Synthesis of 2,3-Disubstituted Carbazoles, Benzo[c]carbazoles, and Phenanthrenes Through FeCl₃-Mediated Cyclization of Triene Frameworks

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Abstract A facile synthesis of 2,3-disubstituted carbazoles through electrocyclization of 2,3-divinylindoles using FeCl₃ in DMF at reflux is reported. The methodology was found to be applicable for smooth transformation of 3-aryl-2-vinylindole as well as 2-styrylbiphenyl into the respective benzo[c]carbazole and phenanthrene.

Key words carbazoles, electrocyclization, Iron(III) chloride, 2,3-divinylindole, benzocarbazole, phenanthrene

Over the years, our research group has exploited electrocyclization of 1-phenylsulfonyl-2,3-divinylindoles as a key step for the syntheses of quinocarbazoles,¹⁻³ staurosporine aglycone,¹³¹ⁱ and also for accessing a wide variety of substituted carbazoles.² We have also accomplished a Lewis acid mediated electrocyclization strategy for accessing calothrixin B and its derivatives.³ In all these reports, the thermal electrocyclization followed by aromatization of 2,3-divinylindoles could be performed using 10% Pd/C in xylenes at reflux to give the respective carbazoles in good yields. However, the inconsistent quality of 10% Pd-C, difficulty in the aromatization of intermediate dihydrocarbazole, coupled with prolonged reaction time at elevated temperature, makes this protocol unsuitable for performing the reaction on a multi-gram scale. We sought to develop an alternative procedure that avoids the use Pd/C and also overcomes the disadvantages noted above. Hence, in a further continuation of our work on the synthesis of carbazoles,¹⁻³ we report herein the synthesis of a wide variety of carbazole derivatives 2 through FeCl₃-mediated⁴,⁵ electrocyclization as a key step. The synthesis of benzo[c]carbazoles 3 could also be achieved from the respective 2-vinyl-3-arylindoles (Scheme 1).

Scheme 1 Synthesis of carbazoles 2 and 3 using FeCl₃-mediated cyclization

To realize this objective, the required 2,3-divinylindoles 1a–v were prepared (Scheme 2) from the respective phosphonate esters.⁶ As a representative case, thermal electrocyclization of 1a in the presence of anhydrous FeCl₃ in anhydrous DMF at reflux for 6h afforded 2-nitrophenyl carbazole 2a in 74% yield (Scheme 3).

To our delight, FeCl₃-mediated electrocyclization of a wide variety of 2,3-divinylindoles could be smoothly performed to afford the respective carbazoles.
The structures of various types of divinylindoles employed and the resulting carbazoles obtained are presented in Table 1. The reaction of 1-phenylsulfonyl-2,3-divinylindoles 1b–d with FeCl3 in anhydrous DMF at reflux afforded carbazoles 2b–d in 71–78% yields, respectively (entry 1). The FeCl3-mediated electrolycization could be smoothly performed with 2,3-divinylindoles 1e–k to afford the expected 4-methylcarbazoles 2e–k in good yields (entry 2). However, the reaction was found to proceed slowly with 2,3-divinylindole 1l/1m, containing a phenyl or p-anisyl unit, yielding the respective carbazole 2l and 2m in 43% and 38% yields (entry 3). The isolation of compounds 2l and 2m in low yields confirms that the electron-donating nature of the aryl unit present in 2,3-divinylindole 1l or 1m is not conducive for the FeCl3-mediated electrolycization reaction. As expected, the 2,3-divinylindoles 1n–q, containing a cyanovinyl unit, upon reaction with 50 mol% FeCl3 in anhydrous 1,2-dichloroethane (DCE) at room temperature or at reflux furnished 2-aryl benzo[c]carbazoles 3a–d in good yields (Scheme 4).

Subsequently, 3-bromo-2-methylindole, upon benzylic bromination followed by hydrolysis and MnO2 oxidation of corresponding alcohol, led to 3-bromoindole-2-carboxaldehyde 7. The Suzuki coupling of bromo compound 7 with veratryl boronic acid using Pd(PPh3)4 in the presence of K3PO4 in DME reflux afforded 2-formyl-3-arylindole 8 as a colorless solid in 87% yield. Indole aldehyde 8, upon Wittig reaction with (carbethoxymethylene)triphenylphosphorane...
anhydrous CH₂Cl₂ at room temperature, led to 3-veratryl-2-vinylindole 9 in 93% yield. The 2-vinyl ester 9, upon cyclization using 50 mol% FeCl₃ in anhydrous 1,2-DCE reflux, furnished benzo[c]carbazole 10 in a moderate yield (Scheme 5). Attempts to improve the yield of the benzo[c]carbazole 10 either by increasing the number of equivalents of FeCl₃ or by prolonging the reaction time was not found to be useful.

Table 1  FeCl₃-Mediated Electrocyclization of 1-Phenylsulfonyl-2,3-divinylindoles 1b–v

<table>
<thead>
<tr>
<th>Entry</th>
<th>2,3-divinylindole a</th>
<th>Carbazole</th>
<th>Yield (%) b</th>
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</thead>
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<tr>
<td>1</td>
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<td><img src="image2.png" alt="Image" /></td>
<td>71 73 78</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td>78 75 76 78 73 71 70</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
<td>43 38</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td>79 82 81 78</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9.png" alt="Image" /></td>
<td><img src="image10.png" alt="Image" /></td>
<td>78 72</td>
</tr>
<tr>
<td>6</td>
<td><img src="image11.png" alt="Image" /></td>
<td><img src="image12.png" alt="Image" /></td>
<td>80 72 74</td>
</tr>
</tbody>
</table>

* Reactions were carried out using 1a–v (1 equiv), FeCl₃ (0.5–2 equiv) in DMF (10 mL) at reflux for 3–12 h.

* Isolated yield by column chromatography.
Next, the Wittig–Horner reaction of phosphonate ester 11 with 2-bromo-veratraldehyde 12 in the presence of t-BuOK in toluene at reflux afforded vinyl compound 13. As expected, the Suzuki coupling of 13 with boronic acids furnished the required triene compounds 14a and 14b in 85% and 91% yields. The triene framework of 14a and 14b underwent cyclization upon interaction with 50 mol% FeCl₃ in anhydrous 1,2-DCE at reflux to give 9-arylphenanthrenes 15a and 15b in 62% and 65% yields, respectively (Scheme 6).

In summary, we have achieved the syntheses of 2,3-disubstituted carbazoles, benzo[cb]carbazoles, and phenanthrene derivatives by employing FeCl₃-mediated cyclization of the corresponding triene frameworks. For the first time, the FeCl₃-mediated cyclization of two vinylic carbons as well as phenyl and vinylic carbons could be achieved in acceptable yields.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1609936.

References and Notes


For FeCl₃-mediated cyclization of indole derivatives, see:


(7) Representative procedure for 3a: To a stirred solution of 2,3-divinyl compound 1a (0.2 mmol) in anhydrous DMF (10 mL) at r.t., anhydrous FeCl₃ (0.4 mmol) was added and the reaction mixture was heated at reflux for 6 h. After completion of the reaction (monitored by TLC), the mixture was poured over crushed ice (50 g) containing conc. HCl (3 mL). The crude product was extracted with ethyl acetate (3 × 20 mL) and the combined organic layer was dried (Na₂SO₄). Removal of solvent followed by column chromatographic purification (1% EtOAc/hexane) afforded 2a (74 mg, 74%) as a colorless solid. Mp 220–222 °C; 1H NMR (300 MHz, CDCl₃): δ = 8.59 (d, J = 8.4 Hz, 1 H), 8.46–8.40 (m, 4 H), 7.97 (d, J = 8.4 Hz, 1 H), 7.73 (d, J = 7.8 Hz, 2 H), 7.60 (t, J = 7.2 Hz, 1 H), 7.42–7.32 (m, 7 H), 7.24–7.17 (m, 2 H), 7.00 (d, J = 8.4 Hz, 2 H), 3.84 (s, 3 H) ppm. 13C NMR (75 MHz, CDCl₃): δ = 159.2, 140.7, 138.2, 137.9, 136.1, 133.8, 133.0, 131.3, 129.8, 129.1, 129.0, 127.6, 127.1, 127.0, 126.3, 126.1, 124.8, 124.4, 123.7, 122.1, 119.0, 115.6, 115.3, 113.8, 55.4 ppm. Dept-135 (75 MHz, CDCl₃): δ = 133.8, 131.3, 129.0, 127.5, 127.1, 126.3, 126.0, 124.8, 124.4, 123.7, 122.0, 115.6, 115.3, 113.7, 55.3 ppm. HRMS (EI): m/z [M⁺] calcd for C₂₉H₂₁NO₃S: 463.1242; found: 463.1220.

Representative procedure for 15a: To a stirred solution of 2-styrylphenyl compound biphenyl vinylene 1a (0.1 g, 0.26 mmol) in anhydrous 1,2-DCE (10 mL) at r.t., anhydrous FeCl₃ (21 mg, 0.13 mmol) was added and the reaction mixture was stirred at reflux for 3 h. Following a similar work up procedure to that for 6a afforded 2,3-dimethoxyphenanthrene 15a (62 mg, 62%) as a colorless solid. Mp 170–172 °C; 1H NMR (300 MHz, CDCl₃): δ = 8.63 (d, J = 8.4 Hz, 1 H), 8.06 (s, 1 H), 7.97 (d, J = 8.4 Hz, 1 H), 7.68–7.62 (m, 2 H), 7.50 (t, J = 7.2 Hz, 1 H), 7.27 (d, J = 3.3 Hz, 1 H), 7.12–7.02 (m, 3 H), 4.17 (s, 3 H), 4.06 (s, 3 H), 4.00 (s, 3 H), 3.93 (s, 3 H) ppm. 13C NMR (75 MHz, CDCl₃): δ = 149.6, 149.3, 148.6, 148.3, 136.9, 133.7, 130.5, 130.0, 127.0, 126.7, 126.5, 126.0, 125.5, 124.4, 122.4, 122.3, 113.5, 111.0, 108.2, 103.2, 56.1, 56.0, 55.9, 55.8 ppm. HRMS (EI): m/z [M⁺] calcd for C₁₉H₁₆O₂: 274.1154; found: 274.1155.