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SUBSTITUTED 4(5H)-OXAZOLONES AND THEIR SALTS. 10.* SYNTHESIS OF 2-[β-(PHENYLAMINO)VINYL]-4(5H)-OXAZOLONES FROM THEIR SALTS AND *Z,E*-ISOMERIZATION AT THE DOUBLE BOND

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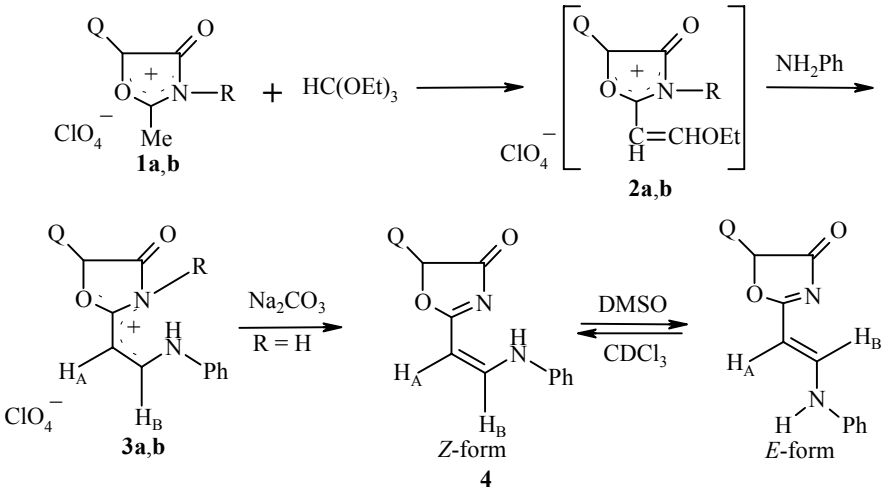
2-[β-(Phenylamino)vinyl]-5-(1,1-dimethyl-2-acetoxyethyl)-4(5H)-oxazolonium perchlorate was synthesized. The deprotonation ability of this compound in chloroform by the action of sodium carbonate to give 4(5H)-oxazolone, containing enamine fragment at $C_{(2)}$ in the ring was studied. Z,E-Isomerization at the double bond was found at room temperature by the action of the solvents.

Keywords: enamine, 4(5H)-oxazolone, *Z,E*-isomerization, NMR spectroscopy, three-component condensation.

We have already described the condensation of 2-methyl-4(5H)-oxazolonium salts **1a**,**b** with ethyl orthoformate, leading to 2-[β-ethoxyvinyl]-4(5H)-oxazolonium perchlorates **2a**,**b**, which proved difficult to crystallize and whose structure was confirmed by consecutive transformations with water and furancarboxylic acid amides [2]. In a continuation of a study of the behavior of perchlorates **2a**,**b** with nucleophilic reagents such as aniline, we are the first to obtain perchlorates **3a**,**b**, containing enamine fragment C=C–NH. New 4(5H)-oxazolone **4** was obtained from salt **3a** by deprotonation using sodium carbonate.



Q = $MeCOOCH_2C(Me)_2$; **1a**, **2a**, **3a** R = H ; **1b**, **2b**, **3b** R = Me

* Communication 9, see ref. [1].

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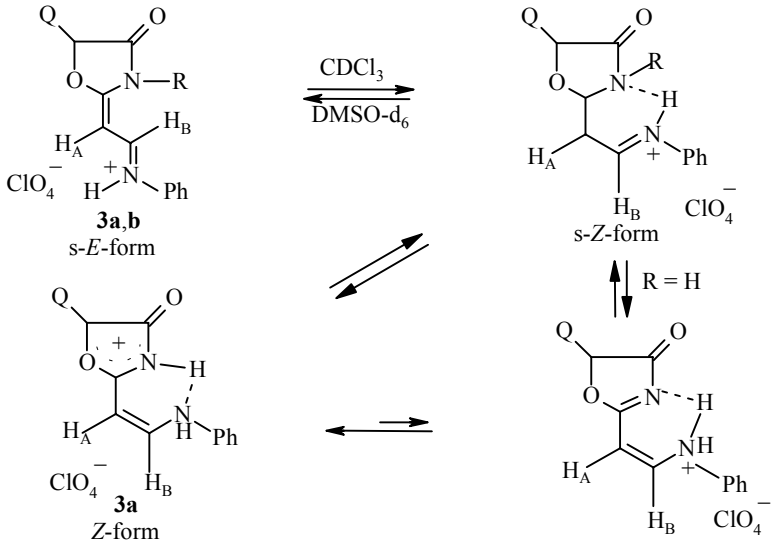
Comparison of the ^{1}H NMR spectra of salt **3b** and 4(5H)-oxazolone **4** in $CDCl_3$ indicates a positive charge in the salt molecule since all the signals of the protons both in the heterocycle and enamine fragment are shifted downfield by ~0.6–0.14 ppm (Table 1). The signal for H_B, which is split into a doublet of doublets on H_A and NH with SSCC $^3J_{AB}$ = 10.0 Hz and $^3J_{CHNH}$ = 12.0 Hz is broadened somewhat due to quadrupole interaction with the nitrogen atom. The downfield position of the signals of the enamine NH proton in salt **3b** (δ_{NH} = 11.13 ppm) and NH proton in oxazolone **4** (δ_{NH} = 10.53 ppm) probably results from intramolecular hydrogen bonding. Salt **3b**, similar to ketoenamines [3], exists in the s-*Z*-form in a weakly polar solvent $CDCl_3$. Salt **3a** is only slightly soluble in $CDCl_3$ and its ^{1}H NMR spectrum will not be discussed thus.



The IR spectra of salts **3a** and **3b** taken for vaseline mulls (Table 2) do not display significant differences in the $\nu_{C=O}$ stretching vibration region of the endocyclic carbonyl group. The shift of the signals of this group towards higher frequencies in methylene chloride results from weakening of intermolecular interactions [4]. The broad, weak band for NH stretching vibrations at 3300-2600 cm^{-1} indicates intramolecular hydrogen bonding. Since there are two hydrogen atoms bound to nitrogen atoms in molecule of the compound **3a**, which give rise to its acid–base properties, the formation of oxazolone **4** does not occur since the leaving proton of cyclic amine may be bound to the enamine nitrogen atom with retention of ionic structure [1, 4]. In this regard, salt **3a** may exist in both s-*Z*- and *Z*-form in slightly polar solvents. Intramolecular hydrogen bonding is indicated by the high-frequency absorption band from stretching vibrations of the carbonyl group of the cyclic fragment ($\nu_{C=O}$ = 1795 cm^{-1}), characteristic of the oxazolonium ring [1, 4]; this band is shifted towards lower frequencies in 4(5H)-oxazolones ($\nu_{C=O}$ = 1720-1750 cm^{-1}) [1].

The ^{1}H NMR spectra of salts **3a** and **3b** taken in DMSO-d_6, which destroys the intramolecular hydrogen bond, differ from the corresponding spectrum of compound **3b** in $CDCl_3$. The upfield shift of the proton H_A for salt **3b** ($\Delta\delta$ = 0.37 ppm) and downfield shift of H_B ($\Delta\delta$ = 0.29 ppm) with a simultaneous increase in the coupling constant ($^3J_{AB}$ = 11.4 Hz) indicate the existence of salts **3a** and **3b** in the s-*E*-form. The lack of spin-spin splitting of the proton H_B on the amino group proton is the result of exchange process of the NH proton with those of water present in DMSO-d_6. The temperature rise to 80°C does not lead to significant change in the ^{1}H NMR spectrum of salt **3a** (Table 1). An upfield shift in the doublet for the proton H_B and the decrease of breadth of this line are observed being caused by intensification of exchange processes and change in the quadrupole relaxation [5].

TABLE 1. ^{1}H NMR Spectral Characteristics (δ, ppm, Coupling Constant, *J*, Hz) of the Synthesized Compounds

Com-pound	Solvent	T, °C	Me_2 s	MeCO s	CH_2	5-H s	H_A d	H_B	H_B (N–Me)	Ph m
1	2	3	4	5	6	7	8	9	10	11
3a	DMSO-d_6		1.03 1.09	2.00	3.90 s	5.03	5.55	8.77 d $^{3}J_{AB}$ = 11.9	12.10 br. s	7.49
		45	1.4 1.10	2.00	3.91 s	4.96	5.51	8.64 d $^{3}J_{AB}$ = 11.8	12.8 br. s	7.36
		60	1.05 1.11	2.00	3.91 s	4.94	5.50	8.63 d $^{3}J_{AB}$ = 11.8	—	7.35
		80	1.03 1.09	1.98	3.91 s	4.89	5.49	8.57 $^{3}J_{AB}$ = 11.8	—	7.31
3b	$CDCl_3$	28	1.10 1.28	2.06	3.87 d, 4.17 d $^{2}J_{HH}$ = -12.0	4.90	6.10	8.58 dd $^{3}J_{AB}$ = 10.0	11.13 br. d $^{3}J_{CHNH}$ = 12.0 (3.08 s)	7.30
	DMSO-d_6	28	1.07 1.17	2.01	3.93 s	5.18	5.73	8.87 d $^{3}J_{AB}$ = 11.4	12.10 br. s (3.18 s)	7.53
4	$CDCl_3$	28	0.98 1.14	2.04	3.99 s	4.33	4.94	7.23 dd $^{3}J_{AB}$ = 8.0	10.53 br. d $^{3}J_{CHNH}$ = 11.9	7.12
	DMSO-d_6	28	0.94 1.04	2.04	4.02 s	4.50	5.46	8.35 dd $^{3}J_{AB}$ = 12.5	10.68 d $^{3}J_{CHNH}$ = 13.1	7.28

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10	11
4	$CDCl_3$–DMSO-d_6 3 : 1	28	0.99 1.13	2.07	4.02 s	4.40	5.05 5.51	7.71d 8.10 d $^3J_{AB}$ = 12.8	10.40 br.	7.18
	1 : 1	28	0.99 1.10	2.06	4.00 s	4.42	5.07 5.49	7.80 d 8.35 d $^3J_{AB}$ = 12.2	10.40 br.	7.20
	1 : 2	28	0.96 1.07	2.04	3.98 s	4.42	5.03 5.50	7.62 d 8.36 d $^3J_{AB}$ = 12.2		7.20
4	C_2D_5OD	28	0.99 1.10	2.02	4.01 s	4.48	5.05 5.51	8.05 d 8.52 d $^3J_{AB}$ = 12.6	—	7.25
		50	0.99 1.04	2.02	4.01 s	4.45	5.08 5.51	8.03 d 8.53 d $^3J_{AB}$ = 12.8	—	7.27
		60	1.00 1.12	2.03	4.03 s	4.45	5.06 5.51	7.93 d 8.45 d $^3J_{AB}$ = 12.8	—	7.26

TABLE 2. IR Spectral Characteristics (ν, cm^{-1}) of the Synthesized Compounds

Compound	Conditions*	C=O	C=C	$O\overset{+}{\cdots}C\cdots N$ (C=N)	C=O ester	NH
3a	A	1770	1655	1580, 1550	1740	3270-2600
	B	1795	1665	1590	1747	3290-2650
3b	A	1788	1660	1590, 1551	1730	3290-2610
	B	1780	1657	1575	1742	3300-2670
4	A	1740	1650	(1575)	1740	3320-2610
	C	1745	1640	(1590)	1740	3260-2860

* A – vaseline mull; B – solution in CH_2Cl_2; C – solution in $CHCl_3$.

The ^{1}H NMR spectrum of 4(5H)-oxazolone **4** in $CDCl_3$, as noted above, indicates strong intramolecular hydrogen bonding due to the presence of the enamine NH group and nitrogen atom in the heterocycle. The broad doublet of the amino group hydrogen atom found in the weak field at 10.53 ppm and coupling constants $^3J_{AB}$ = 8.0 Hz and $^3J_{CHNH}$ = 11.0 Hz indicate the existence of chelate ring of the *Z*-forms (Table 1). The IR spectral data for compound **4** are in good agreement with the ^{1}H NMR spectral data. The *Z*-form and strong intramolecular hydrogen bonding are indicated by the absorption bands at 3260-2860 cm^{-1}, whose position does not change upon going from saturated solution in chloroform to dilute solutions. Intramolecular hydrogen bonding in oxazolone **4** is broken in DMSO-d_6 with formation of intermolecular hydrogen bonds with the solvent molecules. This stabilization of the NH group hydrogen atom by solvent molecules causes splitting of the signal for H_B to give a doublet of doublets, $^3J_{Ab}$ = 12.5 Hz and $^3J_{CHNH}$ = 13.1 Hz, which suggests molecular configuration in the *E*-form.

Taking the ^{1}H NMR spectra of oxazolone **4** in 3:1, 1:1, and 1:2 mixtures of $CDCl_3$ and DMSO-d_6 shows the presence of both *Z* and *E* isomers in 53:47, 46:54, and 10:90 ratio, respectively. The content of the *Z* and *E* isomers was determined using the integral intensities of the proton H_A. The ratio of these isomers in C_2D_5OD (30:70) does not change upon consecutive measurements over 3 h. Thus, as in similar structures [3, 6, 7], *Z–E* isomerization occurs readily in compound **4** at room temperature by the action of solvents and may be considered as *cis-trans* tautomerism.

The spectrum of this compound in C_2D_5OD taken at elevated temperatures – at 50-60°C (Table 1) shows an increase in content of the *Z*-form to 50%, which is attributed to weakening of the intermolecular hydrogen bonding and conversion of the *E*-form to *Z*-form [9].

EXPERIMENTAL

The IR spectra were taken for vaseline mulls and in solution in methylene chloride at room temperature on an IKS-29 spectrometer at 400-4000 cm^{-1}. The ^{1}H NMR spectra were recorded on a Varian FT 80A spectrometer at 80 MHz and 28, 45, 50, 60, and 80°C with HMDS as the internal standard.

Perchlorates 1a,b were prepared according to the method [10].

2-[2-(Phenylamino)ethenyl]-5-(1,1-dimethyl-2-acetoxyethyl)-4(5H)-oxazolonium Perchlorate (3a). A. Salt **3a** was obtained in 80% yield from salt **2a** according to our previous procedure [2] and maintained for 1 h in a mixture with aniline in acetic acid or chloroform at room temperature; mp 191°C. Found, %: C 49.21; H 5.27; Cl 8.44; N 6.60. $C_{17}H_{21}ClN_2O_8$. Calculated, %: C 48.99; H 5.08; Cl 8.57; N 6.72.

B. Ethyl orthoformate (2.0 ml, 0.013 mol) and aniline (0.93 g, 0.01 mol) were added consecutively to mixture of perchlorate **1a** (3.13 g, 0.01 mol), glacial acetic acid (3.4 ml, 0.06 mol), and acetic anhydride (2.8 ml, 0.08 mol). The mixture was maintained for 10 min on a water bath with stirring at 50-60°C. The precipitate formed upon cooling was filtered off and washed consecutively with 1:3 ethyl acetate–ether and with ether to give 2.91 g of compound **3a** (70%).

2-[2-(Phenylamino)ethenyl]-5-(1,1-dimethyl-2-acetoxyethyl)-3-methyl-4(5H)-oxazolonium Perchlorate (3b) was obtained in 85% yield analogously to salt **3a** according to method B; mp 160°C. Found, %: C 50.22; H 5.51; Cl 8.39; N 6.63. $C_{18}H_{23}ClN_2O_8$. Calculated, %: C 50.18; H 5.38; Cl 8.23; N 6.50.

2-[2-(Phenylamino)ethenyl]-5-(1,1-dimethyl-2-acetoxyethyl)-4(5H)-oxazolone (4). Suspension of perchlorate **3a** (3.16 g, 0.01 mol) in chloroform (10 ml) was stirred and shaken for 10-15 min with solution of sodium carbonate (1.06 g) and water (1 ml). The organic layer was removed and the aqueous layer was extracted with chloroform. The extracts were washed with water until the neutral reaction and dried over anhydrous sodium sulfate. The solvent was distilled off and the residue was crystallized from ethanol. Yield of compound **4** 95%; mp 125°C. Found, %: C 64.88; H 6.52; N 9.06. $C_{17}H_{20}N_2O_4$. Calculated, %: C 64.56; H 6.37; N 8.85.

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