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(−)-SICULININE: A LYCORINE-TYPE ALKALOID FROM *STERNBERGIA SICULA*

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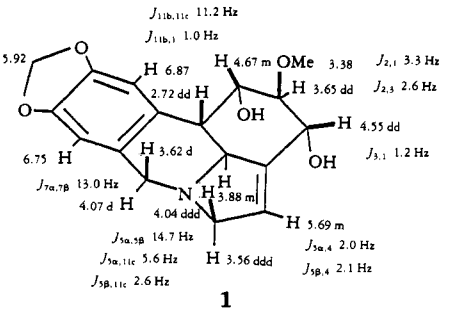
ABSTRACT.—(−)-Siculinine [**2**] was obtained from Turkish *Sternbergia sicula*. (−)-Deacetyllutessine is shown to be identical with (−)-ungiminorine [**1**].

In the wake of our report on the crinine-type alkaloids of *Sternbergia sicula* Tin. ex Guss. and *Sternbergia lutea* Ker-Gawl. ex Schult., we wish to describe the lycorine-type alkaloids obtained from the investigation of these two members of the Amaryllidaceae family. Besides the known (−)-lycorine (1), hippadine (2), and (−)-ungiminorine [**1**], we have isolated and characterized the new alkaloid (−)-siculinine [**2**].

The structure of (−)-ungiminorine [**1**] had been firmly established some years ago through an X-ray analysis (3), as well as through a biomimetic synthesis from (−)-lycorine (4). Even so, reliable high resolution ^{1}H-nmr data for this alkaloid were lacking. We, therefore, initially undertook a complete nmr study of (−)-ungiminorine [**1**], which we thought would assist us in the structure elucidation of the new and related alkaloid (−)-siculinine [**2**]. It was determined that CD_3CN as solvent offered better resolution than $CDCl_3$, and our results have been summarized in Figure 1, around structure **1**. All assignments were supported by interlocking decoupling and nOe measurements.

The signals at δ 2.72 (H-11b), 5.69 (H-4), 5.92 (OCH_2O), 6.75 (H-8), and 6.87 (H-11) are typical values for a lycorine-type system (1). Noteworthy is



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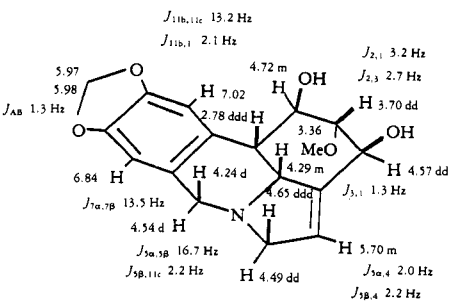

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FIGURE 1. ^{1}H-nmr assignments for compounds **1** and **2**.

the long range W coupling of 1.2 Hz between H-1 (δ 4.67) on the one hand and H-3 (δ 4.55) on the other, indicating that these protons lie in the same plane. But the most telling feature of the spectrum is the 5.6 Hz homoallylic coupling between H-11c (δ 3.88) and H-5α (δ 3.56), which is diagnostic of C-3a, C-4 unsaturation.

Turning now to the new base (−)-siculinine [**2**], its mass spectrum differed from that of **1** only in some of the relative intensities, pointing to a possible diastereomeric relationship between the two compounds (5,6). The CD_3CN nmr spectrum of (−)-siculinine, summarized

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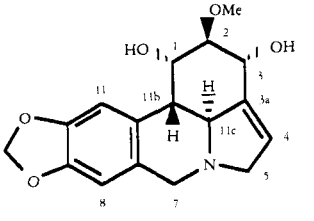
around structure **2** in Figure 1, was quite close to that of **1**. In particular, it indicated a related C-1,2,3 substitution pattern with hydroxyl groups at C-1 and C-3 and a methoxyl at C-2. In this instance, however, no strong homoallylic coupling could be observed between H-11c (δ 4.29) and either H-5α (δ 4.49) or H-5β (δ 4.65). It was, therefore, suspected that the two alkaloids differed in their stereochemistry of fusion for rings B and C.

Indeed, irradiation of (−)-siculinine at δ 2.78 (H-11b) resulted in 39.8% enhancement of the H-11c signal (δ 4.29), pointing to a cisoid orientation for these two protons. Furthermore, long-range W coupling for H-1 (δ 4.72) and H-3 (δ 4.57), as well as strong nOe's between H-11 (δ 7.02) and H-1 (δ 4.72) and between H-3 (δ 4.57) and H-4 (δ 5.70) argued in favor of the all-cis stereochemistry indicated in structure **2**, where ring C is in a near-chair conformation. Significantly, strong allylic coupling between H-3 (δ 4.57) and H-4 (δ 5.70) was lacking because H-3 does not point out in the same direction as the *p* orbitals of the C-3a, C-4 double bond.

The structure of (−)-siculinine [**2**] was then confirmed by a complete nmr nOe study which has been summarized in the Experimental section. Of special interest is the fact that the 2-OMe signal (δ 3.36) showed reciprocating nOe's with H-1 (δ 4.72), H-2 (δ 3.70), and H-3 (δ 4.57). Additionally, H-3 exhibited reciprocating nOe's with H-4 (δ 5.70).

In a recent paper (7), the isolation of (−)-lutessine and (−)-deacetyllutessine from *S. lutea* was described, to which structures **3** and **4**, respectively, were assigned. However, when we compared the specific rotations, mass spectra, and ^{1}H-nmr spectra (in $CDCl_3$) of (−)-deacetyllutessine with those of (−)-ungiminorine [**1**], it became obvious that the two materials are identical. Particularly relevant was the observation that $J_{1,4}$ and $J_{5\alpha,11c}$ in the nmr spectrum of (−)-deacetylutessine, namely, 3.1 Hz and 5.8 Hz, are unlikely for structure **4** and are in fact not reported by the same authors in their nmr spectrum of the related (−)-sternbergine (8). It follows that the name (−)-deacetylutessine should be stricken from the record and should be replaced with the original (−)-ungiminorine [**1**].

The remaining question concerns the true nature of (−)-lutessine, which must be an acetylated derivative of (−)-ungiminorine [**1**]. (−)-3-Acetylungiminorine is already known (9) and from its spectral properties appears to be different from (−)-lutessine. It is likely, therefore, that (−)-lutessine corresponds to (−)-1-acetylungiminorine and possesses structure



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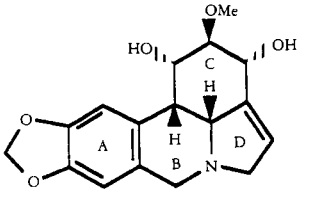

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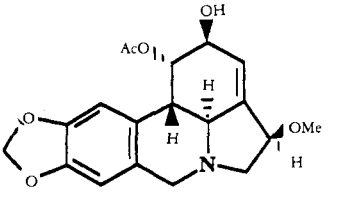

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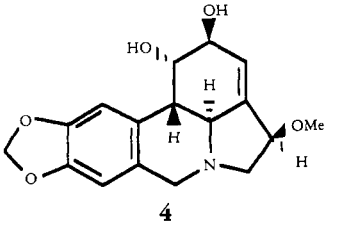

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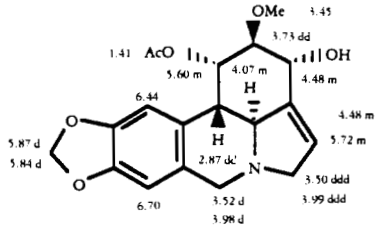
5. A revised interpretation of the nmr spectrum of this alkaloid in $CDCl_3$ is presented around expression **5**. Using the somewhat limited amounts of (−)-ungiminorine at our disposal, a number of unsuccessful attempts were made to obtain **5**. Final confirmation of the structure of (−)-lutessine remains to be achieved.



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EXPERIMENTAL

PLANT COLLECTION AND ALKALOID EXTRACTION.—These are described in detail in Pabuççuoğlu *et al.* (10). Compounds obtained from *S. sicula* were (−)-ungiminorine (25 mg) and (−)-siculinine (15 mg). Compounds from *S. lutea* were (−)-lycorine (1.25 g), hippadine (15 mg), and (−)-ungiminorine (35 mg).

(−)-UNGIMINORINE [**1**].—Significant nmr nOe's are H-1 to H-2 (23%), H-1 to 2-OMe (7%), H-1 to H-11 (50%), H-2 to H-1 (9%), H-2 to 2-OMe (22%), H-2 to H-3 (19%), 2-OMe to H-1 (5%), 2-OMe to H-2 (23%), 2-OMe to H-3 (8%), H-3 to H-2 (18%), H-3 to 2-OMe (10%), H-3 to H-4 (18%), H-4 to H-3 (18%), H-4 to H-5α (12%), H-5α to H-4 (8%), H-5α to H-5β (39%), H-5β to H-5α (37%), H-7α to H-7β (37%), H-7α to H-8 (26%), H-7β to H-11b (19%), H-8 to H-7α (11%), H-11 to H-1 (20%).

(−)-SICULININE [**2**].—Amorphous, $C_{17}H_{19}NO_5$; $[\alpha]_D$ −34° (c = 1.9, MeOH); uv λ max (MeOH) 241, 289 nm (log ε 3.23, 3.38), ir ν max 3400, 910 cm^{-1}; eims *m/z* $[M]^+$ 317 (3), 299 (15), 297 (15), 280 (11), 279 (30), 278 (36), 268 (46), 265 (12), 264 (19), 252 (14), 250 (13), 242 (33), 241 (97), 240 (100), 239 (20), 238 (10), 226 (12), 225 (18), 224 (33), 214 (20), 212 (44), 211 (30). Significant nmr nOe's are H-1 to H-2 (29%), H-1 to 2-OMe (12%), H-1 to H-11 (59%), H-2 to H-1 (9%), H-2 to 2-OMe (30%), H-2 to H-3 (24%), 2-OMe to H-1 (3%), 2-OMe to H-2 (28%), 2-OMe to H-3 (11%), H-3 to H-2 (25%), H-3 to 2-OMe (17%), H-3 to H-4 (25%), H-4 to H-3 (17%), H-4 to H-5α (10%), H-5α to H-4 (12%), H-5α to H-5β (28%), H-5β to H-5α (11%), H-5β to H-7β (8%), H-7β to H-5β (11%), H-7β to H-11b (21%), H-7β to H-7α (38%), H-7α to H-7β (40%), H-7α to H-8 (40%), H-8 to H-7α (14%), H-11 to H-1 (25%), H-11b to H-7β (16%), H-11b to H-11c (40%), H-11c to H-11b (8%).

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