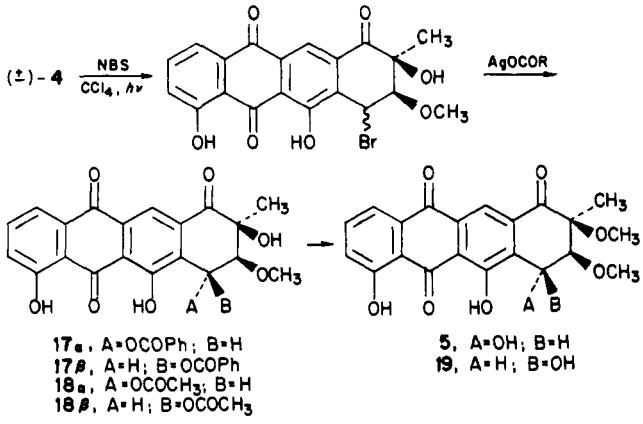
prepared in our laboratory by dithionite reduction of naturally derived aranciamycinone.[11]

Air oxidation of synthetic SM-173B (4) in the presence of base[5] gave intractable products. However, homolytic bromination proceeded smoothly (1.5 equiv of NBS, CCl_4, $h\nu$, 40–45 °C, 1 h) to give 16 which was converted by $AgOCOC_6H_5$ in C_6H_6 (25 °C, 20 m) to an overall 80% yield of 10:1 mixture of 7α/7β-benzoyloxy epimers (17α and 17β). Surprisingly, mild base hydrolysis of this 10:1



17α, A=OCOPh; B=H
17β, A=H; B=OCOPh
18α, A=OCOCH3; B=H
18β, A=H; B=OCOCH3

5, A=OH; B=H
19, A=H; B=OH

mixture gave in nearly quantitative yield a 2:1 mixture of racemic aranciamycinone 5 and its 7β epimer (19). In contrast, reaction of 16 with AgOAc in C_6H_6 (25 °C, 20 min) gave 60–70% of a 10:1 mixture of 7α/7β-acetates (18α and 18β) which with dilute base (1% KOH, aqueous THF, 25 °C, 30 min) gave a corresponding 10:1 ratio of racemic aranciamycinone (5) and its 7β epimer. Hydrolysis of the benzoates (17) but not the acetates (18) thus *takes place in part by alkyl–oxygen scission, probably via a quinone methide mechanism.*

The synthetic (±)-aranciamycinone (5) thus obtained in ca. 60% yield from SM-173B (4) showed TLC and a 400-MHz NMR spectrum [^{1}H NMR ($CDCl_3$) δ 12.73, 11.88 (1 H each, s), 8.41 (1 H, s), 7.91 (1 H, d), 7.76 (1 H, 5), 7.36 (1 H, d), 5.41 (H-7, dd), 3.81 (H-8, d), 3.56 (3 H, s), 3.22 (HO-7, d), 1.52 (3 H, s)] indistinguishable from naturally derived 5 obtained by mild acid hydrolysis[3] of aranciamycin kindly provided by Professor K. Krohn (Braunschweig) and Dr. A. Fujiwara (Nippon Roche).

Efforts to explore the generality of this novel strategy for the synthesis of other anthracyclinones are in progress.[12]

(11) Direct dithionite reduction of natural aranciamycin to SM-173B could not be achieved, although such reductive deglycosidation is common for other anthracyclines (cf. Smith, T. H.; Fujiwara, A. N.; Lee, W. W.; Wu, H. Y.; Henry, D. W. *J. Org. Chem.* **1977**, *42*, 3653).

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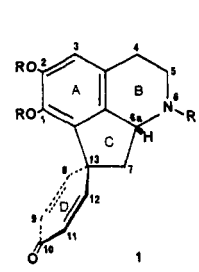
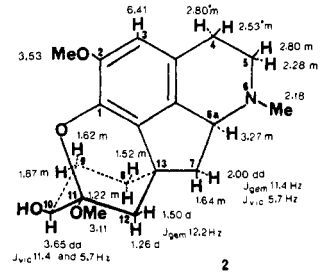
(-)-Misramine: An Unusual Proaporphine Alkaloid

Summary: (-)-Misramine (2), the first pentacyclic proaporphine alkaloid, has been found in Egyptian *Roemeria hybrida* and *R. dodecandra* (Papaveraceae).

Sir: Over 40 naturally occurring monomeric proaporphines are known. These possess skeleton 1. In certain instances, some or all of the double bonds of ring D may be reduced. Proaporphines are optically active and incorporate either the *R* absolute configuration as in 1 or the alternate *S* configuration.[1]



1



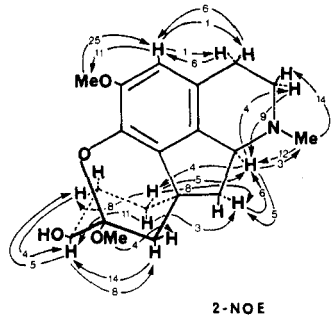
2

We describe the alkaloid (-)-misramine (2), $C_{19}H_{25}O_4N$, mp 103–105 °C (MeOH), found in Egyptian *Roemeria hybrida* (L.) DC. and *R. dodecandra* Stapf (Papaveraceae),[2] which is the first proaporphine to possess a pentacyclic rather than the usual tetracyclic nucleus.

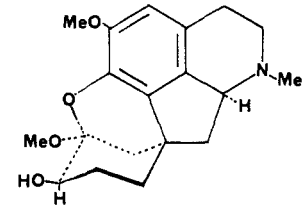
The IR spectrum of misramine is devoid of carbonyl absorption;[3] and the UV spectrum, λ_{max} (MeOH) 231, 285 nm (log ε 4.33, 3.94), is typical of a tetrahydroisoquinoline system possessing two oxygenated substituents on ring A.

The 360-MHz NMR spectrum in C_6D_6 is presented around expression 2. Salient features are an aromatic methoxyl singlet at δ 3.53 and only one aromatic proton in the form of a singlet at δ 6.41. An *N*-methyl absorption falls at δ 2.18, and an aliphatic methoxyl singlet is found relatively upfield at δ 3.11. There is also an aliphatic proton absorption split as a doublet of doublets at δ 3.65 which represents the hydrogen geminal to the alcoholic function.

Assignment of the complex pattern of aliphatic protons in (-)-misramine was made possible by extensive spin decoupling experiments, as well as by a detailed NMR



2-NOE



3

NOEDS study whose results are given in expression 2-NOE.[4] An interconnecting skein of enhancements running from the C-5 to the C-9 hydrogens was of critical importance in settling the relative stereochemistry of the alkaloid, and in eliminating from consideration alternate structure 3. Thus, irradiation of the H-5α absorption at δ 2.28 produced a 9% NOE of the H-6a multiplet at δ 3.27. In turn, irradiation at δ 3.27 led to a 5% enhancement of

(1) For reviews on the proaporphines, see: (a) Stuart, K. L.; Cava, M. P. *Chem. Rev.* **1968**, *68*, 321. (b) Bernauer, K.; Hofheinz, W. *Fortschr. Chem. Org. Naturst.* **1968**, *26*, 245. (c) Shamma, M. "The Isoquinoline Alkaloids"; Academic Press: New York, 1972; Chapter 9. (d) Shamma, M.; Moniot, J. L. "Isoquinoline Alkaloid Research: 1972–1977"; Plenum Press: New York, 1978; Chapter 9.

(2) The above-ground parts of *R. hybrida* were collected in the spring, 30 km west of Alexandria, and weighed 3.3 kg wet. The yield of misramine was 20 mg. The alkaloid was also found in *R. dodecandra*, but in lesser amounts.

(3) (-)-Misramine (2): ν_{max} ($CHCl_3$) 3530, 2470, 1435 cm^{-1}; MS, *m/z* (relative intensity) 332 $(M + 1)^+$ (15), 331 $(M)^+$ (71), 330 (86), 317 (21), 316 (100), 314 (19), 312 (21), 298 (32), 288 (48), 270 (32), 256 (32), 255 (22), 242 (12), 239 (11), 237 (11), 230 (23), 229 (16), 228 (12), 223 (11), 218 (19), 216 (11), 214 (10), 207 (14), 188 (21), 187 (13).

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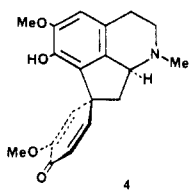
the H-7α signal at δ 2.00 and to a 4% enhancement of the H-8_{eq} multiplet at δ 1.52. It was also possible to interconnect H-8_{eq} (δ 1.52) with H-9_{eq} (δ 1.87) through an 8% NOE. Finally, since H-8_{ax} and H-9_{eq} can be interrelated to H-10_{ax} as shown in diagram **2**-NOE, it follows that the C-10 alcohol is equatorial.

The mass spectrum was in line with the structure assignment for (−)-misramine (**2**). A strong molecular ion (71%), m/z 331, is flanked by an even stronger (86%) m/z 330 peak due to loss of a hydrogen. The base peak, m/z 316, is caused by loss of a methyl from the molecular ion. Another strong peak, m/z 288 (48%), represents the fragment formed from the molecular ion by loss of CH_2-NCH_3 through a retrodiene condensation.[3]

Misramine is levorotatory, $[\alpha]^{25}_D$ −23° (*c* 0.1, MeOH), −26° (*c* 0.1, C_6H_6), −22° (*c* 0.1, acetone), indicating that it possesses the *S* configuration as in expression **2**.[1,5] Additionally, the CD curve of (−)-misramine (**2**) in methanol exhibits $\Delta\epsilon$ (nm) 0 (300), −2.6 (280), −0.6 (225), −5 (242), 0 (230). This pattern with a double minimum is typical of a proaporphine of the *S* configuration possessing a saturated ring D.[6]

The characterization of (−)-misramine (**2**) relates to an interesting facet of proaporphine chemistry. Six "normal" type proaporphine–benzylisoquinoline dimers are known which incorporate an anti relationship between H-6a and the aryloxy substituent on ring D.[7] On the other hand, only two proaporphine–benzylisoquinolines of the alternate "epi" series have been characterized in which H-6a and the ring-D aryloxy substituent lie syn to each other.[7,8] Dimers of the epi series appear to occur less frequently than their counterparts of the normal configuration, although all are known to be present solely among members of the botanical family Berberidaceae.[7,8]

Among the monomeric proaporphines, however, only one alkaloid has been completely characterized which posseses an extra oxygenated function on ring D. This is the Papaveraceae base (−)-orientalinone (**4**) which partakes of the epi configuration[7] and is known to be derived biogenetically from the tetrahydrobenzylisoquinoline (+)-orientaline (**5**).[9]



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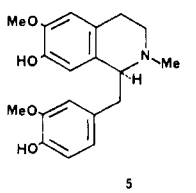
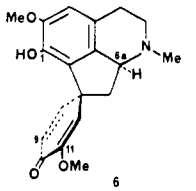


5



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The results presently described indicate that enzymatic oxidation of (+)-orientaline (**5**) may lead to a normal-type monomeric proaporphine such as **6**, which through reduction and intramolecular cyclization can lead to (−)-misramine (**2**) which is also of the normal series.[10] The cyclization to form the fifth ring occurs at C-11 rather than at C-9 since, aside from electronic factors, molecular models and NMR NOEDS studies indicate that for proaporphines or dihydroproaporphines of the *S* configuration the C-1 phenol is closer to C-11 than to C-9.[7] We conclude that the botanical families Papaveraceae and Berberidaceae are both capable of producing proaporphines of the normal as well as of the epi configurations.

Acknowledgment. This research was supported by NSF Grant CHE-8210699 to M.S.

Registry No. **2**, 94801-27-1.

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(8) Weiss, I.; Freyer, A. J.; Shamma, M.; Urzúa, A. *Heterocycles* **1984**, *22*, 2231. *Normal* dimers include (+)-pakistanamine, (+)-valdiberine, (+)-berbivaldine, (+)-valdivianine, (+)-patagonine, and (+)-rupancamine. Epi dimers are (+)-epivaldiberine and (+)-epiberbivaldine.

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Tandem Conjugate Addition–Aldol Reactions Employing 9-(Phenylseleno)-9-borabicyclononane: A Novel Method for Effecting Formal Aldol Condensations at the α-Carbon of α,β-Unsaturated Ketones

Summary: The title compound has been shown to undergo conjugate addition to a variety of α,β-unsaturated ketones to afford β-seleno boron enolates which are convertable to unsaturated ketols upon treatment with aldehydes and subsequent oxidative elimination.

Sir: Over the last several years the general synthetic utility of bifunctional, neutral molecules which contain both hard acid and soft base components has been widely recognized.[2-8] The vast majority of reagents within this category are derived from metals or metalloids (in particular Si and Al) which exhibit a strong affinity for oxygen. In this communication we report the preparation and some of the synthetic applications of the *B*-(phenylseleno)dialkylboranes **1a,b**, members of a new class of highly reactive bifunctional reagents. The synthesis of the selenoborinate reagents **1a,b** can be conveniently accomplished by treating

(1) W.R.L. gratefully acknowledges receipt of an Allied Chemical Dissertation Fellowship.

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