnoni, M. Introduction to Photochemistry for the Synthetic Chemist. In *Enabling Tools and Techniques for Organic Synthesis: A Practical Guide to Experimentation, Automation, and Computation*; Newman, S.G., Ed.; John Wiley & Sons Ltd.: New York, NY, USA, 2023; Chapter 2, pp. 37–72. [CrossRef]
22. Douglas, P.; Evans, R.C.; Burrows, H.D. The Photochemical Laboratory. In *Applied Photochemistry*; Evans, R.C., Douglas, P., Burrows, H.D., Eds.; Springer: Dordrecht, The Netherlands, 2013; Chapter 14, pp. 467–531. [CrossRef]
23. Bochet, C.G. On the Sustainability of Photochemical Reactions. *Chimia* **2019**, *73*, 720–723. [CrossRef]
24. Ravelli, D.; Protti, S.; Fagnoni, M.; Albini, A. Visible Light Photocatalysis. A Green Choice? *Curr. Org. Chem.* **2013**, *17*, 2366–2373. [CrossRef]
25. Koeberg, B.L.; Sagandira, M.B.; Sagandira, C.R.; Watts, P. Paradigm Shift in Medicinal Products Synthesis: Continuous Flow Technology. *Tetrahedron* **2024**, *168*, 134333. [CrossRef]
26. Alfano, A.I.; García-Lacuna, J.; Griffiths, O.M.; Ley, S.V.; Baumann, M. Continuous Flow Synthesis enabling Reaction Discovery. *Chem. Sci.* **2024**, *15*, 4618–4630. [CrossRef] [PubMed]
27. Alfano, A.I.; Pelliccia, S.; Rossino, G.; Chianese, O.; Summa, V.; Collina, S.; Brindisi, M. Continuous-Flow Technology for Chemical Rearrangements: A Powerful Tool to Generate Pharmaceutically Relevant Compounds. *ACS Med. Chem. Lett.* **2023**, *14*, 326–337. [CrossRef] [PubMed]
28. Srivastava, V.; Singh, P.P.; Sinha, S.; Singh, P.K.; Kumar, D. Continuous-Flow Photochemistry: The Synthesis of Marketed Pharmaceutical Compounds. *ChemistrySelect* **2024**, *9*, e202405020. [CrossRef]
29. Fukuyama, T.; Kasakado, T.; Hyodo, M.; Ryu, I. Improved Efficiency of Photo-induced Synthetic Reactions Enabled by Advanced Photo Flow Technologies. *Photochem. Photobiol. Sci.* **2022**, *21*, 761–775. [CrossRef] [PubMed]
30. Politano, F.; Oksdath-Mansilla, G. Light on the Horizon: Current Research and Future Perspectives in Flow Photochemistry. *Org. Process Res. Dev.* **2018**, *22*, 1045–1062. [CrossRef]
31. Rehm, T.H. Flow Photochemistry as a Tool in Organic Synthesis. *Chem. Eur. J.* **2020**, *26*, 16952–16974. [CrossRef]
32. Oelgemöller, M.; Hoffmann, N.; Shvydkiv, O. From 'Lab & Light on a Chip' to Parallel Microflow Photochemistry. *Austr. J. Chem.* **2014**, *67*, 337–342. [CrossRef]
33. Zhang, M.; Roth, P. Flow photochemistry—From Microreactors to Large-scale Processing. *Curr. Opin. Chem. Eng.* **2023**, *39*, 100897. [CrossRef]
34. Yaseen, M.A.; Guo, Z.; Junk, P.J.; Oelgemöller, M. [2+2]-Photocycloadditions of 1,4-Naphthoquinone Under Batch and Continuous-Flow Conditions. *Molecules* **2024**, *29*, 5920. [CrossRef]
35. Khan, H.; Rajesh, V.M.; Ravva, M.K.; Sen, S. Optimization of Blue LED Photo-Flow Synthesis in Continuous Flow Reactors Using Design of Experiments (DoE): Efficient Synthesis of Diverse Diaryl Ketones. *Chem. Eng. J.* **2024**, *501*, 157657. [CrossRef]
36. Yaseen, M.A.; Mumtaz, S.; Hunter, R.L.; Wall, D.; Belluau, V.; Robertson, M.J.; Oelgemöller, M. Continuous-Flow Photochemical Transformations of 1,4-Naphthoquinones and Phthalimides in a Concentrating Solar Trough Reactor. *Austr. J. Chem.* **2020**, *73*, 1149–1157, Erratum in *Austr. J. Chem.* **2020**, *73*, 1301. [CrossRef]
37. Marteaua, C.; Ruyffelaerea, F.; Aubrya, J.-M.; Penvernea, C.; Favier, D.; Nardello-Rataj, V. Oxidative Degradation of Fragrant Aldehydes. Autoxidation by Molecular Oxygen. *Tetrahedron* **2013**, *69*, 2268–2275. [CrossRef]
38. Mumtaz, S.; Robertson, M.J.; Oelgemöller, M. Continuous Flow Photochemical and Thermal Multi-step Synthesis of Bioactive 3-Arylmethylene-2,3-dihydro-1H-isoindolin-1-ones. *Molecules* **2019**, *24*, 4527. [CrossRef] [PubMed]
39. Helferich, B.; Klein, W. Zur Synthese von Disacchariden IV. Zwei Tetra-acetyl-β-d-glucosen. *Liebigs Ann. Chem.* **1926**, *450*, 219–229. [CrossRef]
40. Kraus, G.A.; Kirihara, M. Quinone Photochemistry. A General Synthesis of Acylhydroquinones. *J. Org. Chem.* **1992**, *57*, 3256–3257. [CrossRef]
41. Jha, R.K.; Upadhyay, A.; Kanika Jain, S.; KA, N.; Kumar, S. Light-Driven Carbon−Carbon Coupling of α-sp^3−CH of Aliphatic Alcohols with sp^2−CH Bond of 1,4-Naphthoquinones. *Org. Lett.* **2022**, *24*, 7605–7610. [CrossRef] [PubMed]
42. Hase, J.; Nishimura, T. Antibacterial Properties of Naphthoquinones. I. Syntheses and Antibacterial Properties of Acylnaphthoquinones. *J. Pharm. Soc. Jpn.* **1955**, *75*, 203–207. [CrossRef]
43. Maruyama, K.; Muraoka, M.; Naruta, Y. Photo-oxygenation of Alkenoyl-1,4-quinones by Atmospheric Oxygen. Formation of Stable Cyclic Peroxides. *J. Chem. Soc. Chem. Commun.* **1980**, *24*, 1282–1284. [CrossRef]

44. Batley, G.E. Use of Teflon Components in Photochemical Reactors. *Anal. Chem.* **1984**, *56*, 2261–2262. [CrossRef]
45. Friedrichs, F.; Murphy, B.; Nayrat, D.; Ahner, T.; Funke, M.; Ryan, M.; Lex, J.; Mattay, J.; Oelgemöller, M. An improved Procedure for the Photoacylation of 1,4-Naphthoquinone with Aliphatic Aldehydes. *Synlett* **2008**, *20*, 3137–3140. [CrossRef]
46. Mercier, A.; Monet, A.; Yaseen, M.; Hermanns, M.I.; Oelgemöller, M. Synthesis of Acylated Naphthohydroquinones through Photo-Friedel-Crafts Acylation and Evaluation of their Antibiotic Potential. *Photochem* **2024**, *4*, 501–510. [CrossRef]
47. Chen, Y.; Sabio, J.C.; Hartman, R.L. When Solids Stop Flow Chemistry in Commercial Tubing. *J. Flow Chem.* **2015**, *5*, 166–171. [CrossRef]
48. Wernerova, M.; Hudlicky, T. On the Practical Limits of Determining Isolated Product Yields and Ratios of Stereoisomers: Reflections, Analysis, and Redemption. *Synlett* **2010**, *18*, 2701–2707. [CrossRef]
49. Das, R.; Venkataraman, B. Hydrogen Abstraction from Solvents by the Triplet State of p-Benzoquinone: A Time-resolved Electron Paramagnetic Resonance and Laser Flash Photolysis Study. *Res. Chem. Intermed.* **2005**, *31*, 167–192. [CrossRef]
50. Givens, R.S.; Levi, N. The Photochemistry of Organic Acids, Esters, Anhydrides, Lactones and Imides. In *The Chemistry of Acid Derivatives*; Supplement, B., Patai, S., Eds.; John Wiley & Sons Ltd.: New York, NY, USA, 1979; Part 1, Chapter 11, pp. 641–753. [CrossRef]
51. Capello, C.; Fischer, U.; Hungerbühler, K. What is a Green Solvent? A Comprehensive Framework for the Environmental Assessment of Solvents. *Green Chem.* **2007**, *9*, 927–934. [CrossRef]
52. Montalti, M.; Credi, A.; Prodi, L.; Gandolfi, M.T. *Handbook of Photochemistry*, 3rd ed.; CRC Press: Boca Raton, FL, USA, 2006.
53. Bunce, N.J.; Ridley, J.E.; Zerner, M.C. On the Excited States of p-Quinones and an Interpretation of the Photocycloaddition of p-Quinones to Alkenes. *Theor. Chim. Acta* **1977**, *45*, 283–300. [CrossRef]
54. Kraus, G.A.; Liu, P. Benzophenone-Mediated Conjugate Additions of Aromatic Aldehydes to Quinones. *Tetrahedron Lett.* **1994**, *35*, 7723–7726. [CrossRef]
55. McDowell, C.A.; Sifniades, S. Isomerization as a Primary Process in the Photolysis of Crotonaldehyde. *J. Am. Chem. Soc.* **1962**, *84*, 4606–4607. [CrossRef]
56. Otake, Y.; Nakamura, H.; Fuse, S. Recent Advances in the Integrated Micro-flow Synthesis Containing Photochemical Reactions. *Tetrahedron Lett.* **2018**, *59*, 1691–1697. [CrossRef]
57. Spruit, C.J.P. Carbonyl-substituted Naphthoquinones. Part I. Methyl Ketones Unsubstituted in the Side Chain. *Recl. Trav. Chim. Pays-Bas* **1947**, *66*, 655–672. [CrossRef]
58. Derikvand, F.; Bigi, F.; Maggi, R.; Piscopo, C.G.; Sartori, G. Oxidation of Hydroquinones to Benzoquinones with Hydrogen Peroxide using Catalytic Amount of Silver Oxide under Batch and Continuous-flow Conditions. *J. Catal.* **2010**, *271*, 99–103. [CrossRef]
59. Donnelly, K.; Baumann, M. Scalability of Photochemical Reactions in Continuous Flow Mode. *J. Flow Chem.* **2021**, *11*, 223–241. [CrossRef]
60. Hunter, R.; Josland, S.; Moore, J.; Guthrie, D.; Robertson, M.J.; Oelgemöller, M. Rapid Photochemical Reaction Studies under Continuous-flow Conditions in the Vapourtec UV-150 Reactor—A Technical Note. *Curr. Org. Chem.* **2018**, *22*, 2501–2508. [CrossRef]