N-Cyclohexyl (1-acetyl-5,6-benzindol-3-yl)acetamidine hydrochloride (IIIj) was obtained from 2.0 g (6 mmoles) of compound II in 200 ml of absolute ethanol and 0.6 g (6 mmoles) of cyclohexylamine in 14 ml of absolute ethanol under the conditions of synthesis of IIIg. After cooling, 1.34 g of amidine IIIj was obtained from the reaction mixture by precipitation with hexane.

(1-Acetyl-5,6-benzindolyl-3-yl)morpholylacetamidine hydrochloride (IIIk) was obtained from 1.26 g (4 mmoles) of imino-ether II in 126 ml of absolute ethanol and 0.32 g (4 mmoles) of morpholine in 6 ml of absolute ethanol. Yield 0.94 g.

N,N-Cystaminyl di[1-acetyl-5,6-benzindol-3-yl)acetamidine] dihydrochloride (IIIl) was obtained from 0.5 g (1.5 mmoles) of imino-ether II in 50 ml of absolute ethanol and 0.23 g (1.5 mmoles) of cystamine in 32 ml of dry ether. Yield 0.25 g.

N-Ethyl, N-phenyl (1-acetyl-5,6-benzindol-3-yl)acetamide (IV) was obtained from 1 g (3 mmoles) of imino-ether II and 0.28 g (3 mmoles) of aniline under conditions similar to those used in the synthesis of IIIg. Yield 0.4 g.

Ethyl (1-acetyl-5,6-benzindol-3-yl)acetate (V) was obtained from 0.1 g (0.3 mmole) of imino-ether II and 15 ml of 20% aqueous ethanol at 20-25–C. Yield 0.05 g.

LITERATURE CITED

1. G. M. Ostapchuk, E. I. Voronina, T. M. Ivanova, T. A. Babushkina, L. B. Shagalov, and N. N. Suvorov, *Khim. Geterotsikl. Soedin.*, No. 3, 346 (1984).
2. L. B. Shagalov, G. M. Ostapchuk, T. M. Ivanova, and N. N. Suvorov, *Khim. Geterotsikl. Soedin.*, No. 6, 779 (1987).

TAUTOMERISM AND METHYLATION OF 2-IMINO-4-IMIDAZOLIDINONES

S. M. Ramsh, N. G. Zheltonog, and E. S. Khrabrova

UDC 547.781.5

5-Benzylidenecreatinine and 2'-phenylglycocyamidine exist in DMSO-D_6 in the imino form. In basic medium, the two compounds exhibit a dual reactivity with respect to methylating agents, forming $N_{(2')}$- and $N_{(3)}$-methyl derivatives.

We have previously shown that in basic medium, 2-imino-4-thiazolidinones (pseudothiohydantoins) and 2-imino-4-oxazolidinones exhibit dual reactivity with respect to alkylating agents [1, 2]. The tautomerism of these compounds was also studied [2, 3]. It was of interest to clarify whether anions of 2-imino-4-imidazolidinones (glycocyamidines, creatinines, cyclic derivatives of guanidine) are capable of reacting in dual manner, i.e., whether this mode of reaction is a general property of 2-imino-4-azolidinone anions, the charge of which is delocalized over the amidine system of bonds.

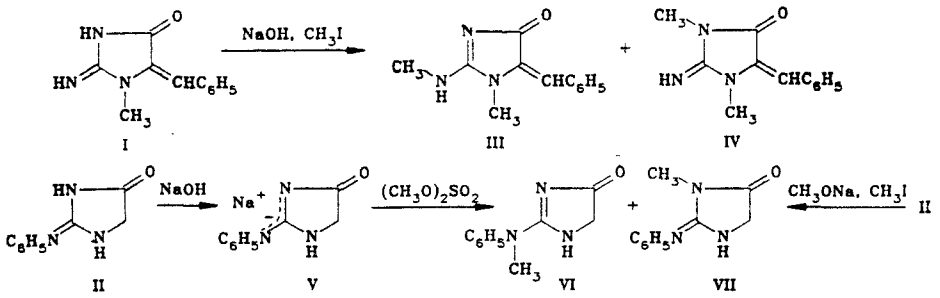
The subjects of the present investigation are 2-imino-5-benzylidene-1-methyl-4-imidazolidinone (I, 5-benzylidenecreatinine) and 2-phenylimino-4-imidazolidonone (II, 2'-phenylglycocyamidine). It is known [4] that in a basic medium compound I is alkylated with the formation of a 2'-methyl derivative. The alkylation of compound II was not previously studied. Since in the investigation of the dual reacting, methylated derivatives were obtained modeling tautomeric forms of compounds I and II, we also studied the tautomeric composition of these compounds, the information on which has not yet been given in the literature.

Lensovet Leningrad Technological Institute, Leningrad 198013.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 62-65, January, 1991. Original article submitted May 19, 1989.

0009-3122/91/2701-0052$12.50

© 1991 Plenum Publishing Corporation



A TLC monitoring of the reaction mixture showed that, in the presence of 1 equivalent of alkali, compound I reacts with methyl iodide in ethanol with the formation of two isomeric methyl derivatives, one of which was found to be identical with 2'-methyl-5-benzylidenecreatinine (III) [4]. The N-methyl structure of the second methyl derivatives is indicated by the presence of a carbonyl absorption band in its IR spectrum, while the position of the methyl proton signals in the PMR spectra of the isomers (Table 1), which is the same as in 2'- and 3-methylpseudothiohydantoins [5] and in 2'- and 3-methylcreatinines [6], indicates that the second methyl derivative is in fact 3-methyl-5-benzylidenecreatinine (IV).

Comparison of the PMR spectra of 5-benzylidenecreatinine (I) and its methylated derivatives III and IV permits us to state that in DMSO-D_6 compound I exists mainly in the imino form [7]. In fact, the aromatic protons resonate in the form of an AA'MM'X system, like the corresponding protons of the model of the imino form IV, while the signal of the aromatic protons of 2'-methyl derivative III does not split. The most probable reason for the difference in the character of the aromatic absorption of isomers III and IV is the existence of compound III in the form of an amino tautomer, in which the conjugation of the phenyl ring (through the $C_{(5)}$=C bond) with the carbonyl group, which is also conjugated with the cyclic $C_{(2')}$=$N_{(3)}$ bond, is weaker than in compound IV with the known imino structure because of the "scattering" effect of the polar conjugation [8]. Moreover, the chemical shifts of the $C_{(5)}$=CH proton of 6.10 ppm and of the 1-NCH_3 protons of 3.10 ppm in compounds I are similar to those in the model of the imino form IV (6.16 and 3.08 ppm, respectively) than in the amino tautomer III (6.36 and 2.94 ppm).

Similarly to 5-benzylidenecreatinine (I), the 2'-phenylglycocyamidine (II) also exhibits a dual reactivity with respect to alkylating agents in a basic medium, forming methyl derivatives VI and VII. The sodium salt V can be isolated in the form of a pure compound. The ratio of yields of isomers VI and VII is about 1:4 during the alkylation of compound II with methyl iodide in methanol and 1:3 during the allylation of salt V by dimethyl sulfate in acetonitrile.

Compound VI is detected by TLC in the reaction mixture from the amination of 2'-methylthiohydantoin by N-methylaniline, and its 2'-methyl structure does not arouse any doubts. Bearing in mind that glycocyamidines in the basic form are never

TABLE 1. Spectral Characteristics of Creatinines I, III, and IV and Glycocyamidines II and V-VII

Compound	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, cm^{-1}		PMR spectrum, ppm			
		C=O	C=N	C_6H_5	NH	$C_{(5)}$=CH or $C_{(5)}H_2$	1-NCH_3*
I	240 (3,98), 280 (4,16), 340 (4,04)	1730	1660	8,00 m, 7,22 m	7,84	6,10	3,10
II	248 (4,32)	1710, 1695	1620	6,98 ... 7,51 m	9,96	3,64	—
III	231 (3,97), 319 (4,23)	1730	1650	7,28 s	7,06	6,36	2,94
IV	235 (4,01), 341 (4,32)	1725	1670	7,82 m; 7,26 m	6,94	6,16	3,08
V	248 (4,32)	1695	1650, 1545	7,20 m; 6,80 m	—**	3,42	—
VI	235 (4,32)	1660	1600	7,30 s	7,52	3,62	—
VII	250 (3,75)	1755	1660	7,22 m; 6,94 m	—**	3,74	—

*$\delta_{N_{(2')}CH_3}$: 2.82 (III) and 3.26 ppm (VI); $\delta_{N_{(3)}CH_3}$: 2.94 (IV) and 2.88 ppm (VII).

**Not detected.

alkylated at the $N_{(1)}$ atom [9], then it is most probable that the second isomer is the 3-methyl derivative VII. The position of the methylation is confirmed by comparison of the chemical shifts (Table 1) of methyl group protons at $N_{(2')}$ atom of 3.26 ppm (compound VI) and t $N_{(3)}$ of 2.88 ppm (compound VII) with the shifts of similar protons in 1-thia analogs of 3.46 and 3.06 ppm, respectively [10].

The model compounds VI and VII, like the corresponding 1-thia analogs [10], have characteristic differences in the absorption region of aromatic protons, which makes it possible to identify with certainty the tautomeric form of compound II predominating in DMSO-D_6 from the form of the PMR spectrum. The aromatic protons signal in the 2'-methyl derivative VI is narrow, and its multiplicity at a working frequency of 100 MHz is not observed. On the contrary, the aromatic protons in the 3-methyl derivative VII absorb in the form of an AA'BB'C spin system, which is characteristic for the imino structure [10] and is attributable to the conjugation of the phenyl ring with the exocyclic $N_{(2')}=C_{(2)}$ bond, while in compound VI, because of the participation of the unshared pair of the $N_{(2')}$ atom in a "competing" conjugation with the $C_{(2)}=N_{(3)}$ and $C_{(4)}=O$ bonds, the chemical shifts of all the phenyl ring protons are similar to one another. As in the model of the imino form VII, the complex multiplet of the aromatic protons of glycocyamidine II represents an AA'BB'C system, which indicates a predominance of the imino form of this compound. In contrast to the 1-thia analog [10], all the protons of compound II are isochronic at room temperatures. Thus, the two compounds studied, I and II, exist in DMSO-D_6 mainly in the imino form. Their anions are ambidentate, i.e., they do not differ in their reactivity from the previously studied thia and oxa analogs.

EXPERIMENTAL

The PMR spectra were run on a Tesla BS-497C spectrometer (100 MHz) in DMSO-D_6 using HMDS as internal standard, the IR spectra – on an IKS-29 spectrophotometer in mineral oil, and the UV spectra – on an SF-16 spectrophotometer in ethanol. The TLC was carried out on Silufol UV-254 plates using as eluents the ethanol–chloroform, 1:4 (compounds II, V-VII) and 1:10 systems (compounds III, IV). The elemental analysis data of compounds IV-VII for C, H, and N correspond to the calculated values.

5-Benzylidene-1-methyl-2-methylamino-4-imidazolinone (III) and 5-Benzylidene-2-imino-1,3-dimethyl-4-imidazolidinone (IV, $C_{12}H_{13}NO$). A mixture of 5.0 g (25 mmoles) of compound I [11], 1.1 g (28 mmoles) of sodium hydroxide and 5.0 g (35 mmoles) of methyl iodide in 200 ml of ethanol was boiled for 10 h. The solvent was evaporated, and the residue was treated with 300 ml of a 5% aqueous solution of sodium hydroxide. The undissolved oily residue was extracted with warm (35-40°C) benzene (3 × 30 ml), the benzene extract was dried overnight over sodium sulfate, benzene was evaporated, and the residue was chromatographed on a 25 × 1 cm column filled with a Silpearl 100/160 μ (CSSR) silica gel with chloroform as eluent. The mixture was deposited on the column in the form of a solution in 10 ml of chloroform, mixed with the adsorbent. Fractions of 10 ml were collected and analyzed by TLC. The corresponding eluates with R_f 0.32 and 0.50 were combined and evaporated. Compounds III and IV that have been isolated were crystallized from chloroform. The yield of the 2'-methyl derivative III was 0.50 g (9%), mp 129-131°C; according to the data in [4], 129°C. The yield of the 3-methyl derivative IV was 0.55 g (10%), mp 110-112°C.

Sodium Salt of 2'-Phenylglycocyamidine (V, C_9H_8NaO). A 0.53-g portion (3 mmoles) of compound II [12] in 6 ml of a 10% aqueous solution of sodium hydroxide was heated at 80°C to complete dissolution. The salt solution was then cooled to 0-5°C and after 10-15 min was poured into 100 ml of acetone cooled to 0-5°C. The precipitate of salt V was filtered off, washed with acetone, dried in vacuo, and held at 100°C (2 mm Hg) in the presence of a 3-Å molecular sieve to a constant weight, mp 250-260°C (decomp.). Yield 0.47 g (80%).

2-Methylphenylamino-4-imidazolidinone (VI, $C_{10}H_{11}N_3O$) and 3-Phenylimino-3-methyl-4-imidazolidinone (VII, $C_{10}H_{11}N_3O$). A. A mixture of 0.35 g (2 mmoles) of compound II and 0.57 g (4 mmoles) of methyl iodide was boiled for 3 h in a sodium methylate solution, obtained from 0.046 g (2 mmoles) of sodium and 30 ml of absolute methanol. The solvent was then evaporated and 10 ml of water was added to the oily residue. The precipitate of the unreacted compound II that separated out was filtered off and the filtrate was extracted with warm (30-35°C) benzene (2 × 40 ml). The benzene extract was dried overnight over sodium sulfate, benzene was evaporated to dryness, and the residue was crystallized from heptane to give compound VII in a yield of 0.11 g (30%), mp 150-152°C. The aqueous layer remaining after the extraction was extracted with chloroform (2 × 40 ml), the extract was dried overnight over sodium sulfate, the chloroform was distilled to dryness, and the residue was crystallized from benzene or toluene to give compound VI in a yield of 0.03 g (8%), mp 189-191°C.

B. A mixture of 0.20 g (1 mmole) of salt V and 0.13 g (1 mmole) of dimethyl sulfate in 25 ml of acetonitrile was boiled for 2 h, the solvent was then distilled off, and the residue was treated according to method A. The yield of compound VI was 0.015 g (8%), and of compound VII – 0.045 g (24%).

The authors wish to express their gratitude to A. V. Dogadin for running the PMR spectra.

LITERATURE CITED

1. Yu. G. Basova, S. M. Ramsh, and A. I. Ginak, *Khim. Geterotsikl. Soedin.*, No. 8, 1046 (1981).
2. S. M. Ramsh, E. S. Khrabrova, and A. I. Ginak, *Khim. Geterotsikl. Soedin.*, No. 3, 388 (1989).
3. S. M. Ramsh, N. A. Smorygo, and A. I. Ginak, *Khim. Geterotsikl. Soedin.*, No. 8, 1066 (1984).
4. V. N. Nicolet and E. D. Campbell, *J. Am. Chem. Soc.*, **50**, 1155 (1928).
5. S. M. Ramsh, S. Yu. Solov'eva, and A. I. Ginak, *Khim. Geterotsikl. Soedin.*, No. 6, 761 (1983).
6. G. L. Kenyon and G. L. Rowley, *J. Am. Chem. Soc.*, **93**, 5552 (1971).
7. B. I. Ionin, B. A. Ershov, and A. I. Kol'tsov, *NMR Spectroscopy in Organic Chemistry* [in Russian], Khimiya, Leningrad (1983).
8. A. S. Dneprovskii and T. I. Temnikova, *Theoretical Principles of Organic Chemistry* [in Russian], Khimiya, Leningrad (1979).
9. C. Lempert, *Chem. Revs.*, **59**, 667 (1959).
10. S. M. Ramsh, N. A. Smorygo, E. S. Khrabrova, and A. I. Ginak, *Khim. Geterotsikl. Soedin.*, No. 4, 544 (1986).
11. R. L. Richardson, C. E. Welch, and S. Calvert, *J. Am. Chem. Soc.*, **51**, 3074 (1929).
12. C. Lempert and J. Breuer, *Magy. Kem. Flurt.*, **69**, 323 (1963).

AMINOMETHYLATION OF 1-R-TETRAZOLES

V. P. Karavai and P. N. Gaponik

UDC 547.796.1.07:542.-953.3:541.124

The reaction of tetrazole and a series of its 1-substituted derivatives with formaldehyde and alkylamines under mild conditions results in aminomethylation of the heterocyclic ring at the carbon atom with the formation of the corresponding Mannich bases. It was found that strong acids (HCl and CF_3COOH) have an activating action during the process. An ylide mechanism of the reaction was proposed from the data obtained.

Tetrazole and its 1H-derivatives have recently become relatively readily available compounds [1, 2] and, therefore, they are of interest as starting materials for the synthesis of various functionally substituted tetrazoles, which are used in medicine, biology, agriculture, and technology [3]. Very promising for this purpose are the reactions at the cyclic carbon atom, which have practically not been investigated until now [3-5], since it had been assumed that the electrophilic substitution of this hydrogen atom is impeded because of the deactivation of this position by annular nitrogen atoms [6].

Scientific Research Institute of Physicochemical Problems, V. I. Lenin Belorussian State University, Minsk 220080. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 66-71, January, 1991. Original article submitted May 29, 1989.

0009-3122/91/2701-0055$12.50 © 1991 Plenum Publishing Corporation