DERIVATIVES OF 1,2-DIAMINOIMIDAZOLE IN REACTIONS WITH ACETYLARENES

V. D. Orlov, I. Z. Papiashvili, M. V. Povstyanoi,
and V. P. Kruglenko

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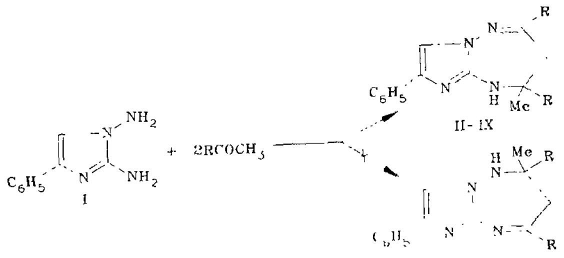
2-Methyl-2,4-diaryl-7-phenyl-5H-3,4-dihydroimidazo[1,2-b]-1,2,4-triazepines have been obtained by reacting 4-phenyl-1,2-diaminoimidazole with acetylarenes in an acid medium. It has been shown that they form monohydrochlorides at the azomethine nitrogen atom of the imidazole ring.

4-Phenyl-1,2-diaminoimidazole (I) reacts with chalcones to form 2,4,7-triaryl-5H-3,4-dihydroimidazo[1,2-b]-1,2,4-triazepines [1]. In our search for new methods for the synthesis of these bicyclic systems we studied the reaction of I with acetyl-containing compounds. It was assumed that 1,2-diamine I, like o-phenylenediamine [2-4], should undergo a three-component condensation with acetyl-containing compounds.

It is known [5] that diamine I reacts with acetophenone in an acidic medium to form a bisazomethine derivative with a melting point of 237-238°C. We studied this reaction in both alkaline and acidic media. It was found that in methanol containing additions of triethylamine (the conditions for the condensation of I with chalcones [1]) or a solution of an alkali metal hydroxide, the formation of a seven-membered triazepine ring is not observed. When the reaction is carried out in an acidic medium, 1,2,4-triazepine II forms, the best yield being achieved when the hydrochloride of diamine I is reacted with acetophenone. This law is also maintained for substituted acetophenones, 2-acetylthiophene, 2-acetylfuran, and acetone, making it possible to obtain a number of 2,2,4-trisubstituted 5H-3,4-dihydroimidazo[1,2-b]-1,2,4-triazepines (II-IX, Table 1).

In the present work we also studied the reaction of 4,5-diphenyl-1,2-diaminoimidazole and 1,2-diaminobenz[b]imidazole with acetophenone. However, the original components were recovered unchanged in both acidic and alkaline media.

Compounds II-IX are individual (TLC), and their structures were confirmed by the data from elemental analysis and spectroscopy. For example, in the IR spectra there are bands for the stretching vibrations of NH and C=N groups (Table 1), as well as alicyclic and methyl C–H bonds (2900-3150 cm^{-1}). An analogy is observed in the nature of the UV spectra of the compounds synthesized and the dihydroimidazotriazepines previously described in [1]. The PMR spectra of compounds II-IX, which were obtained in CF_3COOH (they are insufficiently soluble in neutral organic solvents), show singlets for CH_3 and CH_2 groups (Table 1). Thus, despite the fact that the formation of two isomeric products is possible in the reactions of 4-phenyl-1,2-diaminoimidazole with acetylarenes, only one of them was isolated and identified:



It was shown in [1] that the formation of the C=N bond during the synthesis of 2,4,7-

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A. M. Gor'kii Khar'kov State University, Khar'kov 310077. Kherson Industrial Institute, Kherson 325008. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1396-1398, October, 1984. Original article submitted December 1, 1983; revision submitted March 12, 1984.

TABLE 1. 2-Methyl-2,4-di-R-7-phenyl-5H-3,4-dihydroimidazo[1,2-b]-1,2,4-triazepines

Compound	R	mp, °C	Boiling time, h	IR spectrum, cm^{-1}		UV spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	$\Delta\lambda$*	δ, ppm		Found: N, %	Empirical formula	Calculated: N, %	Yield, %
				νN–H	νC=N			CH_3	CH_2				
II	C_6H_5	171—172	2	3422	1649	341 (7,1), 276 (34,1)	18	2,70	2,76	15,1	$C_{24}H_{22}N_4$	15,3	61
III	4-$CH_3OC_6H_4$	186—187	5	3440	1633	334 (10,4), 287 (43,0)	17	2,68	2,75	12,6	$C_{27}H_{26}N_4O_2$	12,8	51
IV	4-ClC_6H_4	174—175	2	3428	1645	347 (8,2), 279 (44,7)	28	—	—	12,8	$C_{24}H_{20}Cl_2N_4$	12,9	68
V	4-BrC_6H_4	173—174	2	3402	1642	345 (8,9), 277 (44,9)	28	2,72	2,80	10,5	$C_{24}H_{20}Br_2N_4$	10,7	63
VI	4-$O_2NC_6H_4$	231—232	1	3368	1642	383 (7,4), 284 (42,0)	43	—	—	18,0	$C_{24}H_{20}N_6O_4$	18,4	56
VII	2-Thienyl	169—170	3	3429	1644	354 (9,0), 293 (33,5)	26	2,64	2,71	14,4	$C_{21}H_{18}N_4S_2$	14,3	67
VIII	2-Furyl	190—191	3	3308	1659	342 (9,1), 288 (38,5)	19	2,65	2,73	15,7	$C_{21}H_{18}N_4O_2$	15,6	54
IX	CH_3	165—166	3	3414	1628	274 (38,6)	10	—	—	20,5	$C_{15}H_{18}N_4$	20,6	45

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*The difference between the values of λ_{max} for the long-wavelength absorption bands of the basic and salt forms.

triaryl-5H-3,4-dihydroimidazo[1,2-b]-1,2,4-triazepines occurs at the 1-amino group of compound I, which has a hydrazine character. This law should clearly be maintained in the synthesis of compounds II-IX.

In the electronic spectra of compounds II-VI the values of λ_{max} for the long-wavelength absorption bands have undergone 10-43-nm hypsochromic shifts in comparison to the 2,4-disubstituted analogs [1]. This is explained on the basis of an analysis of Dreiding models (with the use of segments reflecting the van der Waals radii), which showed that the seven-membered ring has a rigid "boat" structure and that the presence of two bulky groups in the second position creates steric hindrances to the radical in position 4 of the heterocycle, disrupting its interaction with the remaining conjugated system of the molecule. The UV spectra of dihydroimidazotriazepines II-IX recorded in methanol or benzene with additions of hydrogen chloride ($\sim 10^{-5}$ to 10^{-4} M) show redistribution of the intensities of the absorption of the molecular and ionic forms with a clearly expressed isosbestic point (the same law is also characteristic of compounds not containing a 2-CH_3 group). It may be postulated that a one-step process resulting in the formation of the monochloride takes place. The reaction of II with dry HCl in benzene is accompanied by the precipitation of the salt. After it was separated, washed with benzene, and briefly dried in air at room temperature, an analysis for its chlorine and nitrogen content, which also confirmed the formation of a monohydrochloride, was carried out. A comparison of the IR spectra of the original compound II and its salt revealed a sharp displacement of the νC=N band toward higher frequencies (by 35 cm^{-1}) and a decrease in the νN–H frequency by 45 cm^{-1} for the hydrochloride. It is suggested that the salt-formation process occurs at the N_3 atom of the imidazole heterocycle. In such a case, the skeletal vibrations of the heterocycle, including the C=N bond, undergo changes. The spatial proximity of the N_3 atom of the imidazole ring and the imino group of the triazepine ring is also reflected in the value of νN–H for the hydrochloride of compound II. The hypsochromic shift of λ_{max} for the long-wavelength absorption band in the UV spectra of the hydrochlorides of compounds II-IX in comparison to the absorption of the unprotonated compounds is attributed to the postulated specificity of the protonation. The main chromophoric system HN–C_3N_2H–N=C–R is polarized in the direction of the azomethine bond of the seven-membered ring, and the protonation of the five-membered heterocycle counteracts this polarization. The correctness of the choice of the protonation center is supported by the results of a calculation of the molecular diagram of I performed according to the CNDO/2 method [1], from with it follows that the maximum negative charge is concentrated on the $N_{(3)}$ atom of the imidazole ring. This is also evinced by the experimental data in [6], which indicated that the basicity of imidazoles is approximately two orders of magnitude higher than that of aromatic azomethines. The specificiity of the protonation probably accounts for the increased stability of 2,4-di- and 2,2,4-trisubstituted 5H-3,4-dihydroimidazo[1,2-b]-1,2,4-triazepines with respect to reduction of the seven-membered ring to a five-membered ring, while in the case of the derivatives of 2,3-dihydro-1H-1,5-benzodiazepine in acidic media, this process is one of the most characteristic [7].

EXPERIMENTAL

The electronic absorption spectra of compounds II-IX were measured in methanol (at concentrations from $2 \cdot 10^{-5}$ to $5 \cdot 10^{-5}$ M) on a Specord UV-VIS spectrophotometer, the IR spectra were recorded in KBr tablets on a Specord IR-75 spectrometer, and the PMR spectra were recorded in CF_3COOH on a Varian SL-100 instrument with TMS as an internal reference. The individuality of all the compounds was varified by TLC on Silufol UV-254 plates with a 1:3 methanol–chloroform mixture as the eluent.

1,2-Diamino-4-phenylimidazole (I) was obtained according to the method in [5].

2-Methyl-2,4,7-triphenyl-5H-3,4-diamino-4-phenylimidazo[1,2-b]-1,2,4-triazepine (II). A stream of dry HCl is passed through a solution of 1 g (5.7 mmole) of 1,2-diamino-4-phenylimidazole (I) in 45 ml of benzene until the formation of a yellow precipitate of the salt of the diamine ceases. The salt is filtered out and dissolved in 30 ml of methanol containing 1.4 g (11.4 mmole) of acetophenone. The solution is boiled for 2 h, evaporated to half of the volume of the solvent, and neutralized with ammonia. This gives 1.3 g (61%) of light yellow crystals of base II with mp 171-172°C (from methanol). Compounds III-IX are synthesized in a similar manner, only the boiling time of the solutions being varied (Table 1).

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REACTION OF AROMATIC o-DIAMINES WITH ISATINS.

2.* 2,3-DIAMINONAPHTHALENE

A. G. Drushlyak, A. V. Ivashchenko,
and V. V. Titov

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The reaction of 2,3-diaminonaphthalene with isatins gives a mixture of indolo[2,3-b]benzo[g]quinoxalines, 3-(2-aminophenyl)-2(1H)-benzo[g]quinoxalines, and spiro (2,3-d]imidazoline)-2,3'-indolin-2'ones. The ratio between the products is influenced by the solvent and the relative value of the positive charge on the α-carbon atom in the isatin.

It was previously reported [2] that 2,3-diaminonaphthalene (I) reacts with N-methyl-(IIb) and N-acetylisatin (IIe) in ethanol to form spiro compounds IVb and e, with N-methylisatin (IIb) in acetic acid to form indoloquinoxaline VIb, and with N-acetylisatin (IIe) in acetic acid to form spiro compound IVe with traces of the corresponding indoloquinoxaline. In [1] we showed that the reaction of o-phenylenediamine with N-methylisatin gives a mixture of products and that the reaction of N-acetylisatin results in the formation of aminophenylquinoxaline, rather than the spiro compound.

Investigating the reaction of 2,3-diaminonaphthalene (I) with isatins, we found that spiro compounds IVb-d mainly form with N-methylisatins IIb-d in ethanol, that indoloquinoxalines VIa-c form with isatins IIa-c in acetic acid, and that a mixture of aminophenylquinoxalinones Vd-e and indoloquinoxalines VId and e forms with isatins IId and e in acetic acid. In benzene the reactions with all the isatins investigated predominantly produce aminophenylquinoxalinones Va-e (Table 1).

In contrast to the data in [2] it was found that the reaction of o-diamine I with isatin IIa results in the formation of the corresponding aminophenylbenzoquinoxalinone (Va) along with benzindoloquinoxaline VIa in all solvents except acetic acid. The main product of the reaction of o-diamine I with N-acetylixatin IIe under all the conditions investigated (Table 1) is acetaminophenylbenzoquinoxalinnone Ve, rather than spiro compound IVe [2]. The hydrolysis of this compound in alkaline medium results in the quantitative formation of compound Va. The latter contains and NH_2 group, which is diazotized, and then the compound is coupled with β-naphthol. The IR spectrum of Va contains a band for νCO at 1675 cm^{-1}, which is characteristic of six-membered lactams [3], and its electronic spectrum is similar to the spectra of other aminophenylbenzoquinoxalinones (Table 2). The acetyl derivative Ve again forms when Va is acylated by acetyl chloride. The formation of Ve when 2,3-diamino-

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*For report 1 see [1].

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