Fast and Efficient Synthesis of Pyrano[3,2-c]quinolines Catalyzed by Niobium(V) Chloride

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Abstract: A highly efficient two-step method for the synthesis of pyranoquinoline derivatives from imino-Diels–Alder reactions between aldimines and 3,4-dihydro-2H-pyran using niobium(V) chloride as catalyst under mild conditions is described.

Key words: Diels–Alder reactions, Lewis acids, catalysis, quinolines, Schiff bases

Pyranquinoline derivatives are an important class of natural products that are present in many alkaloids.1,2 They exhibit a wide spectrum of biological activity in various fields,3–6 such as psychotropic, antiallergenic, anti-inflammatory, and estrogenic activity. In addition, these derivatives are also found to possess a vast range of pharmacological activities.7 It is therefore not surprising that many synthetic methods have been developed for these compounds.8–11 Among the various methods, the imino-Diels–Alder reaction between N-arylimines and nucleophilic alkenes is probably one of the most powerful synthetic tools for the construction of nitrogen-containing six-membered heterocyclic compounds.

Generally, Lewis acids11–14 are employed to catalyze such reactions (there are also one-pot versions).15–18 However, several Lewis acids are deactivated or decomposed by nitrogen-containing substrates.19 Some of the Lewis acids are not easily available or are expensive, require longer reaction times, and form the products with poor yields. Therefore, developing simple and efficient synthetic methods for the preparation of this type of compound becomes more and more important.

Niobium(V) chloride, a low-cost and commercially available reagent, has been used by our group and other researchers as an effective catalyst for synthetic methodologies in a variety of reactions.20–32 In the present report a highly efficient two-step method for the synthesis of pyra-noquinolines using niobium(V) chloride as catalyst is described.

For the proposed studies, aldimines 3a–p were prepared in good yields by treatment of the respective aromatic aldehydes 1a–p with aniline (2) at room temperature (Table 1).

Table I Preparation of Aldimines 3a–p

<table>
<thead>
<tr>
<th>Starting aldehyde</th>
<th>R1</th>
<th>R2</th>
<th>R3</th>
<th>R4</th>
<th>R5</th>
<th>Time (h)</th>
<th>Aldimine</th>
<th>Yield (%)</th>
</tr>
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<tbody>
<tr>
<td>1a</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>72</td>
<td>3a</td>
<td>98</td>
</tr>
<tr>
<td>1b</td>
<td>H</td>
<td>H</td>
<td>Me</td>
<td>H</td>
<td>H</td>
<td>72</td>
<td>3b</td>
<td>95</td>
</tr>
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<td>1c</td>
<td>H</td>
<td>Me</td>
<td>H</td>
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<td>72</td>
<td>3c</td>
<td>98</td>
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<td>Me</td>
<td>H</td>
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<td>H</td>
<td>H</td>
<td>72</td>
<td>3d</td>
<td>96</td>
</tr>
<tr>
<td>1e</td>
<td>Me</td>
<td>H</td>
<td>Me</td>
<td>H</td>
<td>Me</td>
<td>72</td>
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<td>94</td>
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<tr>
<td>1f</td>
<td>H</td>
<td>NO2</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>96</td>
<td>3f</td>
<td>92</td>
</tr>
<tr>
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<td>H</td>
<td>H</td>
<td>H</td>
<td>96</td>
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<td>90</td>
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<td>1h</td>
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<td>NO2</td>
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<td>120</td>
<td>3h</td>
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<td>1i</td>
<td>H</td>
<td>OCH3</td>
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<td>120</td>
<td>3i</td>
<td>94</td>
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<td>H</td>
<td>Cl</td>
<td>H</td>
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<td>H</td>
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<td>H</td>
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<td>H</td>
<td>Me</td>
<td>96</td>
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<td>1n</td>
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<td>OMe</td>
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<td>OMe</td>
<td>H</td>
<td>120</td>
<td>3p</td>
<td>90</td>
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Scheme 1 Synthesis of pyranoquinoline derivatives from the imino-Diels–Alder reaction between aldimines 3a–p and 3,4-dihydro-2H-pyran (4) catalyzed by niobium(V) chloride.

Table 2 Niobium(V) Chloride Catalyzed Synthesis of Pyranoquinoline Derivatives 5a–p (endo) and 6a–p (exo)

<table>
<thead>
<tr>
<th>Aldimine</th>
<th>NbCl₅ (equiv)</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>Ratio 5a–p/6a–p (endo/exo)</th>
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</thead>
<tbody>
<tr>
<td>3a</td>
<td>0.500</td>
<td>1</td>
<td>92</td>
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<tr>
<td></td>
<td>0.250</td>
<td>5</td>
<td>89</td>
<td>44:56</td>
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<tr>
<td></td>
<td>0.125</td>
<td>15</td>
<td>90</td>
<td>33:67</td>
</tr>
<tr>
<td>3b</td>
<td>0.500</td>
<td>1</td>
<td>90</td>
<td>44:56</td>
</tr>
<tr>
<td></td>
<td>0.250</td>
<td>5</td>
<td>90</td>
<td>39:41</td>
</tr>
<tr>
<td></td>
<td>0.125</td>
<td>15</td>
<td>84</td>
<td>22:78</td>
</tr>
<tr>
<td>3c</td>
<td>0.500</td>
<td>1</td>
<td>85</td>
<td>31:69</td>
</tr>
<tr>
<td></td>
<td>0.250</td>
<td>5</td>
<td>85</td>
<td>31:69</td>
</tr>
<tr>
<td></td>
<td>0.125</td>
<td>15</td>
<td>81</td>
<td>22:78</td>
</tr>
<tr>
<td>3d</td>
<td>0.500</td>
<td>1</td>
<td>85</td>
<td>31:69</td>
</tr>
<tr>
<td></td>
<td>0.250</td>
<td>10</td>
<td>87</td>
<td>28:72</td>
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<tr>
<td></td>
<td>0.125</td>
<td>15</td>
<td>84</td>
<td>13:87</td>
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<tr>
<td>3e</td>
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<td>30</td>
<td>80</td>
<td>0:100</td>
</tr>
<tr>
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<td>0.250</td>
<td>80</td>
<td>81</td>
<td>0:100</td>
</tr>
<tr>
<td></td>
<td>0.125</td>
<td>150</td>
<td>75</td>
<td>0:100</td>
</tr>
<tr>
<td>3f</td>
<td>0.500</td>
<td>1</td>
<td>85</td>
<td>49:51</td>
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<tr>
<td></td>
<td>0.250</td>
<td>5</td>
<td>82</td>
<td>48:52</td>
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<td>10</td>
<td>82</td>
<td>43:57</td>
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<td>100</td>
<td>85</td>
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<td></td>
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<td>190</td>
<td>84</td>
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<td>60</td>
<td>72</td>
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<tr>
<td></td>
<td>0.125</td>
<td>150</td>
<td>73</td>
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</tr>
<tr>
<td>3j</td>
<td>0.500</td>
<td>1</td>
<td>89</td>
<td>40:60</td>
</tr>
<tr>
<td></td>
<td>0.250</td>
<td>5</td>
<td>90</td>
<td>42:58</td>
</tr>
<tr>
<td></td>
<td>0.125</td>
<td>15</td>
<td>86</td>
<td>34:66</td>
</tr>
<tr>
<td>3k</td>
<td>0.500</td>
<td>1</td>
<td>87</td>
<td>42:58</td>
</tr>
<tr>
<td></td>
<td>0.250</td>
<td>5</td>
<td>87</td>
<td>42:58</td>
</tr>
<tr>
<td></td>
<td>0.125</td>
<td>15</td>
<td>85</td>
<td>35:65</td>
</tr>
<tr>
<td>3l</td>
<td>0.500</td>
<td>1</td>
<td>83</td>
<td>40:60</td>
</tr>
<tr>
<td></td>
<td>0.250</td>
<td>5</td>
<td>84</td>
<td>44:56</td>
</tr>
<tr>
<td></td>
<td>0.125</td>
<td>15</td>
<td>80</td>
<td>35:65</td>
</tr>
<tr>
<td>3m</td>
<td>0.500</td>
<td>1</td>
<td>87</td>
<td>40:60</td>
</tr>
<tr>
<td></td>
<td>0.250</td>
<td>25</td>
<td>81</td>
<td>19:81</td>
</tr>
<tr>
<td></td>
<td>0.125</td>
<td>75</td>
<td>78</td>
<td>0:100</td>
</tr>
</tbody>
</table>

Imino-Diels–Alder reactions between aldimines 3a–p and 3,4-dihydro-2H-pyran (4) in the presence of niobium(V) chloride in acetonitrile at room temperature afforded the corresponding pyranoquinoline derivatives 5a–p and 6a–p in high yields. In most of the cases, a mixture of endo-isomers 5 and exo-isomers 6 were obtained (Scheme 1, Table 2).

All products were isolated and characterized by spectroscopic and spectrometric methods (¹H NMR, ¹³C NMR, IR, and mass spectra). The product ratios were determined by ¹H NMR analysis of the crude product. The relative stereochemistry of the Diels–Alder adducts was determined using the ¹H–¹H scalar coupling constant values between H1 and H2 (J₁,₂) and comparison with literature data. Adducts 5a–p (endo), show smaller coupling constants J₁,₂ (5.5–5.7 Hz), typical for a gauche conformation. This is consistent with an orientation where the pyran ring and the phenyl group are on the same side (Figure 1). In adducts 6a–p (exo), the coupling constants are significantly higher, J₁,₂ between 8.1 and 11.1 Hz, indicative of the anti orientation of H1/H2, which is only possible when the pyran ring and the phenyl group are on opposite sides of the quinoline ring.

As can be observed from Table 2, in all cases the reactions proceed smoothly to give the pyranoquinoline derivatives, which could be separated by column chromatography. Substitution on the aromatic ring has a remarkable influence on reactivity: methylated 3e or oxygenated 3p aldimines, for example, are less reactive. The use of a lower molar ratio of niobium(V) chloride leads to an enhancement of diastereoselectivity, although the required reaction times are longer.
As compared to other Lewis acids (e.g., InCl₃), the reaction was carried out using CDCl₃ as solvent and TMS as internal standard. IR spectra were measured with a Perkin Elmer Spectrum RX IFTIR System, and the most intense or representative bands are reported. ESI-MS were acquired on a high-resolution q-TOF. ESI-MS were also used to determine the molecular mass of the new compounds.

**Table 3** Comparison of Imino Diels-Alder Reactions of Aldimine 3a with 3,4-Dihydro-2H-pyran Catalyzed by Various Lewis Acids

<table>
<thead>
<tr>
<th>Lewis acid</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>Ratio endo/exo</th>
</tr>
</thead>
<tbody>
<tr>
<td>NbCl₅</td>
<td>1</td>
<td>92</td>
<td>44:56</td>
</tr>
<tr>
<td>InCl₃</td>
<td>30</td>
<td>80</td>
<td>41:59</td>
</tr>
<tr>
<td>LiBF₄</td>
<td>120</td>
<td>88</td>
<td>15:85</td>
</tr>
<tr>
<td>K10F₆</td>
<td>1020</td>
<td>86</td>
<td>42:58</td>
</tr>
</tbody>
</table>

In summary, this paper describes an efficient two-step method for the synthesis of pyranooquinoline derivatives from imino Diels-Alder reactions between aldmines and 3,4-dihydro-2H-pyran. This method is more effective, requiring shorter reaction times, giving in most cases better yields and good diastereoselectivity, especially with lower molar concentrations of niobium(V) chloride. These notable features make this procedure an useful and attractive process for the synthesis of fused pyrano[3,2-c]quinolines of biological importance.

NMR spectra were measured using a Bruker DRX 400 instrument (400 MHz for 1H NMR and 100 MHz for the 13C NMR proton-decoupled) using CDCl₃ as solvent and TMS as internal standard. IR spectra were measured with a Perkin Elmer Spectrum RX IFTIR System, and the most intense or representative bands are reported.

**Figure 1** Coupling constant values used for determining stereochemistry

A remarkable aspect of this work is the higher efficiency of niobium(V) chloride, as compared to other Lewis acid catalysts. The strong activation of the aldmine system exerted by niobium(V) chloride is demonstrated by the shorter reaction times required. Table 3 shows some examples comparing our results for aldmine 3a with literature data using other Lewis acids.

In summary, this paper describes an efficient two-step method for the synthesis of pyranooquinoline derivatives from imino Diels-Alder reactions between aldmines and 3,4-dihydro-2H-pyran using niobium(V) chloride as a catalyst. As compared to other Lewis acids (e.g., InCl₃), niobium(V) chloride is more effective, requiring shorter reaction times, giving in most cases better yields and good diastereoselectivity, especially with lower molar concentrations of niobium(V) chloride. These notable features make this procedure an useful and attractive process for the synthesis of fused pyrano[3,2-c]quinolines of biological importance.
**N-[(2-Nitrophenyl)methylene]aniline (3i)**

IR (film): 3056, 2926, 1616, 1565, 1487, 1442, 1272, 1190, 1052, 763 cm⁻¹.

H NMR (400 MHz, CDCl₃): δ = 8.90 (s, 1 H), 8.23 (dd, J₁ = 7.6 Hz, J₂ = 2.5 Hz, 1 H), 7.30–7.42 (m, 5 H), 7.21–7.27 (m, 3 H).

13C NMR (100 MHz, CDCl₃): δ = 156.8 (CH), 151.8 (C), 136.0 (C), 133.2 (CH), 132.1 (CH), 129.9 (CH), 129.2 (CH), 128.5 (CH), 127.1 (CH), 126.3 (CH), 121.0 (CH).

MS: m/z = 217 (M + 2)⁺, 215 (M⁺), 180, 152, 112, 104, 89, 77, 63, 51.

**N-[(2-Chlorophenyl)methylene]aniline (3j)**

IR (film): 3056, 2926, 1616, 1565, 1487, 1442, 1272, 1190, 1052, 763 cm⁻¹.

H NMR (400 MHz, CDCl₃): δ = 8.90 (s, 1 H), 8.23 (dd, J₁ = 7.6 Hz, J₂ = 2.5 Hz, 1 H), 7.30–7.42 (m, 5 H), 7.21–7.27 (m, 3 H).

13C NMR (100 MHz, CDCl₃): δ = 156.8 (CH), 151.8 (C), 136.0 (C), 133.2 (CH), 132.1 (CH), 129.9 (CH), 129.2 (CH), 128.5 (CH), 127.1 (CH), 126.3 (CH), 121.0 (CH).

MS: m/z = 217 (M + 2)⁺, 215 (M⁺), 180, 152, 112, 104, 89, 77, 63, 51.

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Synthesis 2008, No. 16, 2527–2536 © Thieme Stuttgart · New York
raco-(4aS,5S,10bS)-5-Phenyl-3,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (5a)14,45,46
IR (film): 3360, 2940, 2865, 1610, 1488, 1365, 1048 cm⁻¹.

rac-(4aS,5S,10bS)-5-(3-Methylphenyl)-3,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (5b)17
IR (film): 3360, 2940, 2865, 1610, 1488, 1365, 1048, 737 cm⁻¹.

rac-(4aS,5S,10bS)-5-(4-Methylphenyl)-3,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (5c)18

rac-(4aS,5S,10bS)-5-(5-Methylphenyl)-3,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (5d)
IR (film): 3374, 2940, 2865, 1607, 1488, 1365, 1088, 737 cm⁻¹.

rac-(4aS,5S,10bS)-5-(4-Methylphenyl)-3,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (6b)47
IR (film): 3328, 2942, 2850, 1611, 1486, 1366, 1080, 736 cm⁻¹.

rac-(4aS,5S,10bS)-5-(Methylphenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (6c)
IR (film): 3373, 2940, 2865, 1608, 1486, 1316, 1265, 1088, 736 cm⁻¹.

rac-(4aS,5S,10bS)-5-(4-Methylphenyl)-3,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (6d)47
IR (film): 3328, 2942, 2850, 1611, 1486, 1366, 1080, 736 cm⁻¹.

rac-(4aS,5S,10bS)-5-(4-Methylphenyl)-3,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (6e)
IR (film): 3373, 2940, 2865, 1608, 1486, 1316, 1265, 1088, 736 cm⁻¹.

rac-(4aS,5S,10bS)-5-(4-Methylphenyl)-3,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (6f)47
IR (film): 3328, 2942, 2850, 1611, 1486, 1366, 1080, 736 cm⁻¹.
rac-(4aS,5R,10bS)-5-(2-Methylphenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyra
ono[3,2-c]quinoline (6d)
IR (film): 3374, 2935, 2865, 1609, 1485, 1320, 1264, 1088, 736 cm⁻¹.

[1H NMR (400 MHz, CDCl₃):] \( \delta = 7.46 \) (dd, \( J = 4.4 \) Hz, 1 H), 7.28 (d, \( J = 7.6 \) Hz, 1 H), 7.23 (s, 3 H), 7.12 (t, \( J = 7.6 \) Hz, 1 H), 6.75 (t, \( J = 7.6 \) Hz, 1 H), 6.54 (d, \( J = 8.1 \) Hz, 1 H), 5.00 (d, \( J = 10.3 \) Hz, 1 H), 4.49 (d, \( J = 2.6 \) Hz, 1 H), 4.10 (d, \( J = 10.9 \) Hz, 1 H), 3.74 (td, \( J_1 = 10.9 \) Hz, \( J_2 = 1.9 \) Hz, 1 H), 2.50 (s, 3 H), 2.29 (m, 1 H), 1.88–1.66 (m, 2 H), 1.56 (m, 1 H), 1.43 (m, 1 H).

[13C NMR (100 MHz, CDCl₃):] \( \delta = 144.9 \) (C), 140.5 (C), 136.9 (C), 131.2 (CH), 131.1 (CH), 129.7 (CH), 128.2 (CH), 127.9 (CH), 126.9 (CH), 120.9 (C), 117.9 (CH), 114.5 (CH), 74.7 (CH), 68.4 (CH₃), 51.5 (CH), 38.1 (CH), 24.5 (CH₃), 23.3 (CH₃), 20.4 (CH₃).

MS: \( m/z = 279 \) (M⁺), 273, 267, 223, 201, 188, 97, 77, 51.


rac-(4aS,5S,10bS)-5-(3-Nitrophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyra
ono[3,2-c]quinoline (6g)
IR (film): 3399, 2950, 2857, 1606, 1528, 1349, 1087, 759 cm⁻¹.

[1H NMR (400 MHz, CDCl₃):] \( \delta = 8.32 \) (t, \( J = 2.0 \) Hz, 1 H), 8.16 (ddd, \( J_1 = 8.0 \) Hz, \( J_2 = 2.0 \) Hz, \( J_3 = 1.0 \) Hz, 1 H), 7.76 (d, \( J = 7.8 \) Hz, 1 H), 7.56 (dd, \( J_1 = 8.0 \) Hz, \( J_2 = 7.8 \) Hz, 1 H), 7.42 (d, \( J = 7.3 \) Hz, 1 H), 7.12 (dd, \( J = 7.8 \) Hz, \( J_2 = 7.3 \) Hz, 1 H), 6.84 (td, \( J = 7.3 \) Hz, \( J_2 = 0.8 \) Hz, 1 H), 6.67 (dd, \( J = 7.8 \) Hz, \( J_2 = 1.0 \) Hz, 1 H), 5.34 (d, \( J = 5.6 \) Hz, 1 H), 4.79 (d, \( J = 2.3 \) Hz, 1 H), 3.94 (NH, 1 H), 3.59 (m, 1 H), 3.43 (d, \( J = 11.4 \) Hz, \( J_2 = 2.5 \) Hz, 1 H), 2.20 (m, 1 H), 1.46–1.63 (m, 2 H), 1.44 (m, 1 H), 1.26 (m, 1 H).

[13C NMR (100 MHz, CDCl₃):] \( \delta = 148.4 \) (C), 144.5 (C), 143.5 (C), 133.0 (C), 129.4 (CH), 124.3 (CH), 127.6 (CH), 122.6 (CH), 121.7 (CH), 119.9 (C), 119.1 (CH), 114.9 (CH), 72.4 (CH), 60.6 (CH₂), 58.8 (CH), 38.8 (CH), 25.26 (CH₂), 17.9 (CH₃).

MS: \( m/z = 310 \) (M⁺), 266, 251, 205, 179, 130, 115, 97, 77, 65, 51.

rac-(4aS,5R,10bS)-5-(3-Nitrophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyra
ono[3,2-c]quinoline (6f)
IR (film): 3386, 2943, 2828, 1608, 1524, 1482, 1344, 1059, 1795 cm⁻¹.

[1H NMR (400 MHz, CDCl₃):] \( \delta = 8.31 \) (t, \( J = 1.8 \) Hz, 1 H), 8.18 (ddd, \( J_1 = 8.1 \) Hz, \( J_2 = 2.3 \) Hz, \( J_3 = 1.0 \) Hz, 1 H), 7.76 (d, \( J = 7.8 \) Hz, \( J_1 = 8.0 \) Hz, \( J_2 = 7.8 \) Hz, 1 H), 7.23 (dd, \( J_1 = 7.5 \) Hz, \( J_2 = 1.4 \) Hz, 1 H), 7.12 (ddd, \( J_1 = 8.1 \) Hz, \( J_2 = 1.4 \) Hz, 1 H), 6.75 (td, \( J_1 = 7.5 \) Hz, \( J_2 = 1.0 \) Hz, 1 H), 6.57 (d, \( J = 8.1 \) Hz, 1 H), 4.83 (d, \( J = 10.6 \) Hz, 1 H), 4.40 (d, \( J = 2.8 \) Hz, 1 H), 4.11 (m, 1 H), 3.74 (td, \( J_1 = 11.5 \) Hz, \( J_2 = 2.0 \) Hz, 1 H), 2.11 (m, 1 H), 1.84 (m, 1 H), 1.70 (tt, \( J_1 = 13.8 \) Hz, \( J_2 = 5.0 \) Hz, 1 H), 1.40 (m, 2 H).

[13C NMR (100 MHz, CDCl₃):] \( \delta = 148.6 \) (C), 144.8 (C), 144.7 (C), 134.0 (CH), 130.9 (CH), 129.6 (CH), 129.5 (CH), 123.0 (CH), 122.7 (CH), 120.7 (CH), 118.2 (CH), 114.4 (CH), 74.1 (CH), 68.5 (CH), 54.5 (CH), 39.0 (CH), 24.1 (CH₂), 22.1 (CH₂).

MS: \( m/z = 310 \) (M⁺), 266, 251, 205, 179, 130, 115, 97, 77, 65, 51.

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rac-(4aS,5R,10bS)-5-(6-Nitro-1,3-benzodioxol-5-yl)-3,4,4a,5,6,10b-hexahydro-2H-pyraño[3,2-c]quinoline (6h)

IR (film): 3375, 2930, 1729, 1479, 1331, 1271, 1036, 737 cm⁻¹.

rac-(4aS,5S,10bS)-5-(4-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyraño[3,2-c]quinoline (5j)

IR (film): 3387, 2940, 1486, 1276, 1085, 1014, 750 cm⁻¹.

rac-(4aS,5R,10bS)-5-(4-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyraño[3,2-c]quinoline (6j)

IR (film): 3380, 2925, 2851, 1486, 1272, 1050, 913, 750 cm⁻¹.

rac-(4aS,5R,10bS)-5-(3-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyraño[3,2-c]quinoline (5k)

MS: m/z = 309 (M⁺), 279, 265, 225, 233, 218, 188, 121, 91, 77, 51.


rac-(4aS,5S,10bS)-5-(4-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyraño[3,2-c]quinoline (5j)

IR (film): 3387, 2940, 1486, 1276, 1085, 1014, 750 cm⁻¹.

rac-(4aS,5R,10bS)-5-(4-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyraño[3,2-c]quinoline (6j)

IR (film): 3380, 2925, 2851, 1486, 1272, 1050, 913, 750 cm⁻¹.

rac-(4aS,5R,10bS)-5-(3-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyraño[3,2-c]quinoline (5k)

IR (film): 3314, 2941, 2865, 1607, 1476, 1264, 1071, 737 cm⁻¹.

rac-(4aS,5S,10bS)-5-(3-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyraño[3,2-c]quinoline (6k)

IR (film): 3356, 2925, 2839, 1609, 1490, 1368, 1260, 1053, 749 cm⁻¹.

rac-(4aS,5R,10bS)-5-(3-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyraño[3,2-c]quinoline (6k)

IR (film): 3356, 2925, 2839, 1609, 1490, 1368, 1260, 1053, 749 cm⁻¹.
Hz, 1 H), 2.04 (m, 1 H), 1.81 (tt, J1 = 13.1 Hz, J2 = 11.6 Hz, J3 = 4.3 Hz, 1 H), 1.66 (tt, J1 = 13.1 Hz, J2 = 4.5 Hz, 1 H), 1.46 (m, 1 H), 1.36 (m, 1 H).

1H NMR (400 MHz, CDCl3): δ = 7.69 (d, J1 = 7.3 Hz, J2 = 1.0 Hz, 1 H), 7.44 (dt, J1 = 7.3 Hz, J2 = 1.5 Hz, 1 H), 7.30 (td, J1 = 7.6 Hz, J2 = 1.5 Hz, 1 H), 7.24 (td, J1 = 7.6 Hz, J2 = 1.8 Hz, 1 H), 7.16 (td, J1 = 7.3 Hz, J2 = 1.5 Hz, 1 H), 6.82 (td, J1 = 7.3 Hz, J2 = 1.0 Hz, 1 H), 6.62 (dd, J1 = 8.1 Hz, J2 = 1.0 Hz, 1 H), 5.34 (d, J = 5.6 Hz, 1 H), 5.07 (d, J = 2.3 Hz, 1 H), 3.60 (m, 1 H), 3.43 (td, J1 = 11.5 Hz, J2 = 2.5 Hz, 1 H), 2.41 (m, 1 H), 1.52–1.60 (m, 2 H), 1.44 (m, 1 H), 1.22 (m, 1 H).

IR (film): 3375, 2939, 2864, 1605, 1479, 1317, 1089, 928, 754 cm–1.

MS: m/z = 301 (M + 2)+, 299 (M)+, 254, 240, 228, 144, 130, 115, 102, 89, 77, 65, 51.

HRMS (ESI): m/z [M + H] calculated for C14H15CIN0: 300.1149; found: 300.1154.

1H NMR (400 MHz, CDCl3): δ = 7.79 (dd, J1 = 7.6 Hz, J2 = 1.8 Hz, 2 H), 7.44 (dt, J1 = 7.3 Hz, J2 = 1.0 Hz, 1 H), 7.40 (dd, J1 = 7.6 Hz, J2 = 1.5 Hz, 1 H), 7.30 (td, J1 = 7.6 Hz, J2 = 1.5 Hz, 1 H), 7.24 (td, J1 = 7.6 Hz, J2 = 1.8 Hz, 1 H), 7.16 (td, J1 = 7.3 Hz, J2 = 1.5 Hz, 1 H), 6.82 (td, J1 = 7.3 Hz, J2 = 1.0 Hz, 1 H), 6.62 (dd, J1 = 8.1 Hz, J2 = 1.0 Hz, 1 H), 5.34 (d, J = 5.6 Hz, 1 H), 5.07 (d, J = 2.3 Hz, 1 H), 3.60 (m, 1 H), 3.43 (td, J1 = 11.5 Hz, J2 = 2.5 Hz, 1 H), 2.41 (m, 1 H), 1.52–1.60 (m, 2 H), 1.44 (m, 1 H), 1.22 (m, 1 H).

IR (film): 3363, 2939, 2839, 1609, 1464, 1264, 1083, 928, 736 cm–1.


MS: m/z = 301 (M + 2)+, 299 (M)+, 254, 240, 228, 144, 130, 115, 102, 91, 77, 51.

1H NMR (400 MHz, CDCl3): δ = 7.92 (dd, J1 = 7.3 Hz, J2 = 1.3 Hz, 1 H), 7.29 (dd, J1 = 8.1 Hz, J2 = 7.6 Hz, 1 H), 7.09 (ddddd, J1 = 8.1 Hz, J2 = 7.3 Hz, J3 = 1.5 Hz, J4 = 0.7 Hz, 1 H), 6.99 (d, J = 7.6 Hz, 1 H), 6.98 (s, 1 H), 6.84 (ddd, J1 = 8.2 Hz, J2 = 2.5 Hz, J3 = 1.0 Hz, 1 H), 6.79 (td, J1 = 7.3 Hz, J2 = 1.3 Hz, 1 H), 6.60 (dd, J1 = 8.1 Hz, J2 = 1.0 Hz, 1 H), 5.32 (d, J = 5.6 Hz, 1 H), 4.66 (d, J = 2.3 Hz, 1 H), 3.82 (s, 3 H), 3.58 (ddt, J1 = 11.6 Hz, J2 = 4.0 Hz, J3 = 1.7 Hz, 1 H), 3.43 (td, J1 = 11.6 Hz, J2 = 2.5 Hz, 1 H), 2.17 (m, 1 H), 1.47–1.57 (m, 2 H), 1.43 (m, 1 H), 1.35 (m, 1 H).

IR (film): 3370, 2940, 2853, 1608, 1488, 1265, 1154, 1071, 736 cm–1.


IR (film): 3375, 2939, 2837, 1609, 1487, 1253, 1155, 1039, 750 cm–1.


1H NMR (400 MHz, CDCl3): δ = 7.78 (t, J = 7.6 Hz, 1 H), 7.21 (dt, J1 = 7.1 Hz, J2 = 1.3 Hz, 1 H), 7.09 (ddddd, J1 = 7.8 Hz, J2 = 7.3 Hz, J3 = 1.4 Hz, J4 = 0.8 Hz, 1 H), 6.92 (d, J = 8.6 Hz, 2 H), 6.79 (td, J1 = 7.3 Hz, J2 = 1.0 Hz, 1 H), 6.59 (dd, J1 = 8.1 Hz, J2 = 1.0 Hz, 1 H), 5.32 (d, J = 5.6 Hz, 1 H), 4.65 (d, J = 2.5 Hz, 1 H), 3.82 (s, 3 H), 3.59 (m, 1 H), 3.43 (td, J1 = 11.4 Hz, J2 = 2.6 Hz, 1 H), 2.12 (m, 1 H), 1.42–1.60 (m, 3 H), 1.34 (m, 1 H).


1H NMR (400 MHz, CDCl3): δ = 7.47 (dd, J1 = 7.6 Hz, J2 = 2.5 Hz, 1 H), 6.87 (d, J1 = 7.6 Hz, J2 = 2.5 Hz, 1 H), 6.71 (d, J1 = 7.3 Hz, J2 = 1.5 Hz, 1 H), 6.52 (d, J1 = 7.8 Hz, J2 = 1.5 Hz, 1 H), 6.45 (d, J1 = 7.7 Hz, J2 = 1.0 Hz, 1 H), 5.98 (s, 1 H), 4.43 (d, J = 3.3 Hz, 1 H), 4.05 (NH, 1 H), 3.98 (m, 1 H), 3.67 (td, J1 = 11.5 Hz, J2 = 2.7 Hz, 1 H), 2.20 (m, 1 H), 1.92 (m, 1 H), 1.70 (m, 1 H), 1.38–1.51 (m, 2 H).

IR (film): 3362, 2939, 2839, 1609, 1464, 1264, 1083, 928, 736 cm–1.

IR (film): 3373, 2939, 2837, 1609, 1487, 1253, 1155, 1039, 750 cm–1.

HRMS (ESI): m/z [M + H] calculated for C14H15CINO2: 298.1255; found: 298.1254.
rac-(4αS,5R,10bS)-5-(2-Methoxyphenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (50)\(^{31}\)

IR (film): 3373, 2937, 2865, 1602, 1488, 1241, 1090, 753 cm\(^{-1}\).

HRMS (ESI): m/z [M + H] calcd for C\(_{21}\)H\(_{26}\)NO\(_4\): 356.1856; found: 355.1862.

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