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Spiro heterocyclization of 5-methoxycarbonyl-2,3-dihydro-2,3-pyrrolediones by reaction with 1-methyl-3,4-dihydroisoquinoline

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Substituted 1-methyl-3,4-dihydrobenzo[*f*]isoquinoline interacts with substituted 5-methoxycarbonyl-2,3-dihydro-2,3-pyrrolediones to give substituted 1-oxo-1,2,10,11-tetrahydrobenzo[*h*]pyrrolo[2,1-*a*]isoquinoline-2-spiro-2-(4-hydroxy-5-oxo-2,5-dihydropyrroles).

Cross-conjugated olefins and, especially, arylidene derivatives of β-dicarbonyl compounds are widely used in the construction of polycyclic systems.[1] Previously, we found[2] that 1,3,3-trimethyl-3,4-dihydroisoquinoline readily interacts with 3-aroyl-2,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones to form annealated five-membered rings with synchronous introduction of a spiro heterocyclic moiety. These reactions are of great interest for the synthesis of 13-aza analogues of gonanes with a spiro substituent at the 16-position of the tetracyclic system.

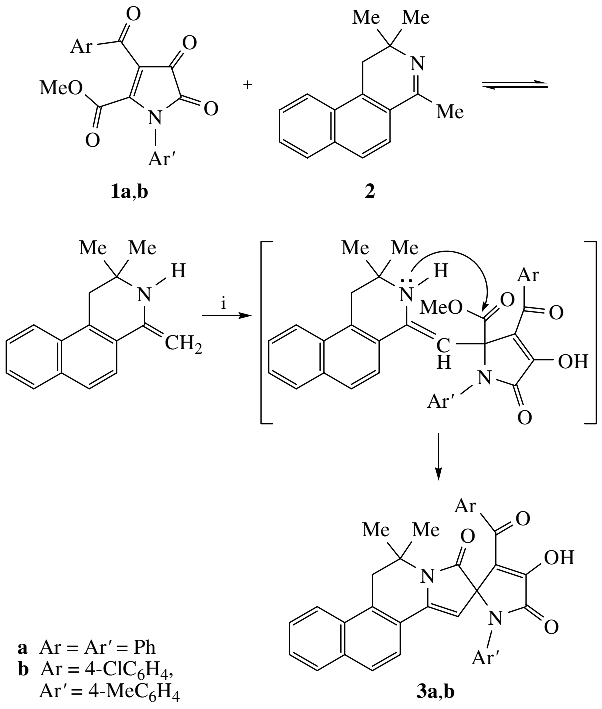
We found that the interaction of 1-aryl-4-aroyl-5-methoxycarbonyl-2,3-dihydro-2,3-pyrrolediones **1a**,**b** (Scheme 1) with 1,3,3-trimethyl-3,4-dihydrobenzo[*f*]isoquinoline **2** on heating for 2–3 min in dry benzene yielded the expected aza analogues of gonanes, 11,11-dimethyl-1-oxo-1,2,10,11-tetrahydrobenzo[*h*]pyrrolo[2,1-*a*]isoquinoline-2-spiro-2-(1-aryl-3-aroyl-4-hydroxy-5-oxo-2,5-dihydropyrroles) **3a**,**b**.[†,‡] The structure of **3a** was confirmed by X-ray diffraction analysis.[§]

At the first step of this reaction, it is likely that the isomeric form of enamine **2** adds to the C(5) atom of pyrrolediones **1a**,**b**, as described for the reactions of these compounds with mono-[3,4] and binucleophiles.[5,6] This step is followed by ring closure due to a *sec*-amino group attack by the isoquinoline ring onto the ester carbonyl of the pyrrolone ring. The reaction presents an example of the regioselective formation of a functionalised spiro-bis(heterocyclic) system of benzopyrroloisoquinoline-spiropyrrole, which was previously inaccessible.

[†] *A typical experimental procedure.* Enamine **2** (0.173 g, 1 mmol) was added dropwise to a solution of pyrroledione **1a** or **1b** (1 mmol) in dry benzene (20 ml). The reaction mixture was heated at 80 °C for 2–3 min and then allowed to cool. The precipitated product was filtered off and recrystallised from an ethyl acetate–1,2-dichloroethane mixture.

[‡] *11,11-Dimethyl-1-oxo-1,2,10,11-tetrahydrobenzo[*h*]pyrrolo[2,1-*a*]isoquinoline-2-spiro-2-(3-benzoyl-4-hydroxy-5-oxo-1-phenyl-2,5-dihydropyrrole)* **3a**: yield 86%, mp 255–257 °C (decomp.). ^{1}H NMR (400 MHz, [^{2}H$_6$]DMSO) δ: 1.28 (s, 3H, Me$_{\text{pseudoeq.}}$), 1.63 (s, 3H, Me$_{\text{pseudoax.}}$), 3.13, 3.28 [dd, 2H, C(10)H$_2$, AB system, J 16.5 Hz], 6.05 [s, 1H, C(3)H], 7.25–7.92 (m, 16H, 2Ph, $\mathrm{C_{10}H_6}$), 12.22 (br. s, 1H, OH). IR (Nujol, ν/cm^{-1}): 3220 (w, OH), 1728, 1703 (2N–C=O), 1638 (COPh). MS (EI, 70 eV) *m/z* (%): 526 (50) [M^{+}], 421 (18), 407 (58), 406 (100), 379 (15), 105 (96) [PhCO]$^+$, 77 (35) [Ph]$^+$. Found (%): C, 77.58; H, 5.00; N, 5.30. Calc. for $\mathrm{C_{34}H_{26}N_2O_4}$ (%): C, 77.55; H, 4.98; N, 5.32.

*11,11-Dimethyl-1-oxo-1,2,10,11-tetrahydrobenzo[*h*]pyrrolo[2,1-*a*]isoquinoline-2-spiro-2-(4-hydroxy-5-oxo-1-*p*-tolyl-3-*p*-chlorobenzoyl-2,5-dihydropyrrole)* **3b**: yield 95%, mp 257–259 °C (decomp.). ^{1}H NMR (400 MHz, [^{2}H$_6$]DMSO) δ: 1.34 (s, 3H, Me$_{\text{pseudoeq.}}$), 1.61 (s, 3H, Me$_{\text{pseudoax.}}$), 2.22 (s, 3H, *Me*$\mathrm{C_6H_4}$), 3.12, 3.28 [dd, 2H, C(10)H$_2$, AB system, J 16.3 Hz], 6.01 [s, 1H, C(3)H], 7.16–8.14 (m, 14H, 2$\mathrm{C_6H_4}$, $\mathrm{C_{10}H_6}$), 12.20 (br. s, 1H, OH). IR (Nujol, ν/cm^{-1}): 3180 (w, OH), 1722, 1688 (2N–C=O), 1636 ($\mathrm{COC_6H_4}$). Found (%): C, 73.13; H, 4.75; N, 4.89. Calc. for $\mathrm{C_{35}H_{27}ClN_2O_4}$ (%): C, 73.10; H, 4.73; N, 4.87.



Scheme 1 *Reagents and conditions*: i, benzene, 80 °C, 2–3 min.

The molecular structure of **3a** is given in Figure 1. All the bond distances and valence angles have values generally accepted for corresponding atoms. The pyridine ring of a pyrroloisoquinoline fragment has an ‘envelope’ configuration. The fold along the line of N(2)···C(19) comprises 42.5°. The C(20) atom deviation from the plane of other five ring atoms sidewards to the phenyl substituent at N(1) of a pyrrole ring comes to 0.60 Å. The conformation of the benzoyl substitutient relative to the pyrrole ring is characterised by the torsion angles C(2)–C(3)–C(4)–C(23) of 29.3° and C(3)–C(4)–C(23)–C(24) of 35.83°; the phenyl ring plane is orthogonal. In a crystal, the molecules of **3a** form dimeric associates held strongly by H-bonds. Parameters for these intermolecular H-bonds are as follows: O(1)···O(4) 2.618(3) Å, H(1)···O(4) 2.02(4) Å, the O(1)–H(1)–O(4) angle is 136(4)°. At the same time, intramolecular hydrogen bonding is also present: O(1)–H(1)···O(2) [O(1)···O(2) 2.826(4) Å, H(1)···O(2) 2.44(4) Å, the O(1)–H(1)–O(2) angle is 113(4)°].

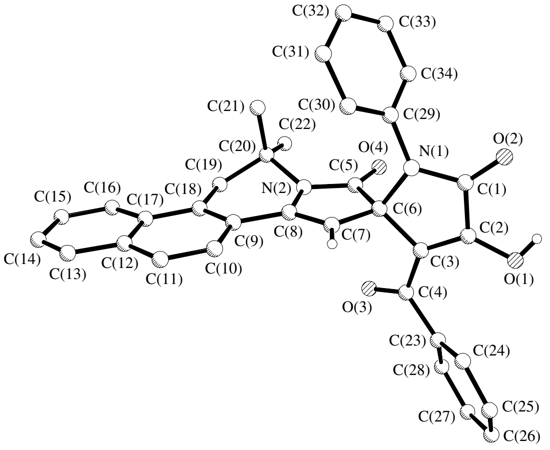


Figure 1 Molecular structure of compound **3a**.

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References

1 A. A. Akhrem, O. V. Gulyakevich and A. L. Mikhalchuk, *Izbrannye metody sinteza i modifikatsii geterotsiklov* (*Selected Methods for Synthesis and Modification of Heterocycles*), eds. V. G. Kartsev, IBS PRESS, Moscow, 2003, vol. 1, p. 22 (in Russian).

2 I. V. Mashevskaya, A. V. Duvalov, Yu. S. Rozhkova, Yu. V. Shklyaev, N. L. Racheva, K. S. Bozdyreva and A. N. Maslivets, *Mendeleev Commun.*, 2004, 75.

3 Yu. S. Andreichikov, A. N. Maslivets, L. I. Smirnova, O. P. Krasnyh, A. P. Kozlov and L. A. Perevozchikov, *Zh. Org. Khim.*, 1987, **23**, 1534 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1987, **23**, 1378].

4 A. N. Maslivets, L. I. Smirnova and Yu. S. Andreichikov, *Zh. Org. Khim.*, 1989, **25**, 1748 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1989, **25**, 1578].

5 A. N. Maslivets, L. I. Smirnova and Yu. S. Andreichikov, *Zh. Org. Khim.*, 1992, **28**, 2141 (*Russ. J. Org. Chem.*, 1992, **28**, 1716).

6 A. N. Maslivets, L. I. Smirnova, O. I. Ivanenko and Yu. S. Andreichikov, *Zh. Org. Khim.*, 1995, **31**, 610 (*Russ. J. Org. Chem.*, 1995, **31**, 563).

7 A. Altomare, G. Cascarano, C. Giacovazzo and A. Gualardi, *J. Appl. Crystallogr.*, 1993, **26**, 343.

8 G. M. Sheldrick, *SHELX-97, Program for Crystal Structure Analysis*, University of Gottingen, Germany.

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§ *Crystallographic data for* **3a**: $C_{34}H_{26}N_2O_4$, monoclinic, space group $P2_1/c$, $a = 7.002(1)$, $b = 14.373(3)$ and $c = 25.522(5)$ Å, $\beta = 94.04(3)°$, $V = 2562.1(8)$ Å^3, $M = 527.58$, $d_{calc} = 1.368$ g cm^{-3}, $Z = 4$. The set of experimental reflections was obtained by the automatic tetra-roundabout diffractometer KM 4 (KUMA DIFFRACTION) with χ-geometry by the $\omega/2\theta$ scanning method using monochromatic MoKα-radiation ($2\theta \le 52.08°$). Altogether 5082 reflections were measured, out of which 4615 were independent ($R_{int} = 0.0495$). The corrections for absorption were not introduced ($\mu = 0.090$ mm^{-1}). The structure was determined by a direct method using the SIR92[7] program with the following series of calculations of the electronic density charts. The hydrogen atom of the carboxyl group was detected from the differential synthesis of the electronic density. The full-matrix anisotropic correction LSM (for non-hydrogen atoms) by the SHELXL-97[8] program was done under $R_1 = 0.0543$, $wR_2 = 0.1620$ on 2542 reflections with $I \ge 2\sigma(I)$ and $R_1 = 0.1400$, $wR_2 = 0.2046$ according to all 2206 reflexes, GOOF = 1.122.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 274698. For details, see ‘Notice to Authors’, *Mendeleev Commun.*, Issue 1, 2005.