Tetrahedron Vol 42, No. 20, pp. 5747 to 5752, 1986
Printed in Great Britain.

0040-4020/86 $5.00+.00
Pergamon Journals Ltd.

FIVE NEW STEROIDAL ALKALOIDS FROM *BUXUS PAPILOSA*. SOME RELATIONSHIPS BETWEEN STRUCTURES AND SPECIFIC ROTATIONS

M. Iqbal Choudhary,[#¶] Atta-ur-Rahman,[¶] Alan J. Freyer[#] and Maurice Shamma[#]

[#] Department of Chemistry, The Pennsylvania State University, University Park, PA 16802, USA

[¶] HEJ Research Institute of Chemistry, University of Karachi, Karachi 32, Pakistan

Buxus papilosa C.K. Schneider (Buxaceae), of Pakistani origin, has yielded the new alkaloids (+)-buxabenzamidienine (1), (+)-16α-acetoxybuxabenzamidienine (2), (+)-buxotrienine (3), (-)-buxanoldine (4), and (+)-buxanaldinine (5). Six generalizations have been drawn which relate specific rotations to structural features.

(*Received in USA* 19 *May* 1986)

A characteristic of the genus Buxus, of the botanical family Buxaceae, is an abundance of steroidal alkaloids. Some 70 of these evergreen shrubs are known, which are spread out from Eurasia to South Africa, Malaysia and Indonesia, and North and Central America.[1]

Previous studies of B. papilosa C.K. Schneider, collected in Pakistan, had yielded the alkaloids (-)-cyclobuxupaline-C,[2] (+)-cyclopapilosine-D,[2] (+)-buxamine-C,[2] (+)-papilicine,[3] (+)-moenjodaramine,[4] (+)-harappamine,[4] (+)-karachicine,[5] (+)-buxaminol-G,[6] (+)-papilinine,[7] (+)-papilamine,[8] (+)-buxaquamarine,[9] (-)-cyclobuxoviricine,[10] and (-)-cycloxobuxoviricine.[11] All of these compounds possess in common either the pentacyclic *cyclo*-9β,19-pregnane-5α or the tetracyclic *abeo*-9(10→19)-pregnane-5α skeletons.

We have now investigated the so-called weakly basic alkaloid fraction of B. papilosa which can be extracted at pH 3.5. This fraction was chromatographed over a silica gel column, with final purification achieved by silica gel TLC. Most of the alkaloids obtained by this procedure proved to be of the tetracyclic *abeo* type, and we herewith describe five of these new bases, namely (+)-buxabenzamidienine (1), (+)-16α-acetoxybuxabenzamidienine (2), (+)-buxotrienine (3), (-)-buxanoldine (4), and (+)-buxanaldinine (5). Additionally, through the use of NMR spin decoupling and NOE experiments, we have made an effort to assign as many specific spectral absorptions as possible.

(+)-Buxabenzamidienine (1), $C_{33}H_{48}N_2O$, shows a UV spectrum with maxima at 238 and 245 nm, and shoulders at 228 and 255 nm, characteristic of 9(10→19)*abeo*diene bases. Similar absorptions have been encountered in the cases of (+)-moenjodaramine,[4] (+)-harappamine[4] and (+)-buxaquamarine.[9] The IR spectrum in chloroform solution displays intense bands at 3680 (NH) and 1652 cm^{-1} (arom. amide).

The 360 MHz ($CDCl_3$) NMR spectrum of (+)-buxabenzamidienine has been summarized around expression 1. Four C-methyl singlets are clearly in evidence. A doublet at δ 0.93 is due to the C-21 methyl group. A singlet at δ 6.00 represents the isolated vinylic H-19, while a doublet of doublets centered at δ 5.56 is due to the vinylic H-11 which is split by the C-12 methylene protons.

The mass spectrum of (+)-buxabenzamidienine (1) includes molecular ion m/z 488. Peak m/z 473 indicates loss of a methyl, and peak m/z 383 reflects the loss of the benzoyl substituent. Base peak m/z 72 represents the trimethyliminium side chain fragment, $H_3C\text{-}CH{=}N^+(CH_3)_2$.

(+)-Buxabenzamidienine (1) is accompanied in the plant by its 16-acetoxyl derivative, (+)-16α-acetoxybuxabenzamidienine (2), $C_{35}H_{50}N_2O_3$. Compound 2 has a UV spectrum nearly identical with that of 1. The IR spectrum is also somewhat similar, but with an additional band at 1732 cm^{-1} because of the ester function.

The NMR spectrum of (+)-16α-acetoxybuxabenzamidienine is presented around expression 2. Significantly, the C-21 methyl doublet at δ 1.26 is appreciably further downfield than in the case of (+)-buxabenzamidienine (1) which lacks the C-16 acetoxyl function. A singlet at δ 1.80 represents the acetyl methyl group, while a multiplet at δ 5.00 is due to H-16.

The mass spectrum of (+)-16α-acetoxybuxabenzamidienine (2) includes molecular ion peak m/z 546, and peak m/z 531 due to loss of a methyl. A peak at m/z 441 represents cleavage of the benzoyl substituent, while base peak m/z 72 is again due to the trimethyliminium cation. Other significant ions are m/z 60 representing acetic acid, and m/z 157 and 171 which are formed by cleavage of ring D along the lines indicated. It follows that the extra acetoxyl group in species 2 must be attached to ring D. More specifically, this function is linked to C-16, since it is known that a C-16α-hydroxyl substituent is present in a wide variety of Buxus alkaloids.

The somewhat unusual nature of (+)-cyclobuxotriene (3), $C_{26}H_{39}NO$, our third alkaloid, was intimated by its yellow color, which could be clearly distinguished on the silica gel TLC plate. The UV spectrum was characterized by an intense absorption maximum at 324 nm, denoting extensive conjugation. The IR spectrum included peaks at 1652 (conj. ketone) and 1600 cm^{-1} (C=C).

The NMR spectrum was extremely informative. Four singlets at δ 0.72, 0.78, 0.96 and 1.17, corresponded to the four tertiary methyl groups. The C-21 secondary methyl group resonated as a doublet at δ 0.93. Two doublets at δ 6.00 and 6.71 were ascribed to the vinylic H-2 and H-1, respectively; whereas the vinylic H-19 appeared as a doublet at δ 7.42. Additionally, the vinylic H-11 appeared as a doublet of doublets centered at δ 6.24.

The mass spectrum of (+)-cyclobuxotriene (3) evidenced molecular ion m/z 381. Loss of the trimethyliminium side chain accounted for base peak m/z 72. Another interesting peak was m/z 167, representing ring D with its substituents, and resulting from retro-Diels-Alder cleavage of ring C along the lines indicated.

Our two remaining new alkaloids are the diolefinic diol (-)-buxanoldine (4) and the monoolefinic aldehydoacetate (+)-buxanaldinine (5).

(-)-Buxanoldine (4), $C_{33}H_{48}N_2O_3$, has a UV spectrum which shows essentially a benzamide chromophore at 228 nm. The IR spectrum includes peaks at 3580 (NH), 3360 (OH), 1640 (arom. amide) and 1600 cm^{-1} (C=C).

The NMR spectrum of (-)-buxanoldine (4) was particularly informative since we had sufficient quantities on hand to allow for a detailed NOE study, in addition to the usual spin decoupling experiments. It featured three tertiary methyl groups as singlets at δ 0.69, 0.72 and 0.90; while a secondary methyl group resonated as a doublet at δ 0.90. Since a hydroxyl group is present at C-30, the C-30 methylene protons appeared as two doublets, centered at δ 3.23 and 3.49. A multiplet at δ 4.11 was due to H-16 which is geminal to a hydroxyl group. A doublet of doublets at δ 5.26 and another at δ 5.43 represented the vinylic hydrogens at C-11 and C-1, respectively. The two double bonds are thus not conjugated, and this finding is in accord with the UV absorption discussed above.

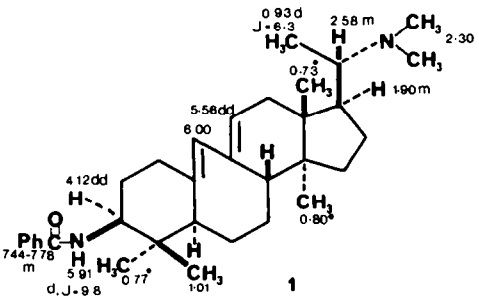
Some of the more salient NMR NOE results are shown in diagram 4a. Irradiation of the H-17 doublet of doublets (δ 1.90) led to a 12.5% enhancement of the C-28 methyl singlet (δ 0.90). Irradiation of the H-16 multiplet (δ 4.11) resulted in no enhancement of the H-17 signal (δ 1.90), but instead led to an increase in the area of the H-15β absorption (δ 1.95), thus furnishing an insight into the stereochemistry of the ring D substituents. Specifically, the C-16 hydroxyl is alpha, as in all other Buxus alkaloids hydroxylated at that site. Another significant NOE result reflected on the spacial proximity of the C-19 methylene protons (δ 2.68 and 2.86) to the vinylic H-1 and H-11 (δ 5.43 and 5.26) since these absorptions showed reciprocating NOE's.

The mass spectrum of (-)-buxanoldine (4) disclosed molecular ion m/z 520, ion m/z 105 for the benzoyl moiety, and the by now familiar base peak m/z 72 representing the trimethyliminium cation.

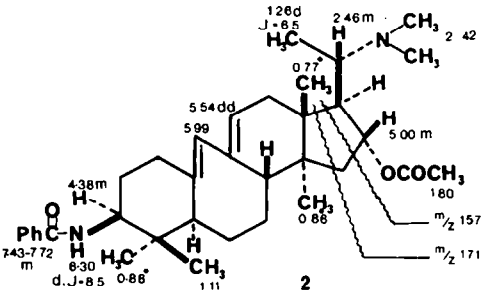
Acetylation of (-)-buxanoldine (4) using acetic anhydride in pyridine afforded as expected (-)-buxanoldine diacetate, $C_{37}H_{52}N_2O_5$, whose IR spectrum incorporates an intense ester carbonyl absorption at 1720 cm^{-1}, in addition to the amidic carbonyl band at 1650 cm^{-1}. The NMR spectrum of the diacetate (Experimental) showed downfield shifts of H-16 from δ 4.11 to 5.15, and of the C-30 methylene protons from δ 3.23 and 3.49 to δ 3.67 and 3.85.

(+)-Buxanaldinine (5), $C_{35}H_{50}N_2O_4$, is the first Buxus alkaloid to incorporate a C-30 aldehydo group in lieu of the more common hydroxyl or ester functions. The UV spectrum displayed a maximum at 228 nm characteristic of the benzamide substituent. The IR spectrum showed absorptions at 3660 (NH), 1735 (ester carbonyl), 1722 (aldehyde carbonyl) and 1656 cm^{-1} (aromatic amide).

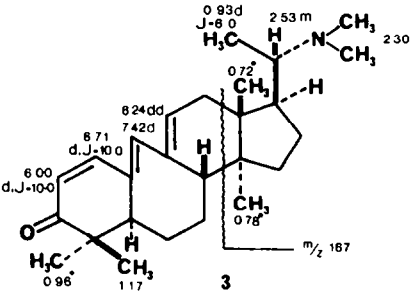
The NMR spectrum exhibits three singlets at δ 0.88, 0.88 and 0.89 for the three tertiary methyl groups. Another singlet at δ 1.91 can be assigned to the acetate methyl group. The doublet at δ 0.88 belongs to the secondary methyl group. A multiplet centered at δ 4.71 represents H-16 which is alpha to the acetate group. The C-1 olefinic proton appears as a doublet of doublets at δ 5.69. Finally, the aldehydic proton absorbed as a singlet at δ 9.50.



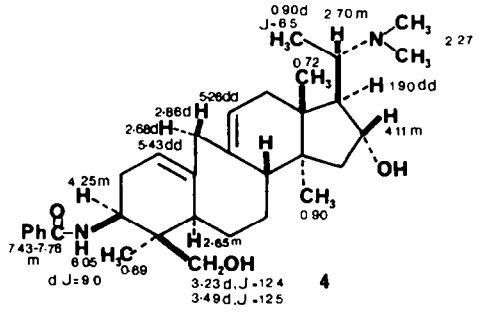
H-3 , J_1 = 18.0 Hz, J_2 = 7.0 Hz
H-11, J_1 = 2.5 Hz, J_2 = 1.8 Hz



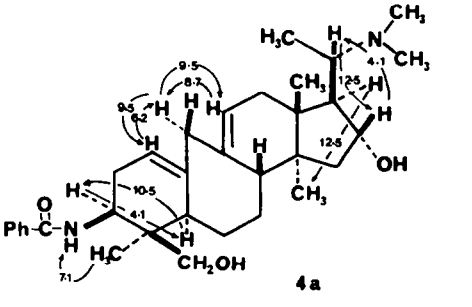
H-11, J_1 = 2.5 Hz, J_2 = 1.5 Hz

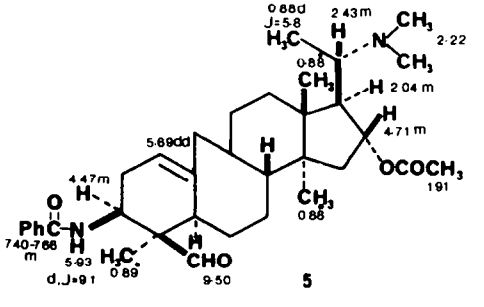


H-11, J_1 = 2.5 Hz, J_2 = 1.8 Hz
H-19, J = 2.2 Hz (long range)



H-1, J_1 = 4.0 Hz, J_2 = 1.8 Hz
H-19α, J = 12.0 Hz; H-19β, J = 12.0 Hz
H-11, J_1 = 2.8 Hz, J_2 = 1.6 Hz
H-17α, J_1 = 12.0 Hz, J_2 = 11.1 Hz





H-1, J_1 = 4.0 Hz, J_2 = 1.8 Hz

The mass spectrum of (+)-buxanaldinine (5) has molecular ion m/z 562 and base peak m/z 72. A relatively large peak m/z 28 is due to loss of carbon monoxide.

Sodium borohydride in methanol reduction of (+)-buxanaldinine (5) supplied the corresponding alcohol (+)-buxanoldinine, $C_{35}H_{52}N_2O_4$, whose NMR spectrum (Experimental) significantly included two one-proton doublets at δ 3.60 and 3.76 representing the C-30 methylene hydrogens, but was devoid of the aldehydic singlet at δ 9.50.

With the characterization of the above five compounds, the number of known Buxus alkaloids reported in the literature is greater than one hundred. An aspect of these species that had never previously been considered is the relationship between structure on the one hand, and specific rotation on the other. Fortunately, the specific rotations for most Buxus alkaloids have been measured in chloroform, so that the values recorded for different alkaloids may be compared. Indeed, a simple measurement of the specific rotation can immediately throw light on some of the structural features of a Buxus base. The following rules relate certain molecular features to specific rotations, with specific rotations quoted between brackets.

(1) 9(10→19)*abeo*dienes of type A are dextrorotatory. Examples are buxamine-E [+42°],[12] papilamine [+23.3°],[8] buxamine-C [+24°],[2] desoxy-16-buxidienine [+33°],[2] buxaquamarine [24°],[9] papilicine [+47°],[3] buxamine-A [+40°],[13] papilinine [+29.4°],[7] buxaminol-B [+20°],[14] buxaminol-E [+40°],[12] and moenjodaramine [+33.3°].[4] The one exception is N-benzoylbuxidienine [-36°],[15] but unfortunately this N-benzoylated compound was not available to us for a redetermination of its optical activity.

(2) 9β,19-Cyclo-11-oxo alkaloids of type B are also dextrorotatory, but the magnitude of the specific rotation is usually larger than for dienes of type A. Examples include baleabuxoxazine-C [+116°],[12] N-benzoylbaleabuxidine-F [+52°],[12] N-isobutyroylcycloxobuxidine-H [+76°],[16] baleabuxidine [+127°],[12] N-isobutyroylcycloxobuxidine-F [+71°],[16] N-isobutyroylbaleabuxidine-F [+71°],[12] N-benzoylcycloxobuxine-F [+90°],[15] N-benzoylcycloxobuxoline-F [+76°],[15] N-isobutyroylcycloxobuxine [+115],[17] buxarine [+98°],[18] N-benzoylcycloxobuxidine-F [+52],[16] N-benzoyl-O-acetylcycloxobuxoline-F [+114°],[15] and buxatine [+108°].[19]

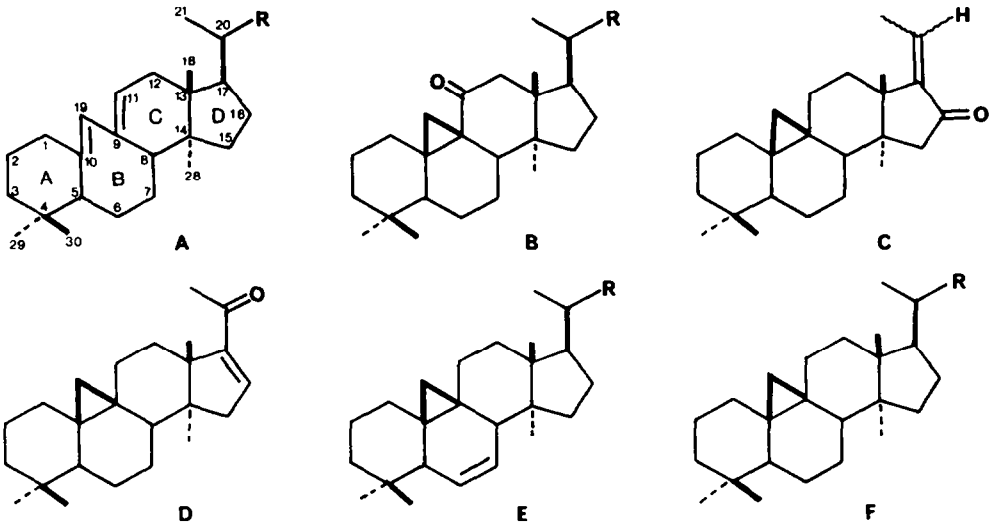
(3) 9β,19-Cyclo-16-oxo-Δ(17→20) alkaloids of type C are levorotatory, regardless of the geometrical isomerism about the C-17(20) double bond. Some examples are cyclobuxophylline-O [-61.5°],[20] buxenone [-48°],[18] cyclobuxophylline-K [-67°],[20] cyclobuxophylline [-72°],[21] methylbuxene [-104°],[22] and cyclobuxosuffrine [-62°].[21]

(4) 9β,19-Cyclo-20-oxo-Δ(16→17) compounds of type D are dextrorotatory. Only two examples are available, namely cyclomicrobuxeine [+126°][21] and cyclobuxomicreine [+37°].[21] The former of these also incorporates an exocyclic methylene at C-4 instead of the usual gem dimethyl.

(5) 9β,19-Cyclo-Δ(6→7) compounds of type E are levorotatory, as exemplified by cyclobuxupaline-C [-37],[2] cyclobullatine-A [-99°],[14] cyclovirobuxeine-B [-80°],[23] cyclovirobuxeine-A [-87°],[23] N-benzoyldihydrocyclomicrophylline-F [-20°],[24] cyclomicrosine [-33°],[21] and cyclomalayanine-B [-61°].[23]

(6) Simple Buxus alkaloids with no unsaturation, but with a 9β,19-cyclo system of type F are dextrorotatory. Relevant examples are cycloprotobuxine-F [+42°],[13] cycloprotobuxine-C [+68°],[14] buxocyclamine-A [+87°],[25] cyclovirobuxine-D [+63°],[23] cyclopapilosine-D [+54°],[2] cyclovirobuxine-C [+62°],[14] cyclorolfoxazine [+106°],[26] buxozine-C [+65°],[27] N-acetylcycloprotobuxine-D [+53°],[15] 16-deoxycyclobuxoxazine [+56°],[28] cyclorolfeibuxine-C [+52°],[26] dihydrocyclomicrophylline-A [+46°],[16] and N-benzoylcycloprotobuxoline [+42°].[15]

It should be noted in conclusion that the oxidation state at C-30 does not appear to have a dominating effect on the specific rotation. C-30 is usually a methyl group, but it could also be hydroxymethyl or part of a 1,3-tetrahydrooxazine ring involving the C-3 nitrogen. Similarly, the presence of a hydroxyl or acetoxyl substituent at C-16 on ring D does not change the direction of the specific rotation.



EXPERIMENTAL

All NMR spectra are at 360 MHz in $CDCl_3$ solution.

Plant Material:- The leaves of B. papilosa (dry weight 50 kg) were collected in the northern regions of Pakistan, in the month of January, 1984, by the Forest Institute, Peshawar. The plant was identified by Prof. S. Irtifaq Ali, Department of Botany, University of Karachi, and a voucher specimen was deposited in the herbarium at the Department of Botany, University of Karachi.

Extraction and Purification:- Extraction of the leaves was with ethanol at room temperature. The solvent was evaporated in vacuo to afford a gum (110 g), which was taken up in 10% acetic acid. The pH was then adjusted by addition of 20% ammonium hydroxide. The fraction obtained at pH 3.5 was loaded on a silica gel column (250 g). The initial solvent was chloroform. Elution was with chloroform and then with chloroform gradually enriched with methanol. Three main fractions were collected: Fraction A, $CHCl_3$-MeOH (95:5), 1.4 g; Fraction B, $CHCl_3$-MeOH (92:8), 1.0 g; and Fraction C, $CHCl_3$-MeOH (90:10), 1.7 g.

(+)-Buxabenzamidienine (1):- Fraction A was again subjected to column chromatography over silica gel. An important fraction (50 mg) was purified by silica gel TLC using the system C_6H_{14}-Me_2CO-Et_2NH (8.5:1.0:0.5) to supply 1 (3.9 mg), amorphous powder; $[\alpha]_D$ +6° (c 1.59, $CHCl_3$); ν max ($CHCl_3$) 3680, 1652 cm^{-1}; λ max (MeOH) 228 sh, 238, 245, 255 sh nm (log ε 4.37, 4.46, 4.49, 4.31); m/z 488 (M^+, 2), 473 (2), 383 (1), 105 (5), 73 (5), 72 (10), 58 (2).

Isolation of (+)-16α-Acetoxybuxabenzamidienine (2) and (+)-buxotrienine (3):- Fraction B was placed on a silica gel column (70 g). Elution was with $CHCl_3$-MeOH-NH_4OH (96:4:4). The major fraction was subjected to preparative TLC on silica gel using C_6H_6:Et_2NH (96.5:3.5) to afford 2 (1.5 mg) and yellow colored 3 (3.5 mg).

(+)-16α-Acetoxybuxabenzamidienine (2):- Amorphous, $[\alpha]_D$ +6° (c 1.02, $CHCl_3$); ν max ($CHCl_3$) 3680, 1732, 1650 cm^{-1}; λ max (MeOH) 228 sh, 237, 245, 254 sh nm (log ε 4.31, 4.34, 4.35, 4.15); m/z 546 (M^+, 3), 531 (3), 441 (1), 171 (2), 157 (3), 105 (45), 72 (100).

(+)-Buxotrienine (3):- Amorphous; $[\alpha]_D$ +13.5° (c 1.81, $CHCl_3$); ν max ($CHCl_3$) 1652, 1600 cm^{-1}; λ max (MeOH) 324 nm (log ε 3.96); m/z 381 (M^+, 1), 366 (2), 167 (2), 72 (100).

Isolation of (−)-Buxanoldine (4) and (+)-Buxanaldinine (5):- Fraction C was placed on a silica gel column (100 g). Elution was with $CHCl_3$-MeOH-NH_4OH (89:10:1). Further purification was by silica gel TLC to supply 4 (14 mg) and 5 (3 mg).

(−)-Buxanoldine (4):- Amorphous; $[\alpha]_D$ −27.4° (c 0.89, $CHCl_3$); ν max ($CHCl_3$) 3580, 3360, 1640, 1600 cm^{-1}; λ max (MeOH) 228 nm (log ε 4.07); m/z 520 (M^+, 1), 505 (2), 105 (8), 72 (100).

(-)-Buxanoldine Diacetate:- (-)-Buxanoldine (4) was acetylated at room temperature using acetic anhydride in pyridine. The diacetate exhibited $[\alpha]_D$ -39° (c 0.62, $CHCl_3$); ν max ($CHCl_3$) 3680, 1720, 1650, 1590 cm^{-1}; δ 0.75 (3H, s, CH_3), 0.85 (3H, s, CH_3), 0.90 (3H, d, J = 6.8 Hz, C-21 CH_3), 1.10 (3H, s, CH_3), 2.00 (6H, s, 2 x $COCH_3$), 2.15 (3H, s, NCH_3), 2.20 (3H, s, NCH_3), 3.67 (1H, d, J = 12 Hz, H-30(a)), 3.85 (1H, d, J = 12 Hz, H-30(b)), 4.48 (1H, m, H-3α), 5.15 (1H, m, H-16β), 5.35 (1H, bm, H-11), 5.50 (1H, bm, H-1), 6.27 (1H, d, NH), 7.42-7.74 (5H, m, ArH); m/z 604 (M^+, 3), 589 (2), 561 (1), 545 (1), 544 (1), 105 (6), 72 (100).

(+)-Buxanaldinine (5):- Amorphous, $[\alpha]_D$ +12° (c 1.39, $CHCl_3$); ν max ($CHCl_3$) 3660, 1735, 1722, 1656, 1600 cm^{-1}; λ max (MeOH) 228 nm (log ε 4.18); m/z 562 (M^+, 1), 171 (3), 157 (2), 105 (7), 72 (100).

Buxanoldinine:- Reduction of 5 with sodium borohydride in methanol supplied the alcohol, ν max ($CHCl_3$) 3680, 1728, 1640 cm^{-1}; λ max (MeOH) 227 nm; amorphous; δ 0.72 (3H, s, CH_3), 0.83 (3H, s, CH_3), 0.88 (3H, d, H = 7.0 Hz, C-21 CH_3), 0.90 (3H, s, CH_3), 2.00 (3H, s, $COCH_3$), 2.17 (6H, s, NCH_3), 3.60 (1H, d, J = 11.0 Hz, H-30a), 3.76 (1H, J = 11.0 Hz, H-30b), 4.30 (1H, m, H-3α), 4.71 (1H, m, H-16β), 5.67 (1H, dd, J = 7.0 Hz, J = 1.5 Hz, H-1), 6.00 (1H, d, J = 10.0 Hz, NH), 7.33-7.77 (5H, m, ArH); m/z 564 (M^+, 1), 505 (1), 171 (1), 157 (2), 105 (9), 72 (100), 58 (3), 44 (2).

Acknowledgment:- This research was supported by NSF grants INT-8217601 and INT-8213225.

REFERENCES

1. J.C. Willis, A Dictionary of the Flowering Plants and Ferns, (revised by H.K.A. Shaw) 8th ed., Cambridge University Press, Cambridge (1980), p. 174.
2. M. Shamma, V.S. Georgiev, G.A. Miana and F.S. Khan, Phytochemistry, 12, 2051 (1973).
3. Atta-ur-Rahman, M. Nisa and T. Zamir, Z. Naturforsch., 39b, 127 (1984).
4. Atta-ur-Rahman, M. Nisa and S. Farhi, Z. Naturforsch., 39b, 524 (1984).
5. Atta-ur-Rahman and M. Nisa, Z. Naturforsch., 39b, 839 (1984).
6. Atta-ur-Rahman, M. Nisa and K. Jahan, Phytochemistry, 24, 1398 (1985).
7. Atta-ur-Rahman, M. Nisa, T. Zamir and W. Voelter, Z. Naturforsch., 40b, 565 (1985).
8. Atta-ur-Rahman, S. Farhi, G.A. Miana, M. Nisa and W. Voelter, Z. Naturforsch., 40b, 567 (1985).
9. Atta-ur-Rahman, M.I. Choudhary and M. Nisa, Heterocycles, 23, 1951 (1985).
10. Atta-ur-Rahman, M.I. Choudhary and M. Nisa, Phytochemistry, 24, 3082 (1985).
11. Atta-ur-Rahman, M.I. Choudhary, I. Ali and Habib-ur-Rahman, J. Nat. Prod., 49, 106 (1986).
12. F. Khuong-Huu, D. Herlem-Gaulier, M.M.Q. Khuong-Huu, E. Stanislas and R. Goutarel, Tetrahedron, 22, 3321 (1966).
13. F. Khuong-Huu, R. Paris, R. Razafindrambao, A. Cavé and R. Goutarel, C.R. Acad. Sci. Paris, 273C, 558 (1971).
14. Z. Voticky, O. Bauerova and V. Paulik, Coll. Czech. Chem. Commun., 40, 3055 (1975).
15. S.M. Kupchan, R.M. Kennedy, W.R. Schleigh and G. Ohta, Tetrahedron, 23, 4563 (1967).
16. D. Herlem-Gaulier, F. Khuong-Huu-Laine and R. Goutarel, Bull. Soc. Chim. France, 763 (1968).
17. D. Herlem-Gaulier, F. Khuong-Huu-Laine and R. Goutarel, Bull. Soc. Chim. France, 3478 (1966).
18. W. Döpke, B. Muller and P.W. Jeffs, Pharmazie, 21, 643 (1966).
19. W. Döpke and B. Muller, Naturwissenschaften, 54, 249 (1967).
20. L.T. Huong, Z. Voticky and V. Paulik, Coll. Czech. Chem. Commun., 46, 1425 (1981).
21. T. Nakano, S. Terao and Y. Saeki, J. Chem. Soc. (C), 1412 (1966).
22. W. Döpke, R. Hartel and H.W. Fehlhaber, Tetrahedron Lett., 27, 4423 (1969).
23. F. Khuong-Huu-Laine, M.-J. Magdeleine, N.G. Bisset and R. Goutarel, Bull. Soc. Chim. France, 758 (1966).
24. W. Döpke and B. Muller, Pharmazie, 21, 666 (1967).
25. W. Döpke, B. Muller and P.W. Jeffs, Pharmazie, 23, 37 (1969).
26. F. Khuong-Huu-Laine, A. Milliet, N.G. Bisset and R. Goutarel, Bull. Soc. Chim. France, 1216 (1966).
27. Z. Voticky, L. Dolejš, O. Bauerova and V. Paulik, Coll. Czech. Chem. Commun., 42, 2549 (1977).
28. R. Hartel, W. Döpke, E. Grundemann and G. Lehmann, Tetrahedron Lett., 29, 2741 (1971).