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SYNTHESIS AND INVESTIGATION OF THE CHEMICAL AND PHYSICOCHEMICAL PROPERTIES OF 6-(1,4,5,6-TETRAHYDRO-6-OXO-3-PYRIDAZINYL)-2,3-DIHYDRO-2-INDOLINONES

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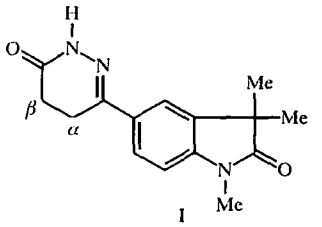
Acylation of 1-ethyl-3-(N,N-dimethyl)aminomethylene-1,2-dihydro-2-indolinone by succinic anhydride in the presence of aluminum chloride has been studied. PMR spectroscopy shows that this acylation leads to formation of a mixture of the 5- and 6-succinoyl derivatives with predominance of the latter (cis and trans isomers of both these products were found). The reaction of the latter with hydrazine hydrate gives hydrazinomethylene derivative of 2-indolinone, in reaction of which with various carbonyl compounds a series of oxindol hydrazones has been obtained. The reaction of these products with primary amines smoothly leads to transamination and the formation of enamines of 1,6-disubstituted 2-indolinone.

Many oxindol derivatives have been found to possess pronounced biological activity [1-3]. In particular, this group features indolidane (I), which is a nonsteroid cardiotonic synthesized by initial acylation of 3,3-dimethyloxindol at $C_{(5)}$ and subsequent closure of the oxopyridazinyl ring [4].



I

In recent work [5], we have established that derivatives with an enamine fragment at $C_{(3)}$ undergo electrophilic substitution at $C_{(6)}$ of the indole system in contrast to oxindol and 1-substituted oxindols, whose nitration occurs at $C_{(5)}$.

These literature results suggested that it would be interesting to study the feasibility of constructing a pyridazinyl substituent starting from enamine derivatives of oxindol, elucidate the predominant site of acylation of these enamines, and, thereby, develop an approach to the synthesis of new hetaryl-2-indolinones with possible cardiotonic activity.

1-Ethyl-(N,N-dimethyl)aminomethyleneoxindol (II) synthesized by us earlier was selected as the starting compound in the present work [6]. The acylation of compound II by succinic anhydride in the presence of aluminum chloride led to a mixture of 5- (III) and 6-succinoyl derivatives (IV) with predominance of the latter. Pure 6-isomer IV was isolated in satisfactory yield from dichloroethane solution (Tables 1 and 2, compound A). The substance obtained from the dichloroethane mother liquor (Table 2, substance B) was a 40:60 mixture of 5- and 6-isomers III and IV.

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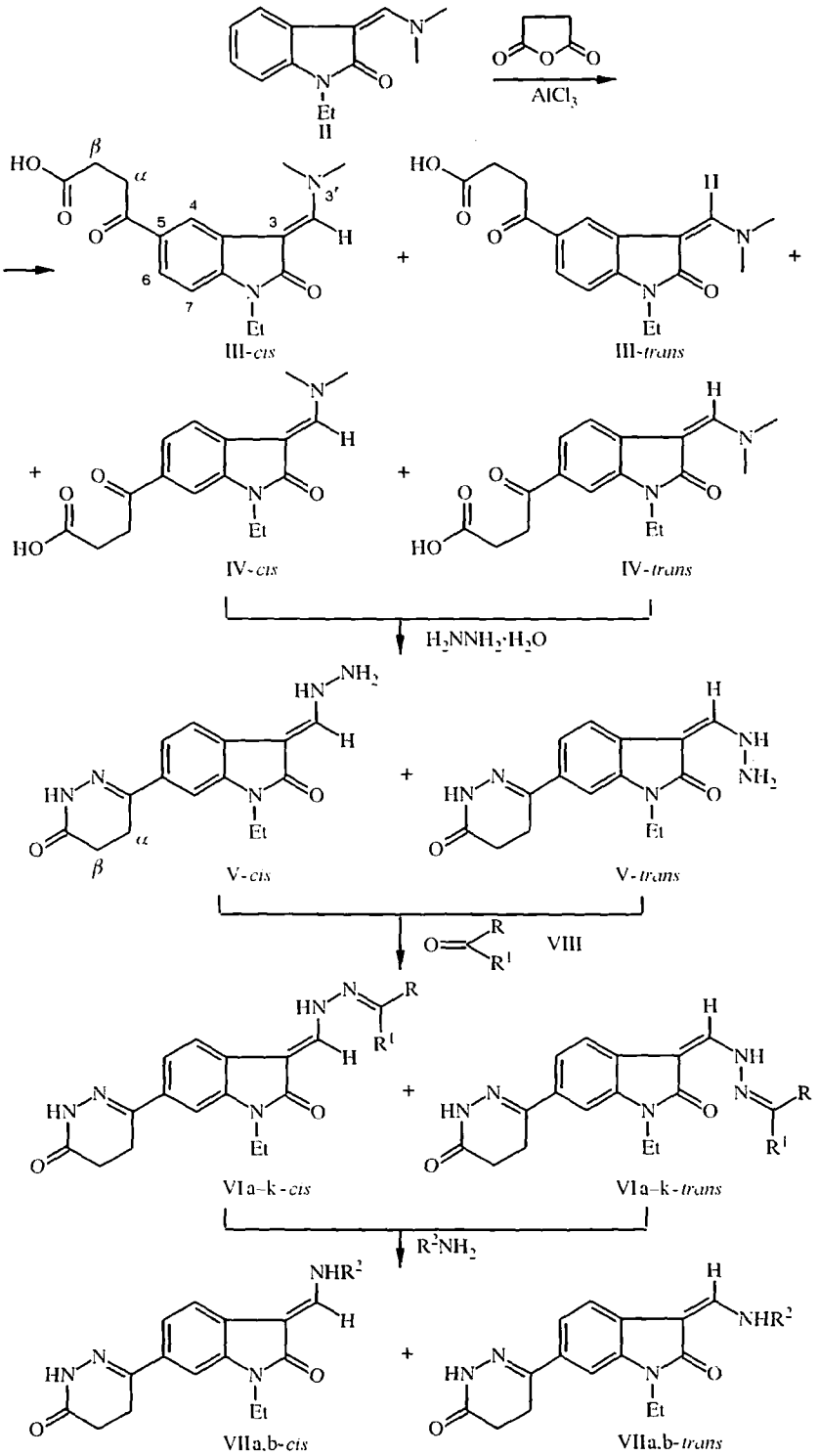


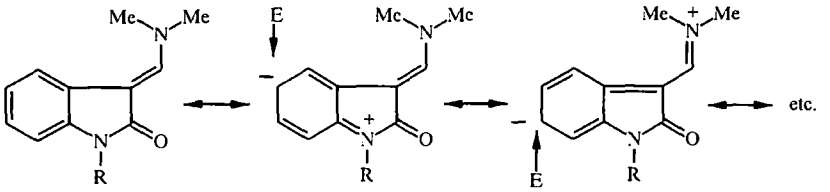
VI a R = Ph, R^1 = H; b R = *p*-$MeOC_6H_4$, R^1 = H; c R = Me, R^1 = Ph; d R = R^1 = $-CH_2CH_2CH_2CH_2-$; e R = R^1 = $-CH_2CH_2CH_2CH_2CH_2-$; f R = Me, R^1 = Bu; g R = H, R^1 = *p*-HOC_6H_4; h R = Me, R^1 = Pr; i R = H, R^1 = *o*-HOC_6H_4; j R = H, R^1 = *m*-MeO-*p*-HOC_6H_3; k R = H, R^1 = *p*-BrC_6H_4.

VII a R^2 = CH_2Ph; b R^2 = CH_2CH_2Ph

The PMR spectrum of the isolated major product A shows a doubling of all signals due to the existence of compound A in solution as a mixture of *cis* and *trans* isomers at the $C_{(3)}$–$C_{(3')}$ bond (Table 2). In the aromatic proton signal region there are doublets at 7.42 ppm with SSCC $^4J_{HH}$ = 1.2 Hz (J_m)* and 7.45 ppm with SSCC $^4J_{HH}$ = 1.4 Hz (J_m)* and doublets at 7.44 ppm with SSCC $^3J_{HH}$ = 8.4 Hz (J_o)* and 7.50 ppm with SSCC $^3J_{HH}$ = 8.4 Hz (J_o)* in addition to doublets of doublets (7.58 and 7.56 ppm). Doublets J_m and J_o are the key signals for determining whether acylation occurs at $C_{(5)}$ or $C_{(6)}$. Nuclear Overhauser effect (NOE) experiments showed that irradiation of the signals of the methylene protons of the N-ethyl substituent at 3.81 and 3.82 ppm leads to the increase in the intensity of the J_m doublets at 7.42 and 7.45 ppm by about 8% and 7.5%, respectively, while the intensity of the J_o doublets at 7.44 and 7.50 ppm remains unchanged. This result permits the unequivocal assignment of the J_m doublets at 7.42 and 7.45 ppm to the proton at $C_{(7)}$ of the indole system, while the signals at 7.44 and 7.50 ppm can be assigned to 4-H, consequently the structure of the major acylation product as 6-acyl derivative IV is solved unequivocally. We should note that, judging from the PMR spectrum of mixture B, 5-acyl derivative features a downfield position for the J_m doublets of 4-H at 8.02 and 8.00 ppm and upfield position of the J_o doublets of 7-H at 6.97 and 7.04 ppm relative to the analogous (according to the type of splitting) signals for 6-isomer IV.

As in the case of 6-substituted isomer IV, 5-substituted isomer III also exists in solution as a mixture of two geometrical isomers. The *cis/trans* isomer ratios*[2] for the studied compounds are given in Table 1, while the assignments of the signals of the geometrical isomers were based on the regulation of chemical shifts of the vinyl proton and 4-H obtained in our previous work [6].*[3]

Thus, acylation of 1-ethyl-3-(N,N-diethyl)aminomethyleneoxindol (II) does not proceed as unequivocally at $C_{(6)}$ as the nitration [5].



II

E = electrophile

However, we may conclude that acylation at $C_{(6)}$ is the predominant reaction. Examination of the structure of starting enamine II, indeed, shows the possibility of acylation at both $C_{(5)}$ and $C_{(6)}$ but the weaker electron-donor effect of the acylamino group relative even to the distant NR_2 group leads to the predominant electrophilic attack at $C_{(6)}$.

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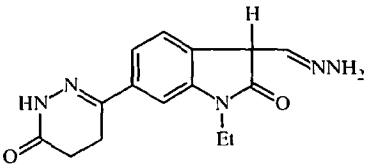
* Here and subsequently, the doublet with SSCC $^4J_{HH}$ ~ 1.2-1.4 Hz is indicated as the J_m doublet and the doublet with SSCC $^3J_{HH}$ = 8.4 Hz is termed the J_o doublet.

*[2] In accord with our previous data [6], the assignment of the *cis* and *trans* isomers was based on the mutual arrangement of vinyl proton 3'-H and carbonyl group $C_{(2)}$=O.

*[3] The comparison was carried out with the spectrum of compound II in DMSO-d_6. *trans* Isomer with 1.09 (3H, t, $NCH_2C\underline{H}_3$); 3.72 (2H, q, $NC\underline{H}_2CH_3$); 3.26; 3.65 (3H each, br. s, $N(CH_3)_2$); 6.80-7.10 (3H, m, arom H); 7.32 (1H, d, 4-H); 7.59 ppm (1H, s, 3'-H). NOE: irradiation of the signal at 7.32 ppm (4-H) led to increase in the intensity of the signal of 3'-H at 7.59 ppm by 25%, irradiation of the signal of 3'-H at 7.59 ppm led to increase in the intensity of the signal of 4-H at 7.32 ppm by 13%, irradiation of the signals of $N(CH_3)_2$ protons led to increase in the intensity of the signal of 3'-H at 7.59 ppm by 20%. *cis* Isomer with 1.10 (3H, t, $NCH_2C\underline{H}_3$); 3.75 (2H, q, $NC\underline{H}_2CH_3$); 3.29 (6H, s, $N(CH_3)_2$); 6.80-7.10 (3H, m, arom H); 7.42 (1H, d, 4-H); 7.48 ppm (1H, s, 3'-H). NOE: irradiation of the signal of $N(CH_3)_2$ protons at 3.29 ppm led to increase in the intensity of the signal of 4-H at 7.42 ppm by 20% and of the signal of 3'-H at 7.48 ppm by 28%.

The reaction of the compound IV with hydrazine hydrate proceeds smoothly. Not only closure of the pyridazine ring but also transamination with formation of hydrazinomethylene derivative V is observed. The PMR spectrum of the compound V features broadened signals in the aromatic region, probably due to exchange processes. The sample was heated to 60°C to reach thermodynamic equilibrium and then cooled. The spectrum of solution of the compound V in DMSO-d_6 indicates the presence of about 60% *trans* isomer stabilized by intramolecular hydrogen bond and about 35% of *cis* isomer. In accord with our previous work [6], for the *trans* isomer the signal of vinyl proton 3'-H is found at significantly low field ($\Delta\delta_{trans-cis}$ = 0.42 ppm), while the signal for 4-H of this isomer is relatively upfield ($\Delta\delta_{trans-cis}$ = -0.26 ppm). It is interesting that about 5% of hydrazone form is found, which features doublets at 5.70 and 6.90 ppm ($^3J_{HH}$ ~ 8 Hz) assigned to 3-H and CH=N protons (the PMR data for the isomer mixture of V are given in Table 3). Product V readily reacts with various carbonyl compounds to give hydrazones VIa-k.



Study of the PMR spectra of hydrazones VIa-k shows that the *trans* isomer, stabilized by intramolecular hydrogen bonding, predominates in all cases (Table 3). We should note that the signals of the aromatic protons of the *trans* isomers of the compounds VIa and VIb are rather narrow with marked multiplicity, while the analogous signals for the *cis* isomers are rather broad, leading to smoothing of multiplicity of the signal. This is true for vinyl protons 3'-H and =CH–Ar and aromatic protons 4-H and 5-H. Significant narrowing of the signals was found when the spectra of the solutions were taken at elevated temperature, and this permitted their reliable assignment. The spectra of the cooled samples were identical to the original spectra. Hence, the broadening of the signals of the sterically hindered *cis* isomers results from hindrance to "rotation" relative to the C=N and N–N bonds, which is more rapid at higher temperature. The PMR spectral data of hydrazones VI are given in Table 2.

Thus, the possibility of transition from hydrazinomethylene derivatives to aminomethylene derivatives has been established. The reaction of hydrazones VIc and VIe with primary amines smoothly leads to transamination to give enamines VIIa and VIIb. The spectral data for these compounds given in Table 3 correspond to these conclusions.

EXPERIMENTAL

The PMR spectra were recorded on a Varian Unity-400 spectrometer for DMSO-d_6 solutions with TMS as the internal standard. The mass spectra were taken on a Finnigan-MAT SSQ-710 mass spectrometer with direct sample inlet into the ion source. The ionizing voltage was 70 eV and the temperature of the ionization chamber was 150°C. The melting points were determined on a Boetius block.

Acylation of 1-Ethyl-(N,N-dimethyl)aminomethylene-2,3-dihydro-2-indolinone. Ground $AlCl_3$ (9.2 g) was added in portions to mixture of the compound II (4.97 g, 0.032 mol) and succinic anhydride (3.85 g, 0.0385 mol) in dichloroethane (115 ml) at 2-5°C. The reaction mixture was stirred for 1 h at 5°C, heated at 50-55°C for 1 h, and then poured into a mixture of ground ice and 11.5 ml of concentrated hydrochloric acid. Mixture (0.7 g) of 5-isomer III (7%) and 6-isomer IV (93%) (as indicated by PMR spectroscopy) was filtered off. Dichloroethane was separated, dried over Na_2SO_4, and filtered to obtain 1.77 g of the compound IV (A). Filtrate was evaporated, the residue was triturated with hexane and then, with ethyl acetate. Filtration gave 1.23 g of substance B (mixture of compounds III and IV, see Table 1). Mass spectrum of the compound IV, *m/z* (I_{rel}, %): 316 M^+ (100), 301 $[M - CH_3]^+$ (32), 288 $[M - CO]^+$ (12), 272 $[M - NMe_2]$ (21), 269 $[M - H - CO_2H]^+$ (49), 243 $[M - C_2H_4CO_2H]^+$ (59), 214 $[M - C_2H_4CO_2H - C_2H_5]^+$ (36), 199 $[M - C_2H_4CO_2H - NMe_2]^+$ (19), 176 $[M - C_2H_4CO_2H - C_4H_5N]^+$ (19), 105 $[PhCO]^+$ (12).

TABLE 1. Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %				mp, °C	Recrystallization solvent	Yield, %
		C	H	N	H_2O			
IV	$C_{17}H_{20}N_2O_4$	64.51 / 64.54	6.81 / 6.37	9.03 / 8.86		239-242 (dec.)	1:1.5 DMF–2-propanol	44
V	$C_{15}H_{17}N_5O_2 \cdot 0.5\ i\text{-}C_3H_7OH$	59.97 / 60.17	6.33 / 6.43	21.23 / 21.26		195-200 (dec.)	2-Propanol	76
VIa	$C_{22}H_{21}N_5O_2 \cdot 0.5\ i\text{-}C_3H_7OH$	67.53 / 67.61	5.71 / 6.04	17.18 / 16.77		245-248	2-Propanol	40*
VIb	$C_{23}H_{23}N_5O_3$	66.17 / 66.17	5.51 / 5.55	16.74 / 16.78		266-267	DMF	99
VIc	$C_{23}H_{23}N_5O_2$	68.60 / 68.81	5.82 / 5.77	17.50 / 17.45		275-276	DMF	98
VId	$C_{20}H_{23}N_5O_2 \cdot 0.5$ DMF	64.26 / 64.23	6.62 / 6.64	19.13 / 19.16		263-264	1:1 DMF–2-propanol	89
VIe	$C_{21}H_{25}N_5O_2$	66.30 / 66.47	6.65 / 6.64	18.48 / 18.46		242-244	Methanol	95
VIf	$C_{21}H_{27}N_5O_2$	66.09 / 66.12	7.09 / 7.13	18.35 / 18.36		228-230	Methanol	79
VIg	$C_{22}H_{21}N_5O_3 \cdot 0.5\ H_2O$	64.14 / 64.06	5.75 / 5.38	17.26 / 16.98	1.72 / 2.18	309-313	65% aqueous DMF	97
VIh	$C_{20}H_{25}N_5O_2$	64.97 / 65.37	6.89 / 6.86	19.07 / 19.06		254-255	Methanol	70
VIi	$C_{22}H_{21}N_5O_3$	65.53 / 65.49	5.66 / 5.25	16.92 / 17.36		273-275	50% aqueous DMF	99
VIj	$C_{23}H_{23}N_5O_4 \cdot 0.25\ H_2O$	62.89 / 63.07	5.69 / 5.41	16.19 / 15.99	1.13 / 1.03	>275	50% aqueous DMF	96
VIk*[2]	$C_{22}H_{20}N_5O_2Br \cdot 0.5\ H_2O$	55.46 / 55.58	4.16 / 4.45	14.58 / 14.73	1.46 / 1.89	263-267	80% aqueous DMF	99
VIIa	$C_{22}H_{22}N_4O_2$	70.53 / 70.57	6.05 / 5.92	14.76 / 14.96		212.5-214.5	2-Propanol	75
VIIb	$C_{23}H_{24}N_4O_2$	70.65 / 71.11	6.13 / 6.23	14.86 / 14.42		189-190	Acetonitrile	88

* 82% yield with regard to compound VIa obtained by evaporation of the mother liquor.

*[2] Found, %: Br 17.28. Calculated, %: Br 16.81.

TABLE 2. ^{1}H NMR Spectral Characteristics of Acylation Products of 3-(N,N-Dimethyl)aminomethylene-2,3-dihydro-2-indolinone (A, B)

Compound mixture	Isomer type	PMR spectrum, δ, ppm (*J*, Hz)								Isomer content, %
		3'-H	4-H	5-H	6-H	7-H	NEt	$COOHCH_2CH_2CO-$	NMe_2	
A	IV-*trans*	7.82 s	7.44 d $^3J_{45}$ = 8.4	7.58 dd	—	7.42 d $^4J_{57}$ = 1.2	1.13 t (CH_3) 3.81 q (CH_2)	3.23 (α-CH_2) t 2.56 (β-CH_2) t ~12.10 (COOH)	3.33 s	70
	IV-*cis*	7.65 s	7.50 d $^3J_{45}$ = 8.4	7.56 dd	—	7.45 d $^4J_{57}$ = 1.4	1.14 t (CH_3) 3.82 q (CH_2)	3.23 (α-CH_2) t 2.57 (β-CH_2) t ~8.50 (COOH)	3.36 s	30
	$\Delta\delta_{trans-cis}$	0.17	-0.06							
B	IV-*trans*	7.82 s	7.43 d	7.58 dd	—	7.42 d	*	*	3.33 s	40
	IV-*cis*	7.65 s	7.49 d	7.55 dd	—	7.45 d			3.36 s	20
	$\Delta\delta_{trans-cis}$	0.17	-0.06							
	III-*trans*	7.85 s	8.02 d $^4J_{46}$ = 1.6	—	7.64 dd	6.97 d $^3J_{67}$ = 8.2	*	*	*[2]	29
	III-*cis*	7.59 s	8.00 d $^4J_{46}$ = 1.6	—	7.73 dd	7.04 d $^3J_{67}$ = 8.3			3.32 s	11
	$\Delta\delta_{trans-cis}$	0.26	0.02							

* For mixture B, the protons of NCH_2CH_3, α-CH_2, and β-CH_2 groups of all the forms give multiplets at ~1.15 ($NCH_2C\underline{H}_3$); ~ 3.20 (N–$C\underline{H}_2CH_3$); ~2.70 (β-CH_2); and ~3.20 ppm (α-CH_2).

*[2] The signal for $N(CH_3)_2$ is masked either by the signals of the other $N(CH_3)_2$ groups or strong H_2O signal (δ 3.38).

TABLE 3. ^{1}H NMR Spectral Data for the Compounds V, VIa-e, VIIa,b

Compound	Isomer type	PMR spectrum, δ, ppm (J, Hz)							Isomer content, %
		3'-H	4-H	5-H	7-H	NEt	pyridazine moiety	R,R'	
1	2	3	4	5	6	7	8	9	10
V*	*trans*	8.00 c	7.42 d $^3J_{45}$ = 8.0	7.29 dd	7.33 d $^4J_{57}$ = 1.2	1.14 t (CH_3) 3.79 q (CH_2)	2.42 t (β-CH_2) 2.96 t (α-CH_2) 10.79 s (NH)	5.30 br. sign. (NH_2) 9.30 br. s (NH)	60*[2]
	cis	7.58 s	7.68 d $^3J_{45}$ = 8.0	7.36 dd	~7.30	1.13 t (CH_3) 3.78 q (CH_2)	2.43 t (β-CH_2) 2.97 t (α-CH_2) 10.82 s (NH)	5.30 (NH_2); 9.80 br. s (NH)	35
	Δδ	0.42	-0.26						
VIa*	*trans*	8.45 br. s (coupled with NH)	7.60 d $^3J_{45}$ = 8.4	7.34 dd	7.38 d $^4J_{57}$ = 1.2	1.19 t (CH_3) 3.85 q (CH_2)	2.44 t (β-CH_2) 2.97 t (α-CH_2) 10.57 s (NH)	8.45 s (=CH); 11.57 br. sign. (NH) 7.38-7.48 m (*m,m,p*-$CH_{arom.}$) 7.66-7.70 (*o,o'*-$CH_{arom.}$)	67
	cis	7.92 br. s	7.86 br. d	7.41 dd $^3J_{45}$ = 8.2	7.35 d $^4J_{57}$ = 1.1	1.16 t (CH_3) 3.80 q (CH_2)	2.46 t (β-CH_2) 3.00 t (α-CH_2) 10.58 s (NH)	8.50 br. s (=CH); 7.38-7.8 m ($CH_{arom.}$) 7.70-7.74 br. m ($CH_{arom.}$) 11.70 br. d (NH) $^3J_{NH3'H}$ = 12	33
	Δδ	0.53	-0.26						
VIb	*trans*	8.44 br. d $^3J_{3'NH}$ ~ 12	7.58 d $^3J_{45}$ = 7.6	7.34 dd	7.38 d $^4J_{57}$ = 1.2	1.19 t (CH_3) 3.84 q (CH_2)	2.43 t (β-CH_2) 2.97 t (α-CH_2) 10.86 s (NH)	8.38 s (=CH); 3.80 s (OCH_3) 6.99-7.05 m (*m,m'*-$CH_{arom.}$) 7.60-7.64 m (*o,o'*-$CH_{arom.}$) 11.70 br. d (NH)	65
	cis	7.85 br. sign.	7.90 br. d	7.40 br. d	~7.36 br. s	1.17 t (CH_3) 3.82 q (CH_2)	2.46 t (β-CH_2) 3.00 t (α-CH_2) 10.90 s (NH)	8.44 s (=CH); 3.81 s (OCH_3) 6.99-7.05 m (*m,m'*-$CH_{arom.}$) 7.64-7.69 m (*o,o'*-$CH_{arom.}$) 11.27 br. d (NH) $^3J_{NH3'H}$ = 12	35
	Δδ	0.59	-0.32						

TABLE 3 (continued)

1	2	3	4	5	6	7	8	9	10
VIc	*trans*	8.63 d $^3J_{5'NH}$ = 8.8	7.63 d $^3J_{45}$ = 8.0	7.38 dd	7.43 d $^4J_{57}$ = 1.6	1.20 t (CH_3) 3.88 q (CH_2)	2.44 t (β-CH_2) 2.98 t (α-CH_2) 10.85 s (NH)	2.35 s (CH_3); 11.90 d (NH) 7.42-7.48 m (*m,m',p*-$CH_{arom.}$) 7.82-7.86 m (*o,o'*-$CH_{arom.}$)	>~95
	*cis**3			~7.32 strongly br. sign.		1.16 t (CH_3) 3.80 q (CH_2)			<~5
VId	*trans*	8.47 d $^3J_{5'NH}$ = 8.0	7.55 d $^3J_{45}$ = 8.0	7.35 dd	7.39 d $^4J_{57}$ = 1.2	1.18 t (CH_3) 3.86 q (CH_2)	2.43 t (β-CH_2) 2.97 t (α-CH_2) 10.83 s (NH)	1.63-1.88 m (2-CH_2); 2.34 m (2-CH_2) 11.37 br. d (NH)	~~95
	*cis**3			~7.30 strongly br. sign.		1.15 (CH_3) 3.80 (CH_2)			<~5
VIe	*trans*	8.50 d $^3J_{5'NH}$ = 9.0	7.54 d $^3J_{45}$ = 7.8	7.35 dd	7.40 d $^4J_{57}$ = 1.2	1.17 t (CH_3) 3.85 q (CH_2)	2.43 t (β-CH_2) 2.97 t (α-CH_2) 10.84 s (NH)	1.54-1.74 m (3-CH_2); 2.32 t (CH_2) 2.39 t (CH_2); 11.80 d (NH)	>~92
	*cis**3			~7.30 strongly br. sign.		1.15 t (CH_3) 3.79 q (CH_2)			<~8
VIIa	*trans*	8.14 d $^3J_{5'NH}$ = 13.5		7.25 - 7.41 m*4		1.15 t (CH_3) 3.80 q (CH_2)	2.43 t (β-CH_2) 2.96 t (α-CH_2) 10.80 s (NH)	4.59 d (CH_2) $^3J_{CH_2,NH}$ = 6.2 9.18 m (NH); 7.25-7.41 m*4	100
VIIb	*trans*	7.97 d $^3J_{5'NH}$ = 13.6		7.17 - 7.35 m*4		1.15 t (CH_3) 3.80 q (CH_2)	2.42 t (β-CH_2) 2.95 t (α-CH_2) 10.80 s (NH)	2.91 t ($\underline{CH_2}$Ph); 3.62 q (NH$\underline{CH_2}$) 8.91 m (NH); 7.17-7.35 m (Ph) *4	77
	cis	7.49 d $^3J_{5'NH}$ = 14.1	7.70 d $^3J_{45}$ = 7.6	7.17-7.35 m		1.11 t (CH_3) 3.75 q (CH_2)	2.44 t (β-CH_2) 2.96 t (α-CH_2) 10.85 s (NH)	~2.95 ($\underline{CH_2}$Ph); ~3.60 (NH$\underline{CH_2}$) 7.89 m (NH); 7.17-7.35 m (Ph)	23
	Δδ	0.48	> -0.35						

* Signals for *i*-PrOH observed in the spectra of these compounds.

*2 5% of hydrazone form is observed for VII, characterized by doublets at 5.70 (3'-H) and 6.90 ppm (CH=N) with SSCC $^3J_{3'\text{-}H=CH}$ = 8 Hz.

*3 Low intensity and considerable broadening of *cis* isomer signals did not permit reliable determination of all the chemical shifts of the protons of this isomer.

*4 Aromatic protons 4-H, 5-H, and 7-H and phenyl ring protons give a multiplet at 7.2-7.4 ppm with intensity 8H.

[1-Ethyl-6-(1,4,5,6-tetrahydro-6-oxo-3-pyridazinyl)-2,3-dihydro-2-indolinone]-3-methylenehydrazine (V). Mixture of the compound IV (1.9 g, 6 mmol), hydrazine hydrate (0.88 g, 1.76 mmol), and 2-propanol (50 ml) was heated at reflux for 2 h, cooled to 3-5°C, and filtered to give the compound V. Mass spectrum: 299 M^+ (13), 284 $[M - CH_3]^+$ (27), 269 $[M - N_2H_2]^+$ (25), 257 $[M - COCH_2]^+$ (100), 242 $[M - CH_2CONH]^+$ (10), 84 $[CH_2=CHCON=NH]^+$ (51).

[1-Ethyl-6-(1,4,5,6-tetrahydro-6-oxo-3-pyridazinyl)-1,2-dihydro-2-indolinone]-3-methylenehydrazones (VI) (General Method). A mixture of the compound V (0.01 mol), 0.015 mol (for compounds VIa-c,e-j) or 0.013 mol (for compound VId) or 0.0133 mol (for compound VIk) of the corresponding ketone VIII, and 2-propanol (150 ml) was stirred at room temperature or at 60°C (for VIh) or at reflux (for VIc) for 1-6 h. The reaction mixture was cooled and hydrazones VIa-k were filtered off. Evaporation of the mother liquor gave an additional amount of compounds VIa-k. Mass spectrum of the compound VIa: 387 M^+ (100), 283 $[M - NCHPh]^+$ (18), 268 $[M - NH–N=CHPh]^+$ (8), 256 $[M - NCHPh - HCN]^+$ (10), 211 $[M - NCHPh - NH_2COC_2H_4]^+$ (12), 104 $[N=CHPh]^+$ (24), 77 $[Ph^+]$ (60).

1-Ethyl-3-benzylaminomethylene-6-(1,4,5,6-tetrahydro-6-oxo-3-pyridazinyl)-1,2-dihydro-2-indolinone (VIIa). Mixture of the compound VIc (0.5 g, 1.25 mmol) and benzylamine (4.91 g, 5 ml, 45.9 mmol) was heated for 1.5 h at 95-100°C with a Dean–Stark trap. The reaction mixture was cooled and triturated with ether and, then, ethyl acetate to give the compound VIIa. Mass spectrum: 374 M^+ (82), 357 $[M - OH]^+$ (16), 345 $[M - H - CO]^+$ (16), 283 $[M - CH_2Ph]^+$ (18), 270 $[M - N=CHPh]^+$ (20), 256 $[M - CHPh - HCN]^+$ (17), 211 $[M - CH_2Ph–NH_2COC_2H_4]^+$ (10), 91 $[CH_2Ph]^+$ (100).

1-Ethyl-3-(β-phenyl)ethylaminomethylene-6-(1,4,5,6-tetrahydro-6-oxo-3-pyridazinyl)-1,2-dihydro-2-indolinone (VIIb). Mixture of the compound VIe (0.4 g, 1.05 mmol) and phenylethylamine (2.7 g, 22.3 mmol) was heated for 2 h at 95-100°C with a Dean–Stark trap. The reaction mixture was washed with heptane and, then, ether to give the compound VIIb. Mass spectrum: 388 M^+ (40), 297 $[M - CH_2Ph]^+$ (100), 267 $[M - NH_2(CH_2)_2Ph]^+$ (7), 226 $[M - CH_2Ph–NHCOC_2H_4]^+$ (8), 105 $[PhC_2H_4]^+$ (7), 91 $[CH_2Ph]^+$ (23).

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