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Transition Metal Complexes in Organic Synthesis – 44.[1]

Iron-Mediated Synthesis of Indolo[2,3-*b*]carbazole

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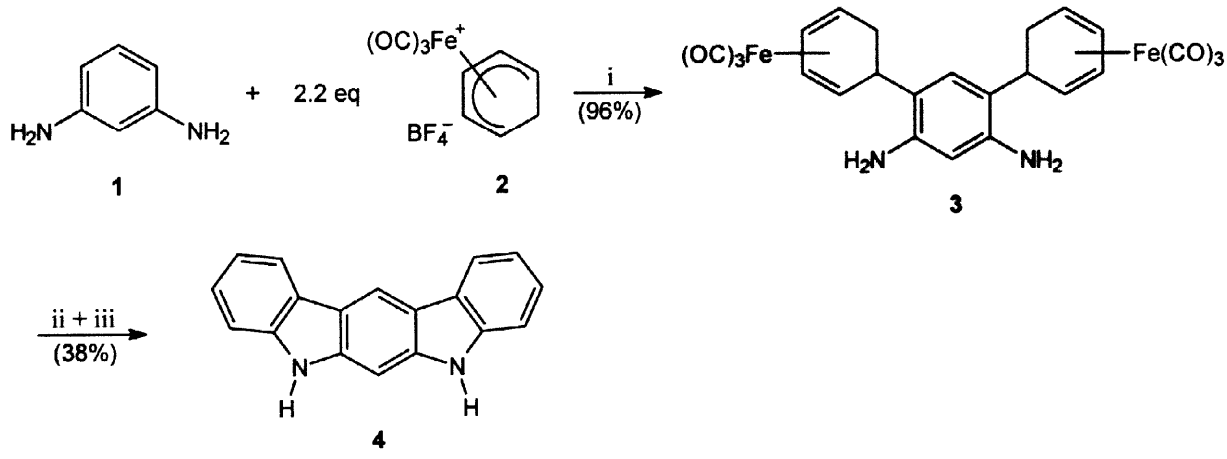
Abstract: A straightforward two-step synthesis of indolo[2,3-*b*]carbazole using a double iron-mediated arylamine cyclization as the key-step is described.

The chemistry of 9*H*-carbazole alkaloids has been extensively investigated and several novel procedures for their synthesis have been developed because of their biological activities and physical properties.[2] All of the five possible isomeric indolocarbazoles were prepared.[3-5] We described a direct synthesis of 9*H*-carbazole derivatives by a consecutive iron-mediated C–C and C–N bond formation, which was applied to the synthesis of many biologically active carbazoles.[6] The crucial steps of this procedure are an *ortho*-selective electrophilic substitution of an arylamine by a tricarbonyliron-complexed cyclohexadienyl cation followed by oxidative cyclization of the resulting substituted tricarbonyl(η^4-cyclohexa-1,3-diene)iron complex with concomitant aromatization to the 9*H*-carbazole (iron-mediated arylamine cyclization).[7] In the present paper we report the first example of an extension of this methodology to a double electrophilic substitution and subsequent double iron-mediated arylamine cyclization. Thus, indolo[2,3-*b*]carbazole, previously obtained by two different syntheses,[3,4] is easily prepared starting from *m*-phenylenediamine (**1**) and the iron complex salt **2** (Scheme).



Scheme. *Reagents and conditions*: i) MeCN, 25°C, 16 h; ii) 3 eq. iodine, pyridine, 25°C, 1 h; iii) 3 eq. iodine, pyridine, 25°C, 18 h and 55°C, 6 h.

Reaction of *m*-phenylenediamine (**1**) with 2.2 equivalents of the iron complex salt **2** provides the dinuclear iron complex **3** as a 1:1 mixture of two diastereoisomers (m.p. 156-158°C). This optimized procedure for double electrophilic substitution at **1** proceeds almost quantitatively without any trace of monosubstitution product.[8]

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The arylamine cyclization with concomitant aromatization and demetalation of the intermediate tricarbonyliron-complexed 4a,9a-dihydro-9*H*-carbazole represents a direct access to the 9*H*-carbazoles and was in most cases achieved by oxidation with very active manganese dioxide[6,7] or with ferricenium hexafluorophosphate/sodium carbonate.[9] However, in case of the double iron-mediated arylamine cyclization required for the transformation of complex **3** into indolo[2,3-*b*]carbazole (**4**) these reagents led exclusively to decomposition. An alternative reagent for this oxidative cyclization is iodine in pyridine.[8,10] We developed a protocol for the conversion of complex **3** into **4** by two consecutive oxidations. Treatment of the dinuclear complex **3** with 3 equivalents of iodine in pyridine for 1 h at room temperature followed by filtration over silica gel (hexane/ether, 2:1) and further oxidation with additional 3 equivalents of iodine in pyridine first for 18 h at room temperature and then for 6 h at 55°C afforded indolo[2,3-*b*]carbazole (**4**) in 38% yield.[11]

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11. **Indolo[2,3-*b*]carbazole**: colorless solid, m.p. 348-350°C; UV (EtOH): λ = 209, 238, 265, 274, 303, 343, 351, 360 nm; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.13 (t, J = 7.6, 2 H), 7.31 (t, J = 7.6, 2 H), 7.37 (s, 1 H), 7.42 (d, J = 7.6, 2 H), 8.13 (d, J = 7.6, 2 H), 8.78 (s, 1 H), 11.04 (s, 2 H); ^{13}C NMR and DEPT (125 MHz, DMSO-d_6): δ = 90.66 (CH), 110.21 (2 CH), 111.15 (CH), 117.19 (2 C), 118.18 (2 CH), 119.26 (2 CH), 123.22 (2 C), 124.36 (2 CH), 140.18 (2 C), 140.30 (2 C); MS (170°C): *m/z* (%) = 256 (M^+, 100), 255 (46), 128 (31); HRMS: calcd. for $C_{18}H_{12}N_2$ (M^+): 256.1000, found: 256.0991.