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LETTERS TO THE EDITOR

SYNTHESIS OF BENZOPYRANO-TRIAZOLOPYRIMIDINE SPIROFUSED WITH AN OXINDOLE FRAGMENT

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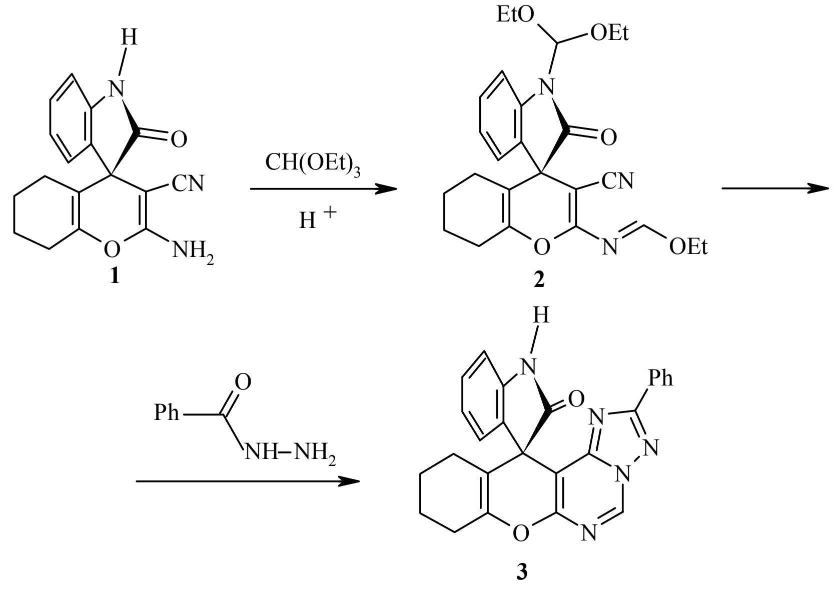
Keywords: oxindole, spirobenzopyranoxindole, triazolopyrimidine, double heteroannelation.

We have developed a convenient method for the double heteroannelation of derivatives of spirooxindolopyrans **1**, which as known exhibit a wide range of biological activity. The reaction of **1** with an excess of orthoformic ester leads to the ethoxymethyleneaminonitrile **2**, which enters into cascade heterocyclization with benzohydrazide and subsequent closure of the pyrimidine and triazole rings, leading to a high yield of compound **3**. The structure of the latter was supported by data from NMR spectroscopy and proved by X-ray crystallographic analysis.



The ^{1}H NMR spectra were recorded on a Varian Unity 300 instrument (300 MHz) in $CDCl_3$ with HMDS as internal standard (δ 0.05 ppm).

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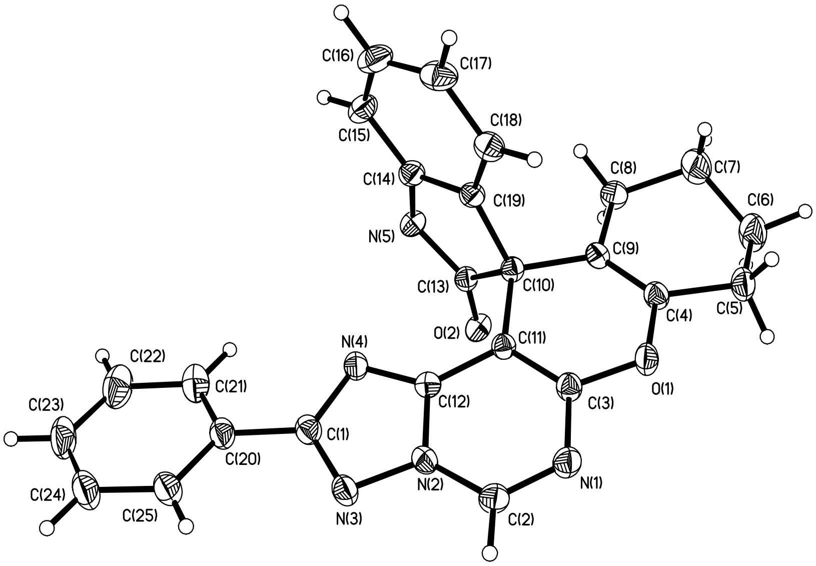
3-Cyano-1'-diethoxymethyl-2-(ethoxymethyleneamino)-2'-oxo-1',2',5,6,7,8-hexahydrospiro[4H-1-benzopyran-4,3'-[3H]indole] (2). A mixture of (1 g, 3.4 mmol) of the *o*-aminocarbonitrile **1** [2], 2 ml (12 mmol) of ethyl orthoformate, and 0.1 ml (50 mol %) acetic acid was boiled for 2 h. It was then evaporated to dryness on a Petri dish, and the residue was recrystallized from methanol. Yield 1.52 g (89%); mp 140°C. ^{1}H NMR spectrum, δ, ppm (J, Hz):1.21-1.32 (6H, m, 2CH_3); 1.39 (3H, t, J = 7.2, CH_3); 1.52-1.86 (6H, m, 3CH_2); 2.33 (2H, t, J = 7.7, CH_2); 3.68-3.88 (4H, m, 2OCH_2); 4.4 (2H, q, J = 7.2, OCH_2); 6.25 [1H, s, $CH(OEt)_2$]; 7.11-7.42 (4H, m, oxindole); 8.24 (1H, s, CH=N). Found, %: C 66.47; H 6.41; N 9.27. $C_{25}H_{29}N_3O_5$. Calculated %: C 66.60; H 6.57; N 9.53.



The molecular structure of compound **3**

2'-Oxo-2-phenyl-1',2',5,6,7,8-hexahydrospiro[1-benzopyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine-2,3'-[3H]indole] (3). A mixture of the imidic ester **2** (0.9 g, 2 mmol), benzohydrazide (0.27 g, 2 mmol), and acetic acid (30 ml) was boiled for 5 h. The acid was removed to dryness under the vacuum of a water-jet pump, the residue was chromatographed on a column of aluminum oxide (with benzene as eluent), and the product was recrystallized from ethanol. Yield 0.31 g (40%); mp 218°C. ^{1}H NMR spectrum, δ, ppm: 1.53-2.40 (8H, m, 4CH_2); 6.91-8.03 (9H, m, C_6H_5, oxindole); 7.82 (1H, s, N=CH); 9.04 (1H, s, N–H). Found, %: C 71.38; H 4.47; N 16.60. $C_{25}H_{19}N_5O_2$. Calculated %: C 71.25; H 4.54; N 16.68.

The product formed colorless prismatic monoclinic crystals, a = 8.2890(6), b = 19.9894(13), c = 12.7615(9) Å; β = 99.706(2)°; V = 2084.2(3) Å^3; space group $P2(1)/n$; Z = 4; d_{calc} = 1.340 g/cm^3. An experimental set of 14412 reflections was obtained on a Bruker diffractometer with a SMART CCD area detector at 120 K (λMoKα radiation, $2\theta_{max}$ = 50°) with a single crystal measuring 0.50 × 0.35 × 0.25 mm. The structure was interpreted by the direct method, and the final uncertainty value was $R1$ = 0.0499. All the computations were performed with SHELXTL PLUS 5 software. The structure has been deposited at the Cambridge structural data bank (No. 608618).

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