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An unexpected rearrangement of 3-unsubstituted-2-acyl substituted indole phenylhydrazones. A new method for benz[*c*]β-carboline synthesis

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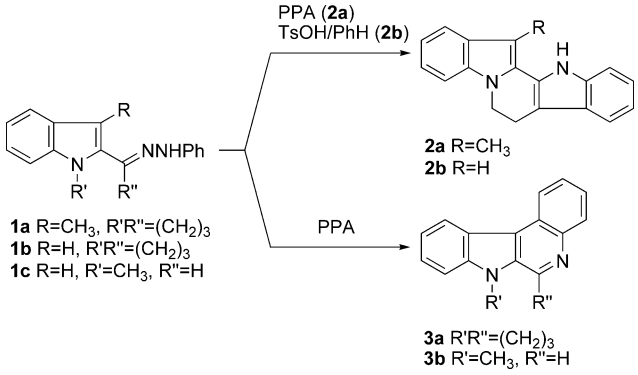
Abstract—A new type of rearrangement of 3-unsubstituted-2-acyl substituted indole phenylhydrazones with formation of a quinoline ring under acid catalysed conditions was observed.

Earlier, for the synthesis of homofascaplysin C, an alkaloid of the marine sponge *Fascaplysinopsis bergquist* sp., we used 10-methyl-7,8-dihydropyrido[1,2-*a*]indol-9(6*H*)-one phenylhydrazone **1a**. It was transformed into the expected 6,7-dihydro-13-methyl-12*H*-pyrido[1,2-*a*:3,4-*b*′]diindole **2a** by Fischer's rearrangement catalysed by polyphosphoric acid (PPA) treatment.[1]

For the synthesis of the alkaloid fascaplysin, 7,8-dihydropyrido[1,2-*a*]indol-9(6*H*)-one phenylhydrazone **1b** was used as the starting material. However, the unexpected rearrangement product 7,8-dihydro-6*H*-benzo[*b*]indolo[3,2,1-*de*]-1,5-naphthyridine **3a**[2] was obtained in 78% yield after treatment of **1b** with PPA (Scheme 1). This reaction is the first example of quinoline ring formation by rearrangement of a phenylhydrazone. At the same time, the product of Fischer's rearrangement, 6,7-dihydro-12*H*-pyrido[1,2-*a*:3,4-*b*′]diindole **2b**, was obtained under the action of TsOH in benzene according to Murakami's method,[3] in 52% yield. The spectral data of **2b** are identical to those from the literature.[4]

This reaction with 1-methyl-1*H*-indole-2-carbaldehyde phenylhydrazone **1c** suggests that this reaction is typical for phenylhydrazone derivatives of 3-unsubstituted-2-acyl substituted indoles. 7-Methyl-7*H*-indolo[2,3-*c*]-quinoline **3b**[5] was obtained in 91% yield.



Scheme 1.

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Keywords: Fischer's rearrangement; Phenylhydrazones; Rearrangement; β-Carbolines.

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References and notes

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2. 7,8-Dihydro-6*H*-benzo[*b*]indolo[3,2,1-*de*]-1,5-naphthyridine **3a**: A mixture of 110 mg (0.4 mmol) 7,8-dihydropyrido[1,2-*a*]indol-9(6H)-one phenylhydrazone **1b** and 4 mL polyphosphoric acid was heated to 120 °C with stirring. The reaction mixture was cooled to room temperature and cold sodium carbonate solution was added carefully. The resulting precipitate was filtered, washed with water and dried to give **3a** (82 mg, 78%) as a yellow precipitate. Mp 179–181 °C (EtOH–H_2O, 5:1). ^{1}H NMR ($CDCl_3$–CF_3COOH) δ: 8.91 (d, $J = 8.3$ Hz, 1H); 8.72 (d, $J = 8.3$ Hz, 1H); 8.17 (d, $J = 8.5$ Hz, 1H); 8.60–7.90 (m, 3H); 7.81 (d, $J = 8.5$ Hz, 1H); 7.67 (t, $J = 7.7$ Hz, 1H); 4.60 (t, $J = 6.0$ Hz, 2H); 3.67 (t, $J = 6.2$ Hz, 2H); 2.73 (q, $J = 6.1$,Hz, 2H). ^{13}C NMR ($CDCl_3$–CF_3COOH) δ: 144.0; 143.4; 132.5; 131.8; 129.9; 129.5; 128.5; 125.1; 124.8; 124.4; 123.2; 123.3; 120.9; 120.8; 111.2; 41.0; 24.4; 21.4. MS m/z 258 (M^+, 100); 243; 229; 190; 176; 151; 128; 114.
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5. 7-Methyl-7*H*-indolo[2,3-*c*]quinoline **3b**: The phenylhydrazone **1c** (500 mg, 2.09 mmol) was treated with polyphosphoric acid (15 mL) as described above to give the compound **3b** (424 mg, 91% yield) as a pale yellow precipitate. Mp 110–112 °C (CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 9.28 (s, 1H); 8.72 (d, $J = 8.0$ Hz, 1H); 8.60 (d, $J = 8.0$ Hz, 1H); 8.30 (d, $J = 8.2$ Hz, 1H); 7.74 (t, $J = 7.2$ Hz, 1H); 7.69–7.60 (m, 3H); 7.44 (t, $J = 7.4$ Hz, 1H); 4.12 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 143.0; 140.7; 136.2; 133.5; 130.5; 127.2; 127.0; 125.7; 124.7; 123.5; 123.3; 122.0; 121.0; 120.6; 110.0; 29.7. MS m/z 232 (M^+, 100); 217; 203; 190; 176; 163; 151; 140; 128; 116.