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A New, Simple, Efficient Synthesis of Benzo[b]carbazoles and Indeno[1,2-b]indoles

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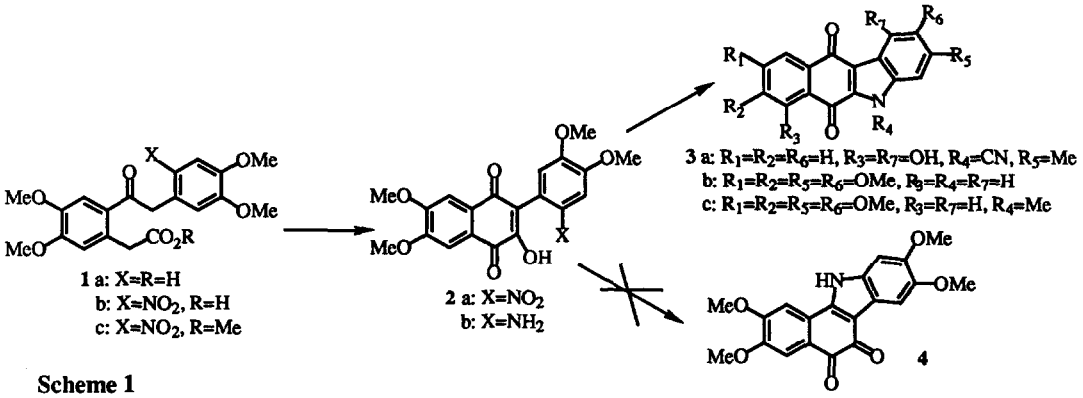
Abstract. A new, efficient synthesis of benzo[b]carbazoles and indeno[1,2-b]indoles from nitrophenylacetylphenylacetic acids and nitrobenzylphthalides respectively is described.

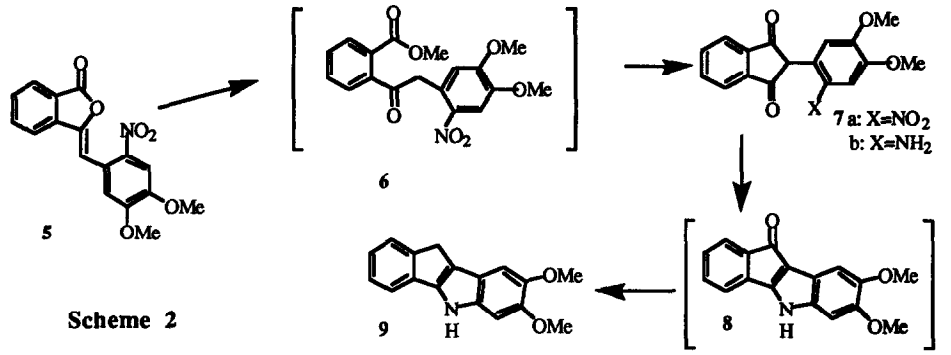
Benzo[b]carbazoles such as prekinamycin (**3a**) are members of the important kinamycin family of antibiotics.[1] Indeno[1,2-b]indoles (**9**) have recently been named as possible inhibitors of radical chain reactions in disease processes,[2] some members of this family being among the most potent antioxidants known.[3] Benzo[b]carbazoles **3**[4,5,6] and indenoindoles **9**[3,7] have previously been obtained by complex or specific synthetic sequences in only poor to moderate yields. We now describe the synthesis of this families from the readily available ketoesters **1c** and **6**.



Scheme 1

Nitroketoester **1c** was easily prepared by nitration of ketoacid **1a**[8] followed by esterification of nitroketoacid **1b**. Treatment of nitroketoester **1c** with aq. sodium hydroxide in refluxing methanol for an hour afforded nitroquinone **2a**[9] in 98% yield, probably by mixed Claisen condensation followed by oxidation of the cyclized product. When nitroquinone **2a** was reduced with $NaBH_4$ in isopropanol at r.t., a 92% yield of a red compound of m.p. 296-298°C (methanol) was obtained. Its spectroscopic data[9] were compatible with both **3b** and **4**, which would have resulted from amino attack at C_2 and C_4 respectively. The α-diketo structure **4** was ruled out on the basis of the *N*-methyl derivative of the red compound did not rearrange to *N*-methylindole under basic conditions.[10]

On the other hand, indenoindole **9**[9] (m.p. 208-210°C (methanol)) was satisfactorily prepared by treatment of nitrolactone **5**[11] with sodium methoxide in methanol (95% yield) followed by catalytic hydrogenation of the resulting indandione **7a**[9] (96% yield) via indenoindole **8**, which is presumed to have resulted from aminoindandione **7b** by intramolecular condensation of the amino and carbonyl groups.



Scheme 2

We are now pursuing the application of this simple, efficient synthetic route to natural benzo[b]carbazoles such as the antibiotic prekinamycin (**3a**) and pyrido[4,3-b]carbazoles, some of which (e.g. ellipticine) show pronounced anticancer activity.[12]

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9. All new compounds gave satisfactory analytical and spectroscopic data. Compound **3b**: IR ($\nu_{máx}$, cm^{-1}, KBr): 3280 (N-H), 1630 (C=O). ^1H NMR (∂, ppm, DMSO): 3.84 (s, 6H, 2x-OCH_3), 3.94 (s, 6H, 2x-OCH_3), 6.93 (s, 1H, Ar-H), 7.50 (s, 2H, 2xAr-H), 7.52 (s, 1H, Ar-H) and 12.79 (s, 1H, N-H). MS (m/z, %): 367 (M^+, 100), 353 (46), 351 (26), 338 (24) and 309 (16). Compound **9**: IR ($\nu_{máx}$, cm^{-1}, KBr): 3460 (N-H). ^1H NMR (∂, ppm, Cl_3CD): 3.67 (s, 2H, -CH_2-), 3.93 (s, 3H, -OCH_3), 3.96 (s, 3H, -OCH_3), 6.94 (s, 1H, Ar-H), 7.08 (s, 1H, Ar-H), 7.17 (d, J=7.7 Hz, 1H, Ar-H), 7.31 (d, J=7.7 Hz, 1H, Ar-H), 7.39 (d, J=7.2 Hz, 1H, Ar-H), 7.50 (d, J=7.2 Hz, 1H, Ar-H) and 8.17 (bs, 1H, N-H). MS (m/z, %): 265 (M^+, 100), 250 (74), 221 (23), 207 (32).
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11. Phthalide **5** was prepared by heating at 240 °C a mixture of phthalic anhydride, 2-nitro-3,4-dimethoxyphenylacetic acid and sodium acetate, as described by Weiss, R. *Org. Synth. Coll. Vol II*, **1943**, 61.
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