(Pyrrol-1-yl)furazans

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Short-time reactions of 3-amino-4-R-furazans with 2,5-dimethoxytetrahydrofuran in boiling acetic acid afford (pyrrol-1-yl)furazans. One of the products was characterized by X-ray diffraction analysis.

Key words: furazans, aminofurazans, pyrroles, Clauson-Kaas reaction, X-ray diffraction analysis, NMR spectroscopy.

A pyrrole ring is contained in a large number of natural compounds such as various enzymes, antibiotics, *etc.* This gives impetus to a search for new biologically active compounds among synthetic pyrrole derivatives. For instance, *N*-substituted pyrroles are important starting reagents for the synthesis of substances of pharmacological interest.[1—4]

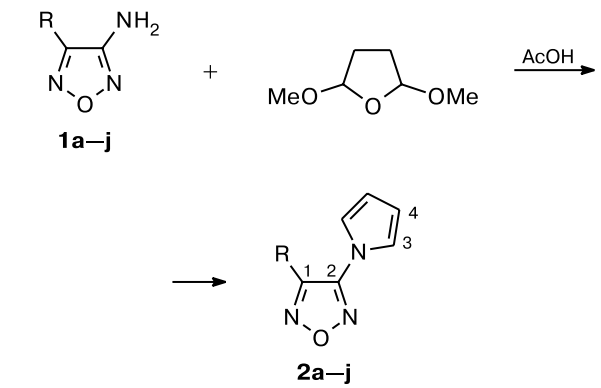
In continuation of our investigations[5—7] into the synthesis of compounds containing the significantly π-deficient furazan ring and the pyrrole ring with a great excess of π-electrons,[8] *N*-(furazanyl)pyrroles were obtained and studied in the present work.

An attractive way of synthesizing *N*-substituted pyrroles is a condensation of primary amines with 2,5-dimethoxytetrahydrofuran (DMT) (the Clauson-Kaas reaction[9]). However, the success of this reaction depends on the properties of an amine used; in some cases, a desired compound is not formed.[10] This reaction is most successfully applied in the synthesis of *N*-alkyl- and *N*-arylpyrroles.[11,12] It shoould be noted that these amines are rather strong bases. A furazan ring is characterized by significant electron-withdrawing properties, which are close to those of dinitrophenyl fragment. As a result, the reduced electron density at the amino group bound to the furazan ring is responsible for an extremely low basicity of aminofurazans.[13,14]

However, we found that 3-amino-4-R-furazans **1a**—**h** containing both donor and acceptor substituents easily react with DMT in boiling acetic acid over a short period of time (15 min) to give the target 3-R-4-(pyrrol-1-yl)furazans **2a**—**h** (Scheme 1) in satisfactory yields (Table 1).

The yields of pyrroles **2i**—**k** from compounds **1i**—**k** are low. In the course of the reaction, aminofurazan **1j** undergoes substantial decomposition; as the result, the yield of pyrrole **2j** does not exceed 30%. Under similar conditions, 3-amino-4-nitrofurazan **1k** affords desired product **2k** only in 8.3% yield. The yield was increased to 15.5% by refluxing the reaction mixture for 1 h; however, a further increase in the refluxing time to 2 h resulted in a lowering of the yield of pyrrole **2k** to 12%. When acetic acid was replaced by trifluoroacetic acid or aqueous 5% HCl, pyrrole **2k** was formed only in trace amounts. Apparently, the low yield of compound **2k** is due to side oxidative process caused by the nitro group. Oxidative reactions are also likely to impede the efficient synthesis of compound **2i**.

Scheme 1



R = Me (**a**), OMe (**b**), Ph (**c**), thien-2-yl (**d**), Ac (**e**), CO_2H (**f**), CO_2Me (**g**), CN (**h**),

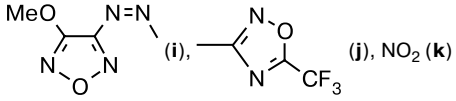


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Table 1. Yields and selected characteristics of (pyrrol-1-yl)furazans

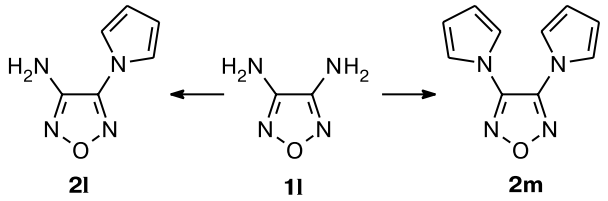
Compound	Yield (%)	M.p. /°C	Found / Calculated (%)			Molecular formula	M_{calc}	MS, *m/z*	IR, ν/cm^{-1}
			C	H	N				
2a	66.6	57—58	56.33 56.37	4.73 4.73	28.10 28.17	$C_7H_7N_3O$	149.15	149 $[M]^+$, 119 $[M - NO]^+$	3112, 1596, 1544, 1464, 1288, 1080, 1040, 744
2b	64	56—61	50.88 50.91	4.17 4.27	25.39 25.44	$C_7H_7N_3O_2$	165.15	165 $[M]^+$, 135 $[M - NO]^+$	3128, 2952, 1616, 1600, 1584, 1472, 1392, 1340, 1264, 1068, 1040, 996
2c	86.9	33—34	68.29 68.24	4.31 4.29	19.82 19.89	$C_{12}H_9N_3O$	211.22	211 $[M]^+$, 181 $[M - NO]^+$	3144, 1584, 1544, 1488, 1448, 1384, 1320, 1072, 992, 888, 768, 728
2d	63.6	Oil	55.31 55.29	3.19 3.25	19.26 19.34	$C_{10}H_7N_3OS$	217.25	217 $[M]^+$, 187 $[M - NO]^+$	3112, 1556, 1496, 1464, 1424, 1384, 1360, 1308, 1232, 1072, 1040, 912, 732
2e	73.6	Oil	54.29 54.24	4.01 3.98	23.70 23.72	$C_8H_7N_3O_2$	177.16	177 $[M]^+$, 147 $[M - NO]^+$	3168, 1720, 1568, 1544, 1496, 1392, 1316, 1160, 1100, 1024, 960, 912, 736
2f	79.6	140—143	46.89 46.93	2.87 2.81	23.41 23.46	$C_7H_5N_3O_3$	179.14	179 $[M]^+$, 149 $[M - NO]^+$, 105	3190—2800, 1728, 1568, 1544, 1512, 1384, 1204, 1112, 1064, 1032, 888
2g	58.6	38—40	49.71 49.74	3.68 3.65	21.69 21.75	$C_8H_7N_3O_3$	193.16	193 $[M]^+$, 163 $[M - NO]^+$	3176, 3144, 1744, 1568, 1544, 1504, 1392, 1336, 1208, 1168, 1112, 1032
2h	50.6	Oil	52.45 52.50	2.49 2.52	34.93 34.99	$C_7H_4N_4O$	160.13	160 $[M]^+$, 130 $[M - NO]^+$	3144, 2928, 2274, 1588, 1544, 1512, 1392, 1288, 1064, 912, 880, 732
2i	13.2	128—131	41.33 41.39	2.64 2.70	37.51 37.54	$C_9H_7N_7O_3$	261.20	261 $[M]^+$, 231 $[M - NO]^+$	3174, 3132, 1627, 1580, 1556, 1542, 1390, 1270, 1220, 1150, 1100, 1016, 932, 880
2j	29.5	Oil	39.85 39.87	1.42 1.49	25.77 25.83	$C_9H_4N_5O_2F_3$	271.16	271 $[M]^+$, 241 $[M - NO_2]^+$	3168, 2928, 2856, 1612, 1564, 1484, 1456, 1384, 1368, 1188, 1148, 1112, 1080, 1064, 1008, 992
2k	15.5	45—48	40.11 40.01	2.18 2.24	31.04 31.10	$C_6H_4N_4O_3$	180.12	180 $[M]^+$, 134 $[M - NO_2]^+$, 104	3152, 1592, 1552, 1496, 1384, 1360, 1240, 1120, 1080, 1064, 1040, 888
2m	9	Oil	60.08 60.00	4.06 4.03	27.89 27.99	$C_{10}H_8N_4O$	200.20	200 $[M]^+$, 170 $[M - NO_2]^+$	3144, 2956, 2924, 2856, 1592, 1572, 1536, 1480, 1356, 1260, 1112, 1080, 1060, 1044, 1004, 928, 884
2n	30.8	142—145	47.23 47.19	3.38 3.39	31.39 31.45	$C_7H_6N_4O_2$	178.15	178 $[M]^+$, 148 $[M - NO]^+$	3256, 3232, 3224, 3128, 1700, 1604, 1576, 1536, 1408, 1384, 1288, 1160, 1076, 920, 868, 744
4	70	Oil	58.95 58.89	5.60 5.56	25.69 25.75	$C_8H_9N_3O$	163.18	163 $[M]^+$, 133 $[M - NO]^+$	3104, 3004, 2936, 1500, 1440, 1284, 1224, 1088, 1072, 1040, 968, 896

In the reaction of 3,4-diaminofurazan **1l** with DMT, the formation of mono- (**2l**) and dipyrroles (**2m**) could be expected (Scheme 2). However, despite a wide variation of the reaction conditions (the ratio of reagents, temperature, reaction time, and replacement of AcOH by CF_3CO_2H), a complex mixture of products was obtained (TLC data), and it was impossible to isolate individual compounds.

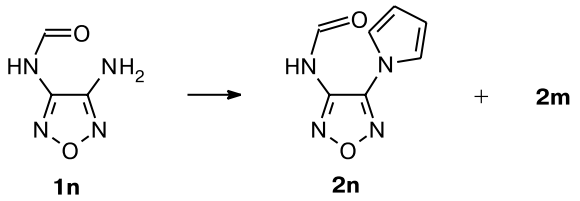
At the same time, the reaction of *N*-formylaminofurazan **1n** with DMT in boiling AcOH affords a mixture of a formyl derivative **2n** and dipyrrole **2m** (Scheme 3) in low yields. These products were isolated from the reaction mixture by chromatography.

An analog of compound **1a**, namely, 3-(aminomethyl)-4-methylfurazan (**3**), in which the amino group

Scheme 2

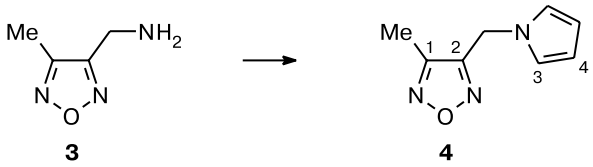


Scheme 3



and the heterocycle are separated by a methylene fragment, reacts with DMT under the same conditions to give pyrrole **4** in 70% yield (Scheme 4).

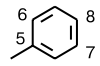
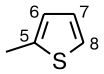
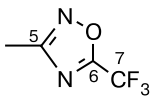
Scheme 4



The structures of the compounds synthesized were unambiguously confirmed by elemental analysis, IR and NMR spectroscopy (^{1}H and ^{13}C), and mass spectrometry (Tables 1, 2).

As can be seen in Table 2, a substituent at the furazan ring of compounds **2a—k** virtually does not affect the chemical shifts of the pyrrole ring. The signals for the C(3) atoms appear at *ca.* δ 121 and the signal for the proton bound to this atom appears at *ca.* δ 7.5. The corresponding signals for the C(4) atom of the pyrrole ring and its proton appear at *ca.* δ 112 and 6.4, respectively. The observed shifts correlate with the literature data.[15] The largest deviations of the shifts of the C(3) atoms (an upfield shift by 1.0—1.5 ppm) was found for compounds **2b**, **2f**,

Table 2. ^{1}H and ^{13}C NMR data for (pyrrol-1-yl)furazans **2a—k,m,n**

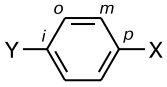
Compound	R	^{13}C NMR, δ					^{1}H NMR, δ
		C(1)	C(2)	C(3)	C(4)	Substituents	
2a[a]	Me	146.7	153.3	121.3	113.0	9.7 (Me)	7.35, 6.45 (both s, 2 H each); 2.65 (s, 3 H)
2b[b]	OMe	158.4	143.3	119.4	112.1	59.6 (OMe)	7.40, 6.40 (both s, 2 H each); 4.20 (s, 3 H)
2c[c]		148.5	151.0	120.7	112.1	124.4 (C(5)); 131.0 (C(6)); 129.0 (C(7)); 128.6 (C(8))	7.60 (s, 3 H); 7.00, 6.40 (both s, 2 H each)
2d[c]		144.7	150.7	121.0	112.2	124.0 (C(5)); 130.0 (C(6)); 128.0 (C(7)); 129.8 (C(8))	7.60 (dd, 1 H); 7.27, 7.16 (both q, 1 H each); 7.07, 6.43 (both t, 2 H each)
2e[c]	COMe	145.8	150.9	121.9	112.4	29.7 (Me); 189.1 (CO)	7.60, 6.48 (both s, 2 H each); 2.90 (s, 3 H)
2f[b]	COOH	140.0	156.4	118.8	112.1	160.2	7.20, 6.30 (both s, 2 H each)
2g[c]	$COOCH_3$	140.6	151.4	121.4	112.4	53.5 (OMe); 158.0 (CO)	7.45, 6.35 (both s, 2 H each); 4.03 (s, 3 H)
2h[c]	CN	125.1	151.7	119.5	114.3	107.2	7.46, 6.49 (both t, 2 H each)
2i[c]		155.6	149.8	120.6	113.5	60.2 (C(7)); 155.5 (C(5)); 158.7 (C(6))	4.26 (s, 3 H); 6.47, 7.58 (both s, 2 H each)
2j[c]		137.2	151.4	121.4	113.1	159.7 (C(5)); 167.7 (C(6)); 115.5 (C(7))	7.45, 6.50 (both t, 2 H each)
2k[c]	NO_2	153	145.7	121.1	113.7	—	7.30, 6.53 (both s, 2 H each)
2m[c]		147.0	147.0	120.8	112.8	—	6.43, 7.41 (both s, 2 H each)
2n[b]	NHCHO	144.4	148.0	120.6	112.2	161.8 (CO)	6.42, 7.34 (both s, 2 H each); 8.49 (s, 1 H)

[a] In acetone-d_6.
[b] In DMSO-d_6.
[c] In $CDCl_3$.

and **2h**, which is probably due to the favorable effect of the methoxy, carboxy, and cyano groups on the conjugation of the furazan and pyrrole rings.

Signals for the furazan ring in compound **2a** were assigned by measuring a coupling constant between the protons of the substituent and the C atoms of the heterocycle. Signal assignment was based[16] on a large difference between the coupling constants for the C(1) atom neighboring to the Me group ($^2J_{C,H}$ = 7.0—7.5 Hz) and the remote C(2) atom ($^3J_{C,H}$ = 2.5—3.2 Hz). In the spectra of compounds **2h** and **2k**, signal assignment was facilitated by respectively a considerable upfield shift of the signal for the C(1) atom due to the effect of the nitrile group and broadening caused by $^{13}C—^{14}N$ quadrupole coupling. Signals for the furazan ring in the spectra of the other compounds were assigned with consideration of the previously revealed additive effect of the substituents.[17—19]

A simple linear equation proposed by Lynch[20] relates the chemical shifts of the ^1H and ^{13}C atoms in *para*-disubstituted benzenes with a fixed substituent Y and variable X to the increments of these substituents in monosubstituted benzenes:



$$Shift_x(Y) = a + b \cdot SCS_x(H). \quad (1)$$

$Shift_x(Y)$ is the chemical shift of the C_x atom in a series of disubstituted benzenes with fixed substituent Y, $SCS_x(H)$ is the corresponding increment of substituent X in a monosubstituted benzene (for Y = H), and a and b are linear regression coefficients.

Recently,[19] we demonstrated that Eq. (1) can be used to predict chemical shifts in ^{13}C NMR spectra of the ring atoms for a series of disubstituted furazans with a fixed substituent through the use of vast literature data on the increments of substituents in monosubstituted benzenes. In our further investigations of the effect of substituents on the chemical shifts of the C atoms of the furazan ring, we determined coefficients of the Lynch equation for pyrrolylfurazans using spectral data for compounds **2a,b,d,e,h,k,m**, for which the signals were assigned by spectroscopic methods:

$$\delta(C(1))(R) = a + b \cdot SCS_i(R), \quad (2)$$
$a = 138.2 \pm 1.0$,
$b = 0.72 \pm 0.06$
(correlation coefficient $r = 0.977$, $n = 7$),
$$\delta(C(2))(R) = a + b \cdot SCS_o(R), \quad (3)$$
$a = 150.7 \pm 0.9$,
$b = 0.53 \pm 0.12$
(correlation coefficient $r = 0.838$, $n = 7$).

As noted by us earlier, the linear regression describing a change in the chemical shifts of the C(2) atom in furazans (equation (3)) shows a low correlation coefficient. The reason for this is a relatively narrow range of variation in the chemical shift of C(2), which is only slightly dependent on the nature of a substituent at the neighboring C(1) atom. Nevertheless, the obtained equation can be useful for qualitative estimation of the replacement effects in substituted pyrrolylfurazans.

Table 3. Correlation between the experimental (I) and calculated (II) chemical shifts (CS)

Compound	CS of the C(1) atom			CS of the C(2) atom		
	I	II[a]	Δδ	I	II[b]	Δδ
2e	148.5	147.5±2.0	−1.0	151.0	150.0	−1.0
2f	140.0	140.5±1.4	0.5	156.4	151.6	−4.8
2g	140.6	139.5±1.3	−1.1	151.4	151.3	−0.1
2i	155.6	157.2±2.8	0.6	149.8	147.0	−2.8
2n	144.4	146.0±1.9	1.4	148.0	145.4	−2.6

[a] Calculated by Eq. (2).
[b] Calculated by Eq. (3).

According to the X-ray diffraction data, the furazan and pyrrole rings in compound **2g** are coplanar, while the deflection angle between their plane and the ester group is 14.9° (Fig. 1). Because the heterocycles are coplanar, they can be slightly conjugated, which is confirmed by a shortened N(1)—C(5) bond length (1.399(3) Å). The Cambridge Crystallographic Database (CCD)[21] contains at least 919 structures with a $N(sp^2)—C(sp^2)$ bond, in which conjugation is insignificant or no present at all (for an angle larger than 40° between the planes of the π-systems of the N and C atoms). The average N—C bond length for these structures was 1.43 Å. Apparently, this conjugation is responsible for a small lengthening of the C(5)—C(6) bond in the furazan ring to 1.446(3) Å

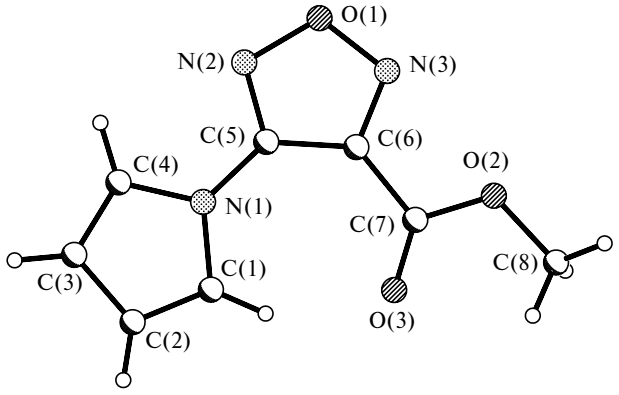


Fig. 1. General view of structure **2g**.

compared to an average value of 1.42 Å found in the CCD structures. Insofar as the C(6)—C(7) bond (1.504(3) Å) is ordinary, one can conclude that the ester group is not involved in conjugation.

As noted earlier,[22] the N—O bond lengths in the furazan ring depend on the character of its substituents. The N—O bond nearest to a donor substituent is lengthened, while that nearest to an acceptor substituent is shortened. Indeed, the N—O bond lengths in compound **2g** are 1.402(2) Å on the pyrrole side and 1.375(2) Å on the ester side.

In crystal, molecules form layers running parallel to the crystallographic plane (100). Neighboring layers are symmetric about one of the two crystallographically nonequivalent centers of inversion; for this reason, two different types of superposition of neighboring layers are present in crystal. For one type, the distance between layers is 3.21 Å, while for the other, 3.25 Å. However, layer superposition is shifted in both cases to give no shortened contacts between molecules in neighboring layers.

The O(3) atom is involved in two hydrogen bonds, namely, intramolecular O(3)...H(1)—C(1) and intermolecular O(3).....H(4)—C(4), with the following bond parameters: O...H 2.11(2) and 2.39(2) Å, O...C 2.970(3) and 3.346(3) Å, and the angle C—H—O 147(2) and 161(2)°, respectively. Molecules in layers are united through intermolecular hydrogen bonding into chains symmetric about a plane of tangential reflection *c*.

Hence, the Clauson-Kaas reaction was found to be an efficient tool for the synthesis of 3-R-4-(pyrrol-1-yl)furazans. Note that an amino group at a furazan ring was involved for the first time in construction of a heterocycle.

Experimental

Melting points were determined on a Kofler stage. Natural-isotope ^{1}H, ^{13}C, and ^{14}N NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13, 75.7, and 21.5 MHz, respectively). Mass spectra were recorded on Varian MAT CH-6 and Varian MAT CH-111 instruments (70 eV). IR spectra were recorded on a Specord IR75 spectrometer (in pellets with KBr for solids and in thin film for liquids). The course of the reaction was monitored and the purity of products was checked by TLC on Silufol UV-254 plates; silica gel was used for preparative chromatography.

3-Methyl-4-(pyrrol-1-yl)furazan (2a). 2,5-Dimethoxytetrahydrofuran (1.32 g, 0.01 mol) was added to a stirred solution of 3-amino-4-methylfurazan **1a** (0.99 g, 0.01 mol) in 3 mL of glacial AcOH. The resulting mixture was refluxed for 15 min, cooled, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 mL) and washed with aqueous 5% K_2CO_3 (20 mL) and water (2×15 mL). The organic layer was dried with $MgSO_4$, filtered through a thin layer of silica gel, and concentrated. The residue was recrystallized from hexane.

Compounds **2b—e** and **2g—k** were obtained analogously. The yields and the physicochemical properties of the products are given in Tables 1 and 2.

4-(Pyrrol-1-yl)furazancarboxylic acid (2f). 2,5-Dimethoxytetrahydrofuran (1.32 g, 0.01 mol) was added to a stirred suspension of 4-aminofurazancarboxylic acid **1f** (1.29 g, 0.01 mol) in 5 mL of AcOH. The resulting mixture was refluxed for 15 min, cooled, and concentrated under reduced pressure. The residue was recrystallized from Pr^{i}OH—water (9 : 1).

Reaction of 3-amino-4-(formylamino)furazan (1n) with 2,5-dimethoxytetrahydrofuran. 2,5-Dimethoxytetrahydrofuran (1.32 g, 0.01 mol) was added to a stirred suspension of 3-amino-4-(formylamino)furazan **1n** (1.28 g, 0.01 mol) in 5 mL of AcOH. The resulting mixture was refluxed for 15 min, cooled, and concentrated under reduced pressure. The residue was treated with CH_2Cl_2 (30 mL). The insoluble precipitate that formed was filtered off, washed with CH_2Cl_2 (3×5 mL), and dried in air to give **4-(formylamino)-3-(pyrrol-1-yl)furazan (2n)** (0.34 g, 19%) as an amorphous light beige powder, m.p. 142—145 °C, R_f 0.4 (CCl_4—MeCN, 3 : 1). Combined mother liquors in CH_2Cl_2 were washed with 5% $NaHCO_3$ (20 mL) and water (20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed on SiO_2 (L100/160 μm) in CH_2Cl_2 to give **3,4-di(pyrrol-1-yl)furazan (1m)** (0.18 g, 9%) as an oil, R_f 0.9 (CH_2Cl_2). After compound **1m** was isolated, elution was continued in CCl_4—MeCN (3 : 1) to give an additional amount of compound **2n** (0.21 g, 11.8%).

4-Methyl-3-(pyrrol-1-yl)methylfurazan (4). Acetic acid (3.5 mL) was added to a mixture of a hydrochloride of compound **3** (0.41 g, 0.003 mol) and NaOH (0.12 g, 0.003 mol) in 2 mL of water. The resulting solution was stirred at ~20 °C for 10 min; then 2,5-dimethoxytetrahydrofuran (0.4 g, 0.003 mol) was added and the reaction mixture was refluxed for 15 min, cooled, and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2, washed with 5% $NaHCO_3$ (20 mL) and water (20 mL), and dried over $MgSO_4$. The solvent was removed, and the residue was dissolved in $CHCl_3$ and passed through a thin layer of silica gel. The resulting solution was concentrated *in vacuo* to give compound **4** (0.42 g, 70%) as a light yellow liquid. ^{1}H NMR ($CDCl_3$), δ: 2.11 (3 H, Me); 5.24 (CH_2); 6.22 (C(3)H); 6.68 (C(4)H). ^{13}C NMR ($CDCl_3$), δ: 7.4 (Me); 41.8 (CH_2); 109.5 (C(4)); 120.8 (C(3)); 150.4 (C(1)); 151.2 (C(2)).

X-ray diffraction analysis. The crystals of compound **2g** at 110 K are monoclinic, space group *C*2/*c*, a = 15.161(6) Å, b = 9.819(4) Å, c = 13.368(6) Å, β = 121.52(1)°, V = 1696(1) Å^3, Z = 8, M = 193.17, d_{calc} = 1.513 g cm^{-3}, μ(Mo-Kα) = 0.119 mm^{-1}, F(000) = 800. The intensities of 6738 reflections were measured on a Bruker SMART 1000 CCD diffractometer (λ(Mo-Kα) = 0.710712 Å, ω scan mode for ω = 0.4° and a 20-s exposure for each frame, 2θ < 60°); 2441 independent reflections were used in refinement (R_{int} = 0.0497). Data processing was performed with the SAINT program.[23] The structure was solved by the direct method and refined by the full-matrix least-squares method in the anisotropic approximation. The H atoms were located from a difference electron-density map and refined isotropically. Final discrepancy factors are wR_2 = 0.1023 for all independent reflections and R_1 = 0.0487 for 1020 reflections with $I > 2\sigma(I)$. All relevant calculations were performed with the SHELXTL PLUS program package.[24] The atomic coordinates and thermal parameters, as well as the bond lengths and angles, have been deposited with the CCD.

References

1. X. Feng, J.-C. Lancelot, H. Prunier, and S. Rault, *J. Heterocycl. Chem*., 1996, **33**, 2007.
2. G. Campiani, E. Morelli, S. Gemma, V. Nacci, S. Butini, M. Hamon, E. Novellino, G. Greco, A. Cagnotto, M. Goegan, L. Cervo, F. D. Valle, C. Fracasso, S. Caccia, and T. Mennini, *J. Med. Chem*., 1999, **42**, 4362.
3. R. Abonia, B. Insuasty, J. Quiroga, H. Kolshorn, and H. Meier, *J. Heterocycl. Chem*., 2001, **38**, 671.
4. M. Kopp, J.-C. Lancelot, P. Dallemagne, and S. Rault, *J. Heterocycl. Chem*., 2001, **38**, 1045.
5. A. B. Sheremetev, I. L. Yudin, and D. E. Dmitriev, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 400 [*Russ. Chem. Bull.*, 1999, **48**, 398 (Engl. Transl.)].
6. I. L. Yudin, A. B. Sheremetev, S. Yu. Shakarvis, and D. E. Dmitriev, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 2375 [*Russ. Chem. Bull.*, 1999, **48**, 2349 (Engl. Transl.)].
7. I. L. Yudin, S. M. Aronova, A. B. Sheremetev, B. B. Averkiev, and M. Yu. Antipin, *Mendeleev Commun*., 2001, 152.
8. A. F. Pozharskii, *Teoreticheskie osnovy khimii geterotsiklov* [*Theoretical Foundations of Heterocyclic Chemistry*], Khimiya, Moscow, 1985, p. 53 (in Russian).
9. N. Clauson-Kaas and Z. Tyle, *Acta Chem. Scand*., 1952, **6**, 667; 867.
10. C. D'Silva and D. A. Walker, *J. Org. Chem*., 1998, **63**, 6715.
11. B. A. Trofimov, *Usp. Khim.*, 1989, **58**, 1703 [*Russ. Chem. Rev.*, 1989, **58** (Engl. Transl.)].
12. S. E. Korostova, A. I. Mikhaleva, A. M. Vasil´tsov, and B. A. Trofimov, *Zh. Org. Khim.*, 1998, **34**, 1767 [*Russ. J. Org. Chem*., 1998, **34** (Engl. Transl.)].
13. I. V. Tselinskii, S. F. Mel´nikova, and S. N. Vergizov, *Khim. Geterotsikl. Soedin*., 1981, 321 [*Chem. Heterocycl. Compd*., 1981, **17**, 228 (Engl. Transl.)].
14. A. B. Sheremetev, N. N. Makhova, and W. Friedrichsen, *Adv. Heterocycl. Chem*., Academic Press, San Diego, 2001, **78**, 65.
15. D. J. Chadwick, in *Comprehensive Heterocyclic Chemistry*, Eds. A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford, 1984, **4**, p. 155.
16. Yu. A. Strelenko, O. A. Rakitin, T. I. Godovikova, and L. I. Khmel´nitskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1987, 2852 [*Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1987, **36**, 2649 (Engl. Transl.)].
17. Yu. A. Strelenko, A. B. Sheremetev, and L. I. Khmel´nitskii, *Khim. Geterotsikl. Soedin*., 1992, 1101 [*Chem. Heterocycl. Compd*., 1992, **28** (Engl. Transl.)].
18. A. B. Sheremetev, O. V. Kharitonova, E. V. Mantseva, V. O. Kulagina, E. V. Shatunova, N. S. Aleksandrova, T. M. Mel´nikova, E. A. Ivanova, D. E. Dmitriev, V. A. Eman, I. L. Yudin, V. S. Kuz´min, Yu. A. Strelenko, T. S. Novikova, O. V. Lebedev, and L. I. Khmel´nitskii, *Zh. Org. Khim.*, 1999, **35**, 1555 [*Russ. J. Org. Chem.*, 1999, **35**, 1525 (Engl. Transl.)].
19. D. E. Dmitriev, Yu. A. Strelenko, and A. B. Sheremetev, *Izv. Akad. Nauk, Ser. Khim.*, 2002, 277 [*Russ. Chem. Bull., Int. Ed.*, 2002, **51**, 290].
20. B. M. Lynch, *Can. J. Chem*., 1977, **55**, 541.
21. F. H. Allen and O. Kennard, *Chem. Des. Auto. News*, 1993, **8**, 31.
22. A. S. Batsanov and Yu. T. Struchkov, *Zh. Strukt. Khim.*, 1985, **26**, 65 [*J. Struct. Chem. USSR,* 1985, **26** (Engl. Transl.)].
23. *SMART V5.051 and SAINT V5.00, Area Detector Control and Integration Software*, Bruker AXS Inc., Madison, WI-53719, USA, 1998.
24. G. M. Sheldrick, *SHELXTL-97, Version 5.10*, Bruker AXS Inc., Madison, WI-53719, USA, 1997.

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