SYNTHESIS, STRUCTURE, AND TAUTOMERISM OF 3*a*,7-DIMETHYL-4,6-DIPHENYL-2-ETHYNYL-7*a*-HYDROXYPERHYDROPYRROLO[3,2-c]PYRIDINE

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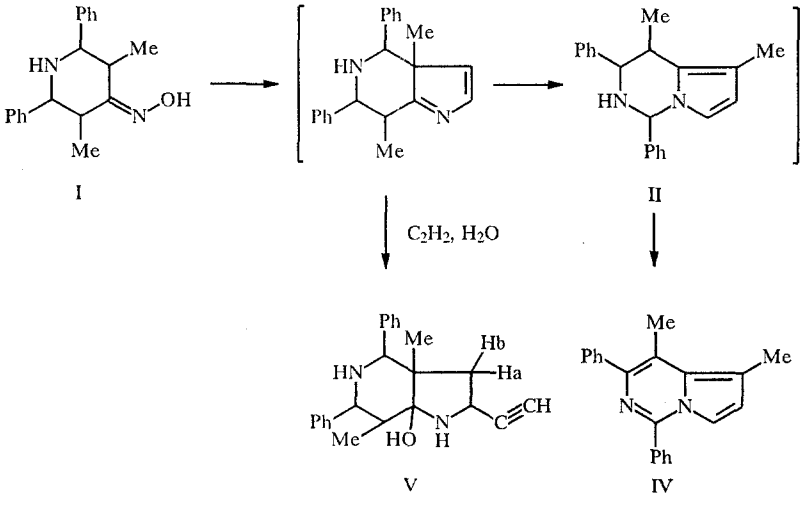
Isomeric [with respect to the fusion of the piperidine and pyrrolidine rings, as well as with respect to the mutual orientation of the substituents attached to the $C_{(2)}$ and $C_{(3a)}$ carbon atoms] 3a,7-dimethyl-4,6-diphenyl-2-ethynyl-7a-hydroxyperhydropyrrolo[3,2-c]pyridines were isolated for the first time in the reaction of 3,5-dimethyl-2,6-diphenyl-4-piperidinone oxime with acetylene under the conditions of the Trofimov reaction under pressure. It was established that, in solutions, the isomers of this compound with an axial-equatorial fusion of the rings exist in the form of ring–chain tautomers.

The Trofimov reaction is a convenient method for obtaining substituted pyrroles and N-vinylpyrroles [1]. 2,4,5-Trimethyl-1,2,3,4-tetrahydropyrrolo[1,2-c]pyrimidine is formed from 1,3,5-trimethyl-4-piperidinone oxime under these conditions as a result of a [1,3]-sigmatropic rearrangement of the reaction intermediate, viz., 3*a*,5,7-trimethyl-3*a*H-4,5,6,7-tetrahydropyrrolo[3,2-c]pyridine [2].

In order to ascertain the principles involved in the [1,3]-sigmatropic rearrangement we studied the heterocyclization of 3,5-dimethyl-2,6-diphenyl-4-piperidinone oxime (I) with acetylene in the presence of potassium hydroxide. The reaction was carried out in an autoclave at 80-90°C and an initial acetylene pressure of 16 atm, as well as at atmospheric pressure at 90-95°C. In both cases the reaction was accompanied by significant resinification. The reaction mixtures were separated by chromatography. The product of a [1,3]-sigmatropic rearrangement, viz., 4,5-dimethyl-1,3-diphenyl-1,2,3,4-tetrahydropyrrolo[1,2-c]pyrimidine (II) was not isolated in either case.

When the reaction was carried out at atmospheric pressure, 3,5-dimethyl-2,6-diphenyl-4-piperidinone (III) and 4,5-dimethyl-1,3-diphenylpyrrolo[1,2-c]pyrimidine (IV) were isolated from the reaction mixture in very low yields. Compound IV is evidently the product of aromatization of the expected tetrahydropyrrolopyrimidine II.



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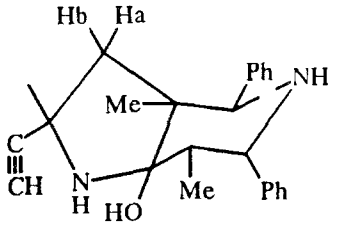
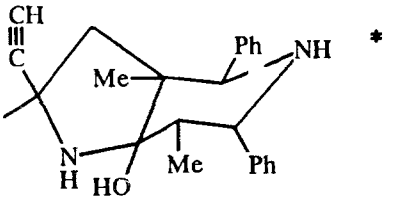
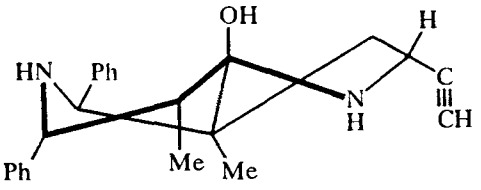


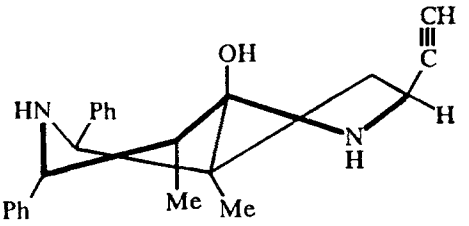
Va



Vb*



Vc



Vd

The mass spectrum of pyrrolopyrimidine IV contains a maximally intense molecular-ion peak at 298,† which corresponds to its empirical formula. Singlet signals of methyl groups attached to the $C_{(4)}$ and $C_{(5)}$ atoms at 2.62 and 2.63 ppm, respectively, are observed in the strong-field part of the PMR spectrum of IV. Signals at 7.34 and 6.63 ppm of coupling 6-H and 7-H protons (^3J = 2.9 Hz), respectively, are located in the weak-field part of the spectrum.

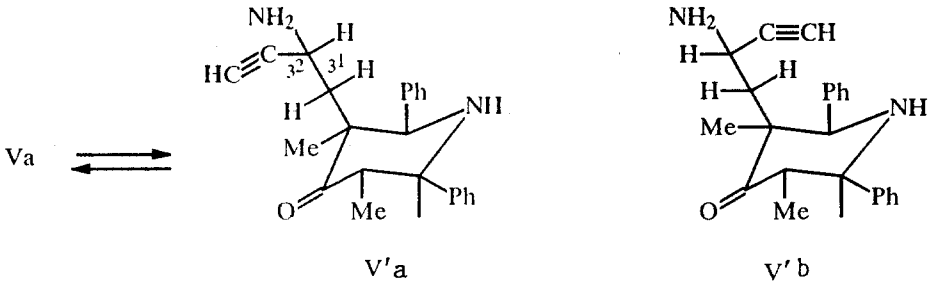
Piperidone III and four substances Va-d (in 11% overall yield), which are isomers of 3*a*,7-dimethyl-4,6-diphenyl-2-ethynyl-7*a*-hydroxyperhydropyrrolo[3,2-c]pyridine (V), were isolated from the reaction mixture when the reaction was carried out in an autoclave. [1,3]-Sigmatropic rearrangement of the intermediate substituted 3H-tetrahydropyrrolopyridine is evidently suppressed under pressure when a large excess of acetylene is present, but acetylene and water add at the 3H-pyrrole fragment with the participation of potassium acetylenide and hydroxide.

The structures of the isomeric perhydropyrrolopyridines Va-d were established by means of ^1H and ^{13}C NMR spectroscopy (Tables 1-7) drawing upon data on the nuclear Overhauser effect (NOE) [3] and the results of calculations by molecular mechanics [4], as well as by means of IR and mass-spectrometric data. The IR spectra of solutions of Va and Vc, d contain bands of stretching vibrations of OH and NH groups at 3610 and 3310 cm^{-1}, respectively. In addition, a band of a hydroxy group at 3342 cm^{-1}, which is associated with an intramolecular hydrogen bond, is present in the spectrum of Vd.

The ^{13}C NMR spectra (see Table 3) of Va-d are similar. The significant difference observed for the Va, b and Vc, d pairs only in the magnitude of the chemical shifts of the quaternary $C_{(7a)}$ carbon atom makes it possible to assume different fusions of the pyrrolidine and piperidine rings in them. According to the ^1H and ^{13}C NMR spectra, Va and Vb exist in solutions as mixtures of two tautomers, the ratio of which depends on the solvent and temperature (see Table 4). Minor tautomers V′a and V′b are characterized by the presence in their ^{13}C NMR spectra (see Table 5) of a signal in the region of carbonyl carbon atoms. This is evidently due to ring–chain tautomerism, similar to the tautomerism of acyl carboxylic acid amides, amino aldehydes, and ketones [5].

*The structures of Va-d and V′a, b, obtained as a result of optimization of the geometry by molecular mechanics, are presented in the schemes.

†Here and subsequently, the m/z values are given in the description of the mass spectra.

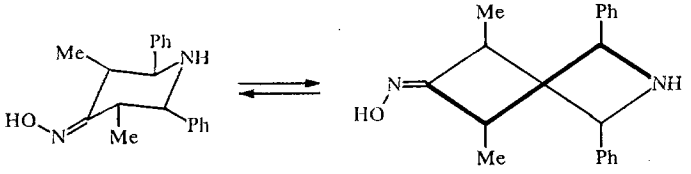


The two-dimensional NOESY spectra of Va and Vb (Fig. 1) contain exchange cross peaks from the 2-H protons of the bicyclic tautomer and the methylidyne (3″-H) proton of the aminobutynyl radical of the keto form, and this confirms the existence of ring–chain tautomerism.

Compounds Vc and Vd are stable in various solvents. An increase in the temperature and the use of acidic and alkaline catalysts do not lead to the development of the keto form. The signal of the terminal acetylenic proton at 2.79 ppm and the corresponding $^4J_{HH}$ constant of spin–spin coupling with the 2-H proton vanish in the PMR spectrum of Vc in CD_3OD in the presence of sodium hydroxide; this serves as additional evidence for the presence of an ethynyl radical attached to the $C_{(2)}$ atom in Va-d.

We used NOE data to establish the mutual orientation of the substituents in the 2 and 3*a* positions in Va-d. The presence of nondiagonal cross peaks from the pairs of 2-H and 3*a*-CH_3 protons with coordinates 0.97-4.76 and 0.91-4.68, respectively, in the two-dimensional NOESY spectra of Vb and Vd indicates a trans configuration of the ethynyl group substituent attached to the $C_{(2)}$ atom and the methyl substituent attached to the $C_{(3a)}$ atom. The absence of similar cross peaks in the spectra of Va and Vc constitutes evidence for a cis configuration of the indicated substituents.

To establish the character of the fusion of the pyrrolidine and piperidine rings in Va-d we studied the stereochemistry of starting system I. According to the ^1H and ^{13}C NMR data (see Tables 6 and 7), it is a mixture of isomers with cis (diequatorial) and trans (axial-equatorial) orientations of the methyl groups attached to the $C_{(3)}$ and $C_{(5)}$ atoms with a ratio of 13:1. Whereas there is no doubt regarding the chair conformation of the trans isomer (see Table 6), the twist–boat conformation assigned to the cis isomer in [6] on the basis of the $^3J_{HH}$ trans spin–spin coupling constants (SSCC) of the protons of the piperidine ring seems less convincing. Our calculations by molecular mechanics showed that the chair conformation of the cis isomer of oxime I is ≈ 10 kJ/mole more stable than the twist–boat conformation. The $^3J_{2,3}$ SSCC calculated from the Karplus equation [7] were 1.7 Hz for the twist–boat conformation [$\varphi_{(H_2,H_3)} = 66°$] and 11.2 Hz for the chair conformation [$\varphi_{(H_2,H_3)} = 176°$]. A comparison of these values with the experimental values and the character of the dependence of the $^3J_{HH}$ trans SSCC (see Table 6) on the solvent make it possible to assume, at least, a two-position conformation equilibrium.



The low yields of Va-d made it impossible a priori to propose from which isomer of oxime I they were formed. To solve this problem we determined the mutual orientation of the 3*a*-CH_3 protons and the axial 4*a*-H proton in bicyclic Va-d and keto forms V′a and V′b. The NOE value ($\approx 5\%$) between the indicated protons in Va-d and V′a and V′b, found by means of differential NOE spectroscopy [8], and the $^3J[C_{(3a)}H_{4a}\text{-}H] \leq 3$ Hz, found by selective proton decoupling, indicate unambiguously a cis orientation of the 3*a*-CH_3 group and the 4*a*-H proton. It hence follows that Va-d were formed from the preponderant isomer of oxime I with a cis-diequatorial orientation of the methyl groups attached to the $C_{(3)}$ and $C_{(5)}$ atoms and that their cis configuration is retained in the isomers of V and in keto forms V′a and V′b (Table 8). Thus the Va, b and Vc, d pairs should differ from one another with respect to the fusion of the pyrrolidine and piperidine rings, while the keto forms

TABLE 1. Chemical Shifts of the Protons in the PMR Spectra of Perhydropyrrolopyridines Va-d

Compound	Solvent	Chemical shift, δ, ppm									
		2-H	3-H*a*	3-H*b*	4-H	6-H	7-H	2-C≡CH	3*a*-CH_3	7-CH_3	4,6-C_6H_5
Va	$CDCl_3$	4,64	3,39	1,50	3,83	3,57	2,00	2,46	1,15	0,74	7,25...7,41
	d_6-DMSO	4,58	2,97	1,14	3,70	3,44	1,91	2,48	0,96	0,56	7,22...7,50
Vб	$CDCl_3$	4,76	3,18	1,68	3,87	3,60	2,42	2,51	0,97	0,79	7,25...7,45
	C_6D_6	4,58	3,21	1,33	3,46	3,45	2,60	2,10	0,73	0,99	7,06...7,38
	d_6-DMSO	4,65	2,97	1,48	3,74	3,49	2,20	2,63	0,80	0,60	7,22...7,50
Vв	$CDCl_3$	4,63	3,51	1,49	3,88	3,65	2,02	2,43	1,09	0,69	7,25...7,42
	C_6D_6	4,46	3,26	1,44	3,72	3,53	1,89	2,09	1,07	0,65	7,13...7,26
	CD_3OD	4,62	3,53	1,37	3,86	3,63	2,06	2,79	1,02	0,64	7,23...7,43
	CD_3OD+NaOH	4,61	3,52	1,36	3,85	3,62	2,05	Center	1,02	0,64	7,23...7,43
	$CDCl_3$+CF_3COOH	5,12	3,76	2,11	4,97	4,68	3,08	2,67	1,49	1,10	7,26...7,47
Vг	$CDCl_3$	4,68	3,32	1,68	3,91	3,68	2,50	2,49	0,91	0,74	7,24...7,45
	d_6-DMSO	4,57	3,11	1,49	3,80	3,60	2,31	2,49	0,77	0,59	7,23...7,40
	d_6-DMSO + CF_3COOH	5,13	3,52	2,13	4,89	4,60	3,05	3,62	1,11	0,95	7,47...7,60

*δ_{1-NH} 5.71 ppm.

**δ_{1-NH} 5.59 ppm.

V′a and V′b with an axial aminobutynyl radical should differ only with respect to the configuration at its asymmetric $C_{(3'')}$ atom.

Only equatorial attack by the amino group on the carbonyl carbon atom can occur in the conversion of keto form V′a or V′b to the bicyclic form. As a result, bicyclic forms Va and Vb with axial-equatorial cis fusion will be formed. The methyl groups and the hydroxy group in these compounds have a cis orientation.

Thus a transoid equatorial–equatorial fusion of the rings can be ascribed to the second pair of compounds Vc and Vd. Their stability in solution is evidently due to the presence of an intramolecular hydrogen bond [5].

The established stereochemistry of perhydropyrrolopyridines Va-d makes it possible to conclude that the addition of the elements of acetylene and water to the intermediate 3H-tetrahydropyrrolopyridine proceeds regiospecifically but not stereospecifically, while the character of the fusion of the pyrrole and piperidine rings is determined by the stereochemistry of the hydration of the imine bond. Nucleophilic attack on the $C_{(7)}$ atom by a hydroxide ion or a water molecule in the cis position relative to the methyl groups attached to the $C_{(3a)}$ and $C_{(7)}$ atoms leads to Va and Vb with an equatorial-axial fusion of the rings, while attack in the trans position leads to Vc and Vd with an equatorial–equatorial fusion of the rings.

Because of their lability under electron-impact conditions, Va, c, d do not form molecular ions. The maximum (with respect to mass number) peaks in the mass spectra are due to $[M - H_2O]^+$ (328) and $[M - NH_2CH - C{\equiv}CH]^+$ (292) ions. Whereas the formation of the former ion is in complete conformity with principle, the existence of a ketone form and subsequent β cleavage should be assumed for the formation of the latter.

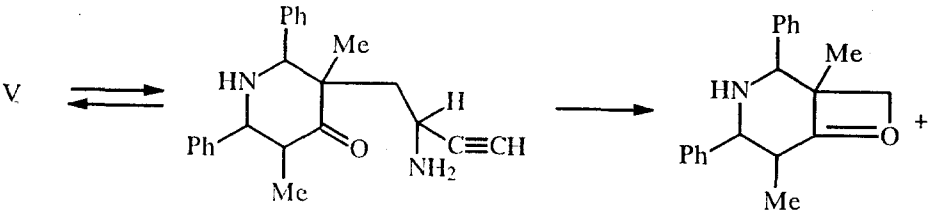


TABLE 2. Spin–Spin Coupling Constants (SSCC) of the Protons in the PMR Spectra of Perhydropyrrolopyridines Va-d (measurement accuracy ± 0.04-0.1 Hz)

Compound	Solvent	SSCC, Hz					
		2,3*a*	2,3*b*	2,C≡CH	3*a*, 3*b*	6,7	7,7-CH_3
Va	$CDCl_3$	10,19	2,44	2,20	-12,45	10,50	6,84
	d_6-DMSO	10,3	2,40	2,2	-12,5	10,6	6,8
Vб	$CDCl_3$*	9,52	7,61	2,16	-12,45	10,74	6,84
	C_6D_6	9,46	7,69	2,08	-12,45	10,68	6,84
	d_6-DMSO	9,28	7,61	2,10	-12,10	10,60	6,83
Vв	$CDCl_3$	10,19	2,62	2,20	-12,51	10,25	6,84
	$CDCl_3$+CF_3COOH	10,13	1,80	2,20	-13,49	12,70	6,84
	C_6D_6 (23°C)	10,20	2,53	2,20	-12,40	10,11	6,84
	C_6D_6 (70°C)	10,16	2,63	2,20	-12,45	10,30	6,82
	CD_3OD	10,20	2,56	2,20	-12,50	10,38	6,92
	CD_3OD+NaOH	10,19	2,62	2,20	-12,57	10,50	6,90
Vг	$CDCl_3$	9,40	7,93	2,08	-12,45	10,50	6,84
	d_6-DMSO	9,5	7,9	2,1	-12,1	10,4	6,8
	d_6-DMSO +CF_3COOH	9,3	7,6	2,0	-13,4	12,3	6,9

*$^4J_{7a\text{-OH}}$ = 1.04 Hz.

TABLE 3. ^{13}C Chemical Shifts (δ, ppm) and Direct $^{13}C—^{1}H$ Spin–Spin Coupling Constants (SSCC) (in parentheses, Hz) in the Spectra of Perhydropyrrolopyridines Va-d ($CDCl_3$)

Compound	Chemical shift, δ, ppm												
	$C_{(2)}$	$C_{(3)}$	$C_{(3a)}$	$C_{(4)}$	$C_{(6)}$	$C_{(7)}$	$C_{(7a)}$	$C_{(2')}$	$C_{(2'')}$	$C_{(3'a)}$	$C_{(7')}$	$C_{(q)}$	$C_{(o)}$, $C_{(m)}$, $C_{(p)}$
Va	62,37	38,00	47,19	65,98	65,14	42,70	107,06	84,54	73,22	19,92	9,59	141,33, 142,70	127,54...128,30
	(154,0)	(134,0), (138,8)	—	(133,6)	(133,6)	(127,3)	—	—	(250,7)	(126,6)	(126,6)	—	*
Vb	63,34	38,96	47,87	65,87	65,49	44,24	106,82	84,97	72,70	18,96	9,47	141,29, 142,80	127,46...128,29
	(153,6)	(133,2), (136,5)	—	(133,6)	(132,4)	(129,0)	—	—	(250,3)	(126,8)	(126,7)	—	*
Vc	61,88	38,88	46,60	65,13	65,72	41,68	96,83	85,23	72,59	20,35	10,05	141,75, 143,07	127,43...128,26
	(152,6)	(134,3), (139,0)	—	(133,8)	(133,8)	(127,9)	—	—	(250,2)	(126,1)	(126,1)	—	*
Vd	62,80	39,64	47,22	65,57	65,67	43,14	96,59	85,93	72,11	19,34	10,02	141,72, 143,22	127,38...128,27
	(152,6)	(132,6), (137,3)	—	(133,5)	(133,5)	(129,7)	—	—	(249,9)	(126,4)	(126,4)		*

*Not measured.

TABLE 4. Correlation of the Tautomers of Perhydropyrrolopyridines Va and Vb

Compound	Solvent	Temp.,°C	Amt., %	
			cyclic form (V)	keto form (V')
Va	$CDCl_3$	20	79	21
	d_6-DMSO	40	68	32
		60	47	53
		80	26	74
		100	23	77
Vb	d_6-DMSO	40	57	43
		60	32	68
		80	25	75
		100	23	77
	$CDCl_3$	-10	68	32
		10	66	34
		20	65	35
		40	63	37
		60	60	40
	C_6D_6	20	77	23

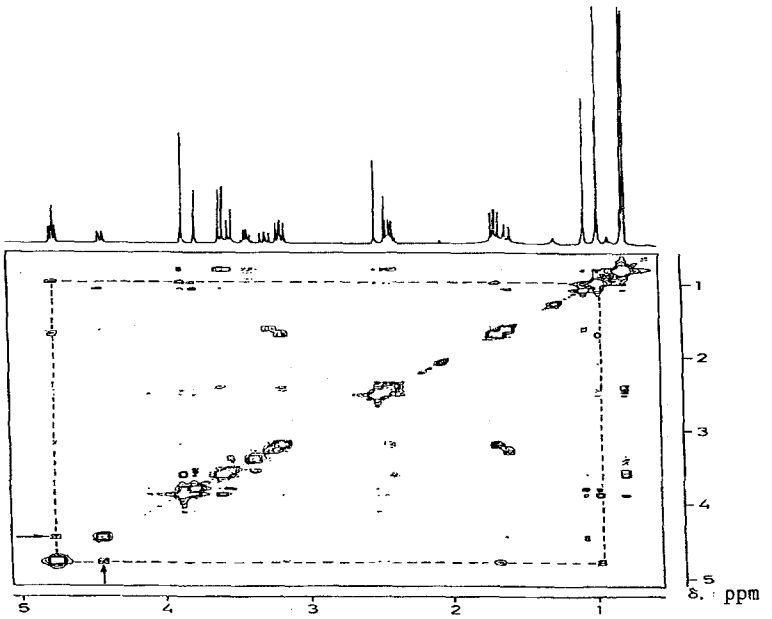


Fig. 1. NOESY spectrum of the mixture of tautomers Vb and V'b. The exchange cross peaks from the 2-H (Vb) and 3″-H (V'b) protons are indicated by arrows. The NOE cross peaks that attest to the spatial closeness of the 2-H and 3*a*'-CH_3 protons for tautomer Vb are indicated by a dotted line.

TABLE 5. ^{13}C Chemical Shifts (δ, ppm) and Direct $^{13}C—^{1}H$ Spin–Spin Coupling Constants (SSCC) (in parentheses, Hz) of V'a and V'b ($CDCl_3$)

Compound	Chemical shift, δ, ppm												
	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	3-CH_3	$C_{(3')}$	$C_{(3'')}$	$C_{(3''')}$	$C_{(3'''')}$	$C_{(5')}$	$C_{(q)}$	$C_{(o)}$, $C_{(m)}$, $C_{(p)}$
V'a	71,87 (135,3)	53,07 —	213,11 —	49,08 (127,6)	69,58 (136,3)	19,07 (126,3)	40,65 (126,9)	59,13 (149,0)	84,38 —	74,65 (250,5)	10,65 (127,6)	138,56 142,04	127,41...128,81 *
V'b	71,44 (134,5)	52,67 —	214,16 —	48,86 (131,8)	69,60 (136,1)	18,86 (126,5)	41,84 (128,1), (131,0)	58,77 (146,4)	85,26 —	72,45 (250,0)	10,78 (126,9)	138,67 141,99	127,40...128,87 *

*Not measured.

TABLE 6. ^{1}H NMR Parameters of the Isomers of Oxime I

Compound	Solvent	Chemical shift, δ, ppm						SSCC (measurement ± 0.04-0.1 Hz)					
		2-H	3-H	5-H	6-H	3-Me	5-Me	2,6-C_6H_5	2,3	3,3-Me	3,5	5,5-Me	5,6
cis-I	CD_3OD	3,83	2,74	3,32	3,73	1,30	1,16	7,23...7,44	5,47	7,49	1,10	7,16	9,46
	CD_3COCD_3	3,88	2,65	3,25	3,80	1,26	1,19	7,22...7,55	5,54	7,43	0,90	7,18	9,13
	$C_6D_5CD_3$	3,41	2,76	3,35	3,44	1,12	1,26	7,07...7,32	6,42	7,39	0,86	7,01	9,22
	CD_3CN	3,86	2,59	3,14	3,77	1,26	1,12	7,23...7,50	5,25	7,48	1,02	7,14	9,14
	$CDCl_3$	3,77	2,78	3,29	3,70	1,26	1,20	7,24...7,43	6,04	7,44	1,00	7,17	9,06
	C_5D_5N	3,91	3,09	3,79	3,87	1,89	1,47	7,27...7,65	5,82	7,38	1,03	6,90	9,18
	C_6D_6	3,39	2,89	3,45	3,42	1,12	1,28	7,07...7,33	6,47	7,32	0,85	7,00	9,28
trans-I	CD_3OD	3,44	2,64	3,76	4,04	0,80	0,89	7,23...7,44	10,45	6,56	—	7,06	3,66
	CD_3COCD_3	3,50	2,65	3,57	4,07	0,81	0,91	7,22...7,55	10,37	6,58	—	7,08	3,60
	$C_6D_5CD_3$	3,18	2,58	3,97	3,81	0,99	1,00	7,07...7,32	10,41	6,56	—	7,06	3,56
	CD_3CN	3,47	2,65	3,68	4,03	0,87	0,75	7,23...7,50	10,55	6,56	—	7,14	3,55
	$CDCl_3$	3,52	2,72	3,79	4,12	0,88	0,98	7,24...7,49	10,46	6,56	—	7,06	3,72
	C_5D_5N	3,59	2,89	—	4,32	1,14	1,19	7,27...7,65	10,51	6,70	—	7,09	3,56
	C_6D_6	3,16	2,60	4,04	3,81	1,02	1,03	7,07...7,33	10,38	6,59	—	7,08	3,54

TABLE 7. ^{13}C Chemical Shifts and Direct $^{13}C—^{1}H$ Spin–Spin Coupling Constants (SSCC) (in parentheses, Hz) of the Isomers of Oxime I

Isomer	Chemical shift, δ, ppm								
	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(3)}$	$C_{(5)}$	$C_{(q)}$	$C_{(o)}$, $C_{(m)}$, $C_{(p)}$
cis-I	66,94	39,76	164,12	42,91	68,16	15,48	20,27	143,47, 144,61	127,20...128,38
	(133,0)	(132,2)	—	(132,3)	(134,3)	(127,9)	(127,4)	—	*
trans-I	62,91	33,85	157,76	38,99	69,50	11,11	11,83	141,73, 142,91	126,91...128,43
	(134,0)	(135,1)	—	(127,4)	(134,6)	(128,1)	(127,3)	—	*

*Not measured.

TABLE 8. Parameters of the PMR Spectra of V′a and V′b

Compound	Solvent	Chemical shift, δ, ppm										SSCC (measurement ±0.04-0.1 Hz)					
		2-H	5-H	6-H	2,6-C_6H_5	3-CH_3	5-CH_3	3′a-H	3′b-H	3′′-H	C≡CH	5,6	5,5-CH_3	3′a, 3′b	3′a, 3′′	3′b, 3′′	3′′, C≡CH
V′a	$CDCl_3$	3,76	3,33	3,55	7,25...7,51	1,08	0,81	3,22	1,76	4,30	2,46	10,50	6,53	−14,04	9,46	5,00	2,20
	d_6-DMSO	3,65	3,32	3,42	7,22...7,50	0,91	0,65	3,10	1,44	4,01	2,48	10,60	6,5	−14,0	9,40	4,90	2,20
V′b	$CDCl_3$	3,79	3,37	3,55	7,25...7,51	1,07	0,81	3,25	1,60	4,43	2,46	10,74	6,47	−14,65	11,23	2,44	2,16
	C_6D_6	3,40	3,48	3,16	7,06...7,27	1,04	0,99	3,44	1,64	4,23	2,01	10,74	6,53	−14,65	11,17	2,36	2,08
	d_6-DMSO	3,66	3,30	3,43	7,22...7,50	0,89	0,61	3,18	1,31	4,07	2,08	10,60	6,4	−14,4	10,60	3,10	2,10

The intensity ratios $J_{[M - NH_2C_3H_2]}^+/J_{[M - H_2O]}^+$ for Vc, Vd, and Va are 1.6, 0.7, and 27.3, respectively, which may serve as yet another piece of evidence for the existence of ring–chain tautomerism for Va. The high-mass region of the mass spectra of stable compounds Vc and Vd is characterized by the presence of ion peaks at 277.

The other most intense peaks in the mass spectra of the investigated compounds are due to cleavage of both the five-membered and six-membered heterorings.

EXPERIMENTAL

The IR spectra of solutions of the compounds in CCl_4 (c 10^{-3}) were obtained with an IR-75 spectrometer. The PMR spectra were recorded with a Bruker WH-400 spectrometer with tetramethylsilane (TMS) as the internal standard. The mass spectra were measured with a Kratos MS-25 RF mass spectrometer. Chromatography with a column and in a thin layer was carried out on L 60 and 40/100 and Silufol UV-254 silica gels.

The results of elementary analysis for C, H, and N were in agreement with the calculated values.

4,5-Dimethyl-1,3-diphenylpyrrolo[1,2-c]pyrimidine (IV, $C_{21}H_{18}N_2$). Acetylene was passed for 5 h at 98-100°C through a solution of 5 g (17 mmole) of oxime I and 0.95 g (17 mmole) of potassium hydroxide in 50 ml of DMSO (with monitoring by TLC), after which the reaction mixture was poured over ice, and the resulting aqueous mixture was extracted with ether. The extract was dried with $MgSO_4$, the ether was removed by distillation, and the brown residue was chromatographed with a column (36 by 2.8 cm). Initial elution with hexane—ethyl acetate (50:1) gave 50 mg (1.2%) of IV in the form of a viscous green oil with R_f 0.49 [ethyl acetate—hexane (1:4)], the crystallization of which from hexane gave 10 mg of yellow crystals with mp 102-104°C. Subsequent elution with a mixture of the same solvents in a ratio of 40:1 gave 100 mg of piperidone III with mp 128-129°C. No melting-point depression was observed for a mixture with a genuine sample.

3*a*,7-Dimethyl-4,6-diphenyl-2-ethynyl-7*a*-hydroxyperhydropyrrolo[3,2-c]pyridines Va-d ($C_{23}H_{26}N_2O$). The heterocyclization reaction was carried out in an autoclave for 3 h at 85-90°C at an initial acetylene pressure of 16 atm using 20.0 g (0.07 mole) of the oxime, 1.4 g (0.07 mole) of potassium hydroxide, and 200 ml of DMSO. The reaction mixture was poured into water, and the aqueous mixture was extracted with ether. The extract was dried with $MgSO_4$, the ether was removed by distillation, and the dark-brown amorphous residue (20.1 g) was refluxed with hexane (8 × 100 ml). Removal of the hexane by distillation gave 4.8 g of a brown resinous mass, a 0.4 g sample of which was taken for chromatography with a column (47 by 2 cm) packed with silica gel. Initial elution with hexane—ethyl acetate (50:1) gave 60 mg (15%) of piperidone III with mp 127-129°C (from hexane). Subsequent elution with a mixture of the same solvents in a ratio of 20:1 gave, successively, 20 mg (5%) of Vb in the form of a white crystalline substance with mp 172-173°C (from hexane) and R_f 0.58 [ethyl acetate—hexane (1:3)] and 32 mg (8%) of Va in the form of a white crystalline substance with mp 157-159°C (from hexane) and R_f 0.53 [ethyl acetate—hexane (1:3)]. Finally, elution with a mixture of the same solvents in a ratio of 10:1 gave 65 mg (16%) of Vd in the form of a white crystalline substance with mp 155-157.5°C (from hexane) and R_f 0.21 [ethyl acetate—hexane (1:3)] and 98 mg (24%) of Vc in the form of white crystals with mp 112-114°C (from hexane) and R_f 0.12 [ethyl acetate—hexane (1:3)]. Mass spectra, m/z (I_{rel}, %): Va: 328 (1.5), 292 (29), 195 (23), 194 (62), 118 (19), 117 (22), 106 (22), 105 (18), 91 (40), 77 (21), 69 (100); Vc: 328 (5), 292 (8), 277 (7), 195 (36), 194 (100), 118 (35), 117 (28), 106 (45), 105 (15), 91 (53), 77 (40), 69 (39); Vd: 328 (3), 292 (2), 277 (3), 195 (48), 194 (100), 118 (32), 117 (27), 106 (39), 105 (15), 91 (52), 77 (29), 69 (15).

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