SYNTHESIS AND ALKYLATION OF 4,6-DIPHENYL-3-THIOCARBAMOYL-3,4,5,6-TETRAHYDROPYRIDINE-2(1H)-ONE AND 4,6-DIPHENYL-3-THIOCARBAMOYL-3,4-DIHYDROPYRIDINE-2(1H)-ONE

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Alkylation of 3-thiocarbamoyl-3,4,5,6-tetrahydropyridine-2(1H)-one with methyl iodide has given 5-methylthio-2,6-diazabicyclo[2.2.2]oct-5-en-3-one and 3-methylthiocarbonyl-3,4-dihydropyridine-2(1H)-one. Alkylation of 3-thiocarbamoyl-3,4-dihydridine-2(1H)-one with iodoacetamide affords 3-(1'-amino-1'-carbamoyl-3,4-methylthiomethylene)-1,4-dihydropyridine-2-one, which in acidic media is converted into 3-(4'-oxo-3',5'-dihydro-1',3'-thiazol-2'-ylidene)-1,4-dihydropyridine-2-one.

Condensation of chalcones with malondiamide or dithiomalondiamide has been reported to give δ-ketodiamides [1] or δ-ketothioamides [2] as the main products, while chalcones condense with cyanothioacetamide giving 6-hydroxy-3-cyano-1,4,5,6-tetrahydropyridine-2-thiolates [3]. Condensation of β-dicarbonyl compounds with monthiomalondiamide in the presence of bases gives exclusively 3-carbamoylpyridine-2(1H)-thiones, i.e. cyclization of the unsaturated δ-ketomonothioamides (intermediates in the Knoevenagel reaction) involves the NH_2 of the thioamide group [4].

We have found tht the cyclization of saturated δ-ketomonothioamides, which are intermediates in the Michael condensation of chalcones with monothiomalondiamide, follows a different course, involving the NH_2 of the amide group to give 2-oxo-derivatives of hydrogenated pyridines [5].

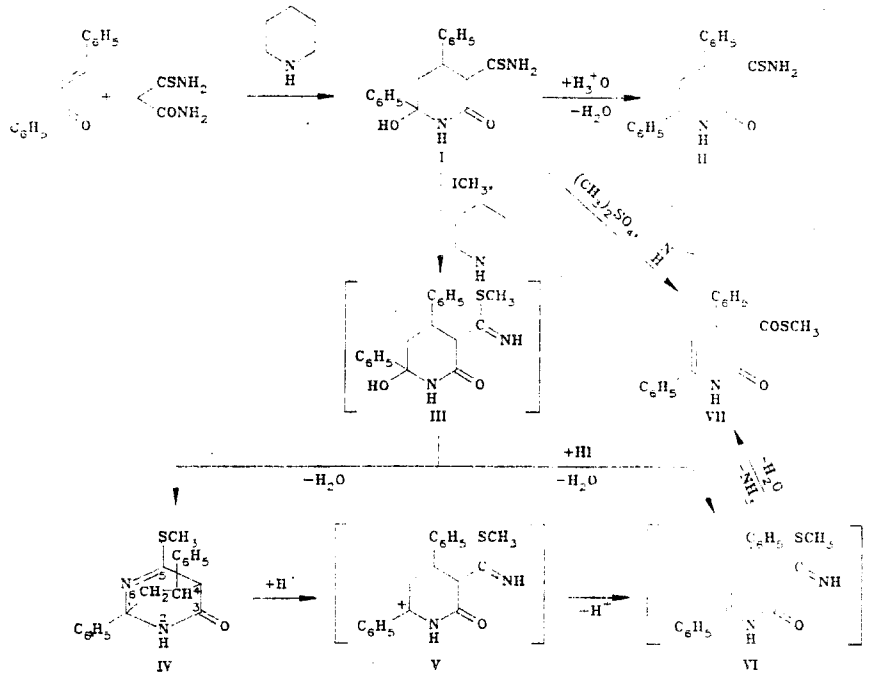

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TABLE 1. Properties of Compounds (I), (II), (IV), (VII), (VIII), and (X-XII)

Compound	Empirical formula	Tmp, °C	R_f	IR spectrum, ν, cm^{-1}		UV spectrum, λ_{max}, nm	Yield, %
				C=O	NH, NH_2, OH		
I	$C_{18}H_{18}N_2O_2S$	194...196	0,10	1676	3158, 3290, 3350, 3406	276	83
II	$C_{18}H_{16}N_2OS$	198...200	0,18	1685	3208, 3300, 3395	223, 276	75
IV	$C_{19}H_{18}N_2OS$	189...191	0,58	1688	3150	237	32
VII	$C_{19}H_{17}NO_2S$	182...183	0,63	1653, 1686	3200	228, 278	56*1, 60*2, 94*3, 94*4
VIII	$C_{19}H_{18}N_2OS$	192...194	0,27	1618	3240, 3462	222, 288, 343	62
X	$C_{20}H_{19}N_3O_2S$	169...171	0,08	1630, 1672	3156, 3290, 3450	226, 288, 343	38
XI	$C_{20}H_{16}N_2O_2S$	238...240	0,45	1628, 1664*5, 1708*5, 1728	3206, 3298	229, 286, 328	69
XII	$C_{19}H_{15}NO_2S$	228...230	0,15	1668, 1726	3124	253, 352	31*1, 25*2

*1 Method A.
*2 Method B.
*3 Method C.
*4 Method D.
*5 Weak Absorption.

TABLE 2. ^{1}H NMR Spectral Parameters for Compounds Obtained (in DMSO-D$_6$)

Compound	Chemical shifts, δ, ppm (multiplicity)							Coupling const., Hz		
	NH_2 (br.s)	NH (br. s)	C_6H_5 (m)	5-H (d.d)	4-H (d)	3-H (d)	SCH_3 or SCH_2 (s)	$J_{H_3H_4}$	$J_{H_4H_5}$	J_{NH,H_5}
I*1	9,31 and 9,21	8,15	7,6...7,1	2,11 and 1,92	4,33*2	3,93	—	11,9	2,6	—
II	9,48 and 9,24	9,87	7,6...7,2	5,33	4,60*3	3,98	—	12,0	3,0	—
VII	—	10,05	7,6...7,2	5,48	4,42	3,97	2,22	8,1	4,0	0,6
VIII	8,27	8,67	7,5...7,1	5,30	4,52	—	2,36	—	6,0	0,8
X	8,58, 7,68 and 7,46	8,76	7,5...7,0	5,30	4,57	—	3,50	—	6,0	0,8
XIA	—	11,60 and 9,60	7,5...7,1	5,42	4,34	—	3,87	—	6,0	0,8
XIB	—	10,98 and 9,30	7,5...7,1	5,48	4,88	—	3,67	—	6,0	0,8
XII	—	12,58	7,9...7,3	6,58*4	—	—	2,32	—	—	—

*1Signal for the OH proton at 6.27 ppm, $^2J_5$-CH_2 = 13.4 Hz.
*2Doublet of triplets.
*3Doublet of doublets, $^5J_{NH,H_4}$ = 1.4 Hz.
*4Singlet.

TABLE 3. ^{13}C NMR Chemical Shifts of Compounds Obtained, in DMSO-D$_6$ (δ, ppm)

Compound	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	4-C_6H_5	6-C_6H_5	Remaining carbon atoms
I	168,57	61,23	40,86	46,07	82,50	146,27 (α), 125,52 (o), 127,95 (m), 126,46 (p)	142,52 (α), 127,60 (o), 128,19 (m), 127,48 (p)	203,21 (C=S)
II	167,39	60,20	44,40	106,33	134,34	142,40 (α), 125,52 (o), 127,92 (m), 126,68 (p)	136,04 (α), 127,92 (o), 128,38 (m), 128,33 (p)	202,41 (C=S)
VII	166,20	61,41	41,67	105,17	134,06	140,88 (α), 125,56 (o), 128,22 (m), 127,05 (p)	137,11 (α), 127,44 (o), 128,61 (m), 128,61 (p)	195,35 (C$\lesssim^{O}_{S}$) 11,22 (SCH_3)
VIII	166,59	91,40	41,87	104,00	134,00	147,05 (α), 125,17 (o), 128,22 (m), 125,67 (p)	134,91 (α), 126,73 (o), 128,22 (m), 127,96 (p)	161,14 (=C$\lesssim^{S}_{N}$) 12,52 (SCH_3)
X	166,78	92,50	42,20	104,26	134,09	147,15 (α), 125,38 (o), 128,43 (m), 125,90 (p)	135,00 (α), 126,88 (o), 128,43 (m), 128,17 (p)	159,76 (=C$\lesssim^{S}_{N}$) 33,23 (SCH_2) 171,26 (C=O)
XIA	165,61	99,76	42,59	103,92	134,49	144,54 (α), 125,55 (o), 128,42 (m), 125,67 (p	135,19 (α), 126,78 (o), 128,57 (m), 128,71 (p)	172,73 (C=O) 151,31 (=C$\lesssim^{S}_{N}$) 32,45 (SCH_2)
XIB	164,79	98,71	42,27	104,83	134,11	143,92 (α), 126,37 (o), 127,19 (m), 126,65 (p)	134,72 (α), 128,42 (o), 128,57 (m), 128,71 (p)	175,19 (C=O) 154,12 (=C$\lesssim^{S}_{N}$) 32,30 (SCH_2)

In continuation of our work with monothilmalondiamide, we have obtained 6-hydroxy-4,6-diphenyl-3-thiocarbamoyl-3,4,5,6-tetrahydropyridin-2(1H)-one and the corresponding 3,4-dihydropyridin-2(1H)-one, and examined their alkylation.

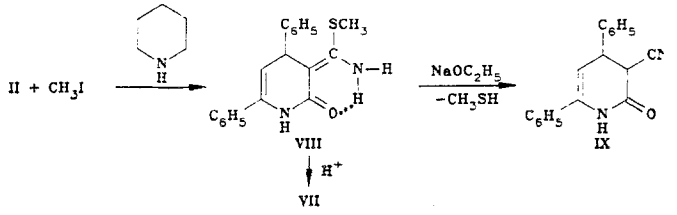
6-Hydroxy-4,6-diphenyl-3-thiocarbamoyl-3,4,5,6-tetrahydropyridin-2(1H)-one (I) was obtained in high yield by condensing benzylideneacetophenone with monothiomalondiamide in the presence of piperidine. This compound (I) is unstable to heat and in solution. Treatment of (I) with a small excess of HCl in ethanol with brief heating results in dehydration to give the more stable 4,6-diphenyl-3-thiocarbamoyl-3,4-dihydropyridin-2(1H)-one (II).

Despite the fact that (I) and (II) contain several nucleophilic centers (S, $C_{(3)}$, O, $N_{(1)}$, and thiamide N), alkylation under mild conditions takes place exclusively at sulfur. Brief heating of the 6-hydroxytetrahydropyridin-2-one (I) with an excess of methyl iodide in the presence of piperidine affords a mixture of 6-methylthio-1,8-diphenyl-2,6-diazabicyclo[2.2.2]oct-5-en-3-one (IV) and 4,6-diphenyl-3-methylthiocarbonyl-3,4-dihydropyridin-2(1H)-one (VII), which are readily separable as a result of their differing solubilities in 50% ethanol. When (I) is alkylated under similar conditions, but with more prolonged heating (15-20 min) followed by keeping at room temperature, the 3,4-dihydropyrid-2(1H)-one (VII) was the sole product. When (I) reacted with dimethyl sulfate, the main product was again the 3,4-dihydropyrid-2(1H)-one (VII). The latter compound was also obtained in high yield by briefly boiling the diazabicyclooctenone (IV) in acidified ethanol, in accordance with the literature [6], the ready hydrolizability of acyclic alkylthioamides being well known [7].

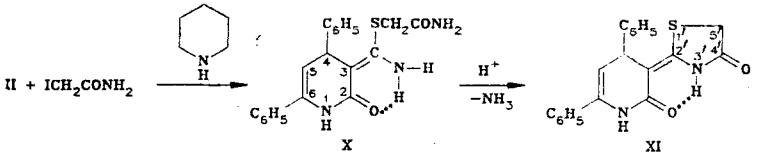
The formation of (IV) and (VII) may be rationalized as follows. First, (I) is alkylated at sulfur, the resulting 6-hydroxy-3-methylthiocarbimino-3,4,5,6-tetrahydropyridin-2(1H)-one (III) then undergoing dehydration with closure of the 2,6-diazabicyclo[2.2.2]oct-5-en-3-one ring to give (IV). The HI liberated then cleaves the $C_{(1)}$—$N_{(6)}$ bond to give the carbocation (V), which is established as 3-methylthiocarbimino-3,4-dihydropyridin-2(1H)-one (VI), this then undergoing hydrolysis to 3-methylthiocarbonyl-3,4-dihydropyridin-2(1H)-one (VII).

In the case of dimethyl sulfate, the 6-hydroxy-3-methylthiocarbimino-3,4,5,6-tetrahydropyridin 2(1H)-one (III) first formed is probably converted directly into the 3,4-dihydropyridin-2(1H)-one (VI) in the acid medium and then into compound (VII).

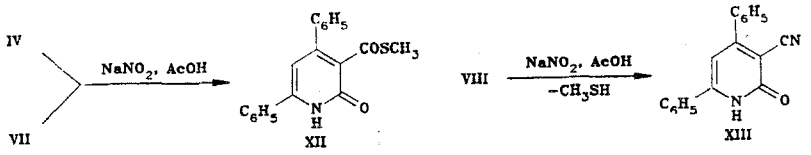
Treatment of the 3-thiocarbamoyl-3,4-dihydropyridin-2(1H)-one (II) with an excess of methyl iodine gives high yields of 3-(1'-amino-1'-methylthiomethylene)-4,6-diphenyl-1,4-dihydropyridin-2-one (VIII). In acid media (VIII) is converted in high yield into 3-methylthiocarbonyl-3,4-dihydropyridin-2(1H)-one (VII), and on brief boiling with sodium ethoxide it loses a molecule of methyl mercaptan to give the known 3-cyano-3,4-dihydropyridin-2(1H)-one (IX) [8].



Alkylation of (II) under similar conditions with iodoacetamide affords 4,6-diphenyl-3-(1'-amino-1'-carbamoylmethylthiomethylene)-1,4-dihydropyridin-2-one (X), which on brief heating in acidified ethanol undergoes intramolecular cyclization with loss of ammonia to give 4,6-diphenyl-3-(4'-oxo-3',5'-dihydro-1',3'-thiazol-2'-ylidene)-1,4-dihydropyridin-2-one (XI).



Oxidation of (IV) and (VII) with sodium nitrite in acetic acid gives low yields of 4,6-diphenyl-3-methylthiocarbonylpyridine-2(1H)-one (XII). Treatment of (VIII) with the same oxidant results in cleavage of a molecule of methyl mercaptan with the formation of the known 3-cyanopyridin-2(1H)-one (XIII) [8].



The structures of the products were confirmed by spectral methods. The IR spectra of (I), (II), (IV), (VII), and (XII) in the crystalline state (Table 1) show ν_{CO} characteristic of the exocyclic carbonyl at 1653-1708 cm^{-1}, and ν_{NH}, ν_{NH_2}, and ν_{OH} at 3150-3406 cm^{-1}. In (VII), (X), (XI), and (XII), ν_{CO} for the exocyclic carbonyl was present at 1686-1728 cm^{-1}. In (VIII), (X), and (XI), the endocyclic ν_{CO} was reduced to 1618-1630 cm^{-1}, and in the case of (X) the exocyclic ν_{CO} was also reduced as a result of the formation of hydrogen bonds between the carbonyl and amino-groups.

In the UV spectra (Table 1), the long-wavelength maximum was shifted bathochromically as the conjugation in the molecule increased.

In the ^1H NMR spectra (Table 2), apart from the signals for the NH, NH_2, OH, and C_6H_5 protons, of the greatest interest for structural proof and elucidation of the steric structure of the hydrogenated ring were the signals for the protons at $C_{(3)}$, $C_{(4)}$, and $C_{(5)}$. In the case of (I), the 3-H, 4-H, and 5-CH_2 signals were present at 3.93, 4.33, 2.11, and 1.92 ppm. The ring coupling constants were $^3J_{H_3H_4}$ = 11.9 Hz, $^3J_{H_4H_5}$ = 12.1 and 2.6 Hz, and $^2J_{5\text{-}CH_2}$ = 13.4 Hz, which according to Kuthan et al. [9] shows that the 3-thiocarbamoyl and 4-phenyl groups are oriented trans-pseudoequatorially.

In the ^1H NMR spectra of the 3,4-dihydropyridin-2(1H)-ones (II) and (VII), the signal for 3-H was seen at 3.98 and 3.97, 4-H at 4.60 and 4.42, and 5-H at 5.33 and 5.48 ppm, with ring coupling constants $^3J_{H_3H_4}$ = 12.0 and 8.1 Hz, and $^3J_{H_4H_5}$ = 3.0 and 4.0 Hz respectively. In the dihydropyridines (II) and (VII), the 3-thiocarbamoyl (or methylthiocarbonyl) and the 4-phenyl groups were, as in (I), preferentially oriented trans-pseudoequatorially.

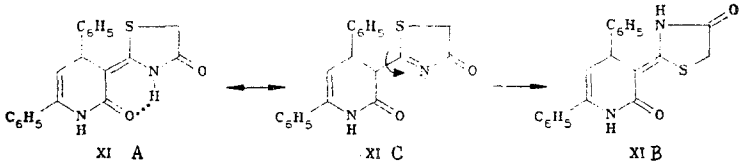
The ^1H NMR spectra of (VIII), (X) and (XI) showed doublets for the 4-H and 5-H protons, confirming the 1,4-dihydropyridin-2-one structure. In (VIII) and (X), signals were also present for the 3-(1'-aminomethylene) substituent, thus excluding the alternative 2-hydroxy-3-methylthiocarbimino-1,4-dihydropyridine structure. The ^1H NMR spectrum of (XI) showed no signals for amino-groups.

In the ^{13}C NMR spectra (Table 3), in contrast to the chemical shifts (CS) of the tertiary $C_{(3)}$ atoms in the hydrogenated pyridin-2-ones (I), (II), and (VII), and the CS of $C_{(4)}$ in the bicyclic compound (IV), present at 61.41-58.06 ppm, in the case of the 3-ylidene-1,4-dihydropyridine-2-ones (VIII), (IX), and (X) the CS for the quaternary carbon $C_{(3)}$ were present at 99.76-91.40 ppm. Of interest is the difference between the CS of $C_{(6)}$ in (I) (82.50 ppm) and the corresponding $C_{(1)}$ in the bicyclic compound (77.17 ppm), and the CS of $C_{(6)}$ in (II), (VII), (VIII), (X), and (XI) (134.49-134.00 ppm).

In addition, in (I) and (II) the CS of the thioamide C=S groups were seen at 203.21-202.41 ppm, and in 3-methylthiocarbonyl-3,4-dihydropyridin-2(1H)-one (VII) the S—C=O lay at 195.35 ppm, in accordance with literature findings [10, 11]. The CS of the quaternary $=C\begin{matrix}S\\ \diagup\\ \diagdown\\ N\end{matrix}$ carbon in (XI), as in (VIII) and (X), was seen at 161.14-151.31 ppm. Furthermore, in the ^{13}C NMR spectra the signals for the C=O groups were present at 172.73 and 165.61 ppm, thus confirming the structure of (XI). The alternative 2,5-dioxo-4,6-diphenyl-1,3,6,9-tetrahydro-1,4-thiazepino [2,3-b]pyridinium structure in ^{13}C NMR spectra would have given rise to signals for $C_{(3)}$ at 110-107 ppm and for S—C=O at 196-195 ppm [10, 11].

The ^{13}C and ^1H spectral data for the bicyclic compound (IV) were in good agreement with those given in [6]. In addition, the ^{15}N NMR spectrum showed signals for the amide nitrogen

N(2) at −242.8 ppm, and for the doubly bonded nitrogen N(6) at −76.0 ppm, also in agreement with reported data [6, 12]. NMR spectroscopy (Tales 2 and 3) showed that on standing for 50 h, (XI) was converted into a mixture of two isomers, (XIA) and (XIB).



XI A XI C XI B

The structure (XIA) was more stable than (XIB) as a result of the possibility of hydrogen bonding between the carbonyl and amino-groups, and in the crystalline state the compound clearly exists in this form. However, the order of the exocyclic C(3)—C(2') bond is considerably reduced by conjugation (according to the canonical form XIC), so that the activational transition XIA→XIB is possible.

In the IR spectrum of (XI), obtained as the saturated solution in DMSO immediately following preparation, two strong bands were present in the carbonyl absorption region, at 1633 and 1732 cm^{-1}, together with two low-intensity bands at 1667 and 1718 cm^{-1}. After keeping for 50 h, the intensity of the absorption at 1633 cm^{-1} had decreased, and absorption appeared at 1650 cm^{-1}. Further, the intensity of the absorption at 1718 cm^{-1} decreased, that at 1667 cm^{-1} remaining of low intensity. It may be assumed that structure (XIA) corresponds to ν_{CO} at 1633 and 1732 cm^{-1}, and (XIB) to ν_{CO} at 1650 and 1718 cm^{-1}. In contrast to (XI), the 1,4-dihydropyridine-2-ones (VIII) and (X) do not isomerize in solution in DMSO, obviously owing to the presence of sufficiently strong intramolecular hydrogen bonds.

EXPERIMENTAL

IR spectra were recorded on a Perkin-Elmer 580B instrument in vaseline grease and in solution in DMSO, and UV spectra on a Specord UV-VIS in ethanol. ^1H NMR spectra were obtained on a WH 90/DC spectrometer (90 MHz), internal standard TMS, and ^{13}C NMR spectra on the same instrument (22.63 MHz), internal standard cyclohexane (δ 27.44 ppm) in DMSO-D_6. The accuracy of measurement of the ^1H chemical shifts was ±0.03 ppm, ^{13}C ±0.07 ppm, and the coupling constants ±0.1 Hz. The ^{15}N NMR spectrum was obtained on a WM 360 instrument at 36.5 MHz, accuracy of measurement of the chemical shifts from the external standard (nitromethane) ±0.2 ppm. The progress of the reactions was followed and the purity of the products established by TLC on Silufol UV-254 plates, eluent chloroform—acetone—hexane (2:1:1). The principal characteristics of the compounds obtained are shown in Tables 1-3. The elemental analyses of (I-XII) for C, H, N, and S were in agreement with the calculated values.

6-Hydroxy-4,6-diphenyl-3-thiocarbamoyl-3,4,5,6-tetrahydropyridine-2(1H)-one (I). A mixture of 2.08 g (10 mmole) of benzylideneacetophenone and 1.18 g (10 mmole) of monothiomalondiamide in 10 ml of abs. ethanol and 1 ml of piperidine was heated briefly to 40-50°C, then stirred for 1 h at room temperature. The mixture was cooled to 0°C, the solid filtered off, and washed with ethanol and water to give 2.79 g (83%) of (I), mp 194-196°C (from ethanol).

4,6-Diphenyl-3-thiocarbamoyl-3,4-dihydropyridine-2(1H)-one (II). A solution of 3.26 g (10 mmole) of the tetrahydropyridine-2(1H)-one (I) was heated briefly in 30 ml of 0.5 N HCl in ethanol, and stirred for 1 h at room temperature. The solid was filtered off and washed with ethanol and water to give 2.31 g (75%) of (II), mp 198-200°C (from ethanol).

Methylation of 3,4,5,6-Tetrahydropyridine-2(1H)-one (I). A solution of 3.26 g (10 mmole) of (I) in a mixture of 25 ml of abs. ethanol, 1 ml (10 mmole) of piperidine, and 2.5 ml (40 mmole) of methyl iodide was heated briefly to 50°C. The mixture was cooled, 0.5 ml of water added dropwise, triturated, and after 10 min filtered, and the solid washed with 20 ml of 50% ethanol to give 1.1 g (32%) of 5-methylthio-1,8-diphenyl-2,6-diazabicyclo[2.2.2]oct-5-en-3-one (IV). ^1H NMR spectrum: 9.12 (1H, s, NH), 7.9-7.2 (10H, m, $2C_6H_5$), 3.53 (1H, d.d J = 1.6 and 2.5 Hz, 4-H), 3.28 (1H, m, 8-H), 2.36 and 2.23 (1H, d.d and d.d, H = 4.6 and 12.6 Hz; 10.2 and 12.6 Hz, 7-CH_2), 2.52 ppm (3H, s, CH_3). ^{13}C NMR spectrum 173.52 (5-C); 169.69 (3-C); 77.17 (1-C); 59.06 (4-C); 44.14 (7-C); 39.45 (8-C); [141.11 (α-C), 126.81 (o-C); 128.30 (m-C); 126.96 (p-C) (8-C_6H_5)]; [140.44 (α-C), 127.72 (o-C), 128.54 (m-C), 128.07 ppm (p-C) (1-C_6H_5)]. ^{15}N NMR spectrum (in DMSO-D_6): -242.8 (NHCO)

and -76.0 ppm (N=C—S). From the filtrate after 24 h there was obtained by filtration 1.15 g (36%) of 4,6-diphenyl-3-methylthiocarbonyl-3,4-dihydropyridine-2(1H)-one (VII).

4,6-Diphenyl-3-methylthiocarbonyl-3,4-dihydropyridine-2(1H)-one (VII). A. A. mixture of 3.26 g (10 mmole) of the tetrahydropyridine-2(1H)-one (I) with 20 ml of absolute ethanol, 1 ml (10 mmole) of piperidine, and 2.5 ml (40 mmole) of methyl iodide was boiled for 15 min on the water bath. The mixture was cooled, and 0.37 g of N-methylpiperidinium iodide filtered off. From the filtrate after 4 h there was obtained by filtration 1.8 g (56%) of (VII).

B. A mixture of 0.98 g (3 mmole) of (I) with 20 ml of abs. ethanol, 0.3 ml (3 mmole) of piperidine, and 0.5 ml (5.3 mmole) of dimethyl sulfate was boiled for 15 min on the water bath, cooled, and 0.6 g (60%) of (VII) filtered off.

C. A mixture of 0.17 g (0.5 mmole) of (IV) in 4 ml of 0.5 N HCl in ethanol was boiled for 2-3 min. The mixture was cooled, and the solid filtered off and washed with water to give 0.15 g (94%) of (VII).

D. Compound (VIII) (0.16 g; 0.5 mmole) was dissolved in 2 ml of 0.5 N HCl in ethanol with heating on the water bath. The mixture was kept for 30 min at room temperature, and the solid filtered off and washed with water to give 0.15 g (94%) of (VII).

4,6-Diphenyl-3-(1'-amino-1'methylthiomethylene)-1,4-dihydropyridine-2-one (VIII). A mixture of 0.62 g (2 mmole) of the 3,4-dihydropyridine-2(1H)- one (II) and 0.62 g (10 mmole) of methyl iodide in 5 ml of abs. ethanol and 0.05 ml (5 mmole) of piperidine was boiled for 5 min on the water bath. The mixture was cooled, kept for 2 h at room temperature, and the solid filtered off and washed with 50% ethanol and water to give 0.6 g (93%) of (VIII), mp 192-194°C (from ethanol).

4,6-Diphenyl-3-cyano-3,4-dihydropyridine-2(1H)-one (IX). A solution of 0.97 g (3 mmole) of (VIII) in 10 ml of 0.5 N sodium ethoxide solution was boiled for 2-3 min on the water bath. The mixture was then cooled, 1 ml of acetic acid added, and the solid filtered off to give 0.51 g (62%) of (IX), which gave no depression of melting point on admixture with an authentic sample [8].

4,6,-Diphenyl-3-(1'-amino-1'-carbamoylmethylthiomethylene)-1,4-dihydropyridine-2-one (X). A mixture of 3.08 g (10 mmole) of the 3,4-dihydropyridine-2(1H)-one (II) and 1.87 g (11 mmole) of iodoacetamide was dissolved with vigorous stirring and heating at 40°C in 50 ml of absolute ethanol and 1.0 ml of piperidine, and filtered. After 5-10 min, the product crystallized, and this was cooled to 0°C, filtered off, and washed with ethanol and water to give 1.39 g (38%) of (X), mp 169-171°C (from ethanol).

4,6-Diphenyl-3-(4'-oxa-3',5'-dihydro-1',3'-thiazol-2'-ylidene)-1,4-dihydropyridine-2-one (XI). A solution of 0.73 g (2 mmole) of (X) in 20 ml of 0.5 N HCl in ethanol was boiled for 2-3 min. After 4-5 min, the product crystallized, and was cooled to 0°C, filtered off, and washed with ethanol to give 0.48 g (69%) of (XI), mp 238-240°C (from ethanol—DMF, 1:1).

4,6-Diphenyl-3-methylthiocarbonylpyridine-2(1H)-one (XII). A. To a mixture of 0.32 g (1 mmole) of the 3,4-dihydropyridine-2(1H)-one (VII) in 5 ml of glacial acetic acid was added 0.7 g (10 mmole) of sodium nitrite, and the mixture heated on the water bath until nitrogen dioxide was no longer evolved. The mixture was then cooled, 5 ml of water added, the solid filtered off, and washed with 10 ml of hot ethanol to give 0.1 g (31%) of (XII), mp 228-230°C (from ethanol).

B. Similarly, from 0.31 g (1 mmole) of the bicyclic compound (IV) there was obtained 0.08 g (25%) of (XII).

Oxidation of 4,6-Diphenyl-3-(1'-amino-1'-methylthiomethylene)-1,4-dihydropyridin-2-one (VIII). To a mixture of 0.1 g (0.3 mmole) of (VIII) in 1 ml of glacial acetic acid was added 0.21 g (3 mmole) of sodium nitrite, and the mixture heated on the water bath until nitrogen dioxide was no longer evolved. It was then cooled, 1 ml of water added, and the solid filtered off and washed with ethanol to give 0.07 g (70%) of 4,6-diphenyl-3-cyanopyrin-2(1H)-one (XIII), which gave no depression of melting point on admixture with an authentic sample [8].

LITERATURE CITED

1. Z. A. Bomika, Yu. E. Pelcher, G. Ya. Dubur, A. A. Krauze, and E. E. Liepin'sh, Khim. Geterotsikl. Soedin., No. 10, 1377 (1979).
2. U. Schmidt, Chem. Ber., 92, 1171 (1959).
3. A. A. Krauze, Z. A. Kalme, Yu. É. Pelcher, E. E. Liepin'sh, I. V. Dipan, and G. Ya. Dubur, Khim. Geterotsikl. Soedin., No. 11, 1515 (1983).
4. W. Schaper, Synthesis, No. 5, 861 (1985).
5. A. A. Krauze, É. É. Liepin'sh, and G. Ya. Dubur, Khim. Geterotsikl. Soedin., No. 7, 994 (1987).
6. Z. A. Kalme, É. É. Liepin'sh, Yu. E. Pelcher, and G. Ya. Dubur, Khim. Geterotsikl. Soedin., No. 5, 620 (1989).
7. R. K. Chaturvedi, A. E. MacMahan, and G. L. Schmir, J. Am. Chem. Soc., 89, 6984 (1967).
8. Z. A. Bomika, M. G. Andaburskaya, Yu. E. Pelcher, and G. Ya. Dubur, Khim. Geterotsikl. Soedin., No. 8, 1108 (1975).
9. J. Kuthan, P. Neswadba, Z. Donnerova, and P. Trška, Coll. Czech. Chem. Communs., 42, 2152 (1977).
10. W. Bremser, B. Franke, and H. Wagner, Chemical Shift Ranges in Carbon-13 NMR Spectroscopy, Weinheim (1982).
11. C. M. Hall and J. Wemple, J. Org. Chem., 42, 2118 (1977).
12. G. J. Martin, M. L. Martin, and J. P. Gouesnard, ^{15}N NMR Spectroscopy, Springer-Verlag, Berlin (1981).

DISSOCIATIVE IONIZATION OF SUBSTITUTED PIPERIDEINES

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The fragmentation of different alkyl(aryl) substituted piperideines [tetrahydropyridines] was studied by analyzing high-resolution mass spectra and DADI [Direct Analysis of Daughter Ions] spectra. It was shown that the retrodiene decomposition of the ring is suppressed by competing processes of elimination of ring substitutents. The nature of the substituents and their mutual disposition on the ring have a substantial influence on the extent of their cleavage from the ring.

The piperideine ring is an important structural element of many natural and synthetic, biologically active substances [1; 2, p. 12]. Determining the position of the double bond in this ring is an important structural/analytical problem, for the solution of which mass spectrometry has been successfully applied [3, 4].

The study of aza analogs of cyclohexane, which are quite unstable compounds, is limited to data on the decomposition of some derivatives of N-acyl substituted 2,3- and 3,4-dehydropiperidines [5-7], the fragmentation of which is basically explained by the cleavage of the acyl group and the localization of the positive charge on it. Here, the fragments, forming via a retrodiene decomposition (RDD), either have these compounds in their mass spectra at low intensities or not at all [6].

It was of interest to investigate the dissociative ionization of alkyl(aryl) substituted piperideines I-IX and also structural analogs of the natural alkaloid anabasine, N-substituted 3-methyl-2-phenyl-6-(3'-methyl-2'-phenylpyridyl-5')-3,4-dehydropiperidines X-XIX, in order to learn the effect of the substituents and their mutual disposition on the ring on the ratio of the fragmentation processes of ring cleavage by an RDD mechanism [8] and elimination of ring substituents. In the present work, the mass spectral behavior of compounds I-IX and XI-XIX are analyzed for the first time; data on the decomposition of X was given in [9].

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