2 (*vicenin*-2 + *vicenin*-1 + *vicenin*-3). Yellow, amorphous powder (MeOH, 80 mg); mp 225–230° (uncorr.); PC, R_f 0.21 (BAW 4:1:2), 0.49 (15% HOAc); UV λ_{max} (see **1**). PM ether: Si gel TLC, R_f 0.38 ($CHCl_3$-EtOAc-Me_2CO, 5:4:1); MS *m/z* (%) 748 ($M_1^{+\cdot}$, 18), 733 ($M_1 - 15$, 33), 717 ($M_1 - 31$, 100), 704 ($M_2^{+\cdot}$, 20), 701 ($M_1 - 47$, 16), 689 ($M_2 - 15$, 22), 685 ($M_1 - 63$, 11), 673 ($M_2 - 31$, 84), 657 ($M_2 - 47$, 13), 645 ($M_1 - 103$, 22), 643 ($M_2 - 61$, 22), 585 ($M_1 - 163$, $M_2 - 119$, 64), 573 ($M_1 - 175$, $M_2 - 131$, 98), 559 ($M_1 - 189$, $M_2 - 145$, 29), 543 ($M_1 - 205$, $M_2 - 161$, 20), 541 ($M_1 - 207$, $M_2 - 163$, 24), 529 ($M_1 - 219$, $M_2 - 175$, 22).

3 (*schaftoside*). Yellow amorphous powder (MeOH, 85 mg); mp 226–228° (uncorr.); PC, R_f 0.28 (BAW 4:1:2), 0.52 (15% HOAc); UV λ_{max} (see **1**). PM ether: Si gel TLC, R_f 0.28 ($CHCl_3$-EtOAc-Me_2CO, 5:4:1); MS, *m/z* (%) 704 (M^+, 31), 689 (M − 15, 35), 673 (M − 31, 100), 601 (M − 103, 25), 585 (M − 119, 19), 573 (M − 131, 25), 541 (M − 163, 40), 529 (M − 175, 50), 515 (M − 189, 27).

4 (*neoschaftoside* + *schaftoside* + 6-C-*hexosylapigenin* 2″-O-*deoxyhexoside*). Yellow amorphous powder (EtOH, 15 mg); PC, R_f 0.32 (BAW 4:1:2) 0.53 (15% HOAc); UV λ_{max} (see **1**). Permethylation and TLC on Si gel gave two bands R_f 0.28 (1) and 0.32 (2). MS (1), *m/z* (%) 704 (M^+, 15), 689 (M − 15, 32), 673 (M − 31, 100), 659 (M − 45, 20), 601 (M − 103, 17), 585 (M − 119, 15), 573 (M − 131, 27), 559 (M − 145, 21), 541 (M − 163, 37), 529 (M − 175, 46), 515 (M − 189, 45), 499 (M − 205, 51), 341 (66). MS (2), *m/z* (%) 704 (M^+, 22), 689 (M − 15, 30), 673 (M − 31, 100), 659 (M − 45, 12), 601 (M − 103, 15), 573 (M − 131, 25), 559 (M − 145, 10), 541 (M − 163, 35), 529 (M − 175, 42), 515 (M − 189, 15).

5 (*isoschaftoside* + *neoisoschaftoside*). Yellow amorphous powder (MeOH); PC, R_f 0.22 (BAW 4:1:2), 0.33 (15% HOAc); UV λ_{max} (see **1**). PC (2% HOAc) R_f 0.22 (isoschaftoside) and 0.10 (neoisoschaftoside).

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TODDALIDIMERINE, A DIMERIC BENZOPHENANTHRIDINE ALKALOID FROM *TODDALIA ASIATICA*[*]

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Key Word Index—*Toddalia asiatica*; Rutaceae; roots; dimeric benzophenanthridine alkaloid; toddalidimerine; dihydrochelerythrine; 8-acetonyldihydrochelerythrine; structural analysis.

Abstract—Toddalidimerine, a new dimeric benzophenanthridine alkaloid, has been isolated from the roots of *Toddalia asiatica.* On the basis of spectral analysis it has been characterized as 1,3-(8-hydrochelerythrinyl-8′-hydro-*N*-norchelerythrinyl) acetone. The presence of dihydrochelerythrine and 8-acetonyldihydrochelerythrine has been confirmed in this plant.

INTRODUCTION

The isolation of corynolamine and bocconoline [1] offered circumstantial evidence to the biogenetic introduction of a carbon unit at C-8 of the benzophenanthridine nucleus. This postulation received further support from the discovery of three dimeric bases, *meso*-1,3-bis(8-hydrosanguinarinyl) acetone (chelidimerine) (**1**) [2], its optically active isomer (sanguidimerine) [3] and 1,3-bis(8-hydrochelerythrinyl) acetone (**2**) [4], each comprising two similar monomeric units. In the present study the isolation of the first benzophenanthridine dimer with dissimilar component units from *Toddalia asiatica* further sustains the above observations. Evidence is presented in this communication for the characterization of the dimer as 1,3-(8-hydrochelerythrinyl-8′-hydro-*N*-norchelerythrinyl) acetone (**3**).

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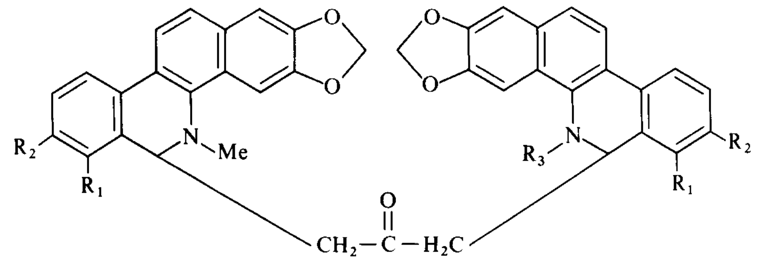
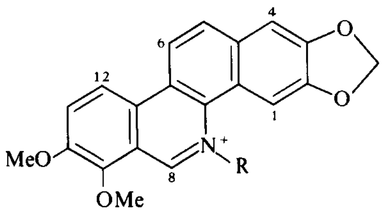


1 $R_1 + R_2 = OCH_2O$, $R_3 = Me$
2 $R_1 = R_2 = OMe$, $R_3 = Me$
3 $R_1 = R_2 = OMe$, $R_3 = H$



4 R = Me, $\Delta^{7,8}$ reduced
5 R = H, $\Delta^{7,8}$ reduced
6 R = Me

RESULTS AND DISCUSSION

The mixture of minor bases from which dihydrochelerythrine (**4**) [5] and 8-acetonyldihydrochelerythrine [6] has been separated on further fractionation afforded the dimer, designated as toddalidimerine (**3**), in 0.0017% yield, mp 307° (CH_2Cl_2–Et_2O); $[\alpha]_D^{20}$ +60° (*c* 2, $CHCl_3$); M^+, *m*/*z* 738.2567 ($C_{44}H_{38}N_2O_9$).

The ill-defined low-field transitions in the ^1H NMR spectrum of **3** included 4 singlets at δ 6.91 (C-4 H), 6.94 (C-4′H), 7.55 (C-1 H) and 7.57 (C-1′ H) and 8 AB doublets at δ 7.37, 7.95 (*J* = 8 Hz, C-5 H, C-6 H); 7.13, 7.72 (*J* = 9 Hz, C-5′ H, C-6′ H); 7.10, 7.54 (*J* = 9 Hz, C-11 H, C-12 H and 6.95, 7.43 (*J* = 8 *Hz*, *C*-11′ H, C-12′ H). Besides the usual resonances for four OMe groups (δ 3.70, 3.75, 3.79 and 3.89 at C-9, C-10, C-9′ and C-10′), two methylenedioxy groups (δ 6.01, 6.09 at C-2, C-3 and C-2′, C-3′) and one *N*-Me group (δ 2.71), the spectrum revealed the presence of a pair of doublets centred at δ 2.92 and 2.99 characterizing the methylenes flanking a carbonyl function (ν_{max} cm^{-1}: 1710 and 1600); one coupled with C-8 H (δ 5.03) and the other with C-8′ H (δ 5.12). This permitted the identification of the two components of **3** as **4** and **5** linked together through a CH_2COCH_2 unit and this is corroborated by the EI high resolution mass spectrum. The presence of the fragment ion at *m*/*z* 391.1410 ($C_{23}H_{21}NO_5$) suggested the cleavage of the molecule accompanying the C-8 H transfer [7]. Subsequent loss of Me_2CO from this fragment afforded an ion of high abundance at *m*/*z* 333.1004 which could also be obtained by the expulsion of a Me radical from the ion at *m*/*z* 348.1237 ($C_{21}H_{18}NO_4$) constituting the base peak. The latter was derived directly from the parent ion without involving H-transfer [4]. Another interesting feature of the spectrum was the absence of fragment ion at *m*/*z* 405 suggesting specific cleavage of the molecule at the side of the dihydrochelerythrine unit of the dimer. The rest of the spectrum displaying fragment ions at *m*/*z* 304.0623 ($C_{18}H_{10}NO_4$), 318.0769 ($C_{19}H_{12}NO_4$) and 290.0826 ($C_{18}H_{12}NO_3$) possessed the usual features of the benzophenanthridine class of alkaloid [4].

An attempted conversion of **3** to **2** by the Eschweiler–Clarke procedure resulted in the isolation of **4** in quantitative yield. Its formation presumably involved the usual *N*-methylation to give **2** which under the influence of acid cleaved to **6**. The latter on attack by hydride ion furnished **4**.

EXPERIMENTAL

All mps are uncorr. The ^1H NMR spectra were recorded at 90 MHz in $CDCl_3$ using HMDS as an int. standard. MS were recorded using a direct inlet system.

Isolation of constituents. Air-dried, powdered roots of *T. asiatica* Lamk. (6 kg) were percolated with 95% EtOH (3 × 7 l.). The residue (800 g) obtained after removal of solvent *in vacuo*, was diluted with H_2O and defatted with hexane (4 × 500 ml). The defatted material was extrd with 2 M HCl (1.4 l.) and the acid layer shaken well with Et_2O (4 × 300 ml) to remove nonbasic material. The aq. acidic layer was basified with NH_4OH and extrd with EtOAc (4 × 300 ml). Removal of solvent under red. pres. yielded a residue (21.5 g) which was chromatographed on a column of basic Al_2O_3 (1 kg) in hexane and eluted with increasing proportions of C_6H_6, followed by EtOAc, to afford dihydrochelerythrine (**4**) (100 mg), mp 190°, 8-acetonyldihydrochelerythrine (20 mg), mp 193° and toddalidimerine (**3**) (60 mg), mp 307° (CH_2Cl_2–Et_2O); $[\alpha]_D^{20}$ +60° (*c* 2, $CHCl_3$); UV λ_{max}^{EtOH} nm: 232 (log ε 5.68), 286 (5.71) and 325 (5.16); IR ν_{max}^{KBr} cm^{-1}: 3470, 1710 and 1600; MS *m*/*z* (rel. int.): 738.2567 (M^+, 4), ($C_{44}H_{38}N_2O_9$), 391.1410 (6), ($C_{23}H_{21}NO_5$), 348.1237 (100), ($C_{21}H_{18}NO_4$), 333.1004 (30), ($C_{20}H_{15}NO_4$), 318.0769 (12), ($C_{19}H_{12}NO_4$), 304.0623 (6), ($C_{18}H_{10}NO_4$) and 290.0826 (16), ($C_{18}H_{12}NO_3$).

Reaction of toddalidimerine (**3**) *with formic acid.* A soln of **3** (10 mg) in HCO_2H (1 ml) and HCHO (1 ml) under reflux (1.5 hr) yielded dihydrochelerythrine (**4**) (7 mg), mp 191°; identical in all respects with an authentic sample.

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