Pure & Appl. Chem., Vol. 62, No. 7, pp. 1385–1388, 1990.
Printed in Great Britain.

Applications of modern 2D-NMR techniques in structure elucidation of natural products

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Abstract- Recent advances in the field of NMR spectroscopy have provided natural product chemists with exciting new tools for structure elucidation of complex molecules, such as HOHAHA, HMBC etc. A number of new natural products have been isolated by us from medicinal plants of Pakistan, Jordan, Ethiopia, Sri Lanka and Turkey and their structures elucidated using these modern spectroscopic techniques.

INTRODUCTION

There has been an explosive growth in NMR spectroscopy in recent years. The advent of such 1D and 2D techniques as DEPT, COSY, NOED, NOESY, 2D J-resolved, one-bond and long range hetero-COSY/COLOC, 2D-INADEQUATE, HOHAHA etc. (ref. 1,2), have provided the organic chemist with powerful new tools for structure elucidation of complex natural products. Inverse measurement techniques such as HMBC and HMQC have allowed substantial enhancements of sensitivity in the heteronuclear shift correlation experiment. These methods have been employed in structure elucidation of new natural products from terrestrial and marine life forms. Some of the recent work carried out in our research laboratories in which such techniques have been used is presented here.

NEW ALKALOIDS FROM *ALSTONIA MACROPHYLLA*

Alstonia macrophylla Wall is reputed for its medicinal and poisonous properties. It is a rich source of monomeric and dimeric indole alkaloids. We have previously reported a number of new alkaloids from A. macrophylla of Sri Lankan origin. As a result of our recent work, alstozine N-oxide (1) was isolated from the leaves of A.macrophylla and its structure established using modern spectroscopic techniques.

STEROIDAL ALKALOIDS FROM *BUXUS HILDERBRANDTII, BUXUS PAPILLOSA* AND *BUXUS SEMPERVIRENS*

Plants of the family Buxaceae find extensive use in folk medicine for the treatment of malaria, rheumatism and skin diseases (ref. 3). The leaves of Buxus hilderbrandtii of Ethiopian origin have afforded four new steroidal alkaloids namely, 31-O-benzoylbuxhilderdienine (2), N-demethyl-31-O-benzoylbuxhilderdienine (3), N,N-dimethyl-31-O-hydroxybuxhilderdienine (4) and N,N-dimethyl-4-demethylbuxhilderdienine (5).

We have previously reported some 40 new steroidal alkaloids from leaves of Buxus papillosa (Buxaceae) of Pakistan origin. We have recently obtained the new alkaloids (+)-buxabenzacine (6), buxoxybenzamine (7), buxapapilinine (8), and N-formylcyclomicrobuxeine (9) from this plant.

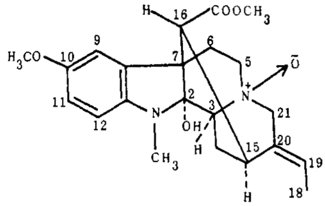
Similarly the leaves of B.sempervirens of Turkish origin have afforded four new steroidal alkaloids, namely (-)-O-acetyl-N-benzoylbuxidienine (10), (+)-nor-16α-acetoxybuxabenzamidienine (11), (+)-31-acetylbuxanolidine (12) and (+)-cyclomicrobuxamine (13).

A NEW SESQUITERPENE LACTONE FROM *FERULA OOPODA*

Work on the ethanolic extract of the leaves of Ferula oopoda (Umbelliferae) has resulted in the isolation of a new sesquiterpene lactone 6-S-11,13-dihydroeremanthine (14).

ALKALOIDS FROM *FUMARIA INDICA*

Fumaria indica (Fumariaceae), a commonly known herb of northern Pakistan, has yielded a new benzylisoquinoline alkaloid, fumarizine (15) and a phthalide isoquinoline alkaloid, (+)-papraine (16).



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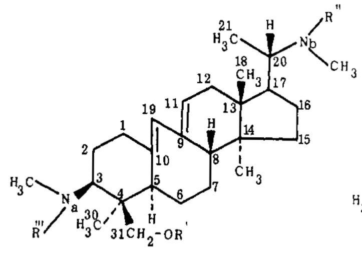
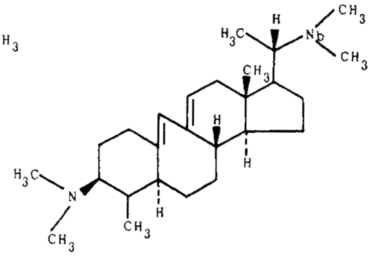


2-4

2 R'=-COPh., R"=CH_3., R'''=H

3 R'=-COPh., R"=H., R'''=H

4 R'= H., R'=CH_3., R'''=CH_3



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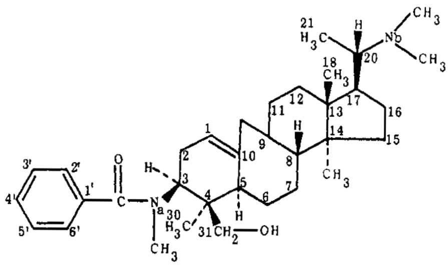

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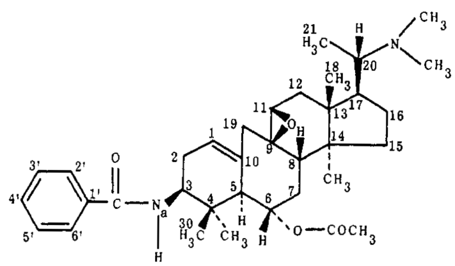

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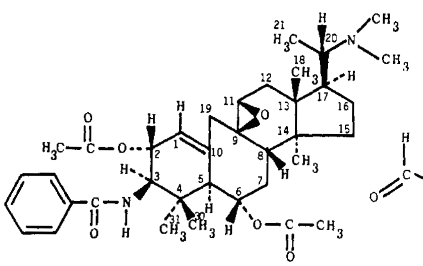

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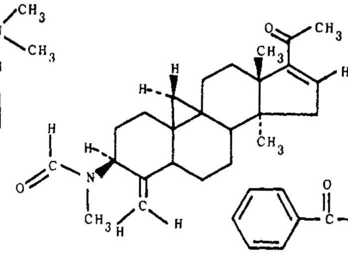

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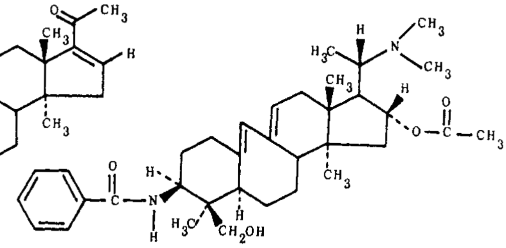

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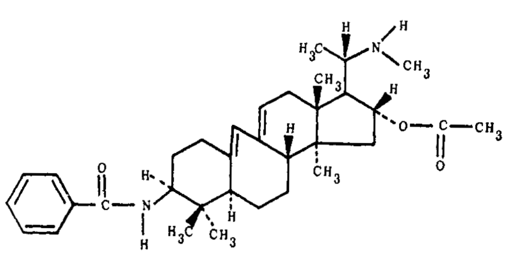

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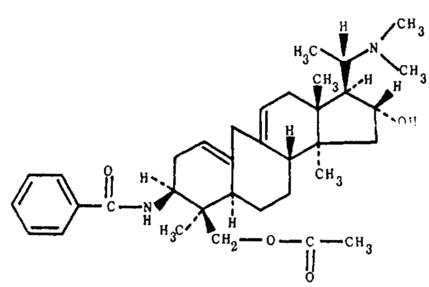

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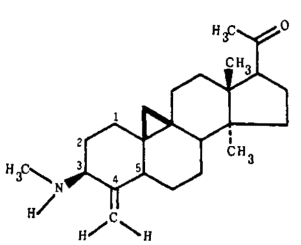

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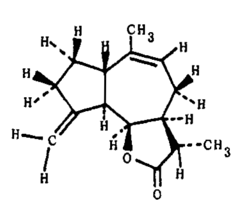

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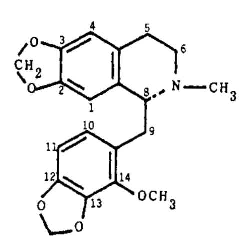

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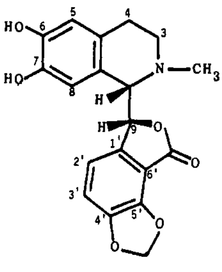

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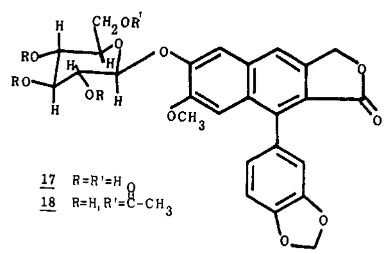
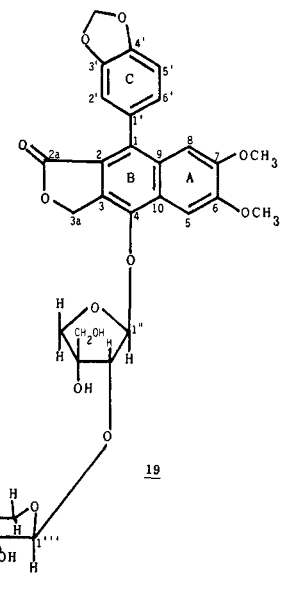


17 R=R'=H

18 R=H, R'=C(=O)−CH$_3$



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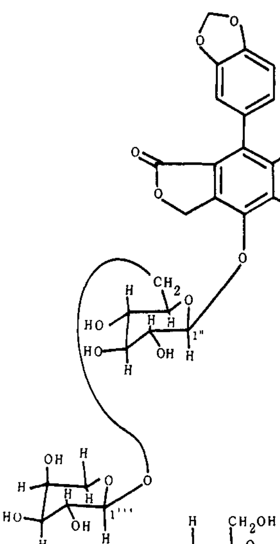

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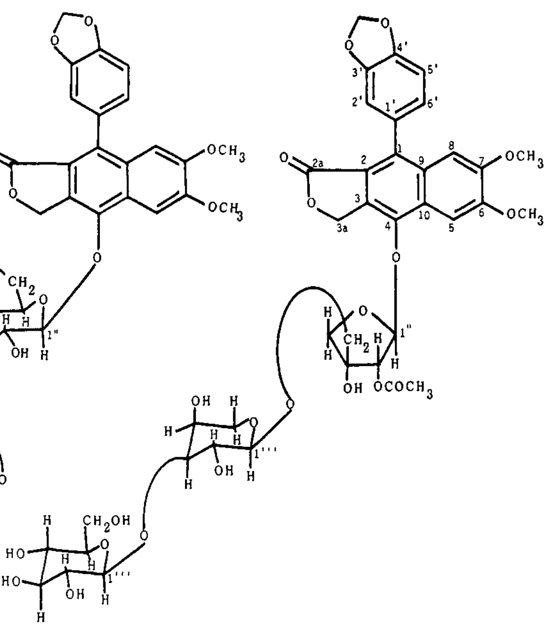

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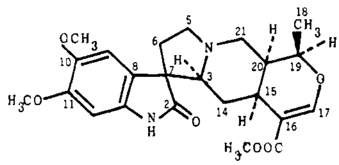

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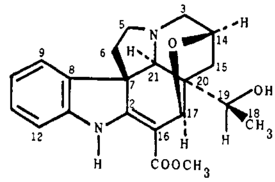

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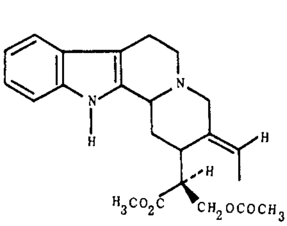

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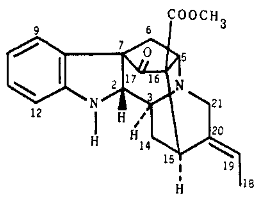

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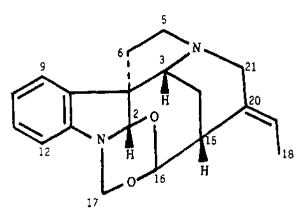

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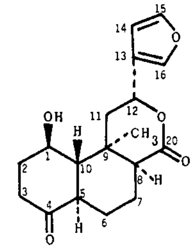

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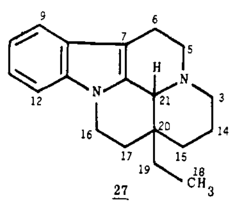

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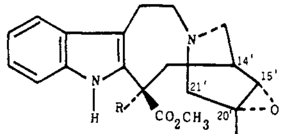

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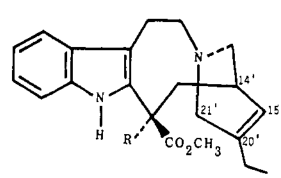

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CHEMICAL CONSTITUENTS OF THE FLORA OF JORDAN

Haplophyllum buxbaumii (Rutaceae) is a yellowish-green perennial herb which is widespread in northern Jordan. As a result of our investigations on the ethanolic extract of the whole plant, we have isolated five new lignan glycosides namely arabelline (17), monoacetylarabelline (18), majidine (19), buxbaumine (20) and qudsine (21). Their structures were established using modern NMR techniques.

A NEW ALKALOID FROM *NEISOSPERMA OPPOSITIFOLIA*

Neisosperma oppositifolia (Apocynaceae), a plant occurring in southern coastal region of Sri Lanka, is a rich source of alkaloids. During the course of our studies on the stem bark of N.oppositifolia, a new oxindole neisosposinine (22), was isolated along with other known compounds.

A NEW ALKALOID FROM *PETCHIA CEYLANICA*

Petchia ceylanica (Apocynaceae) is an evergreen herb indigenous to the lowlands of Sri Lanka and a number of new monomeric and dimeric alkaloids have been reported by us from it (ref. 4,5). A new alkaloid (-)-petchicine (23) has now been obtained and its structure determined with the help of modern spectroscopic methods.

NEW ALKALOIDS FROM *RHAZYA STRICTA*

Rhazya stricta Decaisne (Apocynaceae) is widely distributed in Pakistan and it has been used for the treatment of various ailments. We have previously reported 25 new alkaloids from the plant. We have recently isolated several new alkaloids from R.stricta: 16R-19,20-E-isositsirikine acetate (24), leepacine (25), rhazizine (26) and dihydroeburnamenine (27).

FUNANOID DITERPENE FROM *TINOSPORA MALABARICA*

Tinospora malabarica (Menispermaceae) is cultivated throughout Pakistan and used in the indigenous system of medicine for the treatment of various diseases. The fresh stems of T. malabarica have yielded malabarolonide (28) which is structurally related to a novel furanoid bisnorditerpene, malabarolide reported by us previously.

A NEW PARTIAL SYNTHESIS OF VINBLASTINE FROM LEUROSINE

Vinblastine and vincristine are among the most powerful anti-tumour agents available in medicine for the treatment of a variety of cancers. Leurosine (29) occurs in tenfold higher yields than vinblastine in the leaves. We have previously reported the first partial synthesis of vinblastine (ref. 6) starting from catharanthine and vindoline, two alkaloids first proposed by us to be the biosynthetic precursors to these anti-tumour alkaloids (ref. 7). A one-step conversion of leurosine to anhydrovinblastine (30) has been acheived quantitatively on reaction with chlorotrimethysilane/Zn dust. As anhydrovinblastine has previously been converted by us (ref. 6) and others (ref. 8) into vinblastine, this constitutes an alternative formal synthetic route to vinblastine.

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