Tetrahedron Vol 45, No 7, pp 1887 to 1892, 1989
Printed in Great Britain

0040-4020/89 $3 00 + 00

NEW ALKALOIDS FROM *DELPHINIUM ELATUM* L.

S. William Pelletier*, Samir A. Ross[+] and Palaniappan Kulanthaivel

Institute for Natural Products Research and the School of Chemical Sciences,

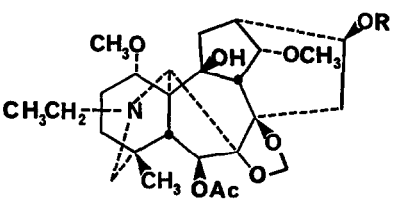
The University of Georgia, Athens, Georgia 30602 U.S.A.

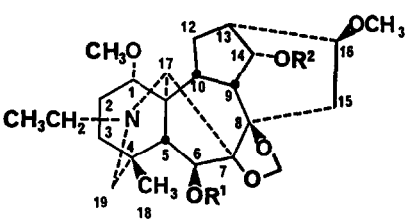
(*Received in USA* 16 *August* 1988)

Abstract. A study of the alkaloids present in the seeds of *Delphinium elatum* L. has led to the isolation of three new C_{19}-diterpenoid alkaloids: elasine (1), isodelpheline (3) and eladine (5), besides seven known alkaloids: delpheline (7), deltaline (8), methyllycaconitine (10), nudicauline (11), 14-deacetylnudicauline (12), lycoctonine and elatine (13). The structures of these alkaloids were determined by spectral data and correlation with alkaloids of established structures. Thus methylation of elasine (1) and eladine (5) yielded deltaline (8) and delpheline (7), respectively.

Previous work on *Delphinium elatum* L. (Ranunculaceae) demonstrated the presence of five diterpenoid alkaloids: delpheline (7)[1], deltaline (8)[2-4], methyllycaconitine (10)[1], elatine (13)[2,5] and delelatine (9).[6] In this paper, we report the isolation and elucidation of the structures of three new alkaloids from the seeds of *D. elatum*: elasine (1), isodelpheline (3) and eladine (5). Also isolated were the known alkaloids nudicauline (11), 14-deacetylnudicauline (12) and lycoctonine, as well as the previously mentioned alkaloids: delpheline (7), deltaline (8), methyllycaconitine (10) and elatine (13).

The seeds of *D. elatum* were extracted with a mixture of 95% ethanol, water and hexane (16:4:5), and the crude alkaloid mixture was obtained as indicated in the Experimental. Extensive chromatographic separation, involving VLC[7], preparative TLC and centrifugally





1 R = H **ELASINE**

2 R = Ac

8 R = CH_3 **DELTALINE**

3 $R^1 = CH_3$; R^2 = H **ISODELPHELINE**

4 $R^1 = CH_3$; R^2 = Ac

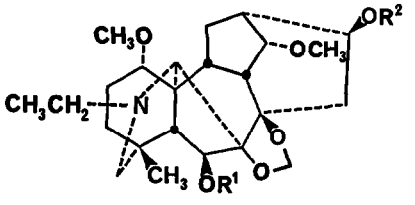
9 $R^1 = R^2$ = H **DELELATINE**

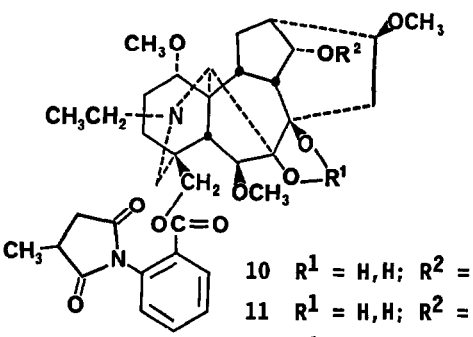
[+]On leave from the Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, Egypt.

accelerated, radial, thin-layer chromatography (Chromatotron)[8,9] afforded ten alkaloids, of which three have not been reported previously.

Elasine (1) was obtained as an amorphous compound; $C_{26}H_{39}NO_8$: M^+ m/z 493; IR (nujol) 3430 (OH) and 1740 (CO) cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.82 (3H, s, *tert*-methyl), 1.01 (3H, t, J = 7.0 Hz, *N*-$CH_2\underline{CH_3}$), 2.03 (3H, s, $OCOCH_3$); 3.21 and 3.45 (3H each, s, OCH_3), 4.28 (1H, t, J = 4.5 Hz, C(14)-β-*H*), 4.86 and 4.91 (1H each, s, -O-CH_2-O-) and 5.43 (1H, brs, C(6)-α-*H*). The presence of two methoxyls, an acetate, an *N*-ethyl and a methylenedioxy group in the molecule suggests that elasine is a new C_{19}-diterpenoid alkaloid. The data for the proton noise-decoupled ^{13}C NMR spectrum appear in the Table. The ^{13}C NMR spectrum of elasine exhibited 6 singlets at 169.7, 92.7, 83.0, 80.1, 55.0 and 33.9 ppm, which can be readily assigned to the carbonyl group of the C(16)-acetate and to C(7), C(8), C(10), C(11) and C(4), respectively. The presence of a methylenedioxy grouping at C(7), C(8) was evident from the above data and a methylene carbon signal at 93.6 ppm. The presence of a hydroxyl group in elasine was established by treatment with Ac_2O and pyridine to afford 2; mp 219.5-221.5°C; $C_{28}H_{41}NO_9$: M^+ m/z 535.

As elasine is a lycoctonine-type alkaloid, the usual oxygen functions at C(1), C(6), C(14) and C(16) can be tentatively assumed to be present. On the basis of these data and comparison of the ^{13}C NMR spectral assignments of related compounds[10], elasine probably possesses the partial structure of deltaline (8). Location of a methoxyl group at C(1) was deduced from the mass-spectrum, which showed facile loss of 31 mass units from molecular ion.[11] The presence of a one-proton triplet (J = 4.5 Hz) at δ 4.28 and a one-proton broad singlet at δ 5.43 indicates that the second methoxyl group is attached to C(14) and the acetate to C(6).



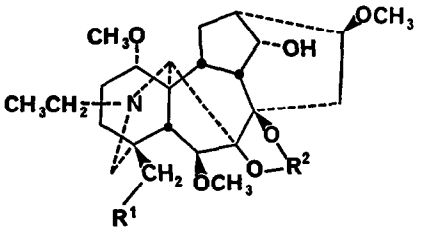


5 $R^1 = R^2 = H$ ELADINE
6 $R^1 = R^2 = Ac$
7 $R^1 = H$; $R^2 = CH_3$

10 $R^1 = H,H$; $R^2 = CH_3$
11 $R^1 = H,H$; $R^2 = Ac$
12 $R^1 = H,H$; $R^2 = H$
13 $R^1 = CH_2$; $R^2 = CH_3$

The chemical shifts of C(14)- and C(16)-methoxyls occur at 57.7 and 56.2 ppm in deltaline (8)[10], respectively. Therefore in elasine the signal at 57.9 ppm is attributed to the C(14)-OCH_3. Thus, the only possibility for the remaining OH group in elasine is at C(16) and elasine may be assigned structure 1. The alternative location of the acyl unit at C(6)-O- can be excluded because methylation of elasine (1) afforded deltaline (8).

Isodelpheline (3), $C_{25}H_{39}NO_6$ (MS), showed hydroxyl absorption at 3500 cm^{-1} (IR). The ^1H NMR spectrum revealed the presence of a quaternary methyl (δ 0.89, s), an *N*-ethyl (δ 1.00, t, J = 7.0 Hz), a methylenedioxy (δ 5.16 and 5.06, each s) and three methoxyl (δ 3.32 (6H) and 3.20 (3H), each s) groups. The ^{13}C NMR spectrum showed resonances for 25 carbons in accord with the molecular composition deduced by the mass spectrum. That the compound was a C(18)-deoxymethylene analog of delbruline (14)[12] was evident from the chemical shifts observed for C(3), C(4) and C(5). When compared with delbruline, C(3) and C(5) showed downfield shifts of 4.9 and 4.8 ppm, respectively, and C(4) showed an upfield shift of 4.2 ppm. These chemical shift changes parallel those of the pair browniine (15)[13] and nudicaulidinine (16).[14] The presence of a hydroxyl group at C(14) was confirmed by acetylation to give a monoacetate (4), mp 116-118°C, which showed in its ^1H NMR spectrum a triplet signal at 4.81 ppm (J = 4.5 Hz) characteristic of a H-14β. The ^{13}C NMR spectrum (Table) also produced the expected spectral changes for an acetate function introduced at C(14). Isodelpheline (3) is therefore a delpheline isomer with the groups at C(6) and C(14) exchanged.



14 $R^1 = OCH_3$; $R^2 = CH_2$
15 $R^1 = OCH_3$; $R^2 = H,H$
16 $R^1 = H$; $R^2 = H,H$

Eladine (5) was obtained as amorphous compound; $C_{24}H_{37}NO_6$: M^+ m/z 435; ^1H NMR ($CDCl_3$): δ 0.94 (3H, s, *tert*-methyl), 1.05 (3H, t, J = 7.0 Hz, *N*-CH_2-CH_3), 3.25 and 3.48 (3H each, s, OCH_3), 4.22 (1H, s, C(6)-α-H), 5.07 and 5.17 (1H each, s, -O-CH_2-O-). The ^{13}C NMR spectrum showed 24 lines for 24 carbon atoms. Four singlets appearing at 93.0, 82.3, 49.8 and 34.2 ppm can be attributed to C(7), C(8), C(11) and C(4), respectively. The presence of a methylenedioxy grouping at C(7), C(8) was evident from the above data and a methylene carbon signal at 93.8 ppm. Acetylation of eladine with Ac_2O and pyridine afforded 6; $C_{28}H_{41}NO_8$: M^+ m/z 519, thus proving the presence of two hydroxyl groups. The presence of two methoxyls, two hydroxyls, an N-ethyl and a methylenedioxy group in the molecule suggests that eladine is a new C_{19}-diterpenoid alkaloid of the lycoctonine type. Comparison of the above spectral data with those of delelatine (9)[6], an alkaloid recently isolated by us from the same plant, suggests that eladine and delelatine possess similar structures. Delelatine (9) and eladine (5) both possess a C(1)-OCH_3 group since both show facile loss of 31 mass units from the molecular ion (M^+-OCH_3).[11] Likewise both have a C(6)-βOH group as indicated by a peak at δ 4.22, 1 H, s, characteristic of C(6)-α-H with a β-OH on C(6). The only difference is in the substitution at C(14) and C(16). Delelatine (9) has a C(14)-OH and C(16)-OCH_3 substitution pattern. Because methylation of eladine afforded delpheline (7), eladine must possess an alternate arrangement of these functional groups, and therefore has structure 5.

^{13}C NMR chemical shifts and assignments for elasine (1), 16-acetylelasine (2), isodelpheline (3), 14-acetylisodelpheline (4), eladine (5) and 6,16-diacetyleladine (6)

Carbon	1	2	3	4	5	6
1	78.9	79.1	83.5	82.1	83.6	82.8
2	26.2	26.9	26 7	26.9	26.2	26.9
3	37.9	38.5	36.8	37.2	36.8	36.8
4	33.9 s	33.8 s	33.7 s	33.5 s	34.2 s	34.0 s
5	50.2	50 5	55.8	56.1	55.7	55.8
6	77.1	77.1	89.2	89.2	79.1	78.4
7	92.7 s	91.9 s	93.7 s	92.5 s	93.0 s	92 2 s
8	83 0 s	83 4 s	80.7 s	83.0 s	82.3 s	82.8 s
9	47.6	50.5	47 8	47.7	47.9	47.9
10	80.1 s	81.1 s	42.1	40.1	39.9	40.2
11	55.0 s	55.9 s	49.2 s	50.3 s	49.8 s	50.2 s
12	36.4	36.5	26.1	27.4	27.1	27.4
13	40.0	38.5	35.8	37.1	38.9	38.7
14	82.5	81.1	74 1	75.5	83.8	82 2
15	37.1	34.0	32.1	35.5	36.1	33.1
16	71.7	73.7	81.8	81.4	71.9	74.3
17	64 0	63.6	64.3	63.7	63.5	64.0
18	25 4	25.6	26.0	26.1	25.3	25.5
19	56.8	56.9	57.1	57.0	57.6	56.9
N-CH_2	50.2	50.2	50.5	50.3	50.4	50.2
CH_3	13.8	13.8	13.9	13.8	13.9	13.8
1′	55.4	55.2	55 6	55.1	56.1	55.3
6′	-	-	58 7	58.5	-	-
14′	57.9	57.8	-	-	58.2	57.6
16′	-	-	56 2	55.9	-	-
-OCH_2O-	93.6	94 0	93.7	93.6	93.8	93.5
C(6)-OCO	169.7 s	169.8 s	-	-	-	170.0[a] s
CH_3	21.4	21.4	-	-	-	21.4[b]
C(14)-OCO	-	-	-	171.4 s	-	-
CH_3	-	-	-	21.4	-	-
C(16)-OCO	-	170.6 s	-	-	-	170.6[a] s
CH_3	-	21.7	-	-	-	21.7[b]

a and b The assignments may be interchanged in any vertical column.

EXPERIMENTAL

Melting points are corrected and were taken on a Thomas-Kofler hot stage equipped with a microscope and a polarizer. Infrared spectra were taken on Perkin-Elmer model 1420 spectrophotometer and rotations were determined on Perkin-Elmer polarimeter model 141. ^1H and ^{13}C NMR spectra were recorded on JEOL FT models FX-60 and FX-90 Q spectrometers in $CDCl_3$. Mass spectra were determined on a Finnegan Quadrupole 4023 instrument. The high resolution mass spectra were run on a VG-ZAB-2F instrument, solid probe at 160°C, 70 ev, 200 ma, resolution 10,000. For chromatographic separations on a Chromatotron[8,9] rotors were coated with either a 1 or 2 mm thick layer of silica gel 60 PF 254 + 365 (EM Art. 7741) or 1 mm thick layer of alumina 60 GF-254 (EM Art. 1092) or 60 PF 254 + 365 (EM Art. 1104), for vacuum liquid chromatography (VLC)[7], silica gel HR (EM Art. 7744), and for PTLC, silica gel PF-254 (EM Art 7747) or alumina 60 HF-254 (EM Art. 1094).

Extraction of plant material. Seeds of *Delphinium elatum* (450 g) from Harris Moran Seeds were ground, suspended in a mixture of 95% ethanol (1.7 l), H_2O (0.42 l) and hexane (0.52 l), heated under reflux for 2 hours and then vigorously stirred at room temperature for 48 hours. The mixture was filtered and the filtrate allowed to stand till the layers separated. Evaporation of the hexane extract gave an oil (73.1 g).

The aqueous ethanolic extract was evaporated to give a yellow solid which was partitioned between CH_2Cl_2 (2 x 2.1 l) and 1.5 N H_2SO_4 (2.1 l). Evaporation of the CH_2Cl_2 extract gave a neutral fraction (4.6 g, fraction 1). Basification of the acidic layer (Na_2CO_3; pH 10) and extraction with ether (3 x 2 l) gave a crude alkaloidal fraction (9.6 g, fraction 2).

Isolation of isodelpheline (3), delpheline (7), methyllycaconitine (10), lycoctonine and elatine (13). About 9.1 g of fraction 2 was chromatographed (VLC) on silica. Elution was performed with hexane, then hexane-ethanol in order of increasing polarity . Fractions eluted with hexane-ethanol (96:4) were combined (1.11 g) and on repeated crystallization from ethanol-hexane gave 683 mg of delpheline (7), m.p. 217.5-219.5°C. The mother liquors were purified on an alumina rotor of a Chromatotron to give 98 mg of isodelpheline (3); $[\alpha]_D^{26}$ -1.2 (c, 1, $CHCl_3$); EIMS: m/z (%) 449 (M^+, $C_{25}H_{39}NO_6$, 2), 418 (M^+ -OCH_3, 85). Hrms: 449.276389. $C_{25}H_{39}NO_6$ requires 449.277742 . For ^{13}C NMR data see the Table.

Fractions eluted with hexane:ethanol (94.6) were combined (0.34 g) and purified twice on a silica rotor of a Chromatotron to give 20 mg of elatine (13); m.p. 222.5-224.5°C, $[\alpha]_D^{24}$ +3.3° (c, 0.42, $CHCl_3$). Elatine was identified by TLC behavior, m.p. m.m.p., IR, ^1H- and ^{13}C NMR spectra.[15,16]

Fractions eluted with hexane:ethanol (85:15 and 75:25) were combined (4.814 g) and separated by VLC (4.814 g) on silica gel, eluting with hexane and increasing amounts (1-15%) of ethanol in hexane. Purification on silica rotors of a Chromatotron (2 mm) afforded methyllycaconitine (10; 3.75 g), identified by TLC behavior, and IR, mass, proton and ^{13}C NMR spectra.[13,17]

The fraction eluted with hexane:ethanol (50:50) was purified on a silica rotor of a Chromatotron to give 31 mg of lycoctonine; m.p. 94-97°C (acetone), $[\alpha]_D^{24}$ +51.9 (c, 0.48, ethanol). Lycoctonine was identified by TLC behavior, m.p., m.m.p., IR, ^1H and ^{13}C NMR spectra.[13,16,18,19]

Isolation of elasine (1), eladine (5), deltaline (8), nudicauline (11) and 14-deacetylnudicauline (12). All the mother liquors and impure fractions left after the separation of the above mentioned alkaloids were combined (3.4 g) and chromatographed (VLC) on silica. Elution was performed with hexane, then hexane:ether in order of increasing polarities. Fractions eluted with hexane:ether (75:25 and 50:50) were combined (200 mg) and when crystallized from ethanol: hexane gave 68 mg of delpheline (7), m.p. 217.5-219.5°C.

Purification of the fraction eluted with hexane:ether (25:75) (0.36 g) on a silica rotor of a Chromatotron and subsequent separation on a preparative TLC plate (alumina) afforded isodelpheline (3; 15 mg), eladine (5, 42 mg) and deltaline (8, 15 mg), m.p. 184-186°C (ether). Eladine (5); amorphous; $[\alpha]_D^{23}$ -57.5° (c, 0.89, $CHCl_3$); EIMS: m/z (%) 435 (M^+, $C_{24}H_{37}NO_6$, 3), 405(25), 404 (M^+ -OCH_3, 100); Hrms: 435.262079. $C_{24}H_{37}NO_6$ requires 435.262091. For ^{13}C NMR data, see the Table. Deltaline was identified by TLC behavior, m.p., m.m.p., IR, ^1H- and ^{13}C- NMR spectra.[16,17,20]

The fraction eluted with ether (0.45 g) was purified twice on alumina rotors to give deltaline (8; 18 mg, m.p. 184-186°C), nudicauline (11; 105 mg) and elasine (1, 50 mg). Nudicauline was identified by TLC behavior and IR, mass, ^1H- and ^{13}C-NMR spectra.[14] Elasine (1); amorphous; $[\alpha]_D^{27}$ -55.7° (c, 0.51, $CHCl_3$); EIMS: m/z(%) 493 (M^+, $C_{26}H_{39}NO_8$, 0.14), 462 (M^+ -OCH_3, 25), 43(100); Hrms: 493.267557. $C_{26}H_{39}NO_8$ requires 493.267570. For ^{13}C NMR data see the Table.

Fractions eluted with ether:chloroform (75:25) and chloroform (0.4 g) were purified twice on an alumina rotor of a Chromatotron to give nudicauline (11; 28 mg), methyllycaconitine (10; 144 mg) and 14-desacetylnudicauline (12; 120 mg). Nudicauline (11) was identified by IR, mass, proton and ^{13}C NMR spectra.[14]

14-Deacetylnudicauline (12); amorphous, $[\alpha]_D^{21}$ +40.7° (c, 0.9, $CHCl_3$); EIMS: m/z(%) 668 (M^+, $C_{36}H_{48}N_2O_{10}$, 0.4), 653(9), 637 (M^+ -OCH_3, 90), 216(73), 44(97), 41(100). This compound was identified by TLC behavior and IR, ^1H- and ^{13}C NMR spectra as 14-desacetylandersoline.[21]

Conversion of elasine (1) to 16-acetylelasine (2). A mixture of 8 mg of 1, 1 ml of pyridine and 1 ml of Ac_2O was kept for 2 days at room temperature. Usual workup gave 8.3 mg of a residue which on crystallization from ether:hexane afforded 6 mg of 16-acetylelasine (2); m.p. 219.5-221.5°, EIMS: m/z (%) 535 (M^+, $C_{28}H_{41}NO_9$, 0.3), 504 (M^+ -OCH_3, 29), 476 (M^+ -59, 3), 43 (100); ^1H NMR ($CDCl_3$): δ 5.48 (1H, br s, C(6)-α-*H*), 4.96 and 4.88 (1H each, s, -O-C*H*$_2$-O-), 4.16 (1H, t, J = 4.5 Hz, C(14)-β-*H*), 3.49 and 3.26 (3H each, s, O*CH*$_3$), 2.08 and 2.05 (3H each, s, OCOC*H*$_3$), 1.07 (3H, t, J = 7 Hz, N-CH_2-C_3), 0.89 (3H, s, CH_3-18); for ^{13}C NMR data see the Table.

Conversion of isodelpheline (3) to 14-acetylisodelpheline (4). A mixture of 40.5 mg of 3, 1 ml of pyridine and 1 ml of Ac_2O was kept for 2 days at room temperature. Usual workup and purification on an alumina rotor of a Chromatotron yielded 40 mg of 14-acetylisodelpheline (4); m.p. 116-118°C (petroleum ether); $[\alpha]_D^{26}$ +13.5° (c, 0.17, $CHCl_3$); IR(KBr): 1730 cm^{-1} (C=O); EIMS: m/z (%) 491 (M^+, $C_{27}H_{41}NO_7$, 2), 460 (M^+ -OCH_3, 8), 431 (M^+ -59, 1); ^1H NMR ($CDCl_3$): δ 5.05 (2H, s, -O-C*H*$_2$-O-), 4.81 (1H, t, J = 4.5 Hz, C(14)-β-*H*), 3.30, 3.27 and 3.24 (3H each, s, O*CH*$_3$), 2.05 (3H, s, OCOC*H*$_3$), 1.03 (3H, t, J = 7 Hz, *N*-CH_2-*CH*$_3$), 0.93 (3H, s, CH_3-

18); for ^{13}C NMR data see the Table.

Conversion of eladine (4) to 6,16-diacetyleladine (6). A mixture of 10 mg of eladine (5), 1 ml of Ac_2O and 1 ml of pyridine was kept for 2 days at room temperature. Usual workup gave 10.5 mg of 6,16-diacetyleladine (6); EIMS: m/z (%) 519 (M^+, $C_{28}H_{41}NO_8$, 0.6), 488 ($M^+ - OCH_3$, 36), 43(100); ^1H NMR ($CDCl_3$): δ 0.84 (3H, s, *tert*-methyl), 1.04 (3H, t, J = 7 Hz, $N\text{-}CH_2\text{-}CH_3$), 2.04 and 2.06 (3H each, s, $OCOCH_3$), 3.24 and 3.45 (3H, s, OCH_3), 4.86 and 4.92 (1H each, s, $-O\text{-}CH_2\text{-}O-$), and 4.53 (1H, brs, C(6)-αH); for ^{13}C NMR see the Table.

Methylation of elasine (1). To 10 mg of elasine (1) in 4 ml of CH_2Cl_2 was added 10 mg of proton sponge [1,8-bis-(dimethylamino)naphthalene] and 16 mg of trimethyloxoniumtetrafluoroborate and the mixture was stirred at room temperature for 2 days. Ice water (15 ml) was added and the reaction mixture was rendered alkaline with $NaHCO_3$. The mixture was extracted with 3 x 20 ml of $CHCl_3$. The combined extracts were dried over anhydrous Na_2SO_4 and evaporated *in vacuo*. The residue was purified by PTLC (alumina) to give 8.3 mg of white foam which on crystallization from ether gave 4.3 mg of deltaline (8), m.p. 184-186 °C. The natural and synthetic deltaline were identical by TLC behavior, m.p., m.m.p. and IR spectra.[16,17,20]

Methylation of eladine (4). To 6 mg of eladine (4) in 4 ml of CH_2Cl_2 was added 6 mg of proton sponge and 8 mg of trimethyloxonium tetrafluoroborate and the mixture was stirred at room temperature for 24 hours. The reaction mixture was worked up as above to give 5 mg residue which was crystallized from ethanol:hexane mixture to give 3.5 mg of delpheline (7), m.p. 217.5-219.5 °C. The natural and synthetic delpheline were identical by TLC behavior, m.p., m.m.p. and IR spectra.[10]

Acknowledgment. We acknowledge with gratitude financial support of this work by the American Cyanamid Company. We are grateful to Mr. Denis Andrejewski, Natural Products Instrumentation Branch, Food and Drug Administration for the high resolution mass spectra. We thank Dr. H. K. Desai for the ^{13}C NMR spectra and Mr. Courtney Pape for the low resolution mass spectra.

REFERENCES

1. J. A. Goodson, *J. Chem. Soc.*, 139 (1942).
2. M. S. Rabinovicl, *J. Gen. Chem. USSR* (English transl.), **24**, 2211 (1954).
3. W. W. Fofilaktov and L. D. Alexejewa, *J. Allg. Chem.*, **24**, 738 (1954); *Chem. Zen.*, 1977 (1955).
4. A. D. Kuzovkov, *J. Gen. Chem. USSR*, **26**, 2063 (1956); *Chem Abs.*, 5099 (1957).
5. M. S. Rabinovich, *J. Gen. Chem. USSR*, **24**, 2242 (1954); *Chem. Zen.*, 10030 (1955).
6. S. A. Ross, H. K. Desai, B. S. Joshi, S. K. Srivastava, J. A. Glinski, S. Y. Chen and S. W. Pelletier, *Phytochemistry*.
7. S. W. Pelletier, H. P. Chokshi and H. K. Desai, *J. Nat. Prod.*, **49**, 5, 892 (1986).
8. H. K. Desai, B. S. Joshi, A. M. Panu and S. W. Pelletier, *J. Chromatogr.*, **322**, 223 (1985).
9. H. K. Desai, E. R. Trumbull and S. W. Pelletier, *J. Chromatogr.*, **366**, 439 (1986).
10. S. W. Pelletier, N. V. Mody, B. S. Joshi and L. C. Schramm, in *Alkaloids: Chemical and Biological Perspectives*, Vol. 2, Ch. 5, John Wiley, New York (1984).
11. M. S. Yunusov, Y. V. Rashkes, V. A. Tel'nov, and S. Y. Yunusov, *Khim. Prir. Soedin.*, 515 (1969).
12. W. Deng and W. L. Sung, *Heterocycles*, **24**, 873 (1986).
13. S. W. Pelletier, N. V. Mody, R. S. Sawhney and J. Bhattacharyya, *Heterocycles*, **7**, 327 (1977).
14. P. Kulanthaivel and M. Benn, *Heterocycles*, **23**, 2515 (1985).
15. S. W. Pelletier, H. K. Desai, P. Kulanthaivel and B. S. Joshi, *Heterocycles*, **26**, 11, 2835 (1987).
16. S. W. Pelletier, N. V. Mody, K. I. Varughese, J. A. Maddry and H. K. Desai, *J. Am. Chem. Soc.*, **103**, 6536 (1981).
17. S. W. Pelletier, O. D. Dailey, Jr., N. V. Mody and J. D. Olsen, *J. Org. Chem.*, **46**, 3284 (1981).
18. A. J. Jones and M. H. Benn, *Can. J. Chem.*, **51**, 486 (1973).
19. S. W. Pelletier, R. S. Sawhney, H. K. Desai and N. V. Mody, *J. Nat. Prod.*, **43**, 395 (1980).
20. S. W. Pelletier, N. V. Mody and O. D. Dailey, Jr., *Can. J. Chem.*, **58**, 1875 (1980).
21. A. M. Panu, Ph.D. Dissertation, University of Georgia, 1986.