Inverse Electron Demand Diels–Alder Reactions of Heterodienes Catalyzed by Potassium Hydrogen Sulfate: Diastereoselective, One-Pot Synthesis of Pyranobenzopyrans, Furanobenzopyrans and Tetrahydroquinolines Derivatives

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Abstract: Potassium hydrogen sulfate catalyzes the one-pot three components coupling of aldehydes, anilines, and electron rich dienes, such as dihydropyran, dihydropyran, ethyl vinyl ether, and cyclopentadiene. With o-hydroxybenzaldehyde, the reaction probably proceeds through the formation of o-quinonemethide, which subsequently undergoes cycloaddition with cyclic and acyclic enol ethers leading to the formation of respective chromanes. However, in case of benzaldehydes with no o-hydroxy group, the imine formed acts as the heterodiene and leads to the formation of tetrahydroquinolines.

Keywords: heterodienes, potassium hydrogen sulfate, pyranobenzopyrans, furanobenzopyrans, tetrahydroquinolines

Nitrogen and oxygen containing heterocycles are ubiquitous in nature and display a wide variety of interesting biological properties. Among the numerous oxygen heterocycles, chromenes (2H-1 benzopyran), chromans (3,4-dihydro-2H-1-benzopyrans), and furanobenzopyrans, which are found in various natural products such as lycorine, haemanthamine, and chelidonine alkaloids.

The classical Diels–Alder reaction, a [4+2] cycloaddition of a diene and dienophile to generate a six membered carbocyclic system, in its modified form can be used to generate nitrogen or oxygen containing six-membered systems by the use of appropriate heterodiene or heterodienophile. However, instead of starting with preformed diene the in situ formation of diene is preferred. This one-pot procedure is especially useful when the diene is unstable and is difficult to purify either by distillation or chromatography. Lewis acids such as lanthanide triflates, Yb(OTf)3, Sc(OTf)3, BF3· OEt2, and GdCl3 were found to catalyze this reaction. However most of these reactions suffer from various disadvantages such as, more than stoichiometric amount of Lewis acid is needed due to strong coordination of it with the heteroatoms, longer reaction time, high cost and use of only aprotic solvents under anhydrous conditions. Also these reactions cannot be performed in one-pot because the amines and water that are present during imine formation can decompose or deactivate these Lewis acids. However to the best of our knowledge there is no report of the use of KHSO4 as catalyst for this type of reactions. The catalyst is inexpensive, mild, and does not require the maintenance of anhydrous conditions.

Treatment of salicylaldehyde, amine, and dihydropyran in the presence of KHSO4 in methanol at room temperature gave an inseparable mixture of linearly cis fused pyranochromanes 3 and 4 with high diastereoselectivity in favor of 3 (Scheme 1). The stereochemistry of the product 3 was assigned based on the coupling constant values and NOE studies. The cis fusion of the tetrahydropyran ring in compound 3 was determined from the coupling constant of 2.5 Hz between H4 and H5. Along with a coupling constant between H3 and H6 of 1.8 Hz and the presence of NOE between H6 and H3 and H3 and H4 proved that H6 is cis to H4. From the coupling constant value and absence of NOE between H5 and H3 and H3 and H4 in compound 4 it is concluded that H6 is trans to H4. Reactions were also performed with substituted anilines and the results are given in Table 1.

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Table 1  Synthesis of Pyrano and Furobenzopyrans

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<thead>
<tr>
<th>Entry</th>
<th>Amine</th>
<th>Dienophile</th>
<th>Product(^a)</th>
<th>Time (min)</th>
<th>Yield(^b) (%)</th>
<th>Product Ratio (^c)</th>
</tr>
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<tbody>
<tr>
<td>a</td>
<td>NH(_2)</td>
<td></td>
<td></td>
<td>50</td>
<td>61</td>
<td>98:2(^d)</td>
</tr>
<tr>
<td>b</td>
<td>NH(_2)</td>
<td></td>
<td></td>
<td>50</td>
<td>50</td>
<td>97:3(^d)</td>
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<tr>
<td>c</td>
<td>NH(_2)</td>
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<td></td>
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<td>71</td>
<td>98:2(^d)</td>
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<tr>
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<td>NH(_2)</td>
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<td>30</td>
<td>60</td>
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<tr>
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<td>77:23</td>
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<tr>
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<td>NH(_2)</td>
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<td></td>
<td>30</td>
<td>80</td>
<td>75:25</td>
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</table>
Similarly when dihydrofuran was treated with salicylaldehyde and amine in the presence of KHSO$_4$ in methanol at room temperature, a mixture of linearly cis fused furanobenzopyrans was obtained in good yield (Scheme 1). The diastereoselectivity, however in this case was moderate and the isomers were separated by column chromatography. From the coupling constant value and a similar NOE study as was done for pyranochromanes, the cis fusion of the furan ring was proven.

When the acyclic dienophile, ethylvinylether was used in the above procedure the corresponding adducts 2-ethoxy-4-N-arylaminobenzopyrans 3g-i and 4g-i were obtained as a separable mixture of diastereomers (Scheme 2). The diastereomers were isolated by column chromatography and the stereochemistry of the products was arrived at from the $^1$H NMR spectroscopy based on the chemical shift and coupling constant values.

One pot cycloaddition of 2,3-dihydropyran with imines generated in situ from aldehydes having no o-hydroxy group was performed in the presence of KHSO$_4$ (Scheme 4). A diastereomeric mixture of the corresponding pyranoquinolines was obtained. The pyran ring is cis

<table>
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<tr>
<th>Entry</th>
<th>Amine</th>
<th>Dienophile</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
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<td>NH$_2$</td>
<td>OEt</td>
<td>3g,4g</td>
<td>70</td>
<td>45</td>
<td>42:58</td>
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<tr>
<td>h</td>
<td>NH$_2$</td>
<td>OEt</td>
<td>3h,4h</td>
<td>60</td>
<td>50</td>
<td>40:60</td>
</tr>
<tr>
<td>i</td>
<td>NH$_2$</td>
<td>OEt</td>
<td>3i,4i</td>
<td>60</td>
<td>50</td>
<td>39:61</td>
</tr>
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</table>

Table 1 Synthesis of Pyrano and Furobenzopyrans (continued)

*a All the products were characterized by IR, NMR, and mass spectroscopy and elemental analysis.
*b The yield is based on isolation by column chromatography.
*c The product ratio is based on isolation by column chromatography.
*d The product ratio is based on $^1$H NMR of product mixture.

Scheme 1

Synthesis 2004, No. 6, 949–959 © Thieme Stuttgart · New York
fused and the stereochemistry of the products was established based on the coupling constant values. In isomer 5c, $J(H_{4a}-H_{5})$ is 4.5 Hz and is significantly smaller and typical for a gauche conformation. This orientation is present in both conformers of the configuration having a cis orientation of the pyran ring and phenyl group. The $J(H_{4a}-H_{5})$ value of 10.6 Hz in isomer 6c is appropriate and indicative of anti reciprocal orientation of protons $H_{4a}$ and $H_{5}$. Similarly with 2,3-dihydrofuran the corresponding furoquinolines were obtained as a mixture of diastereomers with cis fused ring junction.

Cyclopentaquinolines were synthesized by three component coupling reaction of aldehyde, aniline with cyclopentadiene (Scheme 5, Table 2). Imines derived from phenylglyoxal are generally unstable at higher temperatures and are difficult to purify either by distillation or by column chromatography so the one-pot coupling of phenylglyoxal, aniline and cyclopentadiene was attempted successfully (Table 2). In the case of ortho-hydroxy benzaldehyde the reaction probably proceeds through the intermediate formation of o-quinonemethides from the in situ generated imine 3j. A plausible mechanism for the formation of o-quinonemethide, 3k is given in Scheme 3. The o-quinonemethide formed acts as oxadiene and subsequently adds to 2,3-dihydropyran or 2,3-dihydrofuran giving the pyrano or furano benzopyrans. However with aldehydes having no ortho hydroxy group, reaction takes alternative path in which case the imine formed acts as a azadiene giving the pyrano and furoquinolines.

In summary, we have shown for the first time that the salt, KHSO$_4$ can catalyze the one-pot coupling of various aldehydes, amines, and dieneophiles (both cyclic and acyclic) giving the cycloadducts. The catalyst is mild, inexpensive, and easily available and also offers several advantages including shorter reaction times, cleaner reactions as well as simple experimental and isolation procedures, which makes it useful and attractive for the synthesis of chromanes and tetrahydroquinolines.
### Table 2  Synthesis of Tetrahydroquinolines

<table>
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<th>No</th>
<th>Amine</th>
<th>Aldehyde</th>
<th>Dienophile</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>Product Ratio</th>
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<tbody>
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<td>60</td>
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<tr>
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<td>60</td>
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<tr>
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<td>26:73</td>
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<td>60</td>
<td>40</td>
<td>35:65</td>
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<tr>
<td>f</td>
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<td>![Product Image]</td>
<td>75</td>
<td>44</td>
<td>–</td>
</tr>
<tr>
<td>g</td>
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<td>Cl</td>
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<td>75</td>
<td>40</td>
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</table>
Mass spectra were recorded on Varian VG 70-70H mass spectrometer. Analytical TLC was performed on precoated sheets of silica gel G of 0.25 mm thickness containing PF 254 indicator (Merck, Darmstadt). Column chromatography was performed with silica gel (60–120 mesh, S.d Fine, Boisar). IR spectra were recorded as solids in KBr pellets on a Perkin-Elmer FTIR spectrometer. ¹H NMR spectra were recorded on a Bruker spectrometer using TMS as internal standard. ¹³C NMR spectra were recorded on 300, 400, and 500 MHz spectrometer in CDCl₃ and chemical shifts are given relative to the solvent peak. The enol ether used was brought from Lancaster. The procedure does not require dry solvent or an inert atmosphere. All the products obtained were purified by column chromatography using silica gel (Merck, 100–200 mesh).

**Preparation of Pyrano and Furanobenzopyran; General Procedure**

A mixture of o-hydroxybenzaldehyde (4 mmol), aniline (4.8 mmol), dihydropyran or dihydrofuran (10 mmol) and KHSO₄ (0.21 g, 40 mol%) in MeOH (10 mL) was stirred at ambient temperature for the appropriate time. After completion of the reaction, as indicated by TLC monitoring, the excess MeOH was distilled off and the reaction mixture was diluted with water (20 mL) and extracted with CH₂Cl₂ (2 × 30 mL). The combined organic layers were dried over anhydrous Na₂SO₄, concentrated in vacuum and the resulting product was purified by column chromatography (EtOAc and petroleum ether, 1:9) to afford pure cis-fused pyrano and furanochromanes obtained as mixture of 3a-c and 4a-c or pure 3d-f or 4d-f.

**Table 2  Synthesis of Tetrahydroquinolines (continued)**

<table>
<thead>
<tr>
<th>No</th>
<th>Amine</th>
<th>Aldehyde</th>
<th>Dienophile</th>
<th>Product[a]</th>
<th>Time (min)</th>
<th>Yield[b] (%)</th>
<th>Product Ratio[c]</th>
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<td></td>
<td>60</td>
<td>42</td>
<td>–</td>
</tr>
</tbody>
</table>

[a] All the products were characterized by IR, NMR, and mass spectroscopy and elemental analysis.
[b] The yield is based on isolation by column chromatography.
[c] The product ratio is applicable for pyrano and furoquinolines only. In the case of cyclopentaquinolines only one isomer was observed.

Phenyl[3,4,4a,10a-Tetrahydro-2H,5H-pyrano[2,3-b]chromen-5-yl]amine (3a and 4a)

Yield: 0.80 g (60%).

3a

IR (KBr): 3347 (NH), 3029, 1485 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 1.57–1.67 (m, 2 H, H3), 1.87–1.96 (m, 2 H, H2), 3.08–3.15 (m, 1 H, H4), 3.82–3.95 (m, 3 H, including NH), 4.98 (d, 1 H, H6, J = 4.9 Hz), 5.89 (d, 1 H, H5, J = 5.4 Hz), 6.74, (d, 2 H, J = 7.8 Hz), 6.79 (t, 1 H, J = 7.6 Hz), 6.92–6.98 (m, 2 H), 7.19–7.27 (m, 2 H), 7.36 (d, 2 H, J = 7.8 Hz).

¹³C NMR (75 MHz, CDCl₃, proton decoupled): δ = 17.1, 24.2, 34.8, 50.9, 60.9, 96.4, 112.6, 113.2, 116.4, 118.1, 121.1, 126.7, 128.9, 129.5, 146.8, 153.1.

MS: m/z = 281 (M⁺).

Anal. Calcd for C₁₈H₁₉NO₂: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.68; H, 6.94; N, 4.76.

4a

¹H NMR: δ = 4.62 (d, 1 H, H6, J = 2.3 Hz), 5.65 (d, 1 H, H5, J = 5.4 Hz).

¹³C NMR: δ = 21.7, 24.3, 36.6, 53.3, 61.7, 94.6, 112.6, 117.0, 117.8, 118.0, 121.2, 121.8, 129.5, 130.4, 146.2, 153.0.

Yield: 0.60 g (50%).
3b
IR (KBr): 3360 (NH), 3022, 1485 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 1.18–1.62 (m, 4 H, H₂, H₂', H₃, H₃'), 2.18 (s, 3 H, CH₃), 2.38–2.44 (m, 1 H, H₄), 3.62 (br s overlapping, NH, 1 H), 3.62–3.69 (m, 1 H, H₁), 3.89–3.96 (m, 1 H, H¹'), 4.88 (d, 1 H, H₆, J = 1.8 Hz), 5.47 (d, 1 H, H₅, J = 2.5 Hz), 6.45 (d, 1 H, J = 8.3 Hz), 6.55 (d, 2 H, J = 8.3 Hz), 6.81–6.94 (m, 1 H), 6.95 (d, 2 H, J = 7.8 Hz), 7.11–7.17 (m, 1 H), 7.36 (d, 1 H, J = 7.8 Hz).

13C NMR (100 MHz, CDCl₃, proton decoupled): δ = 17.0, 20.4, 24.1, 34.7, 51.1, 60.9, 96.3, 112.7, 113.3, 116.2, 120.7, 126.7, 127.0, 128.9, 130.0, 144.5, 153.0.

MS: m/z = 295 (M⁺).

Anal. Calcd for C₁₈H₁₈BrNO₂: C, 60.01; H, 5.04; N, 3.89. Found: C, 76.62; H, 6.23; N, 5.36.

Phenyln(2,3,3a,9a-tetrahydro-4H-furo[2,3-b]chromen-4-yl)amine (4d)
Yield: 0.15 g (23%); colorless solid; mp 90–92 °C.

IR (KBr): 3363 (NH), 3022, 1454 cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ = 1.23–1.70 (m, 1 H, H₂), 2.12–2.19 (m, 1 H, H₂'), 2.89–2.96 (m, 1 H, H₃), 3.90 (br s, 1 H, NH overlapping), 3.91–3.98 (m, 1 H, H₁), 4.01–4.08 (m, 1 H, H¹'), 4.51 (br s, 1 H, H₅), 5.66 (d, 1 H, H₆, J = 4.7 Hz), 6.63 (d, 2 H, J = 8.0 Hz), 6.76 (t, 1 H, J = 7.3 Hz), 6.91–6.95 (m, 2 H), 7.16–7.24 (m, 4 H, H₃).

13C NMR (75 MHz, CDCl₃, proton decoupled): δ = 26.9, 43.3, 50.5, 67.8, 99.9, 113.0, 117.6, 118.1, 121.6, 121.7, 124.2, 129.5, 129.8, 146.3, 152.5.

MS: m/z = 267 (M⁺).


(4-Methylphenyl)2,3,3a,9a-tetrahydro-4H-furo[2,3-b]chromen-4-ylamine (3e)
Yield: 0.5 g (77%); colorless solid; mp 80–82 °C.

IR (KBr): 3386 (NH), 2976, 1482 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 1.56–1.64 (m, 1 H, H₂), 1.87–1.94 (m, 1 H, H₂'), 2.27 (s, 3 H, CH₃), 3.08–3.14 (m, 1 H, H₃), 3.70 (br s, 1 H, NH), 3.84 (q, 1 H, H₁, J = 8.6 Hz), 3.92 (dt, 1 H, H¹', J = 4, 8.9 Hz), 4.95 (d, 1 H, H₅, J = 4.6 Hz), 5.88 (d, 1 H, H₄, J = 5.7 Hz), 6.67 (d, 2 H, J = 8.5 Hz), 6.91–6.99 (m, 2 H), 7.04 (d, 2 H, J = 8.0 Hz), 7.20–7.29 (m, 1 H), 7.38 (d, 1 H, J = 7.4 Hz).

13C NMR (125 MHz, CDCl₃, proton decoupled): δ = 25.0, 24.0, 43.3, 49.1, 68.1, 102.4, 113.7, 117.2, 122.9, 124.8, 126.3, 127.7, 128.8, 130.1, 144.7, 153.0.

MS: m/z = 281 (M⁺).

Anal. Calcd for C₁₇H₁₈N₂O₂: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.64; H, 6.53; N, 4.76.

(4-Methylphenyl)2,3,3a,9a-tetrahydro-4H-furo[2,3-b]chromen-4-ylamine (4e)
Yield: 0.15 g (23%); colorless solid; mp 108–110 °C.

IR (KBr): 3384 (NH), 3022, 2948, 1486 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 1.65–1.73 (m, 1 H, H₂), 2.13–2.10 (m, 1 H, H₂'), 2.27 (s, 3 H, CH₃), 2.91–2.96 (m, 1 H, H₃), 3.79 (br s, 1 H, NH), 3.96 (q, 1 H, H₁, J = 8.0 Hz), 4.07 (dt, 1 H, H¹', J = 4, 8.6 Hz), 4.50 (d, 1 H, H₅, J = 2.2 Hz), 5.68 (d, 1 H, H₄, J = 5.1 Hz), 6.59 (d, 2 H, J = 8.0 Hz), 6.91–6.98 (m, 2 H), 7.04 (d, 2 H, J = 8.0 Hz), 7.24–7.26 (m, 2 H).

13C NMR (125 MHz, CDCl₃, proton decoupled): δ = 20.5, 27.0, 43.3, 50.8, 67.9, 100.0, 113.3, 117.6, 121.7, 124.9, 129.8, 129.9, 130.1, 144.1, 152.5.

MS: m/z = 281 (M⁺).

Anal. Calcd for C₁₇H₁₈N₂O₂: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.75; H, 6.46; N, 4.89.

(4-Bromophenyl)2,3,3a,9a-tetrahydro-4H-furo[2,3-b]chromen-4-ylamine (3f)
Yield: 0.15 g (23%); colorless solid; mp 107–109 °C.

IR (KBr): 3383 (NH), 3038, 1493 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 1.54–1.83 (m, 1 H, H₂), 1.90–1.94 (m, 1 H, H₂'), 3.08–3.14 (m, 1 H, H₃), 3.84–3.96 (m, 3 H, H₁, including NH), 4.93 (br s, 1 H, H₅), 5.90 (d, 1 H, H₄, J = 5.4 Hz), 6.63 (d, 2 H, J = 8.8 Hz), 6.94–7.00 (m, 2 H), 7.22–7.27 (m, 2 H), 7.31 (d, 2 H, J = 8.8 Hz).

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Synthesis 2004, No. 6, 949–959 © Thieme Stuttgart · New York
2.78 (m, 1 H), 2.21 (m, 1 H), 1.52 (m, 1 H).

(1) \( \text{H NMR (400 MHz, CDCl}_3 \):} \delta = 7.47–7.25 (m, 6 H), 7.10 (td, 1 H, \( J = 8.0, 1.1 \text{ Hz} \)), 6.80 (t, 1 H, \( J = 7.4 \text{ Hz} \)), 6.60 (d, 1 H, \( J = 8.0 \text{ Hz} \)), 5.28 (d, 1 H, \( J = 7.4 \text{ Hz} \)), 4.60 (d, 1 H, \( J = 2.8 \text{ Hz} \)), 3.76 (m, 3 H), 2.78 (m, 1 H), 2.21 (m, 1 H), 1.52 (m, 1 H).

(1) \( \text{C NMR (75 MHz, CDCl}_3 \):} \delta = 145.0, 142.2, 130.2, 128.7, 128.4, 127.7, 126.6, 127.7, 119.2, 115.0, 76.0, 66.9, 57.6, 45.8, 24.7.

MS: \( m/z = 251 \) (M⁺).

Anal. Calcd for \( \text{C}_9\text{H}_8\text{BrNO} \): C, 80.90; H, 7.67; N, 5.58. Found: C, 80.90; H, 7.66; N, 5.53.

4-Phenyl-2,3a,4,5,9b-hexahydropyran[3,2-c]quinoline (5a)

Yield: 0.510 g (60%); colorless solid; mp 115–117°C (Lit.25 117–118°C).

IR \( (\text{KBr}) \): 3345, 1484 cm⁻¹.

\( ^1\text{H NMR (300 MHz, CDCl}_3 \):} \delta = 7.47–7.25 (m, 6 H), 7.10 (td, 1 H, \( J = 8.0, 1.1 \text{ Hz} \)), 6.80 (t, 1 H, \( J = 7.4 \text{ Hz} \)), 6.60 (d, 1 H, \( J = 8.0 \text{ Hz} \)), 5.28 (d, 1 H, \( J = 7.4 \text{ Hz} \)), 4.60 (d, 1 H, \( J = 2.8 \text{ Hz} \)), 3.76 (m, 3 H), 2.78 (m, 1 H), 2.21 (m, 1 H), 1.52 (m, 1 H).

(1) \( \text{C NMR (75 MHz, CDCl}_3 \):} \delta = 145.0, 142.2, 130.2, 128.7, 128.4, 127.7, 126.6, 127.7, 119.2, 115.0, 76.0, 66.9, 57.6, 45.8, 24.7.

MS: \( m/z = 251 \) (M⁺).

Anal. Calcd for \( \text{C}_9\text{H}_8\text{BrNO} \): C, 80.90; H, 7.67; N, 5.58. Found: C, 80.90; H, 7.66; N, 5.53.

4-Phenyl-2,3a,4,5,9b-hexahydropyran[3,2-c]quinoline (6a)

Yield: 0.340 g (40%); viscous oil.

IR \( (\text{KBr}) \): 3324, 1483 cm⁻¹.

\( ^1\text{H NMR (300 MHz, CDCl}_3 \):} \delta = 7.47–7.25 (m, 6 H), 7.10 (td, 1 H, \( J = 8.0, 1.1 \text{ Hz} \)), 6.80 (t, 1 H, \( J = 7.4 \text{ Hz} \)), 6.60 (d, 1 H, \( J = 8.0 \text{ Hz} \)), 5.28 (d, 1 H, \( J = 7.4 \text{ Hz} \)), 4.60 (d, 1 H, \( J = 2.8 \text{ Hz} \)), 3.76 (m, 3 H), 2.78 (m, 1 H), 2.21 (m, 1 H), 1.52 (m, 1 H).

(1) \( \text{C NMR (75 MHz, CDCl}_3 \):} \delta = 145.5, 141.7, 131.3, 129.0, 128.7, 128.3, 128.2, 120.1, 118.4, 114.8, 76.3, 65.3, 57.8, 43.4, 28.9.

MS: \( m/z = 251 \) (M⁺).

Anal. Calcd for \( \text{C}_9\text{H}_8\text{BrNO} \): C, 81.28; H, 6.77; N, 5.58. Found: C, 80.92; H, 6.66; N, 5.31.

4-(4-Chlorophenyl)-2,3a,4,5,9b-hexahydropyran[3,2-c]quinoline (5b)

Yield: 0.450 g (65%); colorless solid; mp 129–130°C.

IR \( (\text{KBr}) \): 3321, 1486 cm⁻¹.

\( ^1\text{H NMR (300 MHz, CDCl}_3 \):} \delta = 7.42–7.32 (m, 5 H), 7.09 (t, 1 H, \( J = 8.5 \text{ Hz} \)), 6.82 (t, 1 H, \( J = 7.4 \text{ Hz} \)), 6.60 (d, 1 H, \( J = 8.0 \text{ Hz} \)), 5.26 (d, 1 H, \( J = 8.0 \text{ Hz} \)), 4.67 (d, 1 H, \( J = 2.9 \text{ Hz} \)), 4.01 (m, 1 H), 3.82–3.69 (m, 3 H), 2.76–2.71 (m, 1 H), 2.19–2.10 (m, 1 H), 1.53–1.46 (m, 1 H).

\( ^1\text{C NMR (75MHz, CDCl}_3 \):} \delta = 144.7, 140.7, 133.3, 130.2, 128.9, 128.5, 127.9, 122.7, 119.5, 115.1, 75.8, 66.8, 57.0, 45.7, 24.6.

MS: \( m/z = 287 \) (M⁺ + 2), 285 (M⁺).
9-Methoxy-5-phenyl-3a,4,5,9b-tetrahydro-2H-pyran[3,2-c]quinoline (6d)
Yield: 0.280 g (27%); viscous liquid.

IR (KBr): 3379, 2928, 1492, 1261 cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ = 7.35–7.27 (m, 5 H), 7.21 (s, 1 H), 6.76–6.66 (m, 1 H), 6.54 (d, 1 H, J = 8.1 Hz), 5.23 (d, 1 H, J = 5.4 Hz), 4.84 (s, 1 H), 3.91 (br s, 1 H, NH), 3.71 (d, 1 H, J = 11.3 Hz), 3.64–3.43 (m, 1 H), 1.98–1.81 (m, 1 H), 1.79–1.54 (m, 4 H).

13C NMR (75 MHz, CDCl₃): 144.1, 140.6, 133.0, 130.4, 129.1, 128.8, 128.5, 120.6, 117.4, 113.9, 74.5, 68.3, 53.9, 38.8, 24.0, 21.9.

MS: m/z = 299 (M⁺); 301 (M + 2).

Anal. Calcld for C₁₈H₁₈ClNO: C, 72.11; H, 6.05; N, 4.67. Found: C, 72.38; H, 5.98; N, 4.65.

4-(4-Chlorophenyl)-3a,4,5,9b-tetrahydro-2H-cyclopenta[c]quinoline (5f)
Yield: 0.398 g (40%); colorless solid; mp 141–142 °C.

IR (KBr): 3384, 1469 cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ = 7.80 (d, 1 H, J = 8.0 Hz), 7.38 (m, 5 H), 6.64 (m, 2 H), 5.81 (m, 1 H), 5.65 (m, 1 H), 4.75 (d, 1 H, J = 2.7 Hz), 4.48 (s, 1 H), 4.13 (d, 1 H, J = 8.4 Hz), 3.02 (m, 1 H), 2.58 (m, 1 H), 1.82 (m, 1 H).

13C NMR (75 MHz, CDCl₃): δ = 173.3, 150.2, 142.1, 135.5, 134.9, 130.6, 130.0, 128.6, 128.2, 127.1, 127.0, 126.8, 126.1, 116.2, 111.8, 56.4, 45.8, 45.3, 31.7.

MS: m/z = 291 (M⁺). Anal. Calcld for C₁₉H₁₇NO₂: C, 78.33; H, 5.88; N, 4.81. Found: C, 77.99; H, 5.86; N, 4.82.

6,7-Dimethyl-4-phenyl-3a,4,5,9b-tetrahydro-2H-cyclopenta[c]quinoline-8-carboxylic acid (5h)
Yield: 0.530 g (41%); colorless solid; mp 114–115 °C.

IR (KBr): 3384, 1469 cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ = 7.62–7.40 (m, 5 H), 6.97 (d, 1 H, J = 7.5 Hz), 6.71 (d, 1 H, J = 7.5 Hz), 5.98 (m, 1 H), 5.79 (s, 1 H), 4.65 (d, 1 H, J = 2.7 Hz), 4.42 (d, 1 H, J = 8.1 Hz), 3.80 (br s, 1 H, NH), 3.33–3.25 (m, 1 H), 2.96–2.87 (m, 1 H), 2.48 (s, 3 H), 2.26 (s, 3 H), 2.04–1.96 (m, 1 H).

13C NMR (75 MHz, CDCl₃): δ = 144.8, 142.9, 134.2, 130.6, 128.4, 127.6, 126.4, 124.4, 120.5, 119.7, 58.5, 46.1, 45.6, 32.0, 19.5, 17.0.


4-Benzoyl-3a,4,5,9b-tetrahydro-2H-cyclopenta[c]quinoline (5j)
Yield: 0.480 g (50%); colorless solid; mp 157–158 °C.

IR (KBr): 3384, 1681 cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ = 7.93–7.85 (m, 2 H), 7.60–7.47 (m, 3 H), 7.06–6.98 (m, 2 H), 6.76–6.67 (m, 2 H), 6.57 (t, 1 H), 5.36 (s, 1 H), 5.05 (d, 1 H, J = 3.1 Hz), 4.42 (br s, 1 H), 4.21 (d, 1 H, J = 8.9 Hz), 3.37–3.27 (m, 1 H), 2.47–2.38 (m, 1 H), 1.94–1.86 (m, 1 H).
$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 199.1, 143.9, 135.5, 133.9, 133.2, 129.5, 128.7, 128.0, 126.5, 125.8, 118.9, 115.8, 59.7, 46.9, 42.5, 31.4.

MS: $m/z = 275$ (M$^+$).

Anal. Calcd for C$_{19}$H$_{17}$NO: C, 82.88; H, 6.22; N, 5.08. Found: C, 83.69; H, 6.19; N, 5.16.

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References


(23) Wildman, W. C. Alkaloids 1986, 60, 289; and references therein.


