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SYNTHESIS OF 2-*spiro*-(1,2-DIHYDROPERIMID-2-YL)-5,5-DIALKYL-2,3,5,6-TETRAHYDROPYRROLO[2,1-*a*]-ISOQUINOLIN-3-ONES

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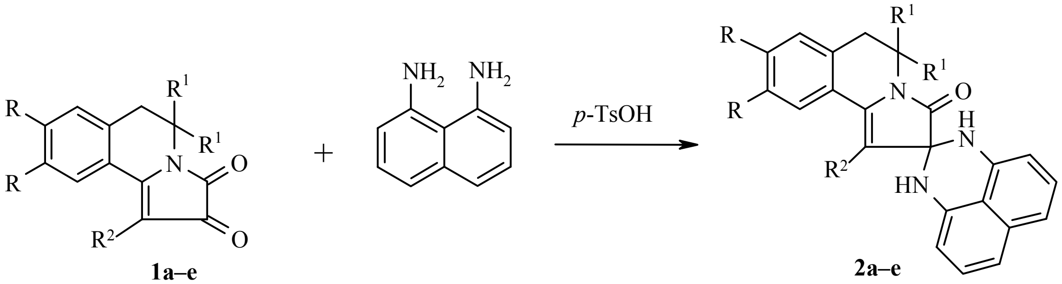
2,3-Dioxpyrrolo[2,1-a]isoquinolines react with 1,8-naphthalenediamine in 2-propanol in the presence of p-toluenesulfonic acid to give 2-spiro-(1,2-dihydroperimid-2-yl)-5,5-dialkyl-2,3,5,6-tetrahydro-pyrrolo[2,1-a]isoquinolin-3-ones whose structure was confirmed by X-ray analysis.

Keywords: 5,5-dialkyl-2,3-dioxopyrrolo[2,1-*a*]isoquinolines, 1,8-naphthalenediamine, 2-*spiro*-(1,2-dihydroperimid-2-yl)-5,5-dialkyl-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinolin-3-ones, acid catalysis, X-ray structural analysis.

We have previously studied the reactions of 2,3-dioxopyrrolo[2,1-*a*]isoquinolines with *o*-phenylenediamine. It was found that the products can have different structures depending on the reaction conditions [1-3]. Treatment of these compounds with other aromatic diamines has not been reported before. The aim of this work was to study the reaction of 2,3-dioxopyrrolo[2,1-*a*]isoquinolines with 1,8-naphthalenediamine.

The study has shown that refluxing dioxopyrrolines of general formula **1a-e** with 1,8-naphthalenediamine under acid catalytic conditions using *p*-toluenesulfonic acid gave the *spiro* compounds **2a-e**. The course of the reaction was readily observed by the change in color of the solution of starting material from dark-red. In the process of forming the new compound (TLC monitoring) the solution color change to yellow. When refluxed in glacial acetic acid unreacted starting material was returned unchanged.

The spiro compounds prepared are yellow, crystalline materials (Table 1).



1,2 a R = R^2 = H, R^1 = Me; **b** R = R^2 = H, R^1+R^1 = $(CH_2)_4$; **c** R = MeO, R^1 = Me, R^2 = H;
d R = H, R^1 = Me, R^2 = $C(O)N(CH_2)_5$; **e** R = H, R^1 = Me, R^2 = $C(O)N(CH_2)_2O$

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TABLE 1. Characteristics of the Compounds Synthesized

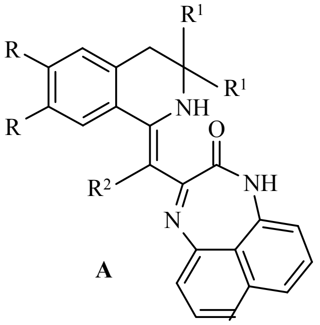
Compound	Empirical formula	Found, % Calculated, %			mp., °C	Yield, %
		C	H	N		
2a	$C_{24}H_{21}N_3O$	74.8 74.9	6.4 6.3	8.8 8.7	170-171	51
2b	$C_{21}H_{22}N_2O_2$	75.2 75.4	6.5 6.6	8.4 8.4	143 - 145	55
2c	$C_{28}H_{27}N_3O_2$	69.8 70.0	6.7 6.8	8.5 8.6	154-156	45
2d	$C_{20}H_{19}N_3O_4$	65.6 65.7	5.1 5.2	11.6 11.5	179-181	60
2e	$C_{20}H_{19}N_3O_4$	65.5 65.7	5.1 5.2	11.6 11.5	155-157	56

By contrast with the spectra of the starting compounds the ^1H NMR spectra (Table 2) of the lactams **2a-e** show the presence of NH group singlets at 6.34-6.47 ppm and multiplets for the additional eight aromatic protons of the 1,2-dihydroperimidine fragment.

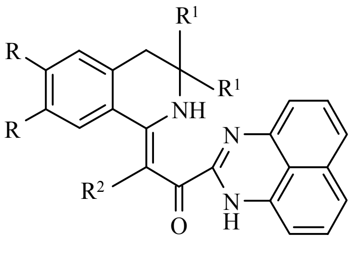
The IR spectra of the lactams **2a-e** show the presence of lactam carbonyl stretching vibrations (1730-1745) and the NH groups (3170-3210 cm^{-1}). The amide carbonyl in compounds **2d,e** absorbs in the region 1640-1650 cm^{-1}.

The mass spectrum of amide **2a** shows a molecule ion peak at 367 (42%) and more intense peaks corresponding to fission of the CO group (*m/z* 339, I_{rel} 90%) with further loss of a methyl group (*m/z* 324, I_{rel} 95%). The methoxy derivative **2c** has *m/z* (I_{rel}, %): 427 $[M]^+$ (5), 399 $[M-CO]^+$ (15), and 384 $[399-Me]^+$ (35).

It should, however, be noted that the ^1H NMR, IR, and mass spectroscopic data presented do not contradict two further possible structure, i.e. dibenzazepinone **A** and perimidine derivative **B**:



A



B

TABLE 2. ^1H NMR Spectra of the Compounds Synthesized

Compound	Chemical schifts, δ, ppm					
	5-CR^{1}R^1	6-CH$_2$, s	1-HC=, s	Aromatic protons, m	2NH, 2 s	Other protons
2a	1.39 (6H, s, 2CH$_3$)	2.84	5.86	6.81-7.75 (10H)	6.34, 6.41	—
2b	1.15-1.76 (8H, m, (CH$_2$)$_4$)	2.88	5.78	6.46-7.16 (10H)	6.46, 6.48	—
2c	1.40 (6H, s, 2CH$_3$)	2.75	5.82	6.83-7.62 (8H)	6.34, 6.40	3.75 (3H, s, CH$_3$O); 3.78 (3H, s, CH$_3$O)
2d	1.35 (6H, s, 2CH$_3$)	2.78	—	7.10-8.13 (8H)	6.39, 6.45	1.03-1.39 (6H, m, C(CH$_2$)$_3$C); 3.27-3.36 (4H, m, 2CH$_2$–N)
2e	1.42 (6H, s, 2CH$_3$)	2.80	—	7.10-8.50 (8H)	6.40, 6.47	2.90-3.70 (8H, m, N(CH$_2$)$_2$O

Hence, in this case, the structure could only be established using X-ray analysis. A suitable single crystal was obtained for compound **2c**.

The **2c** molecule crystallizes with an equimolar amount of an acetonitrile molecule. The overall view of the molecule is given in Fig. 1. All of the bond lengths and valence angles (Tables 3 and 4) agree with standard

TABLE 3. Basic Valence Angles (φ) in the Compound **2c** Molecule

Angle	φ, deg	Angle	φ, deg
C(8)–O(2)–C(15)	117.7(3)	C(8)–C(9)–C(10)	120.7(4)
C(7)–O(3)–C(16)	116.7(3)	C(5)–C(10)–C(9)	119.4(4)
C(2)–N(1)–C(4)	109.4(3)	C(5)–C(10)–C(11)	119.5(4)
C(2)–N(1)–C(12)	127.0(3)	C(9)–C(10)–C(11)	120.8(4)
C(4)–N(1)–C(12)	123.1(3)	C(10)–C(11)–C(12)	112.7(4)
C(17)–N(2)–C(1)	119.2(3)	C(13)–C(12)–N(1)	109.1(4)
C(25)–N(3)–C(1)	119.0(3)	C(13)–C(12)–C(11)	112.0(4)
N(2)–C(1)–N(3)	107.6(3)	N(1)–C(12)–C(11)	108.8(3)
N(2)–C(1)–C(3)	114.4(3)	C(13)–C(12)–C(14)	109.8(5)
N(3)–C(1)–C(3)	111.1(3)	N(1)–C(12)–C(14)	110.7(4)
N(2)–C(1)–C(2)	112.5(3)	C(11)–C(12)–C(14)	106.5(4)
N(3)–C(1)–C(2)	109.8(3)	C(18)–C(17)–N(2)	122.7(4)
C(3)–C(1)–C(2)	101.3(3)	C(18)–C(17)–C(26)	119.6(4)
O(1)–C(2)–N(1)	126.6(3)	N(2)–C(17)–C(26)	117.6(3)
O(1)–C(2)–C(1)	125.7(3)	C(17)–C(18)–C(19)	119.1(4)
N(1)–C(2)–C(1)	107.7(3)	C(20)–C(19)–C(18)	122.2(4)
C(4)–C(3)–C(1)	110.8(3)	C(19)–C(20)–C(21)	122.2(4)
C(3)–C(4)–N(1)	110.4(3)	C(26)–C(21)–C(20)	118.9(4)
C(3)–C(4)–C(5)	131.2(3)	C(26)–C(21)–C(22)	118.3(4)
N(1)–C(4)–C(5)	118.4(3)	C(20)–C(21)–C(22)	122.8(4)
C(10)–C(5)–C(6)	119.5(3)	C(23)–C(22)–C(21)	120.4(4)
C(10)–C(5)–C(4)	119.5(3)	C(22)–C(23)–C(24)	121.4(4)
C(6)–C(5)–C(4)	120.9(3)	C(25)–C(24)–C(23)	119.9(4)
C(7)–C(6)–C(5)	120.8(3)	C(24)–C(25)–N(3)	122.0(4)
O(3)–C(7)–C(6)	125.9(3)	C(24)–C(25)–C(26)	119.8(4)
O(3)–C(7)–C(8)	114.3(3)	N(3)–C(25)–C(26)	118.1(3)
C(6)–C(7)–C(8)	119.8(3)	C(21)–C(26)–C(25)	120.2(4)
O(2)–C(8)–C(9)	124.7(4)	C(21)–C(26)–C(17)	119.9(4)
O(2)–C(8)–C(7)	115.6(3)	C(25)–C(26)–C(17)	119.7(3)
C(9)–C(8)–C(7)	119.6(3)	N(4)–C(27)–C(28)	178.0(7)

TABLE 4. Bond Lengths (*d*) in the Compound **2c** Molecule

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
O(1)–C(2)	1.213(4)	C(1)–C(2)	1.556(5)	C(17)–C(18)	1.373(6)
O(2)–C(8)	1.360(4)	C(3)–C(4)	1.328(5)	C(17)–C(26)	1.429(5)
O(2)–C(15)	1.419(5)	C(4)–C(5)	1.454(5)	C(18)–C(19)	1.418(6)
O(3)–C(7)	1.365(4)	C(5)–C(10)	1.391(5)	C(19)–C(20)	1.346(7)
O(3)–C(16)	1.400(5)	C(5)–C(6)	1.396(5)	C(20)–C(21)	1.415(7)
N(1)–C(2)	1.358(5)	C(6)–C(7)	1.373(5)	C(21)–C(26)	1.408(5)
N(1)–C(4)	1.436(5)	C(7)–C(8)	1.406(5)	C(21)–C(22)	1.418(6)
N(1)–C(12)	1.485(5)	C(8)–C(9)	1.375(6)	C(22)–C(23)	1.361(7)
N(2)–C(17)	1.389(5)	C(9)–C(10)	1.402(6)	C(23)–C(24)	1.398(6)
N(2)–C(1)	1.451(5)	C(10)–C(11)	1.521(6)	C(24)–C(25)	1.374(6)
N(3)–C(25)	1.389(5)	C(11)–C(12)	1.529(6)	C(25)–C(26)	1.414(6)
N(3)–C(1)	1.460(5)	C(12)–C(13)	1.475(8)	N(4)–C(27)	1.101(6)
C(1)–C(3)	1.483(5)	C(12)–C(14)	1.540(6)	C(27)–C(28)	1.446(9)

values for the corresponding atoms. The pyrazine ring has a *boat* conformation twisted along the N(2)–N(3) line by 39.6° with a deviation of atom C(1) from the plane of the remaining five ring atoms of 0.55 Å. The piperidine ring of the isoquinoline is strongly distorted. The deviations of atoms N(1) and C(12) from the plane of the four atoms are 0.38 and 0.75 Å respectively and are to the same side. The methoxy groups are situated in the plane of the benzene ring. Hydrogen bonds and shortened intermolecular contacts are absent in the crystal.

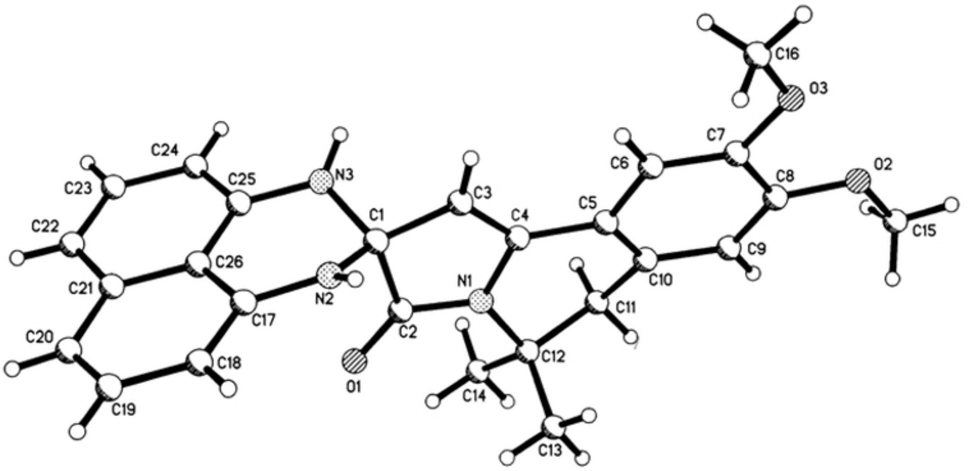


Fig. 1. X-ray structure of the compound **2c** molecule.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker 300 (300 MHz) instrument using DMSO-d$_6$ (compounds **2a, c-e**) or CDCl$_3$ (compound **2b**) with HMDS as internal standard at δ 0.05. IR spectra were obtained on a Specord M-80 spectrometer using vaseline oil. Mass spectra were taken on a MAT-311 instrument (70 eV, EI).

Checking the purity of the compounds obtained was carried out using TLC on Silufol UV-254 plates using the system acetone–ethanol–chloroform (1:3:6), compounds being colored.

Compounds **2a,b,d,e** were recrystallized from isopropyl alcohol and compound **2c** from acetonitrile.

The synthesis of the starting materials has been reported in [1, 4].

X-ray Structural Analysis of Compound 2c. Crystals of $C_{26}H_{25}N_3O{\cdot}MeCN$ belong to the monoclinic crystal system with a = 12.298(1), b = 19.583(4), c = 10.310(1) Å, β = 98.99(1)°, V = 2452.5(6) Å^3, M = 468.54, d_{calc} = 1.269 g/cm^3, Z = 4, space group $P2_1/c$. The set of experimental reflections was obtained on a KM-4 (Kuma Diffraction) automatic four-circle diffractometer, geometry χ-4, using ω/2θ-scanning method with monochromatic MoKα radiation (2θ ≤ 50°). In all, 3617 independent reflections (R_{int} = 0.0241) were measured. Corrections for absorption were not introduced (μ = 0.084 mm^{-1}). The structure was determined by a direct method using the SIR92 [5] program with a subsequent series of calculations of the electron density maps. All of the hydrogen atoms were assigned geometrically. Full-matrix anisotropic (non-hydrogen atoms) least-squares refinement using the SHELXL-97 [6] program was performed to R_1 = 0.0760 for 2489 reflections with $I \geq 2\sigma(I)$. *GOOF* = 1.033.

1-R^2-2-*spiro*-(1,2-Dihydroperimid-2-yl)-5,5-(R^1)$_2$-6,7-(R)$_2$-2,3,5,6-tetrahydroisoquinolinones (2a-e) (General Method). Approximately 10 mg (1-2 crystals) of *p*-toluenesulfonic acid were added to a solution of the dioxopyrroline **1a-e** (10 mmol) and 1,8-naphthalenediamine (1.58 g, 10 mmol) in isopropyl alcohol (30 ml). Refluxing the solution for 30 min caused the solution color to change from red to dark-yellow. The mixture was cooled to 20°C and the precipitate was filtered off, washed on the filter with water, dried, and recrystallized.

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