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REACTION OF FUNCTIONALLY SUBSTITUTED VINYL ETHERS WITH 3,4-DIAMINOFURAZAN AND FURAZAN-3,4-DICARBOXYLIC ACID DIHYDRAZIDE

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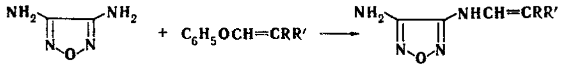
UDC 547.793.2

Enaminofurazans were obtained by reaction of vinyl ethers with 3,4-diaminofurazan. It was established by IR and PMR spectroscopy that enaminofurazans exist in the form of a chelate complex. The structure of the chelate complex is discussed. Enehydrazides were obtained by reaction with furazan-3,4-dicarboxylic acid dihydrazide. When there is a cyano group in the ether molecule, the reaction does not stop with the formation of the enehydrazide but continues with its cyclization to give a pyrazole ring.

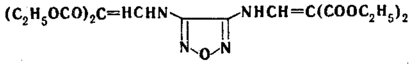
Diverse condensed systems are obtained by the reaction of functionally substituted vinyl ethers with aromatic and heterocyclic amines. We have investigated the reactions of 3,4-diaminofurazan (I) and furazan-3,4-dicarboxylic acid dihydrazide (II) with vinyl ethers containing keto, ester, and cyano groups.

The corresponding enamines III-IX were obtained in all cases in the reactions of the vinyl ethers with furazan I. Dienamine X was obtained when the reaction was carried out with excess ethoxymethylenemalonic ester. An analysis of the PMR spectra shows that the enamines obtained exist in the form of a chelate cyclic complex with a hydrogen bond between the proton of the amino group and the oxygen atom of the C =O group (XI). The formation of a hydrogen bond leads to slow exchange of the NH proton, as a result of which spin-spin coupling of the NH and CH protons with a constant of 13 Hz shows up in the PMR spectra. Such a large constant is characteristic for coupling of the NH and CH protons in the anti orientation that is realized in the chelate-bonded cis-s-cis form [1]. The presence of this form is also confirmed by the characteristic marked shift of the signal of the NH proton to weak field (10-12 ppm) [1].

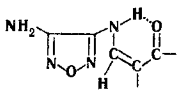


I

III-IX



X



XI

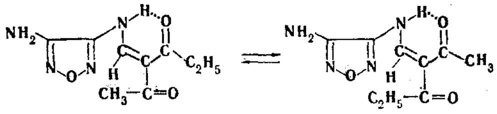
Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga 226006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 319-323, March, 1979. Original article submitted January 20, 1978.

0009-3122/79/1503-0261$07.50

TABLE 1. PMR Spectra of Enaminofurazans III-X

Compound	R	R′	Chemical shifts, δ, ppm						
			CH	NH	NH_2	$COCH_3$	$COOC_2H_5$		Other
III	$COCH_3$	$COCH_3$	8,14	11,38	6,36	2,24 2,32	—	—	
IV	$COCH_3$	COC_2H_5	8,26	11,49	6,34	2,32 2,44	—	—	1,00 (CH_3); 2,64 (CH_2) 1,10 2,94
V	$COCH_3$	COPh	7,84	11,68	6,33	2,42	—	—	7,38—7,69 (Ph)
VI	$COCH_3$	$COOC_2H_5$	8,27	11,40	6,38	2,41	1,22	4,20	—
VII	$COOC_2H_5$	$COOC_2H_5$	8,13	10,03	6,33	—	1,16 1,20	4,07 4,17	—
VIII	C≡N	$COOC_2H_5$	8,29	10,65	6,29	—	1,19	4,16	—
IX	C≡N	C≡N	7,93	10,78	6,31	—	—	—	—
X	$COOC_2H_5$	$COOC_2H_5$	8,02	10,73	—	—	1,16 1,21	4,07 4,19	—

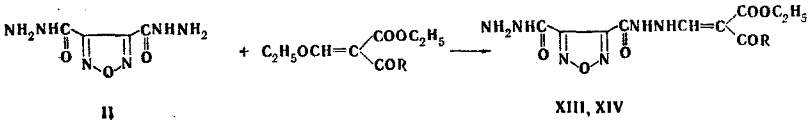
In the case of III, VII, and X with R = R' nonequivalence of the cis- and trans-acetyl (III) and ester (VII and X) groups is observed in the PMR spectra (Table 1). If R ≠ R', one might expect that the enamines would exist in two isomeric forms. In fact, doubling of the signals of the protons of the methyl and ethyl groups is observed in the spectrum of enamine IV, and both signals have approximately identical intensities.


IV a

IV b

It is known [2] that the barrier to rotation about the double bond in enamines is small and that rotation can be realized at room temperature. This leads to the impossibility of isolation of isomers IVa and IVb in individual form. In contrast to this, similar doubling of the signals is observed in the spectra of enamines V, VI, and VIII. The greater difference in the R and R' groups in their ability to form hydrogen bonds in this case evidently makes one of the isomers more stable, as a result of which the equilibrium is shifted to favor the formation of the most stable product. A band above 1710 cm^{-1}, which is associated with the stretching vibrations of the free ester carbonyl group, is observed in the IR spectra of enamines VI-VIII and X. A band of the stretching vibrations of the free ketone carbonyl group in enamines III and IV appears at 1680 cm^{-1}. The absence of this band in the spectra of V and VI and the presence in the spectrum of enamine VI of a band at 1721 cm^{-1} constitute evidence that the acetyl group rather than the ester or benzoyl group participates in the formation of a hydrogen bond. This is also confirmed by the fact that the signal of the NH proton in the PMR spectrum of enamine VI is observed in the region characteristic for III-V, in which the carbonyl group participates in the formation of a hydrogen bond. The fact that the NH signal in the spectra of III-V is found at weaker field than in the spectra of VII and X indicates that the hydrogen bond with the ketone group is stronger than the bond with the ester group. Thus the material set forth above makes it possible to conclude that enamines V and VI exist in the form of a chelate complex in which the oxygen atom of the acetyl group participates in the formation of a hydrogen bond. A comparison of the IR spectra of III-IX and X at 3100-3500 cm^{-1} makes it possible to assign the two narrow bands at 3232-3292 and 3330-3362 cm^{-1} to the stretching vibrations of the NH_2 group and the broad band at 3212-3242 cm^{-1} and the band of lower intensity at 3270-3290 cm^{-1} to vibrations of the NH group. The nonequivalence of the cyano groups in IX shows up in the IR spectrum, in which two narrow bands at 2248 and 2254 cm^{-1} are observed.

In an attempt to cyclize the enamines obtained to furazanodiazepines by refluxing in an alcohol solution of sodium ethoxide [3] we observed cleavage of the enamine to give the starting 3,4-diaminofurazan.


II

XIII, XIV

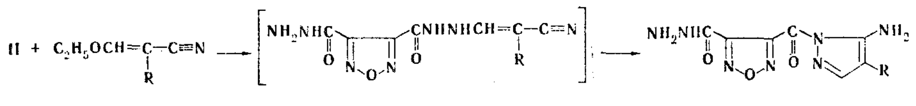
XIII $R=OC_2H_5$; XIV $R=CH_3$

The corresponding enehydrazides XIII and XIV were obtained by the reaction of ethoxymethylenemalonic and ethoxymethyleneacetoacetic esters with dihydrazide II. As in the case of enamines, nonequivalence of the protons of the two esters groups shows up in the PMR spectrum of enehydrazide XIII. However, in contrast to enamine VI, two signals of protons of both methyl and ethyl groups are observed in the spectrum of enehydra-

TABLE 2. IR Spectra of Enaminofurazans III-X

Compound	Characteristic absorption frequencies, ν, cm^{-1}			
	NH_2	NH	$COOC_2H_5$	C≡N
III	3392, 3330	3276, 3221	—	—
IV	3400, 3332	3270, 3220	—	—
V	3415, 3348	3280, 3236	—	—
VI	3400, 3362	3290, 3242	1721	—
VII	3403, 3354	3282, 3230	1740	—
VIII	3410, 3355	3283, 3242	1710	2246
IX	3432, 3330	3272, 3212	—	2248, 2254
X	—	3280, 3212	1738	—

zide XIV. This indicates that XIV is a mixture of interconverting cis and trans isomers. Spin–spin coupling of the CH and NH protons is not displayed in the spectra of the enehydrazides. The signal of the enehydrazide NH proton also cannot be recorded.



XV, XVI

XV R = C≡N; XVI R = $COOC_2H_5$

In the case of the reaction of hydrazide II with ethoxymethylenemalonic acid dinitrile and ethoxymethylenecyanoacetic ester the reaction does not stop with the formation of the enehydrazide but continues with its cyclization to give a pyrazole ring.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in Nujol were recorded with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in d_6-DMSO were recorded with a Bruker WH-90 spectromter at 20 deg C with tetramethylsilane as the internal standard.

The characteristics of all of the products obtained are presented in Table 3.

General Method for the Preparation of Enaminofurazans III-VII. A mixture of 1.0 g of furazan I and 0.011 mole of the appropriate vinyl ether was heated at 100-120 deg C for 5-10 min until a homogeneous mixture formed. The mixture cooled, and the reaction product began to crystallize.

3,4-Bis(β,β-dicarbethoxymethyleneamino)furazan (X). This compound was similarly obtained by using a threefold excess of ethoxymethylenemalonic ester.

Enaminofurazans VIII and IX. A solution of 1.0 g (0.01 mole) of furazan I and 0.012 mole of the appropriate vinyl ether in 7 ml of alcohol was refluxed for 1 h, after which the alcohol was removed by evaporation, and the product was recrystallized.

Action of Sodium Ethoxide on Enaminofurazans III-VIII. A 0.01-mole sample of the appropriate enaminofurazan was added to a solution of sodium ethoxide obtained from 0.3 g of sodium and 15 ml of alcohol, and the mixture was cooled and neutralized with acetic acid. The solvent was removed by evaporation, and the residue was recrystallized from water to give 0.5-0.7 g (50-70%) of 3,4-diaminofurazan.

Diethyl Furazan-3,4-dicarboxylate. A solution of 15.8 g (0.1 mole) of furazan-3,4-dicarboxylic acid in 100 ml of alcohol was refluxed in the presence of 5 ml of thionyl chloride for 3 h, after which the alcohol was removed by evaporation, and the residue was dissolved in ether. The ether solution was washed with a solution of sodium carbonate and dried over anhydrous sodium sulfate. The ether was removed by evaporation, and the product was distilled at 80-83 deg C (1 mm) to give 19.0 g (89%) of a colorless liquid. Found: C 44.6; H 4.6; N 13.3%. $C_8H_{10}N_2O_5$. Calculated: C 44.9; H 4.7; N 13.1%.

Furazan-3,4-dicarboxylic Acid Dihydrazide (II). A solution of 21.4 g (0.1 mole) of diethyl furazan-3,4-dicarboxylate in 20 ml of alcohol was added dropwise at room temperature to a solution of 40 ml of hydrazine hydrate in 50 ml of alcohol, and the mixture was stirred for 8 h. The resulting precipitate was removed by filtration. IR spectrum: 1680 (C=O); 3190 and 3320 cm^{-1} ($NHNH_2$).

TABLE 3. Characteristics of II-X and XIII-XVI

Compound	mp, deg C*	Found, %			Empirical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
II	182—184	25,6	3,2	45,0	$C_4H_6N_6O_3$	25,8	3,2	45,2	85
III	144—146	45,2	4,7	26,8	$C_8H_{10}N_4O_3$	45,7	4,8	26,7	75
IV	123—125	48,1	5,3	25,0	$C_9H_{12}N_4O_3$	48,2	5,4	24,8	72
V	158—160	57,1	4,5	20,3	$C_{13}H_{12}N_4O_3$	57,4	4,4	20,6	64
VI	143—144	44,4	4,9	23,6	$C_9H_{12}N_4O_4$	45,0	5,0	23,3	80
VII	128—129	44,3	5,1	20,5	$C_{10}H_{14}N_4O_5$	44,4	5,2	20,7	68
VIII	162—164	43,3	4,1	31,2	$C_8H_9N_5O_3$	43,0	4,0	31,4	52
IX	139—141	41,0	2,3	47,5	$C_6H_4N_6O$	40,9	2,3	47,7	55
X	141—143	49,4	5,4	12,8	$C_{18}H_{24}N_4O_9$	49,1	5,5	12,7	61
XIII	106—108	40,3	4,6	23,5	$C_{12}H_{16}N_6O_7$	40,5	4,5	23,6	59
XIV	113—115	40,7	4,4	26,0	$C_{11}H_{14}N_6O_6$	40,5	4,3	25,8	48
XV	>300	36,3	2,3	42,5	$C_8H_6N_8O_3$	36,6	2,3	42,8	64
XVI	160—162	39,1	3,5	31,9	$C_{10}H_{11}N_7O_6$	38,8	3,6	31,7	67

*All of the reaction products were recrystallized from alcohol.

(3-Carbhydrazido-4-furazanoyl)hydrazinomethylenemalonic Ester (XIII). A solution of 1.86 g (0.01 mole) of hydrazide II and 2.16 g (0.01 mole) of ethoxymethylenemalonic ester in 10 ml of alcohol was refluxed for 15 min, after which it was cooled, and the resulting precipitate was removed by filtration. PMR spectrum: 1.15 and 1.18 (6H, two triplets, $2CH_3$), 4.01 and 4.13 (4H, two quartets, $2CH_2$), and 7.82 ppm (1H, s, CH). IR spectrum: 1670 (C=O), 1700 (C=O), and 3100-3300 cm^{-1} (NH, NH_2).

(3-Carbhydrazido-4-furazanoyl)hydrazinomethyleneacetoacetic Ester (XIV). A 1.86-g (0.01 mole) sample of hydrazide II was added to a solution of 1.86 g (0.01 mole) of ethoxymethyleneacetoacetic ester in 6 ml of alcohol, during which the mixture became warmer, and the hydrazide gradually dissolved. The mixture was then allowed to stand for 3 h, after which the precipitate was removed by filtration. PMR spectrum: 1.16 and 1.22 (3H, two triplets, CH_3), 4.11 and 4.22 (2H, two quartets, CH_2O), 2.33 and 2.38 (3H, two singlets, CH_3CO), and 8.04 ppm (1H, s, CH).

3-(3-Amino-4-cyanopyrazolyl)furazan-4-carboxylic Acid Hydrazide (XV). A solution of 1.86 g (0.01 mole) of hydrazide II and 1.22 g (0.01 mole) of ethoxymethylenemalonic acid dinitrile in 10 ml of alcohol was refluxed for 20 min, after which the precipitate was removed by filtration. IR spectrum: 3100-3480 (NH, NH_2), 2226 (C≡N), and 1680 cm^{-1} (C=O). PMR spectrum: 7.60 ppm (1H, s, CH).

3-(3-Amino-4-carbethoxypyrazoyl)furazan-4-carboxylic Acid Hydrazide (XVI). This compound was obtained by a method similar to that used to prepare XV. PMR spectrum: 1.18 (3H, t, CH_3), 4.09 (2H, q, CH_2), 7.49 ppm (1H, s, CH). IR spectrum: 3100-3480 (NH, NH_2) and 1705 cm^{-1} (C=O).

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