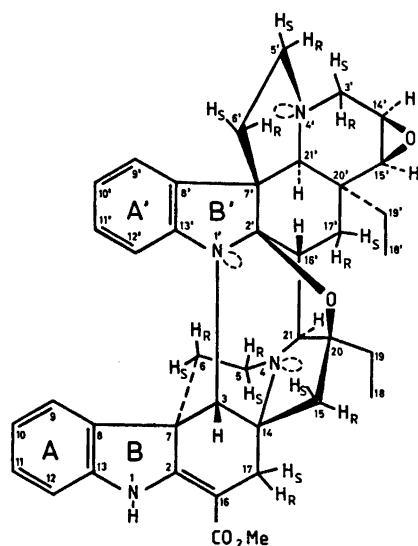


A 400 MHz ¹H NMR Study of the Dimeric Indole Alkaloid Ervafoline

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From the leaves of *Stenosolen heterophyllus* (Vahl.) Mgf (Apocynaceae) several dimeric indole alkaloids have recently been isolated.¹ One of these, ervafoline, was shown by X-ray crystallography to possess the structure *1*. In order to get useful ¹H NMR data for the structure determinations of the other dimeric indole alkaloids present,² we undertook a 400 MHz ¹H NMR study of ervafoline *1*. The results of this NMR study are presented in the present communication.



1

The application of consecutive double resonance experiments permitted all of the 44 protons in ervafoline *1* to be discovered. The chemical shifts and the coupling constants that were assigned are presented in Table 1.

The three-proton singlet resonance at δ 3.75 was assigned to the $-\text{CO}_2\text{Me}$ group. The other singlet signals (one proton each) at δ 9.20, 3.86 and 2.58 were assigned to protons H-1 (NH), H-3 and H-21', respectively.

The doublet signal at δ 3.54 ($J_{21,16'} < 0.3\text{Hz}$) (*vide infra*) was assigned to the proton H-21,

Table 1. ¹H NMR data of ervafoline *1*. Spectra were run in CDCl_3 at 400 MHz. Values are in δ (TMS=0), s, singlet, d, doublet, t, triplet, q, quartet, m, multiplet, br, broad. The coupling constants between the aromatic protons are not included. The Hanson prochirality nomenclature system³ is applied to distinguish between the H-atoms of different $-\text{CH}_2-$ groups.

Chemical shifts

H-3	3.86 s	H _R -3'	3.10 br d
H _R -5	2.8 ^a m	H _S -3'	3.47 dd
H _S -5	3.5 ^a m	H _R -5'	3.10 ^c m
H _R -6	1.8 m	H _S -5'	3.15 ^c m
H _S -6	1.68 br dd	H _R -6'	2.15 br dd
H-9	6.36	H _S -6'	1.24 br dd
H-10	6.35	H-9'	7.17
H-11	6.97	H-10'	6.50
H-12	6.72	H-11'	6.59
H _R -15	2.11 d	H-12'	5.64
H _S -15	2.00 d	H-14'	3.25 br dd
H _R -17	2.94 d	H-15'	3.03 d
H _S -17	2.49 d	H-16'	3.10 br d
H-18	0.96 t	H _R -17'	1.92 dd
H _R -19	1.78 ^b br q	H _S -17'	1.35 dd
H _S -19	1.80 ^b br q	H-18'	0.97 t
H-21	3.54 d	H _R -19'	1.51 ^d dq
CO ₂ Me	3.75 s	H _S -19'	1.63 ^d dq
N-H	9.20 s	H-21'	2.58 s

Coupling constants

$J_{2,3}^{\text{R,S}} \sim 1\text{ Hz}$; $J_{2,3}^{\text{S,S}} = 6.5\text{ Hz}$; $J_{4,5}^{\text{R,S}} = 13.5\text{ Hz}$; $J_{14,15}^{\text{R,S}} = 12\text{ Hz}$; $J_{14,15}^{\text{R,R}} = 17.5\text{ Hz}$; $J_{16,17}^{\text{R,S}} = 7.5\text{ Hz}$; $J_{16,17}^{\text{S,S}} = 7.5\text{ Hz}$; $J_{21,16'} < 0.3\text{ Hz}$; $J_{1,2}^{\text{R,S}} = 14\text{ Hz}$; $J_{1,2}^{\text{R,R}} < 0.3\text{ Hz}$; $J_{2,3}^{\text{S,S}} = 1.5\text{ Hz}$; $J_{1,2}^{\text{R,R}} = 12\text{ Hz}$; $J_{2,3}^{\text{R,S}} \sim 0.5\text{ Hz}$; $J_{2,3}^{\text{S,R}} = 6\text{ Hz}$; $J_{1,2}^{\text{S,S}} = 6\text{ Hz}$; $J_{4,5}^{\text{R,S}} = 15\text{ Hz}$; $J_{4,5}^{\text{R,R}} = 4.5\text{ Hz}$; $J_{16,17}^{\text{R,S}} = 12\text{ Hz}$; $J_{16,17}^{\text{S,S}} \sim 2.5\text{ Hz}$; $J_{17,18}^{\text{R,S}} = 13\text{ Hz}$; $J_{17,18}^{\text{R,R}} = 7\text{ Hz}$; $J_{17,18}^{\text{S,S}} = 7\text{ Hz}$; $J_{17,18}^{\text{R,S}} = 14\text{ Hz}$.

a, b, c, d Assignments can be interchanged.

and the doublet signal at δ 3.03 ($J_{15,14'} = 4.5\text{ Hz}$) to H-15'. The irradiation of the latter signal permitted the identification of H-14' which appeared as a multiple resonance at δ 3.25. Subsequent irradiation at δ 3.25 allowed the identification of both H-3' signals (δ 3.47 and 3.10).

The doublet absorption signals at δ 2.94 and 2.49, and δ 2.11 and 2.00 represent two AX systems (geminal couplings) which were assigned to H_R-17 and H_S-17 (allylic positions) and to H_R-15 and H_S-15, respectively.

The doublet-of-doublet signal at δ 1.35, the triplet-like signal at δ 1.92 and the broad doublet signal at δ 3.10 were found to form a system which could be assigned to H_S-17', H_R-17' and H-16', respectively. The chemical shift of

H_R-17' was assigned on the basis of its proximity to the lone-pair of electrons on $N-1'$. The absorption due to $H-16'$ was assigned on its proximity to the oxygen atom between $C-20$ and $C-2'$, as well as on the basis of a weak coupling with the proton $H-21$. The latter observation confirms the correctness of the assignment of the δ 3.54 signal to $H-21$ (*vide supra*).

The protons of the two ethylene bridges ($C(5)-C(6)$ and $C(5')-C(6')$) form two separate systems which were easily resolved. The distinction between these systems (Table 1) is based on the assumption that the highest field signal (δ 1.24) belongs to H_S-6' as it appears to be the most shielded by the π -system of ring A' .

The triplet signal at δ 0.96 and the quartet signals centered at δ 1.78 and 1.80 were found to form a system which could be distinguished from a similar system comprising a triplet signal at δ 0.97 and two multiple signals centered at δ 1.51 and 1.63. These systems were assigned to the two ethyl side-chains (Table 1). The distinction between these systems was based on the inspection of a molecular model that revealed that, due to steric hindrance to the rotation of the $C(18')-C(19')$ side-chain, the chemical shifts of H_R-19' and H_S-19' can be expected to be clearly different.

The assignment of the aromatic proton signals of *ervafoline 1* has been discussed earlier.¹

As far as we know, the present case is the first one in which it has been possible to assign all the protons in the 1H NMR spectrum of a dimeric indole alkaloid.

Experimental. The NMR spectra were recorded on a laboratory-built 400 MHz 1H high resolution spectrometer (I.E.F. 400)⁴⁻⁶ and obtained by collecting 8 to 64 free-induction decay signals for a 0.01 M solution of the sample in 450 μ l of $CDCl_3$.

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- Henriques, A., Kan-Fan, C., Ahond, A., Riche, C. and Husson, H.-P. *Tetrahedron Lett.* (1978) 3707.
- Henriques, A., Kan-Fan, C., Husson, H.-P. and Lounasmaa, M. *Work in progress*.
- Hanson, K. R. *J. Am. Chem. Soc.* 88 (1966) 2731; Bentley, R. *Molecular Asymmetry in Biology*, Academic, New York 1969, p. 172.
- Gonord, P., Kan, S. and Sauzade, M. *J. Magn. Res.* 24 (1976) 457.
- Kan, S., Gonord, P., Fan, M., Sauzade, M. and Courtieu, J. *Rev. Sci. Instrum.* 49 (1978) 785.
- Lounasmaa, M. and Kan, S. *Tetrahedron. In press*.

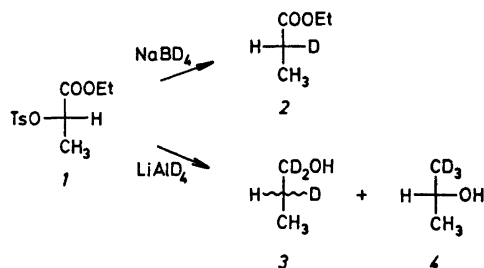
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Deuteride Reduction of Ethyl (S)-2-Tosyloxypropionate

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In connection with stereochemical studies of reactions mediated by citrate synthase, we undertook reductions of ethyl (S)-2-tosyloxypropionate (*1*) with sodium borodeuteride (SBD) and lithium aluminium deuteride (LAD). Since both reactions constituted simple syntheses of versatile, stereospecifically deuterated compounds (*2* and *4* respectively) a detailed account is presented.



Reduction of *1* with SBD was carried out at 100 °C without the use of solvent. Ethyl (*R*)-(2-²H₁)propionate (**2**) and triethyl borate were the principal products. Hydrolysis of **2** gave sodium (*R*)-(2-²H₁)propionate with a slightly weaker specific rotation than that of a sample in which the chirality had been introduced microbially.¹ The specific rotation of the corresponding acid was, however, distinctly stronger than the rotations previously reported for this acid^{2,3} or its enantiomer.²⁻⁴ Sodium cyanoborodeuteride in HMPA (110 °C) has been used in the case of (+)-methyl *O*-mesylmandelate to obtain an analogous substitution.⁵

Reduction of *1* with LAD in refluxing tetrahydrofuran gave a product mixture which contained ethanol, optically active (1,1,2-²H₃)-1-propanol (**3**) and (*R*)-(1,1,1-²H₃)-2-propanol (**4**) in the molar ratios 1.00:0.47:0.52 (GLC). The components were separated by spinning band column distillation and **3** was oxidised to sodium (2-²H₁)propionate which showed $[\alpha]_{D}^{25} = -1.13^\circ$. For the optically pure *R* isomer a value of -3.61° has been estimated.¹ The enantiomeric composition of **3** should thus be 66% *R*, 34% *S*. This low optical purity as well as the formation of **4** can be accounted for by a reduction along the paths in Fig. 1. Support for the view that **5** is formed initially was obtained from a reaction carried out at 23 °C which yielded ethanol but practically no