Supporting Information

A glycerol mediated domino reaction: an efficient, green synthesis of polyheterocycles incorporating a new thiochromeno[2,3-b]quinoline unit

Narsidas J. Parmar*, Hitesh A. Barad*, Bailvant Singh L. Labana, Rajnikant, Vivek K. Gupta

*Department of Chemistry, Sardar Patel University, Vallabh Vidyanagar-388120. Dist. Anand, Gujarat, India
bPost graduate Department of Physics, University of Jammu, Jammu Tavi-180006, India

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1.1 General methods

All solvents and reagents were used as supplied from commercial sources. The recorded melting points are uncorrected. IR spectra were recorded in KBr on Shimadzu FT-IR 8401 spectrometer and are reported in wave numbers (cm$^{-1}$). A single crystal-X-ray diffraction data were collected on X'calibur CCD area-detector diffractometer equipped with graphite monochromated MoK$\alpha$ radiation ($\lambda=0.71073$ Å). $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker Avance 400 spectrometer operating at 400 MHz for $^1$H NMR and 100 MHz for $^{13}$C NMR as solutions in CDCl$_3$, unless otherwise indicated. Chemical shifts are reported as parts per million (ppm, d) and referenced to the residual protic solvent. Coupling
constants are reported in Hertz (Hz). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; br, broad; m, multiplet; comp, complex multiplet. The degree of substitution (C, CH, CH₂, and CH₃) was determined by the APT method. The ESI mass spectra were measured on Shimadzu LCMS-2010 spectrometer. TLC was performed on Merck 60 F254 pre-coated silica plates, spots were detected either by UV (254 nm, 366 nm) or dipping into a permanganate [KMnO₄ (3 g), K₂CO₃ (20 g), NaOH (5 mL, 5% in H₂O), H₂O (300 mL)] or an anisaldehyde solution [3% p- methoxybenzaldehyde and 1% H₂SO₄ in MeOH] or 2,4 Dinitro phenyl hydrazine solution [2,4-DNP (12 g), Conc. H₂SO₄ (6 mL), Water (8 mL), EtOH (20 mL)] followed by heating.

1.2 General Procedure for Synthesis of 2-mercaptopquinoline-3-carbaldehydes (1a-c)

1.2.1 2-chloroquinoline-3-carbaldehyde:

POCl₃ (98.28 mmol) was added drop wise to DMF (34.65 mmol) while maintaining the temperature at 0–5 °C. The mixture was allowed to stir for about 5 min. Acetanilide (10.37 mmol) was then added and the resulting solution heated for 8 h at 75–80 °C. The reaction mixture was cooled to room temperature and then poured into crushed ice with stirring. A pale yellow precipitate appeared immediately and was filtered and washed with water and then dried. The crude compound was recrystallized from ethyl acetate.

1.2.2 2-mercaptopquinoline-3-carbaldehyde 1a-c:

To a solution of 2-chloroquinoline-3-carbaldehyde (1 mmole) in dry DMF (5 mL), powder sodium sulphide (1.5 mmole) was added and stirred for 1-2 h at room temperature. On completion of the reaction, the reaction mixture was poured into ice-water and made acidic with acetic acid. The product was filtered off, washed well with water, dried and was pure enough for further use.
1.3 General Experimental Procedure and analytical data for Synthesis of thiopyrano[2,3-b]quinoline-3-carbaldehydes (3a-c)

2-mercaptoquinoline-3-carbaldehyde (1a-c) (2.0 mmol) and citral (2) (2.4 mmol) were dissolved in xylene (20 mL), and ethylenediamine diacetate (0.4 mmol) was added at room temperature. The mixture was refluxed for 3-3.5 h and then cooled to room temperature. Removal of solvent at reduced pressure left an oily residue, which was then purified by column chromatography on silica gel using a mixture of hexane/ethyl acetate (10 : 1) as an eluent to give product 3a-c as a yellow solid.

**2-methyl-2-(4-methylpent-3-en-1-yl)-2H-thiopyrano[2,3-b]quinoline-3-carbaldehyde (3a):**

<table>
<thead>
<tr>
<th>Chemical Shifts</th>
<th>ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1H (400 MHz, CDCl3)</td>
<td>1.53 (s, 3H, CH3), 1.63 (s, 3H, CH3), 1.69-1.79 (m, 2H, CH2), 1.83 (s, 3H, C(2)CH3), 1.96-2.28 (m, 2H, CH2), 2.35 (s, 1H, C(4)H), 5.04 (t, 1H, J = 6.8 Hz, CH), 7.45-7.95 (m, 5H, Ar-H), 9.63 (s, 1H, CHO) ppm</td>
</tr>
<tr>
<td>δC (100 MHz; CDCl3)</td>
<td>24.46, 25.55, 29.19, 41.86, 51.33, 123.18, 123.73, 126.26, 128.05, 128.55, 131.56, 136.82, 137.01, 141.33, 145.46, 145.76, 149.28, 158.74, 191.33 ppm</td>
</tr>
</tbody>
</table>

Isolated Yield (0.46 g, 72 %) as yellow crystals, mp 70-72 °C; νmax/cm⁻¹ = 3054.20, 2973.43, 2900.84, 2852.91, 1683.90, 1608.90, 1553.70, 1374.75, 1177.35, 1094.67, 920.27, 741.27; δH (400 MHz, CDCl3) 1.53 (s, 3H, CH3), 1.63 (s, 3H, CH3), 1.69-1.79 (m, 2H, CH2), 1.83 (s, 3H, C(2)CH3), 1.96-2.28 (m, 2H, CH2), 2.35 (s, 1H, C(4)H), 5.04 (t, 1H, J = 6.8 Hz, CH), 7.45-7.95 (m, 5H, Ar-H), 9.63 (s, 1H, CHO) ppm; δC (100 MHz; CDCl3) 24.46, 25.55, 29.19, 41.86, 51.33, 123.18, 123.73, 126.26, 128.05, 128.55, 131.56, 136.82, 137.01, 141.33, 145.46, 145.76, 149.28, 158.74, 191.33 ppm; m/z (ESI) 323.9 [M + H⁺].
1.4 General experimental procedure for synthesis of pyrazolo[4\'',3\'':5\','6]' pyrano[4\',3\':5,6] thiochromeno[2,3-b]quinolines (5a-r)

Some 3 mL glycerol were added to an equimolar (3 mmol of each) mixture containing thiopyrano[2,3-b]quinoline-3-carbaldehyde (3a-c) and 5-pyrazolone (4a-f) taken in a 50 mL round-bottomed flask connected to a reflux condenser. The mixture was then stirred at 120 °C. The progress of reaction was monitored by TLC using EtOAc–n-hexane (1:4) as an eluent. After completion of the reaction, 5 mL warm water was added to flask. Insoluble crude products thus precipitated were isolated simply by filtration. The filtrate upon water evaporation under reduced pressure at 100 °C left glycerol. The recovered glycerol was reused for the preparation of next product. All the compounds 5a-r were received quantitatively with an excellent purity.

1.5 Analytical data for compounds (5a,15b,S)1,5,5,7a-tetramethyl-3-phenyl-5,5a,6,7,7a,15b-hexahydro-3H-pyrazolo[4\'',3\'':5\',6]pyrano[4\',3\':5,6] thiochromeno[2,3-b]quinoline (5a)

Isolated Yield (1.30 g, 91 %) as yellow crystals, mp 260-262 °C; \( \nu_{\text{max}} / \text{cm}^{-1} = 3059.33, 2979.50, 2946.72, 2917.59, 1648.57, 1598.74, 1510.21, 1390.82, 1119.83, 749.23, 689.78; \delta_H (400 MHz, CDCl_3) 1.28 (s, 3H, C(5)CH_3), 1.50 (s, 3H, C(5)CH_3), 1.64 (s, 3H, C(7a)H), 1.99-2.10 (m, 4H, C(6)&C(7)CH_2), 2.30 (s, 4H, C(1)CH_3), 2.40-2.47 (m, 1H, C(5a)H), 3.70 (d, 1H, \( J = 8.4 \) Hz, C(15b)H), 6.40 (s, 1H, C(15)H), 7.22-7.97 (m, 10H, Ar-H) ppm; \delta_C (100 MHz; CDCl_3) 13.28, 21.07, 22.08, 28.13, 30.25, 30.86, 31.91, 33.49, 41.02, 48.01, 84.58, 93.99,
120.10, 122.17, 125.33, 125.83, 126.43, 126.76, 127.63, z127.77, 128.85, 129.59, 132.61, 138.92, 143.27, 147.19, 147.34, 150.46, 158.08 ppm; m/z (ESI) 479.7 [M + H+].

**\((5aR,15bS)1,5,5,7a-tetramethyl-3-(p-tolyl)-5,5a,6,7a,15b-hexahydro-3H-pyrazolo[4'',3'':5',6']pyrano[4',3':5,6]thiochromeno[2,3-b]quinoline (5b):**

Isolated Yield (1.4 g, 90 %) as yellow crystals, mp 228-230 °C; \(\nu_{\text{max}}/\text{cm}^{-1} = 3034.40, 2921.48, 1605.22, 1581.97, 1517.87, 1391.67, 1100.35, 818.66, 749.54; \)
\(\delta_{\text{H}} (400 \text{ MHz, CDCl}_3) 1.27 (\text{s, 3H, C(5)CH}_3), 1.48 (\text{s, 3H, C(5)CH}_3), 1.64 (\text{s, 3H, C(7a)H}), 1.82-2.07 (\text{m, 4H, C(6) & C(7)CH}_2), 2.29 (\text{s, 3H, C(1)CH}_3), 2.39 (\text{s, 3H, p-CH}_3), 2.41-2.44 (\text{m, 1H, C(5a)H}), 3.70 (\text{d, 1H, J} = 8.4 \text{ Hz, C(15b)H}), 6.40 (\text{s, 1H, C(15)H}), 7.23-7.96 (\text{m, 9H, C(Ar)H}) \text{ ppm;} \)
\(\delta_{\text{C}} (100 \text{ MHz; CDCl}_3) 13.35, 20.71, 20.94, 22.13, 28.31, 30.29, 31.96, 33.57, 41.13, 41.35, 47.99, 69.80, 84.26, 120.28, 122.17, 125.87, 126.45, 126.80, 127.57, 129.50, 132.21, 132.49, 135.05, 136.47, 143.25, 143.97, 147.02 \text{ppm; m/z (ESI) 493.9 [M + H+].}

**\((5aR,15bS)5,5,7a-trimethyl-1,3-diphenyl-5,5a,6,7a,15b-hexahydro-3H-pyrazolo[4'',3'':5',6']pyrano[4',3':5,6]thiochromeno[2,3-b]quinoline (5d)\)**

Isolated Yield (1.5 g, 91 %) as yellow crystals, mp 234-236 °C; \(\nu_{\text{max}}/\text{cm}^{-1} = 3052.94, 2931.77, 3856.28, 1596.64, 1509.94, 1484.66, 1386.03, 1136.04, 1070.22, 752.18, 691.55; \)
\(\delta_{\text{H}} (400 \text{ MHz, CDCl}_3) 1.32 (\text{s, 3H, C(5)CH}_3), 1.53 (\text{s, 3H, C(5)CH}_3), 1.68 (\text{s, 3H, C(7a)H}), 1.88-2.17 (\text{m, 4H, C(6) & C(7)CH}_2), 2.52-2.59 (\text{m, 1H, C(5a)H}), 4.09 (\text{d, 1H, J} = 8.4 \text{ Hz, C(15b)H}), 6.30 (\text{s, 1H, C(15)H}), 7.31-7.99 (\text{m, 15H, Ar-H}) \text{ ppm;} \)
\(\delta_{\text{C}} (100 \text{ MHz; CDCl}_3) 13.33, 20.76, 22.06, 28.31, 30.32, 31.88, 33.49, 41.05, 48.07, 84.98, 117.71, 119.99, 121.98, 125.12, 125.19, 126.49, 126.87, 127.02, 128.70, 129.96, 132.10, 134.71, 135.37, 143.49, 147.54, 147.89, 159.48 \text{ ppm.}

Electronic Supplementary Material (ESI) for RSC Advances
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**Isolated Yield (1.4 g, 90 %) as yellow crystals, mp 170-172 °C; ν_max/cm⁻¹ = 3071.39, 2929.44, 2856.39, 1607.66, 1593.91, 1505.63, 1478.33, 1387.09, 1199.11, 1078.51, 927.51, 881.80, 774.60, 751.77; δ_H (400 MHz, CDCl₃) 1.27 (s, 3H, C(5)CH₃), 1.51 (s, 3H, C(5)CH₃), 1.63 (s, 3H, C(7a)H), 1.81-2.11 (m, 4H, C(6) & C(7)CH₂), 2.28 (s, 3H, C(1)CH₃), 2.40-2.47 (m, 1H, C(5a)H), 3.69 (d, 1H, J = 6.8 Hz, C(15b)H), 6.35 (s, 1H, C(15)H), 7.19-7.94 (m, 8H, Ar-H) ppm; δ_C (100 MHz; CDCl₃) 13.33, 20.76, 22.06, 28.31, 30.32, 31.88, 33.49, 41.05, 48.07, 84.98, 117.71, 119.99, 121.98, 125.12, 125.19, 126.49, 126.87, 127.02, 128.70, 129.96, 132.10, 134.71, 135.37, 143.49, 147.54, 147.89, 159.48 ppm; m/z (ESI) 547.9 [M + H⁺].

**Isolated Yield (1.5 g, 90 %) as yellow crystals, mp 138-140 °C; ν_max/cm⁻¹ = 3070.95, 2923.80, 2858.22, 1605.67, 1512.87, 1476.11, 1138.50, 1092.57, 927.73, 870.76, 806.87, 771.99, 656.08, 581.54; δ_H (400 MHz, CDCl₃) 1.26 (s, 3H, C(5)CH₃), 1.38 (s, 3H, C(5)CH₃), 1.63 (s, 3H, C(7a)H), 1.81-2.11 (m, 4H, C(6) & C(7)CH₂), 2.28 (s, 3H, C(1)CH₃), 2.38-2.43 (m, 1H, C(5a)H), 3.70 (d, 1H, J = 8.4 Hz, C(15b)H), 6.38 (s, 1H, C(15)H), 7.33-7.95 (m, 7H, Ar-H) ppm; δ_C (100 MHz; CDCl₃) 13.44, 20.27, 22.10, 28.33, 30.55, 31.90, 33.57, 40.95, 48.12, 85.02, 117.88, 120.09, 122.08, 125.27, 125.37, 126.65, 126.98, 127.92, 128.70, 130.12, 132.08, 135.55, 143.65, 147.78, 147.98, 160.04 ppm.
(5aR15bS) 1,5,5,7a,10-pentamethyl-3-(p-tolyl)-5,5a,6,7,7a,15b-hexahydro-3H-pyrazolo[4",3":5,6"]pyrano[4',3':5,6"]thiochromeno[2,3-\text{b}]quinoline (5n):

Isolated Yield (1.3 g, 89 %) as yellow crystals, mp 236-238 °C; \( \nu_{\text{max}}/\text{cm}^{-1} = 3033.95, 2950.81, 2920.92, 1608.16, 1515.93, 1390.42, 1327.19, 1105.03, 817.96, 756.88; \delta_{\text{H}} \) (400 MHz, CDCl3) 1.26 (s, 3H, C(5)CH3), 1.48 (s, 3H, C(5)CH3), 1.64 (s, 3H, C(7a)H), 1.98-2.03 (m, 4H, C(6) & C(7)CH2), 2.29 (s, 3H, C(1)CH3), 2.33 (s, 3H, C(41)CH3), 2.40 (m, 1H, C(5a)H), 2.77 (s, 3H, C(10)CH3), 3.70 (d, 1H, J = 8.4 Hz, C(15b)H), 6.39 (s, 1H, C(15)H), 7.25-7.79 (m, 8H, C(Ar)H) ppm; \delta_{\text{C}} \) (100 MHz; CDCl3) 12.88, 13.31, 17.89, 20.68, 20.95, 21.05, 22.09, 28.29, 30.24, 31.85, 33.58, 41.13, 47.87, 84.43, 93.82, 120.31, 121.10, 122.23, 125.58, 126.11, 126.72, 129.43, 129.46, 129.72, 132.88, 135.08, 135.86, 138.17, 142.76, 146.54, 147.09, 156.76 ppm.

(5aR15bS) 1,5,5,7a,10-pentamethyl-3-(4-nitrophenyl)-5,5a,6,7,7a,15b-hexahydro-3H-pyrazolo[4",3":5,6"]pyrano[4',3':5,6"]thiochromeno[2,3-\text{b}]quinoline (5r):

Isolated Yield (1.4 g, 86 %) as yellow crystals, mp 248-250 °C; \( \nu_{\text{max}}/\text{cm}^{-1} = 3119.95, 2947.44, 2917.86, 1595.17, 1511.41, 1392.17, 1336.60, 1106.03, 851.67, 750.97, 511.18; \delta_{\text{H}} \) (400 MHz, CDCl3) 1.29 (s, 3H, C(5)CH3), 1.65 (s, 3H, C(7a)H), 2.01-2.06 (m, 4H, C(6) & C(7)CH2), 2.31 (s, 3H, C(1)CH3), 2.40-2.45 (m, 1H, C(5a)H), 2.77 (s, 3H, C(10)CH3), 3.71 (d, 1H, J = 7.2 Hz, C(15b)H), 6.34 (s, 1H, C(15)H), 7.28-8.32 (m, 8H, Ar -H) ppm; \delta_{\text{C}} \) (100 MHz; CDCl3) 13.41, 17.87, 19.10, 20.85, 22.05, 23.33, 28.38, 30.22, 31.81, 33.54, 40.95, 47.78, 48.96, 85.81, 95.49, 117.68, 118.79, 122.39, 124.76, 125.01, 125.71, 125.87, 126.68, 132.90, 135.91, 142.16, 143.97, 146.31, 149.68 ppm; m/z (ESI) 538.7 [M + H+].
1.6 Single crystal X-Ray data

Figure 3: ORTEP view of the molecule 5a.

Figure 4: The packing arrangement of molecules 5a.
<table>
<thead>
<tr>
<th><strong>Table 1 Crystal and experimental data of 5a</strong></th>
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<tr>
<td><strong>CCDC No</strong></td>
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<tr>
<td><strong>Crystal description</strong></td>
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<td><strong>Radiation, Wavelength</strong></td>
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<td><strong>Unit cell dimensions</strong></td>
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<td><strong>Space group</strong></td>
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<tr>
<td><strong>Unit cell volume</strong></td>
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<tr>
<td><strong>No. of molecules per unit cell, Z</strong></td>
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<tr>
<td><strong>Absorption coefficient(μ)</strong></td>
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<td><strong>F (000)</strong></td>
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<tr>
<td><strong>θ range for entire data collection</strong></td>
</tr>
<tr>
<td><strong>Reflections collected / unique</strong></td>
</tr>
<tr>
<td><strong>Reflections observed [I &gt; 2σ(I)]</strong></td>
</tr>
<tr>
<td><strong>No. of parameters refined</strong></td>
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<tr>
<td><strong>Final R</strong></td>
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<tr>
<td><strong>wR(F$^2$)</strong></td>
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<tr>
<td><strong>Goodness-of-fit</strong></td>
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<td><strong>(Δ/σ)$_{max}$ in the final cycle</strong></td>
</tr>
<tr>
<td><strong>Final residual electron density</strong></td>
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</table>
1.7 2D NMR experiments: NOE and Cosy for 5a

NOE for 5a
Cosy for 5a
1.8 $^1$H NMR, $^{13}$C NMR, Mass and IR Spectral Data

$^1$H NMR spectrum of compound 3a
APT spectrum of compound 3a
ESI-MS of compound 3a

FT-IR spectrum of compound 3a
$^1$H NMR spectrum of compound 5a
$^{13}$C NMR spectrum of compound 5a
DEPT-135 spectrum of compound 5a
ESI-MS of compound 5a

FT-IR spectrum of compound 5a
$^1$H NMR spectrum of compound 5b
APT spectrum of compound 5b
FT-IR spectrum of compound 5b

FT-IR spectrum of compound 5d
$^1$H NMR spectrum of compound 5d
$^1$H NMR spectrum of compound 5i
APT spectrum of compound 5i
ESI-MS of compound 5i

FT-IR spectrum of compound 5i
$^1$H NMR spectrum of compound 5k
FT-IR spectrum of compound 5k

FT-IR spectrum of compound 5n
The image shows a NMR spectrum of compound 5n. The spectrum is labeled with peaks at various chemical shifts, indicating the presence of hydrogen nuclei at different positions within the compound's structure.
APT spectrum of compound 5n
**1H NMR spectrum of compound 5r**
APT spectrum of compound 5r
ESI-MS of compound 5r

FT-IR spectrum of compound 5r