Ruthenium-catalysed C-alkylation of 1,3-dicarbonyl compounds with primary alcohols and synthesis of 3-keto-quinolines

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GENERAL EXPERIMENTAL DETAILS

All reagents were used as purchased from commercial suppliers without further purification. The reactions were carried out in oven dried or flamed vessels. Solvents were dried and purified by conventional methods prior use. Toluene was distilled from sodium. Flash column chromatography was performed with Merck silica gel 60, 0.040-0.063 mm (230-400 mesh). Merck aluminium backed plates pre-coated with silica gel 60 (UV254) were used for analytical and preparative thin layer chromatography and were visualized by staining with a KMnO₄ solution. NMR spectra were recorded at 25 °C and 400 MHz for ¹H and 100 MHz for ¹³C. The solvent is specified for each spectrum. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Chemical shifts (δ) are given in ppm relative to the resonance of their respective residual solvent peak. GC/MS analyses were performing using a ion-trap detector equipped with a 30 m OV-101 capillary column, splitting injector at 280 °C, method: 80 °C - 200 °C 30 min. High and low resolution mass spectroscopy analyses were recorded by electrospray ionization. Melting points were determined in open capillary tubes and are uncorrected. MW heated reaction were carried out with a CEM Discover oven, the temperature recorder through the IR sensor. The internal pressure was monitored during the reaction and the max value is reported.

2-Benzyl-1,3-indandione

Yield: 64% Solid that decomposes on heating. ¹H-NMR (400 MHz, CDCl₃): δ 7.87 – 7.82 (m, 2H), 7.71 (d, J = 5.7 Hz, 2H), 7.15 – 7.03 (m, 5H), 3.30 (s, 3H). ¹³C-NMR (100 MHz, CDCl₃): δ 199.6, 142.1, 136.7, 135.1, 129.1, 127.8, 126.2, 122.6, 54.6, 31.8. GC/MS: Rₜ 20.23 min; m/z 236 (C₁₆H₁₂O₂). HRMS (EI): Calcd for C₁₆H₁₂O₂Na [M+Na]⁺ 259.0735, found 259.0738.

2-Ethyl-1,3-indandione


Yield: 61%  Mp 53-54 °C (Lit mp: 55 °C). \( ^1 \)H-NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.16 – 7.49 (m, 4H), 2.98 – 2.90 (m, 1H), 2.07 – 1.94 (m, 2H), 0.95 (t, \( J = 7.6 \) Hz, 3H). \( ^{13} \)C-NMR (100 MHz, CDCl\(_3\)): \( \delta \) 200.8, 142.3, 133.9, 127.6, 51.1, 17.0, 11.5. GC/MS: R\(_t\) 14.01 min; m/z 174 (C\(_{11}\)H\(_{10}\)O\(_2\)). HRMS (EI): Calcd for C\(_{11}\)H\(_{10}\)O\(_2\)Na [M+Na\(^+\)] 197.0579, found 197.0576.

2-Hexyl-1,3-indandione

Yield: 57% Dense waxy material. \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.23 – 7.51 (m, 4H), 2.97 (t, \( J = 6.0 \) Hz, 1H), 1.95 – 1.75 (m, 2H), 1.36 – 1.10 (m, 8H), 0.79 (d, \( J = 16.9 \) Hz, 3H). \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): \( \delta \) 201.0, 140.9, 132.6, 127.2, 53.0, 31.9, 29.5, 29.0, 22.3, 15.1. GC/MS: R\(_t\) 18.81 min; m/z 230 (C\(_{15}\)H\(_{18}\)O\(_2\)). HRMS (EI): Calcd for C\(_{15}\)H\(_{18}\)O\(_2\)Na [M+Na\(^+\)] 253.1204, found 253.1206.

2-Furfuryl-1,3-indandione

Yield: 66% Mp 96-98 °C (Lit mp 97.5-98.0 °C) \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.91 (dt, \( J = 6.8, 3.4 \) Hz, 2H), 7.81 – 7.73 (m, 2H), 7.05 (d, \( J = 1.9 \) Hz, 1H), 6.10 (d, \( J = 2.7 \) Hz, 1H), 5.96 (d, \( J = 3.2 \) Hz, 1H), 3.34 (d, \( J = 5.4 \) Hz, 2H), 3.31 – 3.26 (m, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 199.6, 151.9, 142.4, 141.3, 134.6, 123.7, 110.3, 107.5, 53.0, 24.5. HRMS (EI): Calcd for C\(_{14}\)H\(_{10}\)O\(_3\)Na [M+Na\(^+\)] 249.0528, found 249.0527.

2-(3-Benzeyloxycarbonylaminopropyl)-1,3-indandione

Yield: 76% Dense material that tends to solidify. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.09 – 7.69 (m, 4H), 7.42 – 6.98 (m, 5H), 4.98 (m, 3H), 3.18 (q, \( J = 6.3 \) Hz, 2H), 2.98 (t, \( J = 6.1 \) Hz, 1H), 1.98 – 1.82 (m, 2H), 1.64 (dq, \( J = 14.3, 6.9 \) Hz, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 204.1, 145.8, 139.3, 132.0, 131.6, 126.8, 70.2, 56.4, 44.2, 30.5, 27.6. HRMS (EI): Calcd for C\(_{20}\)H\(_{19}\)NO\(_4\)Na [M+Na\(^+\)] 360.1212, found 360.1210.
2-(3-Benzoylcarbonylaminoethyl)-1,3-indandione

Yield: 64% M.p. 67-68 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.09 – 7.62 (m, 4H), 7.44 – 7.09 (m, 5H), 5.24(bs, 1H) 4.99 (m, 2H), 3.44 (m, 2H), 3.04 (t, \(J = 6.4\) Hz, 1H), 2.18 – 1.94 (m, 2H). \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 199.8, 155.8, 141.6, 136.2, 135.3, 128.0, 127.6, 123.7, 122.9, 66.2, 51.3, 38.6, 29.2, 26.4. HRMS (EI): Calcd for C\(_{19}\)H\(_{17}\)NO\(_4\)Na [M+Na]+ 346.1055, found 346.1053.

2-Benzy-1,3-cyclohexanedione

Yield: 62% M.p. 179-181 °C (Lit m.p. 180 °C). \(^1\)H NMR (400 MHz, CD\(_2\)OD) \(\delta\) 7.37 – 6.86 (m, 5H), 4.83 (s, 2H), 3.30 (s, 1H), 2.43 (t, \(J = 6.2\) Hz, 4H), 1.94 (p, \(J = 5.4, 4.6\) Hz, 2H). \(^1^3\)C NMR (100 MHz, CD\(_2\)OD) \(\delta\) 199.2, 139.7, 126.1, 125.5, 122.9, 113.3, 30.4, 27.4, 25.0, 20.9, 18.6. GC/MS: R\(_t\) 18.34 min; m/z 202 (C\(_{13}\)H\(_{14}\)O\(_2\)). HRMS (EI): Calcd for C\(_{13}\)H\(_{14}\)O\(_2\)Na [M+Na]+ 225.0892, found 225.0895.

2-(3-Benzoylcarbonylaminopropyl)-1,3-cyclohexanedione

Yield: 52% M.p. 94-96 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.43 – 7.20 (m, 5H), 5.06 (d, \(J = 9.2\) Hz, 3H), 3.15 (t, \(J = 10.6\) Hz, 1H), 3.06 (q, \(J = 6.2\) Hz, 2H), 2.58 (m, 1H), 2.45 (m, 2H), 2.32 (m, 2H), 2.14 (m, 1H) 1.90 (m, 2H), 1.55 (m, 2H). \(^1^3\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 209.4, 161.4, 132.1, 131.6, 131.5, 70.6, 43.7, 40.7, 39.7, 33.3, 27.3, 24.4, 22.0. HRMS (EI): Calcd for C\(_{17}\)H\(_{23}\)NO\(_4\)Na [M+Na]+ 326.1369, found 326.1365.

2-Hexyl-1,3-cyclopentanedione

Yield: 64% M.p. 67-68 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.09 – 7.62 (m, 4H), 7.44 – 7.09 (m, 5H), 5.24(bs, 1H) 4.99 (m, 2H), 3.44 (m, 2H), 3.04 (t, \(J = 6.4\) Hz, 1H), 2.18 – 1.94 (m, 2H). \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 199.8, 155.8, 141.6, 136.2, 135.3, 128.0, 127.6, 123.7, 122.9, 66.2, 51.3, 38.6, 29.2, 26.4. HRMS (EI): Calcd for C\(_{19}\)H\(_{17}\)NO\(_4\)Na [M+Na]+ 346.1055, found 346.1053.
Yield: 51% Solid that decomposes on heating (Lit m.p. 240 °C)\(^5\) \(^1\)H NMR (400 MHz, CD\(_3\)OD) \(\delta\) 2.47 (s, 4H), 2.09 (t, \(J = 7.4\) Hz, 2H), 1.42 – 1.23 (m, 9H), 0.89 (t, \(J = 6.7\) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 203.5, 49.6, 31.2, 30.2, 29.8, 26.9, 22.3, 20.3, 13.2. HRMS (EI): Calcd for C\(_{11}\)H\(_{18}\)O\(_2\)Na [M+Na]\(^+\) 205.1205, found 205.1203.

2-(3-Phenylpropyl)-1,3-cyclopentanedione

\[
\begin{align*}
\text{O} & \\
\text{O} & \\
\end{align*}
\]

Yield: 47% Gum that tends to solidify on standing. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.36 – 6.99 (m, 5H), 2.54 (d, \(J = 33.1\) Hz, 7H), 2.22 (t, \(J = 7.6\) Hz, 2H), 1.75 (p, \(J = 7.8\) Hz, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 197.8, 142.4, 127.5, 125.2, 43.5, 38.8, 35.6, 28.8, 20.3. HRMS (EI): Calcd for C\(_{14}\)H\(_{16}\)O\(_2\)Na [M+Na]\(^+\) 239.1048, found 239.1050.

2-Benzyl-1,3-cyclopentanedione

\[
\begin{align*}
\text{O} & \\
\text{O} & \\
\end{align*}
\]

Yield: 49% Solid that decomposes on heating. \(^1\)H NMR (400 MHz, CD\(_3\)OD) \(\delta\) 7.25 – 6.98 (m, 5H), 3.49 – 3.15 (m, 3H), 2.48 (s, 4H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 198.2, 140.3, 128.2, 128.2, 127.7, 125.5, 116.6, 36.9, 32.9, 26.1. HRMS (EI): Calcd for C\(_{12}\)H\(_{12}\)O\(_2\)Na [M+Na]\(^+\) 211.0735, found 211.0733.

3-(3-Benzylxycarbonylaminopropyl)-6-undecyl-5,6-dihydro-3H-pyran-2,4-dione

\[
\begin{align*}
\text{H}_{25}\text{C}_{11} & \\
\text{O} & \\
\text{O} & \\
\text{NH} & \\
\text{Cbz} & \\
\end{align*}
\]

Yield: 44% Dense waxy material \(^1\)H NMR (400 MHz, CDcl\(_3\)); the spectrum is refereed to the prevalent enolic form: \(\delta\) 7.33 (s,5H), 5.09 (d, \(J = 19.3\) Hz, 3H), 4.29 (m, 1H), 3.10 (m, 2H), 2.58 – 2.26 (m, 2H), 1.83 – 1.48 (m, 4H), 1.24 (s, 20H), 0.86 (t, \(J = 6.6\) Hz, 3H). \(^{13}\)C NMR (101 MHz, ) \(\delta\) 174.9, 169.6, 154.9, 132.1, 131.7, 99.8, 81.0, 80.7, 80.3, 79.2, 71.9, 70.6, 70.4, 41.1, 41.1, 40.8, 40.6, 39.8, 38.1, 37.0, 36.1, 33.7, 33.7, 33.3, 33.3, 27.4, 26.7, 26.5, 25.9, 24.4, 24.0, 23.5, 22.5, 22.3, 22.1. A preparative TLC gave the analytical sample. HRMS (EI): Calcd for C\(_{27}\)H\(_{41}\)NO\(_3\)Na [M+Na]\(^+\) 482.2883, found 482.2880.
3-Hexyl-6-undecyl-5,6-dihydro-3H-pyran-2,4-dione

Yield: 50% M.p 110-112 °C (Lit. m.p. 112 °C).¹ H NMR (400 MHz, CDCl₃) enol form: δ 4.64 (m, 1H), 2.74 – 2.59 (m, 1H), 2.38 (dd, J = 18.8, 11.8 Hz, 1H), 1.98 – 1.69 (m, 3H), 1.41 – 1.22 (m, 28H), 0.85 (t, J = 5.8 Hz, 6H). A preparative TLC gave the analytical sample. HRMS (EI): Calcd for C₂₂H₄₀O₃Na [M+Na]+ 375.2876, found 375.2873.

2,3,4,4a-Tetrahydro-1H-indeno[1,2-b]pyridin-5(9bH)-one acetate

In a round bottom flask containing a magnetic stirrer bar, 2-(3-benzyloxy carbonylaminopropyl)-1,3-indandione 16 (67 mg, 0.2 mmol) was solubilized in 20 mL of MeOH under nitrogen. Acetic acid (25 mg, 24 µL, 0.42 mmol) and 20% Pd(OH)₂ on charcoal (3 mg, 0.021 mmol) were added and reaction mixture was stirred under H₂ for 72 h. The reaction mixture was then filtered on celite and the catalyst washed with MeOH. The solvent was evaporated and the crude purified by flash chromatography (CH₂Cl₂ to CH₂Cl₂/MeOH, 80:20). Obtained 22 mg, (47 % yield) of a solid that decomposes on heating. Major diastereoisomer (trans)¹ H NMR (400 MHz, CDCl₃) δ 7.81 – 7.71 (m, 1H), 7.23 (d, J = 3.8 Hz, 4H), 4.19 (d, J = 11.4 Hz, 1H), 3.37 – 3.29 (m, 2H), 2.97 (dd, J = 14.7, 6.8 Hz, 1H), 2.78 (s, 3H), 2.52 (dd, J = 14.7, 11.3 Hz, 1H), 2.33 (m, 1H), 2.13 (m 1H), 1.94 (m, 2H), 1.67 (m, 1H).¹³C NMR (101 MHz, CDCl₃) δ 200.5, 134.3, 128.8, 128.5, 127.4, 127.1, 124.8, 61.6, 55.1, 46.0, 34.2, 27.5. GC/MS: Rᵣ 15.36 min m/z 187 (C₁₂H₁₃ON). HRMS (EI) Calcd. for C₁₂H₁₄NO [M+H]⁺ 188.1076, found 188.1074.
6-Chloro-3,4-dihydro-2H-acridin-1-one

Yield: 70 % Waxy material. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.49 (s, 1H), 7.75 (d, $J$ = 9.4 Hz, 1H), 7.58 (d, $J$ = 8.7 Hz, 1H), 7.25 (d, $J$ = 8.6 Hz, 1H), 3.33 – 2.97 (m, 2H), 2.86 – 2.50 (m, 2H), 2.08 (dt, $J$ = 12.5, 6.1 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 197.2, 163.0, 149.6, 138.1, 136.5, 136.3, 130.6, 128.1, 127.5, 127.1, 126.2, 124.9, 38.8, 33.2, 21.5. HRMS (EI): Calcd for C$_{13}$H$_{11}$ClNO [M+H]$^+$ 232.0529, found 232.0526.

5-Methyl-3,4-dihydro-2H-acridin-1-one

Yield 62%. M.p. 76-78 °C. $^1$H NMR (400 MHz, CDCl$_3$): δ 8.69 (s, 1H), 7.66 (d, $J$ = 8.1 Hz, 1H), 7.55 (d, $J$ = 6.9 Hz, 1H), 7.34 (t, $J$ = 7.6 Hz, 1H), 3.35 – 3.20 (m, 2H), 2.72 (d, $J$ = 9.9 Hz, 5H), 2.19 (p, $J$ = 6.4 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 197.7, 160.3, 148.3, 136.5, 136.2, 131.7, 127.2, 126.2, 125.8, 125.4, 38.7, 33.2, 21.5, 17.5. HRMS (EI): Calcd for C$_{14}$H$_{14}$NO [M+H]$^+$ 212.1075, found 212.1077.

2-Azatricyclo[7.4.0.0$^{3,7}$]trideca-1(9),2,7,10,12-penta-6-one

Yield 49%. Gum $^1$H NMR (400 MHz, CDCl$_3$) δ 8.53 (s, 1H), 8.09 (d, $J$ = 8.6 Hz, 1H), 7.94 (d, $J$ = 8.1 Hz, 1H), 7.81 (t, $J$ = 7.4 Hz, 1H), 7.55 (t, $J$ = 7.5 Hz, 1H), 3.45 – 3.39 (m, 2H), 2.90 – 2.82 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 204.8, 151.7, 133.5, 133.2, 132.6, 130.4, 129.4, 129.0, 127.8, 126.8, 36.3, 28.9. HRMS (EI): Calcd for C$_{12}$H$_{10}$NO [M+H]$^+$ 184.0762, found 184.0765.
9-Azatetracyclo[8.7.0.0³,8.0¹¹,16]heptadeca-1,3(8),4,6,9,11,13,15-octaen-17-one

Yield: 61%  M.p. 172-174°C. Lit m.p. (175-176 °C)¹ H NMR (400 MHz, CDCl₃) δ 8.30 (s, 1H), 8.05 (t, J = 8.7 Hz, 2H), 7.79 (dd, J = 14.2, 7.7 Hz, 2H), 7.71 (t, J = 7.7 Hz, 1H), 7.64 (t, J = 7.4 Hz, 1H), 7.47 (td, J = 7.5, 3.6 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 190.4, 161.6, 150.2, 143.4, 137.0, 135.1, 133.9, 132.0, 131.6, 131.1, 130.1, 129.6, 129.4, 127.8, 127.2, 126.8, 123.7, 121.4. HRMS (EI): Calcd for C₁₆H₁₀NO [M+H]⁺ 232.0762, found 232.0764.

3,3-Dimethyl-3,4-dihydro-2H-acridin-1-one

Yield: 67% M.p. 101-102°C. Lit m.p. (101-102 °C)⁷ H NMR (400 MHz, CDCl₃) δ 8.72 (s, 1H), 7.96 (d, J = 8.6 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.75 – 7.65 (m, 1H), 7.45 (t, J = 7.5 Hz, 1H), 3.11 (s, 2H), 2.56 (s, 2H), 1.06 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 197.4, 160.3, 149.5, 136.0, 131.7, 129.3, 128.1, 126.3, 126.2, 124.8, 52.0, 46.7, 32.3, 29.2, 27.9. HRMS (EI) Calcd for C₁₅H₁₆NO [M+H]⁺ 226.1232, found 226.1234.

1-(2-Methyl-3-quinolyl)-1-ethanone

Yield: 58% M.p. 72-74°C. Lit m.p. (73-74 °C)⁷ H NMR (400 MHz, CDCl₃) δ 8.40 (s, 1H), 7.98 (d, J = 8.5 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.75 – 7.68 (m, 1H), 7.48 (t, J = 7.5 Hz, 1H), 2.86 (s, 3H), 2.65 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 200.4, 158.0, 148.7, 138.8, 132.2, 131.4, 128.9, 128.7, 127.0, 125.9, 29.7, 26.1. HRMS (EI): Calcd for C₁₂H₁₂NO [M+H]⁺ 186.0919, found 186.0916.
1-(2-Phenylquinolin-3-yl)ethanone

Yield: 52% M.p. 131-133 (Lit m.p. 132-133) $^9$ $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.07 (d, $J = 12.1$ Hz, 1H), 7.86 – 7.70 (m, 2H), 7.70 – 7.39 (m, 5H), 7.22 (dq, $J = 19.3$, 6.8 Hz, 3H), 2.73 (s, 3H). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.07 (d, $J = 12.1$ Hz, 1H), 7.86 – 7.70 (m, 3H), 7.70 – 7.39 (m, 5H), 7.22 (dq, $J = 19.3$, 6.8 Hz, 3H), 2.73 (s, 2H). HRMS (EI): Calcd for C$_{17}$H$_{14}$NO $[M+H]^+$ 248.1075, found 248.1078.

3-(5-Undecene-1,3-diynyl)-2-oxa-10-aza-3,4-dihydroanthracen-1-one

Yield: 44% Waxy material $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.89 (s, 1H), 8.03 (d, $J = 8.6$ Hz, 1H), 7.91 (d, $J = 8.1$ Hz, 1H), 7.81 (t, $J = 7.6$ Hz, 1H), 7.56 (t, $J = 7.5$ Hz, 1H), 4.72 – 4.60 (m, 1H), 3.36 – 3.16 (m, 2H), 1.97 – 1.84 (m, 1H), 1.85 – 1.71 (m, 1H), 1.57 – 1.43 (m, 2H), 1.25 (d, $J = 21.4$ Hz, 16H), 0.84 (t, $J = 6.7$ Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 164.6, 156.6, 149.3, 139.8, 132.2, 128.9, 128.3, 126.7, 118.5, 78.0, 36.6, 34.6, 31.5, 29.2, 29.1, 28.9, 24.5, 22.2, 13.7. HRMS (EI): Calcd for C$_{23}$H$_{32}$NO$_2$ $[M+H]^+$ 354.2433, found 354.2436

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