(91), 71 (62), 69 (62). Measurement of the masses of the ions with m/e 111 and 83. Found: 111.0813, 83.0869. Calculated: 111.0810, 83.0861. Composition: 111 ($C_7H_{11}O$), 83 (C_6H_{11}).

SUMMARY

A new phytoecdysone has been isolated from the flower heads of *Rhaponticum integrifolium*, and for it the structure of 24(28)-dehydromakisterone A has been established.

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INFLUENCE OF SOLVENTS ON THE PARAMETERS OF THE PMR SPECTRA OF THE PHTHALIDE-ISOQUINOLINE ALKALOIDS. VI

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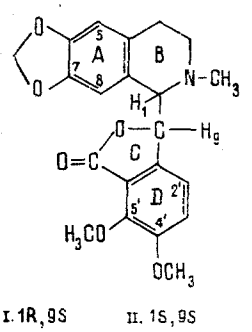
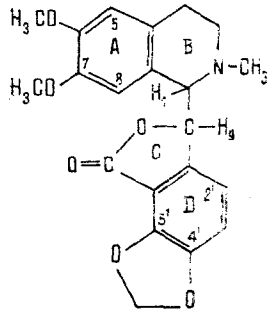
UDC 577.94.543.42:542.61

In the present work, which is a continuation of our investigations of the influence of solvents on the parameters (CSs and SSCCs) of the NMR spectra of alkaloids [1], we give the results of d-β- and d-α-hydrastines (I) and (II), respectively, corlumine (III), and adlumine (IV). The structures of these bases have been established previously [2-5]. The determination of the absolute configurations and stereochemical features of the phthalide-isoquinoline alkaloids has been considered by Znatzke et al. [6] and by Sate and Moir [7]. Later, summarizing the available information and basing his considerations on the results of his own NMR investigations, Shamma [8] suggested that the erythro (I, III) and threo (II, IV) conformations were the most likely for the bases of this series. We have studied the influence of solvents on the parameters of the NMR spectra of alkaloids (I-IV) in the following 10 solvents: $CDCl_3$, CCl_4, CD_3CN, CD_3OD, $(CD_3)_2CO$, DMF, DMSO, TFA, C_5D_5N, and C_6D_6. The results for four solvents are given in Tables 1 and 2.



I. 1R, 9S II. 1S, 9S



III. 1S, 9R IV. 1R, 9R

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TABLE 1. Chemical Shifts of the Protons in Various Solvents and Their Relative Difference $\Delta = \delta_{CDCl_3} - \delta_{solvent}$

Solvent	N=CH₃	4'-OCH₃	5'-OCH₃	H_1	H_9	OCH_2O	H_8	H_5	H_3'	H_2'
d-β-Hydrastine										
$CDCl_3$	2,57	3,92	4,08	3,99	5,49	5,92	6,39	6,58	7,08	6,52
TFA	3,24	4,08	4,17	5,09	6,27	5,94	5,82	6,81	7,61	7,35
	−0,67	−0,16	−0,09	−1,10	−0,78	−0,02	+0,57	−0,23	−0,53	−0,83
C_5D_5N	2,55	3,77	4,12	4,14	5,73	5,98	6,80	6,70	7,18	6,58
	+0,02	+0,15	−0,04	−0,15	−0,14	−0,06	−0,41	−0,12	−0,10	−0,06
C_6D_6	2,42	3,27	4,03	3,84	5,11	5,38	6,34	6,43	6,52	6,10
	+0,15	+0,65	+0,05	+0,25	+0,38	−0,54	+0,05	−0,15	+0,56	+0,42
d-α-Hydrastine										
$CDCl_3$	2,56	3,86	3,99	3,99	5,54	5,81	6,66	6,37	7,04	7,30
TFA	3,14	4,09	4,29	4,45	5,83	6,11	6,62	6,94	7,00	7,54
	−0,58	−0,23	−0,30	−0,46	−0,32	−0,30	−0,04	−0,57	+0,04	−0,24
C_5D_5N	2,40	3,70	4,05	4,14	5,80	5,83	7,03	6,51	7,26	7,50
	+0,16	+0,16	−0,06	−0,15	−0,26	−0,02	−0,37	−0,14	−0,22	−0,20
C_6D_6	2,15	3,21	3,98	3,77	5,22	5,20	6,87	6,29	6,62	7,06
	+0,41	+0,65	+0,01	+0,22	+0,32	+0,61	−0,21	+0,08	+0,58	−0,24

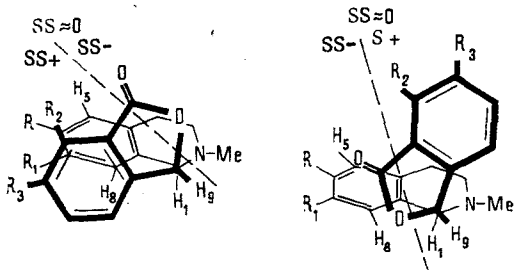
TABLE 2. Chemical Shifts of the Protons in Various Solvents and Their Relative Difference $\Delta = \delta_{CDCl_3} - \delta_{solvent}$

Solvent	N=CH₃	7-OCH₃	6-OCH₃	H_1	H_9	OCH_2O	H_8	H_5	H_3'	H_2'
Corlumine										
$CDCl_3$	2,60	3,74	3,89	4,09	5,66	6,15	6,40	6,61	6,93	6,22
TFA	3,27	3,57	3,96	5,15	6,37	6,23	5,98	6,91	7,37	7,15
	−0,67	+0,17	−0,07	−1,06	−0,71	−0,08	+0,42	−0,30	−0,44	−0,93
C_5D_5N	2,60	3,77	3,78	4,22	5,88	6,15	6,82	6,75	7,01	6,23
	0,00	−0,03	+0,11	−0,13	−0,22	0,00	−0,42	−0,14	−0,08	−0,01
C_6D_6	2,52	3,45	3,50	3,90	5,30	5,26	6,38	6,38	6,44	5,75
	+0,08	+0,29	+0,39	+0,19	+0,36	+0,89	+0,02	+0,23	+0,49	+0,47
Adlumine										
$CDCl_3$	2,67	3,77	3,83	4,08	5,68	6,07	6,70	6,38	6,87	7,17
TFA	3,14	3,94	4,06	4,53	5,95	6,29	7,07	6,70	7,25	7,65
	−0,47	−0,17	−0,23	−0,45	−0,27	−0,22	−0,37	−0,32	−0,38	−0,48
C_5D_5N	2,57	3,57	3,84	4,20	5,92	5,78	7,12	6,56	7,05	7,30
	+0,17	+0,20	−0,01	−0,12	−0,24	+0,29	−0,42	−0,18	−0,18	−0,13
C_6D_6	2,27	3,21	3,72	3,93	5,36	5,00	6,98	6,16	6,50	6,94
	+0,40	+0,56	+0,11	+0,15	+0,32	+1,07	−0,28	+0,22	+0,37	+0,23

Influence of Aromatic Solvents. In our case, the influence of benzene must be described in conformity with the rule of the carbonyl plane of reference (RCPR) [9], which has been used in the series of methyl- and methoxy-substituted coumarins [10]. As can be seen from Fig. 1, as applied to the bases (I-IV) investigated, this plane is shifted relatively to the carbonyl carbon atom in the direction of the C_6 and C_9 atoms, separating the protons characterized by solvent shifts (SSs) of opposite signs.

Analysis of the results obtained (see Tables 1 and 2) shows that in (I) and (II) the value $\Delta^{C_6D_6}_{CDCl_3}$ is the maximum at +0.65 ppm for 4'-OCH_3 while 5'-OCH_3 is practically unaffected by the action of benzene. The chemical shifts of these OCH_3 groups in $CDCl_3$ solution appear in the 3.86-3.99 ppm region, in view of which their assignment in the NMR spectra is difficult.

The values of Δ that we have established for the methoxy protons of ring D can be used successfully in the identification of these protons. In addition, $\Delta^{C_6D_6}_{CDCl_3}$ for the N–CH_3 group in the erythro alkaloids is +0.10 ppm, and in the threo alkaloids + 0.40 ppm. The values of Δ for the methoxy groups in bases (I) and (II) and the substantial difference in the values of Δ for N–CH_3 in (I, III) and (II, IV) are explained by the following considerations. From Fig. 1 and Dreiding stereomolds it can be seen that the 5'-OCH_3 group in the diastereoisomers (I) and (II) and also the N–CH_3 groups in the erythro alkaloids are located either in the



I $R+R_1=OCH_2O$, $R_2=R_3=OCH_3$ d-β-Hydrastine
II $R+R_1=OCH_2O$, $R_2=R_3=OCH_3$ d-α-Hydrastine
III $R=R_1=OCH_3$, $R_2+R_3=OCH_2O$ Corlumine
IV $R=R_1=OCH_3$, $R_2+R_3=OCH_2O$ Adlumine
ERYTHRO
THREO

Fig. 1. Conformations of phthalide-isoquinoline alkaloids.

intersecting plane of reference or close to it and therefore the action of benzene on them is insignificant. Conversely, the 4'-OCH_3 and N-CH_3 groups in the threo bases fall into the positive zone of the CPR and are shifted substantially upfield. The influence of benzene on the H_1 and H_9 protons (Δ = +0.20 and +0.35 ppm, respectively) is explained by the distance of the latter from the CPR. Tables 1 and 2 show that the H_8 aromatic proton in the erythro alkaloids is scarcely affected by benzene (Δ = + 0.03 ppm) while in the threo alkaloids it shifts downfield (Δ = −0.25 ppm). Figure 1 shows that in the erythro bases this proton, although it is present on the positive side of the plane of reference, is nevertheless remote from it, and in the threo bases H_8 is located close to the plane of reference on the negative side. Thus, the value of $\Delta^{C_6D_6}_{CDCl_3}$ for the H_1, H_9, and H_8 protons enables us to make an assignment of the latter and a stereochemical identification of the erythro and threo alkaloids of the phthalide-isoquinoline series. The established values of $\Delta^{C_6D_6}_{CDCl_3}$ of the N-CH_3 group can serve the same aim.

As can be seen from Tables 1 and 2, pyridine mainly causes diamagnetic shifts of the signals of the methyl proton and paramagnetic shifts of the methylene and methine protons, the 5'-OCH_3 group being practically unaffected by C_5D_5N, and the 4'-OCH_3 group having the value $\Delta^{C_5D_5N}_{CDCl_3}$ = +0.15 ppm, which may be a factor facilitating the identification of the methoxy groups in the NMR spectra of alkaloids of this series.

Since the aromatic solvents cause considerable changes in the CSs of the protons of the compounds investigated, we have performed additional experiments involving the nuclear Overhauser effect (NOE). It has been established that in benzene solution with irradiation by frequencies of 327 and 321 Hz corresponding to the resonance transition of the protons of the OCH_3 group, the intensity of the one-proton doublets with δ = 6.52 ppm (I) and 6.62 ppm (II) increases by 14%. These results permit the unambiguous assignment of the 4'-OCH_3, 5'-OGH_3, H_3', and H_2' signals. In pyridine, the assignments of the methoxy groups in bases (I) and (II) were also made with the aid of the NOE.

On the superimposition of additional frequencies corresponding to the resonance transition of the protons of the OCH_3 groups (377 and 370 Hz) in d-β- and d-α-hydrastines, the intensities of the one-proton doublets δ = 7.18 and 7.26 ppm relating to H_3' (I and II, respectively) increased by 12%. Consequently, the irradiated protons belong to the 4'-OCH_3 groups. In corlumine and adlumine the CSs of the 6-OCH_3 and 7-OCH_3 groups were elucidated in aromatic solvents similarly, with the aid of the NOE.

Influence of Polar Solvents. Polar solvents cause substantial changes in the CSs of the protons. Thus, for example, $\Delta^{CD_3CN}_{CDCl_3}$ in d-β-hydrastine changes from +0.27 ppm for H_8 to −0.24 ppm for H_2', and $\Delta^{DMSO}_{CDCl_3}$ amounts to 0.24 ppm (5'-OCH_3) and −0.27 ppm (H_3'). Similar changes in the CSs of the protons have been established in polar solvents for others of the studied compounds (I-IV) which is apparently explained by the action of the "reaction field

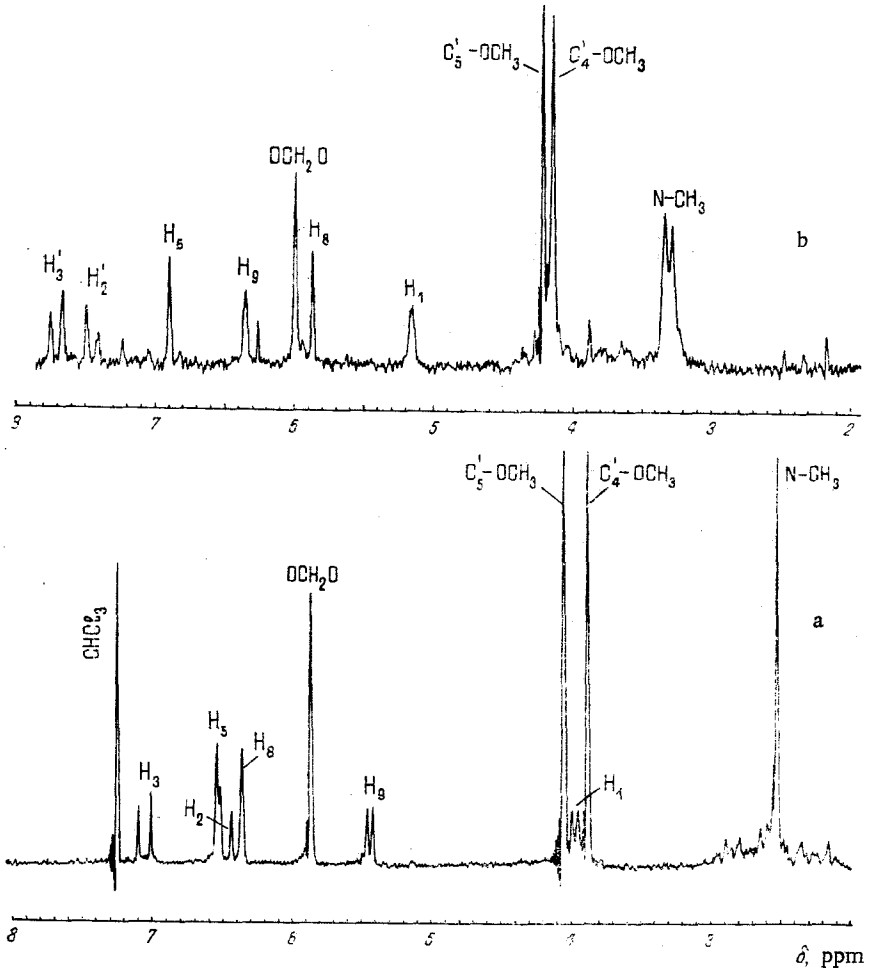


Fig. 2. NMR spectra of d-β-hydrastine in $CDCl_3$ (a) and TFA (b).

of the solvent," arising as a consequence of the presence of highly polar groups in the alkaloids (I-IV). The most considerable changes in the CSs of the protons in bases (I-IV) are observed in TFA.

As a consequence of the protonation of the nitrogen atom, the signal of the N—CH_3 group shifts downfield by an average of —0.6 ppm and is converted into a doublet through coupling with the N^+—H proton with $J_{CH_3 \cdot N^+-H}$ = 5.0 Hz. The values of $\Delta^{TFA}_{CDCl_3}$ for the H_1 and H_9 protons in the erythro bases are —1.10 and —0.75 ppm, and in the threo bases —0.45 and —0.30 ppm, respectively, which may serve as a stereochemical test for phthalide-isoquinoline alkaloids. Furthermore, it follows from Tables 1 and 2 that the H_8 aromatic proton in the erythro alkaloids undergoes a considerable diamagnetic shift in TFA solutions of from +0.40 to +0.60 ppm. Such an upfield shift may be a consequence of the screening influence of ring D (see Fig. 1).

Influence of Solvents on the SSCCs. A study of the results obtained shows that the SSCCs of the H_1 and H_9 protons in solutions in different solvents (apart from TFA) vary within very narrow limits. The values of the SSCCs of H_1 and H_9 in TFA and other solvents differ greatly. While in aromatic and polar solvents the SSCCs average 3.5 Hz, in the acid the value of $J_{H_1 \cdot H_9}$ in the erythro bases (d-β-hydrastine and corlumine) becomes close to 0 Hz (Fig. 2), and in the threo bases (d-α-hydrastine and adlumine), $J_{H_1 \cdot H_9}$ = 9.2 Hz (Fig. 3). This is explained by a change in the mutual orientation of the isoquinoline and phthalide moieties of the molecule, which corresponds to a change in the dihedral angle between the interacting H_1—C—C—H_9 protons.

Dreiding stereomodels show that the H_1—C—C—H_9 dihedral angle in the erythro bases changes to 90°, and this must lead to screening of the H_8 proton of the aromatic ring D in THF, as

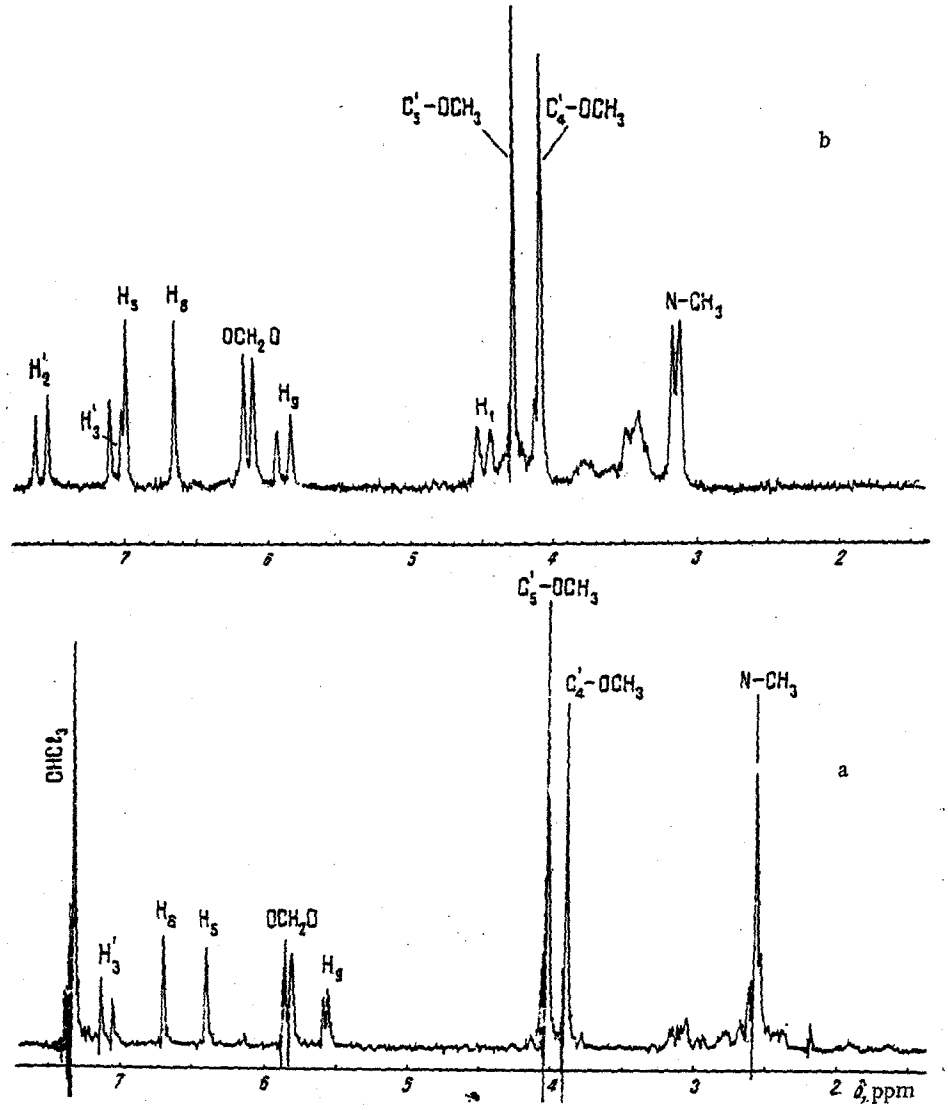


Fig. 3. NMR spectra of d-α-hydrastine in $CDCl_3$ (a) and TFA (b).

does in fact take place. In the threo alkaloids and, in particular, in d-α-hydrastine, insignificant screening of the H_8 atom of ring D in TFA is observed with a change in the H_1—C—C—H_9 dihedral angle under consideration to 160°, which corresponds to an increase in the SSCC of the H_1 and H_9 protons to 9.2 Hz.

The decrease in the vicinal SSCC of the H_1 and H_9 protons in the erythro bases corlumine and d-β-hydrastine from 3.5 to 0 Hz can be explained not only by a change in the H_1—C—C—H_9 dihedral angle but also by an increase in the electronegativity of the nitrogen present in the α position to the C_1 atom when it is protonated in TFA solution [11], while in the threo alkaloids d-α-hydrastine and adlumine the increase in $J_{H_1-H_9}$ from 3.5 to 9.2 Hz obviously takes place mainly because of the increase in the H_1—C—C—H_9 dihedral angle. Thus, the values of $J_{H_1-H_9}$ in TFA that have been found may serve as a reliable criterion in the study of the stereochemistry of alkaloids of the phthalide-isoquinoline series.

All the spectra were taken on a JNM 4H-100/100 MHz instrument with T_{room} = 22-24°C, c = 5% by weight, internal standard TMS, δ scale [the assignments of the CSs of the aromatic and methoxy protons in the NMR spectra of compounds (I-IV) were refined by N. D. Abdullaev].

SUMMARY

As the result of a study of the influence of solvents on the parameters of the NMR spectra of a number of phthalide-isoquinoline alkaloids it has been established that benzene

causes changes of different magnitudes in the CSs of the 4'-OCH_3, 5'-OCH_3, and N-CH_3 protons in the erythro and threo series. Furthermore, it has been found that TFA causes specific changes in the CSs and SSCCs of the H_1 and H_9 protons in the bases of these series. The possibility has been shown of using the results of the influence of different solvents to solve structural and stereochemical problems in the study of the alkaloids phthalide-isoquinoline series.

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ALKALOIDS OF *Thalictrum isopyroides*

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and D. Kurbakov

UDC 547.944/945

Thalisopine, thalisopidine, cryptopine, thalicmine, thalicminine, dehydrothalicmine, and magnoflorine have been isolated previously from *Thalictrum isopyroides* [1]. The present paper gives the results of a study of the roots of *Th. isopyroides* C.A.M. collected on the Ustyurt plateau in the period of fruit-bearing on May 25, 1973. From the nonphenolic fraction of the ether-extractable total, by chromatography on a column of alumina we isolated a crystalline base (I) with mp 104-105°C (ether).

The UV spectrum of (I) [λ_{max}, nm, 249, 268 (sh.), 271, 283, 294, 324, 330 infl.] is characteristic for 1,2-dihydroisoquinolin-1-ones [2]. IR spectrum: 1658 cm^{-1} (conjugated C=O group). Mass spectrum: m/e 219 (M^+), 204, 190, 176, 109.5 (M^{++}).

The NMR spectrum of (I) ($CDCl_3$, ppm) contains a singlet at 3.67 (3 H, NCH_3), a singlet at 3.93 (6 H, 2 × OCH_3), two one-proton singlets at 6.88 and 7.65 (H-5 and H-8, respectively), and two one-proton doublets at 7.06 and 6.68 (J = 7 Hz, H-3 and H-4). A comparison of the results obtained and those given in the literature enabled (I) to be identified as 6,7-dimethoxy-2-methyl-1,2-dihydroisoquinolin-1-one, which has been isolated previously only from *Hernandia ovigere* [3].

From the phenolic fraction of the combined alkaloids we obtained in the form of an oil an optically active base (II) with $[\alpha]_D$ +45° (c 0.13; CH_3OH). The UV spectrum (II) showed three maxima: at 282 nm, 305 nm, and 316 nm, infl., which are characteristic for 1,2,9,10-tetrasubstituted aporphine alkaloids [4]. The PMR spectrum of (II) showed signals at (ppm) 2.49 (3 H, NCH_3), 3.65 (3 H, OCH_3 at C-1), 3.82 (3 H, OCH_3), 3.85 (3 H, OCH_3), and 3.90 (3 H, OCH_3), and in the region of aromatic protons two one-proton singlets were observed at 6.73 and 7.85 (H-8 and H-11, respectively). The mass spectrum of (II) contained the peaks of ions with m/e 371 (M^+), 370 (M − 1), 356 (M − 15), 340 (M − 31), and 328 (M − 43).

The methylation of (II) with diazomethane gave thalicsimidine [5]. Consequently, the base (II) is a new one and we have called it thalisopynine. Since the base (II) possesses distinct phenolic properties (it dissolves in alkali and is readily methylated and acetyl-

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