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Synthesis and rearrangement of benzopirano[4,3-*c*]pirazole derivatives

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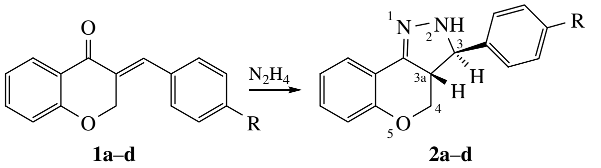
Benzopirano[4,3-*c*]pirazole derivatives have been synthesised, and their intramolecular disproportionation and stereochemical features have been discussed.

Benzopyrano[4,3-*c*]pyrazole derivatives **2a**–**d** were synthesised by condensation of arylidenechromanones **1a**–**d** with hydrazine (Scheme 1). The structures of these compounds were studied by ^{1}H NMR spectroscopy.† The ^{1}H NMR spectra of benzopyrano[4,3-*c*]pyrazoles **2a**–**d** contain signals of protons in the 3-, 3a- and 4-positions of the heterocycle with appropriate multiplicity, peaks of aromatic protons and, in the case of **2b**, a singlet of the methoxy group.

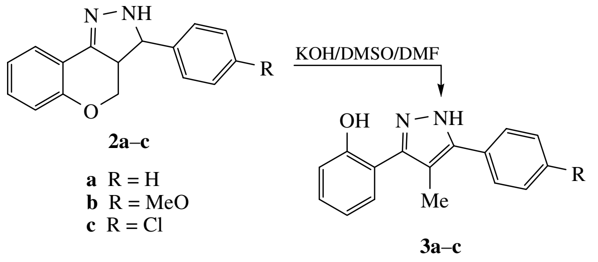
Compounds **2a**–**d** contain two chiral centres in the 3- and 3a-positions. Published data suggest a possibility of forming both *cis* and *trans* isomers in the reactions of arylidenechromanones **1a**–**d** with hydrazine.[1–3] However, the ^{1}H NMR spectra



a R = H **c** R = Cl
b R = MeO **d** R = NO_2

Scheme 1

of **2a–d** do not contain signs of doubling the signals. It points to the formation of only one of possible diastereomers. Analysis of spin–spin coupling constants of the CH–CH–CH_2 fragment of the heterocycle and NOE data allow us to fix a relational configuration of substituents in **2a–d**: the values of J_{3aH-3H} (13.3–14.3 Hz) are more typical of axial–axial coupling constants. The NOE experiment shows a spatial nearness of protons in the 3-, 3a- and 4-positions. Analysis of the geometry of compound **2a** obtained from quantum chemical calculations (GAMESS,[4] HF 6-31G**) indicates that protons at the 3- and 3a-positions are able to give NOE in both *cis* and *trans* orientations, but 3H and a proton in the 4-position can reveal NOE only in the case of *trans* orientation of 3 and 3a. Thus, compounds **2a–d** were obtained as *trans* isomers containing aryl substituents in equatorial positions.



a R = H
b R = MeO
c R = Cl

Scheme 2

The molecules of compounds **2a–d** contain partially hydrogenated pyran and pyrazoline rings. It was established that the refluxing of **2a–c** in a mixture of DMSO and DMF in the presence of KOH leads to rearrangement with pyran ring opening, and the oxidation of a pyrazoline fragment gave pyrazoles **3a–c** (Scheme 2). Under the same conditions, compound **2d** decayed and no product was isolated from the reaction mixture.

In the ^{1}H NMR spectra of **3a–c**,[‡] the signals of the CH–CH–CH_2 fragment of pyranopyrazoline bicycle disappeared but peaks attributed to protons of methyl and hydroxyl groups appeared.

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[†] A solution of arylidenechromanone **1a** (0.005 mol, 1.18 g) and hydrazine hydrate 99% (0.008 mol, 0.4 ml) in 15 ml of MeOH was boiled for 30 min. After cooling, the precipitate was filtered off and crystallised from methanol; 64% of product **2a** was obtained. Compounds **2b**, **2c** and **2d** in 68, 74 and 75% yields, respectively, were synthesised in a similar manner.

2a: mp 132 °C. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 3.38 (ddd, 1H, 3a-H, *J* 12.3, 6.0 and 13.8 Hz), 4.20 (dd, 1H, 4-H_A, *J* –11.2 and 12.3 Hz), 4.56 (dd, 1H, 4-H_B, *J* –11.2 and 5.9 Hz), 4.66 (d, 1H, 3-H, *J* 13.6 Hz), 6.9–7.7 (m, 9H, ArH).

2b: mp 137 °C. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 3.42 (ddd, 1H, 3a-H, *J* 12.4, 6.1 and 13.8 Hz), 3.74 (s, 3H, OMe), 4.18 (dd, 1H, 4-H_A, *J* –11.6 and 10.7 Hz), 4.51 (dd, 1H, 4-H_B, *J* –11.7 and 6.1 Hz), 4.58 (d, 1H, 3-H, *J* 13.8 Hz), 6.8–7.7 (m, 8H, ArH).

2c: mp 152 °C. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 3.40 (ddd, 1H, 3a-H, *J* 12.4, 6.3 and 14.3 Hz), 4.20 (dd, 1H, 4-H_A, *J* –11.3 and 10.4 Hz), 4.55 (dd, 1H, 4-H_B, *J* –11.4 and 5.8 Hz), 4.66 (d, 1H, 3-H, *J* 14.3 Hz), 6.85–7.7 (m, 8H, ArH).

2d: mp 214 °C. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 3.43 (ddd, 1H, 3a-H, *J* 11.1, 6.0 and 13.3 Hz), 4.25 (dd, 1H, 4-H_A, *J* –11.3 and 10.9 Hz), 4.61 (dd, 1H, 4-H_B, *J* –11.4 and 6.0 Hz), 4.82 (dd, 1H, 4-H, J_{CH-NH} 13.5 and 5.0 Hz), 6.9–8.3 (m, 9H, ArH + NH).

[‡] Compound **2a** (0.002 mol, 0.5 g) was dissolved in a mixture of 5 ml DMF and 1 ml DMSO and 0.1 g KOH was added. The mixture was boiled for 3 h, poured into water and neutralised with a 10% HCl solution. The product was filtered off and crystallised from EtOH; 30% of pyrazole **3a** was obtained. Compounds **3b** and **3c** in 42 and 35% yields, respectively, were synthesised in a similar manner.

3a: mp 142 °C. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 2.17 (s, 3H, Me), 6.9–7.7 (m, 9H, ArH), 10.4 (br. s, 1H, OH). MS, *m/z* (%): 250 (75), 146 (100), 55 (30).

3b: mp 126 °C. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 2.19 (s, 3H, Me), 3.82 (s, 3H, OMe), 6.9–7.6 (m, 8H, ArH), 10.3 (br. s, 1H, OH). MS, *m/z* (%): 280 (65), 146 (100), 55 (32), 73 (20), 60 (18).

3c: mp 186 °C. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 2.15 (s, 3H, Me), 6.9–7.8 (m, 8H, ArH), 10.4 (br. s, 1H, OH). MS, *m/z* (%): 284 (86), 146 (100), 130 (66), 43 (34).