QUATERNARY AZO COMPOUNDS BASED ON ADENINE DERIVATIVES

P. B. Zikmanis

UDC 547.857.7:543.422.25.4.6

The structure of quaternary azo compounds containing an azo group and an acrylic acid residue attached to the exocyclic nitrogen atom of adenine is proposed for the products of coupling of N^6-furfuryladenine with resorcinol, orcinol, and m-cresol after reaction of N^6-furfuryladenine with nitrous acid on the basis of the UV, PMR, and IR spectral data and the results of electrochemical reduction.

The analytical application of the colorimetric reaction of N^6-furfuryladenine (kinetin) (I) with N-(1-naphthyl)ethylenediamine after reaction of I with nitrous acid was mentioned in [1]. We have reported similar reactions of the natural compound N^6-(Δ^2-isopentenyl)adenine [2] and zeatin [3] with aromatic amines and phenols. These reactions have been suggested for analytical application [3, 4].

An assumption regarding the possible similarity in the structures of the compounds formed and the products of diazo coupling of 4-aminoimidazole-5-carboxamide [5], which is formed in the acid hydrolysis of the reduced adenine ring, was expressed in [1].

The UV spectra (Table 2) of the products of coupling of reduced and unreduced N^6-furfuryladenine I with aromatic compounds and the UV spectrum of the intermediate of the reaction of I with nitrous acid (Fig. 1) constitute evidence for retention of the purine system in the reaction products, in contrast to azo derviatives based on 4-aminoimidazole-5-carboxamide; this is in agreement with the data obtained in a spectroscopic study of the diazo coupling reactions of reduced purine compounds [5]. Retention of the purine system in the products of the reactions of I is also confirmed by the presence of characteristic signals of the protons attached to 2-C and 8-C in the PMR spectra (Table 1).

These data and the conformity of the qualitative characteristics of the substances obtained in this study and the azo compounds make it possible to assume that the reaction proceeds at the exocyclic nitrogen atom of adenine. According to our observations, coupling with aromatic compounds containing oriented +M substituents (resorcinol, m-cresol, m-aminophenol, orcinol, and β-naphthol) is characteristic for the products of the reaction of I with nitrous acid. This sort of fusion could not be realized with phenol, pyrocatechol, and α-naphthol. It is unlikely that reactions of this sort proceed via the mechanism of the Bamberger reaction, which assumes the formation of a diazonium cation and is not characteristic for secondary amines [6]. One may assume the existence of an intermediate of the product of the reaction of I with nitrous acid in a form similar to the N^6-isonitroso derivative of substituted adenine and subsequent direct coupling with activated

TABLE 1. PMR Spectra of II

Compound	Solvent	Chemical shifts, δ, ppm							SSCC, Hz			
		purine (2-H, 8-H)	10-H	11-H	12-H	13-H	14-H	CH_3	$J_{10.11}$	$J_{12.13}$	$J_{13.12}$	$J_{13.14}$
IIa	$(CD_3)_2SO$	7,99; 7,76	7,01	5,78	8.14	6,74	6,82	2.62	12,5	9,3	9,3	2,5
IIb	$(CD_3)_2SO$	8.06. 7,78	6,97	5.70	8.01	6,47	6.40	—	12.5	9,4	9.4	2.5
IIc	$(CD_3)_2SO$	7.96; 7,63	7,05	5.78	—	6,21	6,39	2,61	11,8	—	—	2,4
IIa	CF_3COOH		7.08	6.31					12,4			
IIa —Si	CF_3COOH		7.02	6,24					12,4			

Institute of Microbiology, Academy of Sciences of the Latvian SSR, Riga. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 986-990, July, 1976. Original article submitted June 11, 1975; revision submitted January 7, 1976.

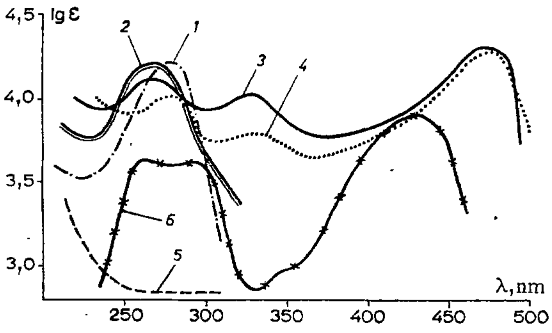
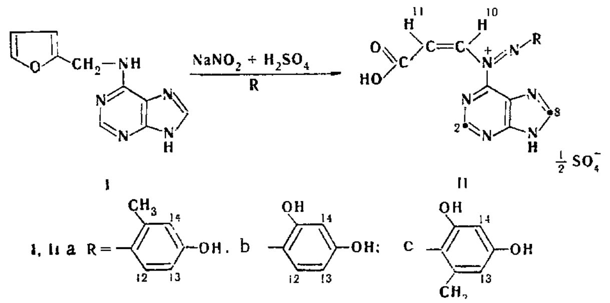


Fig. 1. UV spectra of azo compounds of purines and intermediates: 1) N^6-furfuryladenine (I), 0.1 N H_2SO_4; 2) intermediate in the reaction of I with nitrous acid*; 3) IIc (ethanol, pH 1.5); 4) 2.6-dihydroxypurine-8-azobenzene-4'-sulfonic acid (0.1 N NaOH); 5) reduced I; 6) azo compound of reduced I with orcinol.*

TABLE 2. Characteristics of II

Compound	Dec. temp., °C	Empirical formula	Found, %				Calculated, %				UV spectrum, nm (in ethanol)		IR spectrum, cm^{-1} (in mineral oil and hexachlorobutadiene)	Yield, %
			C	H	N	S	C	H	N	S	λ_{max} (lg ε) pH 1,5	λ_{max} (lg ε) pH 13		
IIa	280	$C_{15}H_{13}N_6O_3 \cdot$ $\cdot 1/2H_2O \cdot$ $\cdot 1/2(SO_4^{--})$	46,8	4,1	21,6	4,2	47,1	3,7	21,9	4,2	272(4,18), 327(4,14), 443(4,22)	280(4,11), 347(4,14). 490(4,37)	1320, 1385, 1440, 1470, 1490, 1580, 1615, 1655, 2380, 2700, 3120, 3460,	45
IIb	310	$C_{14}H_{11}N_6O_4 \cdot$ $\cdot 1/2H_2O \cdot$ $\cdot 1/2(SO_4^{--})$	43.6	3,7	21.4	4.1	43.7	3,1	21,9	4.2	270(4,14), 328(4,10), 478(4,35)	282(4,16), 353(4,12), 511(4.40)	1350, 1390, 1420, 1480, 1560, 1610, 1655 (sh.) 2600, 3140, 3410	50
IIc	300	$C_{15}H_{13}N_6O_4 \cdot$ $\cdot 1/2H_2O \cdot$ $\cdot 1/2(SO_4^{--})$	44,9	4.0	20.8	3,8	45.3	3.5	21.2	4,0	269(4,12), 328(4,04), 471(4.31)	282(4,04), 354(4,07). 520(4.42)	1320, 1350, 1395, 1460, 1490, 1540, 1570, 1625, 1650 (sh.) 2400, 2700, 3120, 3155, 3350	60

aromatic compounds. The structure of the intermediates of the reaction of I with nitrous acid was not studied experimentally because of the nonquantitative character of the reactions, the limited possibilities of extraction of them from dilute strongly acidic reaction solutions, and their considerable instability (rapid loss of the ability to undergo coupling with aromatic compounds and resinification of the products). The conformity between the products (of the presumed II structure) of the reaction of N^6-furfuryladenine with nitrous acid and subsequent coupling with activated phenols was verified by a study of the UV,* PMR, and IR spectra and the results of electrochemical reduction and elementary analysis of the final reaction products.



The UV spectra of II (Fig. 1 and Table 2) are characteristic for conjugated heterocyclic systems, particularly azo compounds [7, 8], and display a certain similarity to the UV spectrum of 2,6-dihydroxypurine-

---

*The UV spectra were recorded for dilute reaction solutions against the appropriate controls, and the log ε values were found on the basis of the molecular weight of I.

8-azobenzene-4'-sulfonic acid, which was obtained in [9] by diazo coupling of diazosulfanilic acid with xanthine.

Compounds II are readily reduced by zinc dust and $SnCl_2$ and, after reduction, give positive reactions with p-dimethylaminobenzaldehyde and bindone. After diazotization, the products of reduction of II are capable of coupling with aromatic compounds, and this confirms the presence of an azo group in the investigated compounds [10, 11]. Compounds II display reversible shifts of the absorption maxima in the visible region of the UV spectrum (Table 2) as the pH changes. Compounds IIb and IIc have complexing properties with Cu^{2+}, Co^{2+}, U^{5+}, and Fe^{3+} ions at pH 4-6, values that are characteristic for o-hydroxyazo compounds. Compound IIa has the selective complexing properties with the Hg^{2+} ion that are characteristic for heterocyclic azo compounds with similar structures [12].

Three waves corresponding to the number of equilibrium ionic forms with $E_{1/2}$ values of, respectively, -0.33, -0.75, and -1.04 V relative to a saturated calomel electrode (for IIc) are characteristic for the polarographic reduction of II in anhydrous dimethylformamide (DMF). The low reduction potentials, the substantial differences in the heights of the waves, and the effects of the addition of strong and weak proton donors constitute evidence in favor of the azonium structure of II [13].

The PMR spectra of II (Table 1) display characteristic singlets of 2-H and 8-H protons of the purine system, absorption signals of aromatic protons with chemical shifts and spin–spin coupling constants (SSCC) corresponding to substitution of the 12-H–14-H type, and signals of methyl groups (IIa, IIc). In addition, two characteristic doublets related to the signals of protons attached to the 10-H and 11-H double bond are present in the PMR spectra. The chemical shifts and SSCC of these signals are in complete agreement with the signals of the cis-ethylene protons of α,β-unsaturated carboxylic acids [14, 15]. No other signals than those presented in Table 1 are present in the PMR spectra of II at δ 15 ppm. The PMR spectra in the strong-field region were recorded from pyridine solutions in order to exclude the possibility of overlapping with the signals of the protons of the methyl groups of the phenols and dimethyl sulfoxide (DMSO). It follows from the PMR data that the most likely structural unit that fastens the ethylene grouping is the carboxyl group.

The possibility of the existence of quinonehydrazone form II, which includes, in particular, possible cyclization of the ethylene grouping with respect to the $N_{(1)}$ atom of purine, was verified by a study of the PMR spectra of II and their silyl derivatives in CF_3COOH. The PMR spectrum confirms the presence of a trimethylsilyl group (δ 9.51 ppm) in silylated IIa. The silylation of the hydroxyl group of the phenol is confirmed by the δ value of the trimethylsilyl group relative to tetramethylsilane (TMS), the practically coinciding δ values of the characteristic doublets of the ethylene 10-H and 11-H grouping of IIa and its silylated derivative (Table 1), and the shifts of the δ values of the aromatic protons of the latter, which, however, do not yield to precise assignment with the additional signals of protonation [16] of the heterocyclic system of purine in CF_3COOH in the region of aromatic proton absorption. Thus structure IIa is confirmed for the investigated compound, and this assignment also corresponds to the results of polarographic reduction of azonium and quinoid structures [13].

Steric factors [the possibility of interaction of the $N_{(1)}$ atom of purine with the carboxyl hydroxyl group] or even unsuitable selection of the reagent and silylation conditions probably hinder the formation of the trimethylsilyl ester of the carboxyl group. In particular, we were also unable to realize the N-silylation of both IIa and 6-chloropurine.

The interpretation of the IR spectra of II (Table 2) is hindered because of the presence of heterocyclic and aromatic systems, considerable conjugation, and the possibility of the formation of hydrogen bonds. The absorption of the azo group in the IR spectra of aromatic compounds of complex structure also cannot be precisely assigned [17]. The absorption bands at 3410-3500 cm^{-1} are characteristic for hydroxyl groups with intermolecular hydrogen bonds. The broad bands at 2600-2800 cm^{-1} are characteristic for the ν_{OH} bands of carboxyl groups with strong hydrogen bonds. The bands at 1560-1580, 1610-1625, and 1650 cm^{-1} correspond to $\nu_{C=C}$ and $\nu_{C=O}$ bands (the precise assignment is hindered because of the possibility of considerable lowering and partial "mixing" of the absorption frequencies of such structures [18]). Because of the strong mesomeric effect of conjugation between the systems of double bonds, the characteristic carbonyl absorption may also be absent [19].

With respect to the formation of an acrylic acid residue during cleavage of the furan ring, it should be noted that reactions of this sort involving acid cleavage of the furan ring are well known [20]. One cannot exclude the possibility that the inductive effect of the purine system and nitrosation of the furan ring promote this.

It might be assumed that the subsequent cleavage is associated with the subsequent α-C-nitrosation relative to the carboxyl group, which promotes decarboxylation [21], with subsequent transformations of the C-nitroso (or isonitroso) derivatives to a carboxyl group with simultaneous migration of the double bond to give a stabilized structure, in this case an acrylic acid residue, which forms an enamine grouping with the exocyclic nitrogen atom of adenine. A large diversity of reactions, tautomeric transformations, and physicochemical peculiarities [18] are characteristic for this grouping, and this generates interest in a further study of heterocyclic compounds of this type.

EXPERIMENTAL

The UV spectra of ethanol solutions of the compounds were recorded with a Specord UV-vis spectrophotometer [the appropriate pH values (Table 2) were established by the addition of 1 N HCl and 1 N NaOH] in 0.1 N NaOH and in 0.1 N HCl. The UV spectra of the intermediate in the reaction of I with nitrous acid and of the products of reduction of I (Fig. 1) were recorded in dilute (1 : 10-1 : 40) reaction solutions using the reaction solutions of corresponding concentrations that did not contain I as the control. The IR spectra of mineral oil and hexachlorobutadiene suspensions of the compounds were recorded with IKS-14 and UR-20 spectrometers. The PMR spectra of 7-10% solutions in d_6-DMSO, pyridine, and CF_3COOH were obtained with a Perkin–Elmer R-12A spectrometer; the chemical shifts were measured relative to TMS (the internal standard).

Compounds II. A total of 50 ml of 10 M H_2SO_4 and 15 ml (2.5 mmole) of 1% $NaNO_2$ were added to a solution of 0.215 g (1 mmole) of N^6-furfuryladenine (Chemapol, Czechoslovakia) in 100 ml of 0.1 N H_2SO_4. The color of the mixture changed to greenish-yellow after 35-40 min, after which 15 ml (7.5 mmole) of 5% sulfamic acid solution was added to remove the excess nitrous acid (test with starch-iodide paper), and 10 ml (2 mmole) of a 2% solution of the aromatic compound in alcohol was added. The resulting precipitate was centrifuged, washed with small portions of water, ethanol, and acetone, and purified by reprecipitation by the addition of water to concentrated DMF solutions and crystallization from a large volume of ethanol (with removal of the excess solvent by distillation). Compounds II (Table 2) were orange-red (IIa) and red (IIb, c) powders that were practically insoluble in nonpolar solvents and acids, slightly soluble in alcohol and water, and quite soluble in DMF, DMSO, pyridine, and alkalis.

Silylation of IIa. Compound IIa was silylated by refluxing for 2 h with a fourfold excess of hexamethyldisiloxane (HMDS), after which the HMDS was removed by distillation.

Reduction and Diazo Coupling of the Products of the Reduction of I. Zinc dust (1 g) was added to 0.005 g ($2.5 \cdot 10^{-5}$ mole) of I in 20 ml of 2 N HCl, and the mixture was heated on a boiling-water bath for 15 min. It was then filtered, and 5 ml of the filtered reaction solution was diazotized by the addition of 1 ml of a 1% of a 1% $NaNO_2$ solution in the course of 30 min. The mixture was then treated with 1 ml of 5% sulfamic acid solution and 2 ml of a 0.5% solution of orcinol in alcohol.

The author sincerely thanks his co-workers of the Institute of Organic Synthesis of the Academy of Sciences of the Latvian SSR, V. T. Glezer and Yu. Yu. Popelis for their valuable assistance in this research.

LITERATURE CITED

1. R. K. Atkin and R. L. Wain, Nature, 214, 530 (1967).
2. P. B. Zikmanis, Izv. Akad. Nauk LatvSSR, Ser. Khim., No. 5, 620 (1973).
3. P. B. Zikmanis, Izv. Akad. Nauk LatvSSR, No. 7, 69 (1975).
4. P. B. Zikmanis, Izv. Akad. Nauk LatvSSR, No. 11, 94, (1973).
5. S. Friedman and J. S. Gots, Arch. Biochem. Biophys., 39, 254 (1952).
6. A. N. Nesmeyanov and S. G. Ioffe, Zh. Obshch. Khim., 11, 392 (1941).
7. O. V. Sverdlova, Electronic Spectra in Organic Chemistry [in Russian], Leningrad (1973), p. 117.
8. C. N. R. Rao, Electronic Spectra in Chemistry [Russian translation], Vol. 30, Moscow (1964), p. 105.
9. J. R. Spies and T. H. Harris, J. Am. Chem. Soc., 61, 351 (1939).
10. E. Van Gulle, in: Houben-Weil, Methoden der Organische Chemic, edited by Eugen Müller, Georg Thieme Verlag, Stuttgart (1952-1958).
11. E. N. Moundrianakis and M. Beer, Biochim. Biophys. Acta, 95, 23 (1965).
12. L. P. Kolesnikova, Author's Abstract of Candidate's Dissertation, Rostov-on-Don (1972).
13. V. T. Glezer and P. B. Zikmanis, Summaries of Papers Presented at the Sixth All-Union Conference on Polarography [in Russian], Riga (1975).
14. J. M. Purcell, S. G. Morris, and H. Susi, Anal. Chem., 38, 588 (1966).
15. F. C. Stehling and K. W. Bartz, Anal. Chem., 38, 81 (1966).

16. R. Wagner and W. von Philipson, Helv. Chim. Acta, 54, 1543 (1971).
17. L. Bellamy, Infrared Spectra of Complex Molecules, Methuen (1958).
18. Ya. F. Freimanis. The Chemistry of Enamino Ketones, Enamino Imines, and Enamino Thiones [in Russian], Riga (1974).
19. J. C. Brand and T. Eglington, Application of Spectroscopy in Organic Chemistry [Russian translation], Moscow (1967), p. 149.
20. R. Elderfield and T. Dodd, in: Heterocyclic Compounds, Vol. 1, Wiley (1950).
21. S. Patai (editor), The Chemistry of the Carbon–Nitrogen Double Bond, London–New York–Sydney–Toronto (1970), p. 86.

HETEROCYCLIC NITRO COMPOUNDS

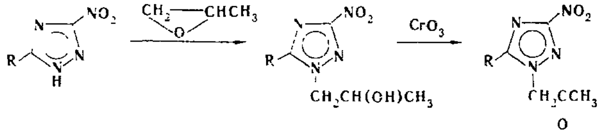
XX.* KETONES OF THE 1,2,4-TRIAZOLE SERIES

T. P. Kofman, T. L. Uspenskaya,
N. Yu. Medvedeva, and M. S. Pevzner

UDC 547.792.3.5:542.953.943

A number of triazolylpropanones were synthesized by oxidation of 1-(2-hydroxypropyl)-3-nitro-5-R-1,2,4-triazoles obtained by condensation of 3-nitro-5-R-1,2,4-triazoles with propylene oxide. Similar triazolylbutanones were obtained by reaction of 3-nitro-5-R-1,2,4-triazoles with methyl vinyl ketone.

It has been previously shown that the reaction of 3-nitro-5-R-1,2,4-triazoles with substituted α-oxides gives secondary alcohols, which can be oxidized with dichromate in sulfuric acid to the corresponding ketones [2, 3]. We obtained a number of 1-(2-oxopropyl)-3-nitro-5-R-1,2,4-triazoles in high yields via this scheme by using milder oxidation conditions (chromic anhydride in acetone):



I-III V-VII VIII-X

I, V, VIII $R = NO_2$; II, VI, IX $R = Br$; III, VII, X $R = H$

Oxidation with dichromate at elevated temperatures gives lower yields of ketones IX and X.

The alkylation of triazoles I-III with propylene oxide to alcohols V-VII occurs under conditions determined by the pK_a value of the starting triazole. A change in the alkylation mechanism and conditions is observed on passing from 3,5-dinitro- and 3-nitro-5-bromo-1,2,4-triazole (pK_a of I 0.66 [4] and of II 3.05 [2]), the acidities of which are sufficient for realization of the process in the absence of external catalysts [2, 3], to the less acidic 3-nitro-1,2,4-triazole (pK_a of III 6.05 [4]). The reaction of triazoles III with propylene oxide proceeds in proton-donor (water and alcohols) and aqueous aprotic solvents (acetonitrile and dioxane) at room temperature only in the presence of bases. The mechanism of the alkylation is similar to that observed for 3,5-dichloro-1,2,4-triazole.

Alcohols VI and VII [2] were obtained as uncrystallizable oils, which were subjected to oxidation without purification.

---

*See [1] for communication XIX.

Lensovet Leningrad Technological Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 991-994, July, 1976. Original article submitted July 8, 1975.