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,² staurosporine aglycone,¹ and also for accessing a wide variety of substituted carbazoles.¹ 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-arylidynes (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.

EWG = CO₂Et, CN

EWG/Ar

SO₂Ph

EWG/Ar

SO₂Ph

R1

R3

R2

40–88%

reflux

24 examples

38–82%

R1 = H (62%)

R1 = OMe (65%)

EWG = CO₂Et, CN

EWG/Ar

SO₂Ph

EWG/Ar

SO₂Ph

R1

R3

R2

reflux

38–82%

22 examples

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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 electrocyclization 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 electrocyclization 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-bromomidoled-2-aldehyde 7. The Suzuki coupling of bromo compound 7 with veratryl boronic acid using Pd(PPh₃)₄ in the presence of K₂PO₄ 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 in

The synthesis of benzo[c]carbazole analogues employing the FeCl₃-mediated cyclization was then initiated. Accordingly, Wittig–Horner reaction of phosphonate ester 4 with substituted benzaldehydes in the presence of NaH in tetrahydrofuran (THF) at 0°C for 3 h afforded 3-bromo-2-arylindoles 5a and 5b. As expected, the Suzuki coupling of bromo compound 5a/5b with aryl boronic acid using Pd(PPh₃)₄ and Na₂CO₃ in 1,2-dimethoxyethane (DME) at reflux furnished 3-aryl-2-styrylindoles 6a–d as colorless solids in good yields. As expected, the reaction of 6a–d 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-bromomidoled-2-aldehyde 7. The Suzuki coupling of bromo compound 7 with veratryl boronic acid using Pd(PPh₃)₄ in the presence of K₂PO₄ 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 in
anhydrous CH₂Cl₂ at room temperature, led to 3-veratryl-2-vinylindole 9 in 93% yield. The 2-vinyl ester 9, upon cyclization using 50mol% 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.

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

| Entry | 2,3-divinylindole* | Carbazole | Yield (%)b |
|-------|-------------------|-----------|------------|
| 1     | ![Image](image1)   | ![Image](image2) | 71/73/78   |
| 2     | ![Image](image3)   | ![Image](image4) | 78/75/76   |
| 3     | ![Image](image5)   | ![Image](image6) | 43/38/78   |
| 4     | ![Image](image7)   | ![Image](image8) | 79/82/78   |
| 5     | ![Image](image9)   | ![Image](image10) | 78/72/72   |
| 6     | ![Image](image11)  | ![Image](image12) | 80/72/74   |

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

b 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 frameworks 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[c]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.

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Representative procedure for 6a: To a stirred solution of 3-aryl-biphenyl compound biphenyl vinylene (0.2 mmol) in anhydrous DMF (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 1a, 2a, 3a as a colorless solid. Mp 170–172 ºC; 1H NMR (300 MHz, CDCl₃): δ = 8.69 (d, J = 8.4 Hz, 1 H), 8.46–8.40 (m, 2 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⁺] cacld for C₂₀H₁₄NO₃S: 374.1518; found: 374.1515.

Representative procedure for 15a: To a stirred solution of 2-styrlybenzophenone (62 mg, 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 ºC; 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), 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⁺] cacld for C₂₂H₁₉NO₅: 374.1518; found: 374.1515.