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SYNTHESIS AND STRUCTURE OF N-SUBSTITUTED 2-AMINO-3-PHENACYLIDENE-3,4-DIHYDROQUINOXALINES

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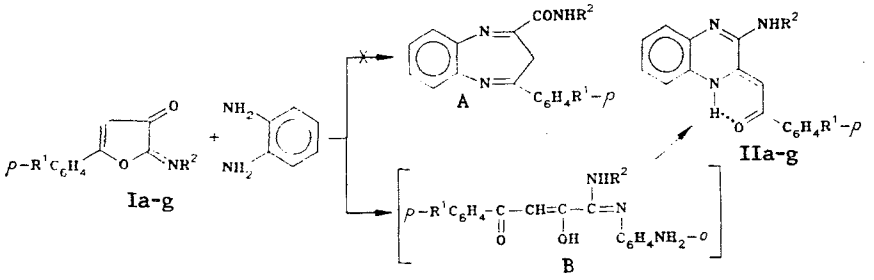
UDC 547.863.1'728.2'553.1.04

N-Substituted 2-imino-5-aryl-2,3-dihydro-3-furanones react with o-phenylenediamine to form N-substituted 2-amino-3-phenacylidene-3,4-dihydroquinoxalines.

It is known that N-substituted 2-imino-5-aryl-2,3-dihydro-3-furanones are readily decyclized by amines and water with nucleophilic attack occurring at $C_{(5)}$ of the heterocycle [1]. N-Substituted 2-imino-4,5-diaryl-2,3-dihydro-3-furanones [2] behave similarly with amines but hydrazines can attack both $C_{(5)}$ and $C_{(2)}$ [2].

With the aim of studying the chemical properties of N-substituted 2-imino-5-aryl-2,3-dihydro-3-furanones I we have investigated their reaction with o-phenylenediamine. The direction of nucleophilic attack at the $C_{(5)}$ atom or $C_{(2)}$ atom of compound I can lead to formation of either 1,4-benzodiazepine-2-carboxiamides A or to 2,3-disubstituted quinoxalines II, respectively.



I, II a–d $R^2=C(CH_3)_3$, a $R^1=H$, b $R^1=CH_3$, c $R^1=Br$, d $R^1=Cl$; e, f $R^2=p$-$CH_3C_6H_4SO_2CH_2$, e $R^1=H$, f $R^1=Cl$; g $R^2=2,5$-$(CH_3)_2C_6H_3$, $R^1=H$

We have shown that reaction of iminofuranones Ia-g with o-phenylenediamine at room temperature for 2-4 h gives the N-substituted 2-amino-3-phenacylidene-3,4-dihydroquinoxalines IIa-g. Evidently nucleophilic attack occurs only at atom $C_{(2)}$ of heterocycle I in this case with opening to the substituted amidines B and subsequent cyclization to the quinoxalines II.

The spectral characteristics of the compounds obtained confirmed their structure. The IR spectra of the alternative 1,4-benzodiazepin-2-carboxamides A show an "amide I" band near 1670 cm^{-1} [3] but this was absent in the spectra of IIa-g. The mass spectrum of IIc showed a molecular ion peak with m/z 399 and 397 together with fragment ion peaks at 384, 382 $[M - CH_3]^+$, 343, 341 $[M - C_4H_8]^+$, 185, 183 $[BrC_6H_4CO]^+$, and 158 $[M - C_4H_8 - BrC_6H_4CO]^+$.

Thanks to the presence of the amidine and aminovinylketone fragments the quinoxalines can exist in one of several tautomeric forms and a choice can be made based on their spectral data.

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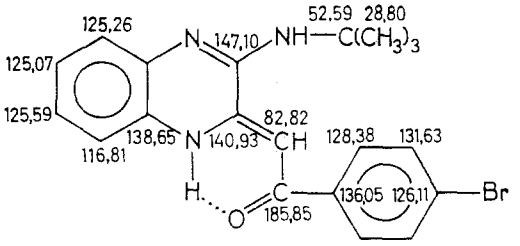


Fig. 1. ^{13}C NMR signal assignments for IIc.

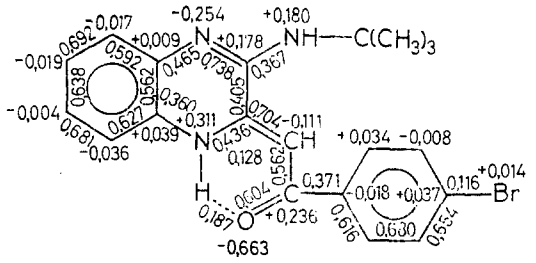
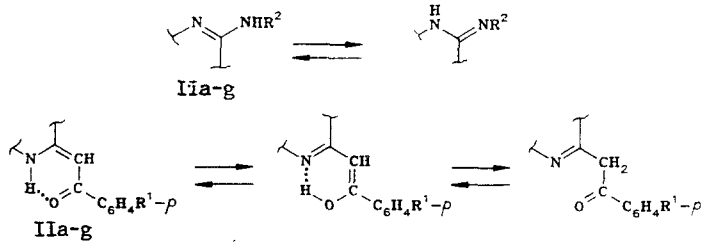


Fig. 2. Molecular diagram for IIc.



The ^1H NMR spectra of IIa-g show a singlet methine proton in the region 5.75-6.62 ppm and the absence of a methylene proton singlet allowing elimination of a structure with a phenacyl substituent at $C_{(3)}$. Signals in the ^{13}C NMR spectrum of IIc can be assigned to aromatic ring carbons and those at 82.82 and 185.85 ppm to the vinyl and carbonyl carbon atoms, respectively (Fig. 1). The latter points to the phenacylidene form for the $C_{(3)}$ substituent. The signal at 116.81 ppm apparently corresponds to the electron rich $C_{(5)}$ atom in agreement with calculations for the IIc molecule in the HMO approximation (Fig. 2).

The shift of the ^{13}C NMR signals for the vinyl and carbonyl carbons of IIc to high field when compared to several enaminoketones [4] and the significant chemical shift of the $N_{(4)}$–H proton signals in their ^1H NMR spectra (15.43-15.95 ppm) for IIa-d, g point to the presence of a strong intramolecular hydrogen bond [4, 5]. A similar NH signal in the spectra of IIe,f was not observed by reason of extensive broadening due to exchange with the solvent. Formation of this intramolecular hydrogen bond is accompanied by redistribution of electron density within the enaminoketone fragment [6] with an increasing bond order for $N_{(4)}$–$C_{(3)}$ and $C_{(exo)}$–$C_{(C=O)}$ and a decreasing bond order for $C_{(3)}$–$C_{(exo)}$ and C=O. This correlates with the lowering of the ketonic carbonyl frequency to 1607-1600 cm^{-1} in the IR spectra of IIa-g.

Spin-spin interaction with the N–H proton causes the methylene protons of the p-$CH_3C_6H_4$-SO_2CH_2 fragment of IIe,f to appear as a doublet at 5.42-5.62 ppm ($J \approx 6.3$ Hz) in the PMR spectrum. This means that it is a substituted amino group which is attached to the $C_{(2)}$ position of the heterocycle.

EXPERIMENTAL

IR spectra were taken on an IR-20 instrument in paraffin oil. ^1H NMR spectra were obtained on RS-60 (compounds IIa-d) and RY-2310 instruments (IIe-g) at 60 MHz with HMDS internal standard and ^{13}C NMR spectra on a Bruker HX-90 (90 MHz) using internal TMS. Mass spectra were

TABLE 1. Physical Data for IIa-g

Compound	Empirical formula	mp, °C	IR spectrum, δ, ppm		^{1}H NMR spectrum, δ, ppm	Yield, %
			N—H	C=O		
IIa	$C_{20}H_{21}N_3O$	122...123	3385	1607	1,58 (s 9H, $C(CH_3)_3$); 4,91 (br 1H, NH); 5,92 (s 1H, =CH); 7,65 (m, 9H, Ar); 15,85 (br 1H, $N_{(4)}$—H) ($CDCl_3$)	69
IIb	$C_{21}H_{23}N_3O$	143...145	3378	1604	1,58 (s 9H, $C(CH_3)_3$); 2,35 (s 3H, CH_3); 4,82 (br 1H, NH); 5,85 (s 1H, =CH); 7,58 (m 8H, Ar); 15,72 (br 1H, $N_{(4)}$—H) ($CDCl_3$)	71
IIc	$C_{20}H_{20}BrN_3O$	165...166	3380	1603	1,55 (s 9H, $C(CH_3)_3$); 6,08 (br 1H, NH); 6,45 (s 1H, =CH); 7,63 (m, 8H, Ar); 15,95 (br 1H, $N_{(4)}$—H) [$(CD_3)_2CO$]	87
IId	$C_{20}H_{20}ClN_3O$	151...152	3384	1603	1,58 (s 9H, $C(CH_3)_3$); 4,82 (br 1H, NH); 5,75 (s 1H, =CH); 7,38 (m 8H, Ar); 15,76 (br 1H, $N_{(4)}$—H) ($CDCl_3$)	80
IIe	$C_{24}H_{21}N_3O_3S$	172...174	3366	1600	1,85 (s 3H, CH_3); 5,42 (d 2H, CH_2); 6,62 (s 1H, =CH); 7,12 (m 13H, Ar); 9,60 (br 1H, NH) (C_5D_5N)	76
IIf	$C_{24}H_{20}ClN_3O_3S$	175...177	3360	1600	2,38 (s 3H, CH_3); 5,62 (d 2H, CH_2); 6,72 (br 1H, =CH); 7,55 (m 12H, Ar); 8,55 (br 1H, NH) [$(CD_3)_2SO$]	70
IIg	$C_{24}H_{21}N_3O$	168...170	3380	1600	2,25 (s 3H, CH_3); 2,35 (s 3H, CH_3); 4,60 (br 1H, NH); 6,15 (s 1H, =CH); 7,40 (m 12H, Ar); 15,43 (br 1H, $N_{(4)}$—H) ($CDCl_3$)	59

recorded on a Varian MAT-311A. Quinoxaline IIc molecular calculations were carried out using Streitwieser parameters [7] with intramolecular hydrogen bonding evaluated according to [8].

The course of the reaction and purity of the products was monitored by TLC on Silufol plates in the solvent system 1:1 benzene-ether.

Physical data for IIa-g is given in Table 1. Elemental analytical data for C, H, and N agreed with that calculated.

2-tert-Butylamino-3-(p-R^1-phenylacylidene)-3,4-dihydroquinoxalines (IIa-d). A solution of o-phenylenediamine (0.005 mole) in absolute chloroform (10 ml) was added to the iminofuranone (Ia-d, 0.005 mole) in absolute chloroform (20 ml). After 3-4 h the solvent was removed and the residue recrystallized from ethanol.

2-Tosylmethylamino-3-phenacylidene-3,4-dihydroquinoxaline (IIe). A solution of o-phenylenediamine (0.76 g, 0.007 mole) in absolute THF (10 ml) was added to the iminofuranone (Ie, 2.40 g, 0.007 mole) in absolute THF (30 ml). The reaction mixture was held for 2 h at room temperature and the precipitated solid was filtered off and recrystallized from DMF-2-propanol (1:1) in 2.45 g yield.

2-Tosylmethylamino-3-p-chlorophenacylidene-3,4-dihydroquinoxaline (IIf). o-Phenylenediamine (0.25 g, 0.002 mole) in absolute dioxane (10 ml) was added to the iminofuranone (If, 0.80 g, 0.002 mole) in absolute dioxane (20 ml). The reaction mixture was held for 2 h at room temperature, raised to reflux, and filtered hot. The filtrate was cooled to room temperature and the precipitated solid was filtered off and recrystallized from acetonitrile in 0.70 g yield.

2-(2,5-Xylylamino)-3-phenacylidene-3,4-dihydroquinoxaline (IIg). o-Phenylenediamine (0.40 g, 0.0036 mole) in absolute chloroform (10 ml) was added to the iminofuranone (Ig, 1.00 g, 0.0036 mole) in absolute chloroform (20 ml). The reaction mixture was held for 3 h at room temperature and filtered. The filtrate was evaporated and the residue recrystallized from benzene in 0.77 g yield.

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MASS SPECTROMETRY OF NITROGENOUS HETEROCYCLES.

1. MASS SPECTROMETRIC EVALUATION OF STABILITY OF TETRAHYDROPYRAZINES ANNELATED TO FIVE- AND SIX-MEMBERED HETEROCYCLES

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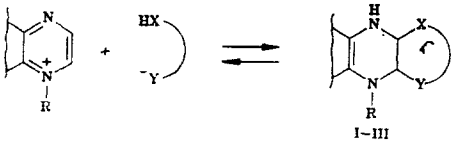
V. N. Charushin, and O. N. Chupakhin

UDC 543.51:547.863

Based on a study of electron impact mass spectra of a large number of tetrahydropyrazines, which are joined to five- and six-membered heterocyclic and carbocyclic residues, the trends which characterize the stability of these condensed systems are found. The proposed criteria can be used for evaluation of the chemical stability of these compounds, for example, their propensity toward the reverse dissociation reaction.

Recently, a series of studies have appeared in which mass spectrometric methods are used for evaluation of the stability of hydrogenated heterocycles and for prediction of reaction directions [1-4]. In the present work, experimental material on mass spectrometry of condensed tetrahydropyrazines is correlated. These data were accumulated during a study of the fragmentation patterns of hydrogenated heterocycles, the cyclization products of 1,4-diazine cations with bifunctional nucleophiles.

Annelation of azines by carbo- and heterocycles through reaction of bifunctional nucleophilic reagents to the two ortho-carbon atoms of the azine ring is a general method for synthesis of pyrazines and condensed systems based on them. Cyclizations of this type are known in a series of pyrazine derivatives, quinoxaline, pyrido[2,3-b]pyrazine, and pteridine, including both 1,4-diazinium cations [5-7] and neutral 1,4-diazines activated by acceptor substituents, in particular, pteridine derivatives [8, 9].



I–III

The cyclizations examined are reversible and, as was shown in a number of works [5-7, 10-12], dissociation of the cycloadducts I-III creates grounds for various types of isomerization which lead to regio- [10, 11] and stereoisomeric compounds [12] as well as to a change in the annelated ring [10]. The result of these complicated reverse reactions which as a rule have a few possible directions is largely determined by the thermodynamic stability of the adducts I-III which are formed. Chemical experiments [10] have shown that dissociation of cyclic adducts occurs with rupture of both C–X and C–Y bonds and leads to final addends, cations of 1,4-diazine and the corresponding dinucleophiles. The tendency of the condensed

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