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 ^{1}H NMR spectrum of a dimeric indole alkaloid.

Experimental. The NMR spectra were recorded on a laboratory-built 400 MHz ^{1}H 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 μl of $CDCl_3$.

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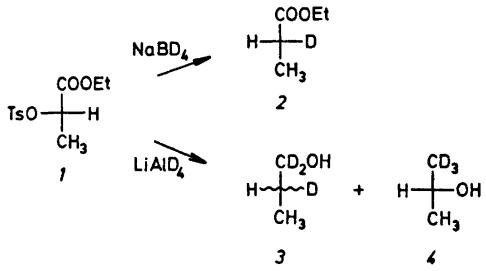
Deuteride Reduction of Ethyl (*S*)-2-Tosyloxypropionate

SVANTE BRANDÄNGE and LARS MÖRCH

Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm, Sweden

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-$^2H_1$)propionate (*2*) and triethyl borate were the principal products. Hydrolysis of *2* gave sodium (*R*)-(2-$^2H_1$)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-$^2H_3$)-1-propanol (*3*) and (*R*)-(1,1,1-$^2H_3$)-2-propanol (*4*) ni 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-$^2H_1$)propionate which showed $[\alpha]_{365}^{23} - 1.13°$. 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

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propanols or ethyl propionate (GLC). If it is assumed that (*R*)-*3* formed by path B is optically pure, then one finds from the ratio *3*/*4* and the enantiomeric composition of *3* that *6* is reductively ring-opened in a 3.3:1 manner (in favour of *4*) and that the importance of path A is about twice that of path B.

Information about a previous reduction of *1* with LAD is given in brief in a review article.[6] Oxidation of the (1,1,2-$^2H_3$)-1-propanol obtained gave a (2-$^2H_1$)propionic acid which was optically impure and it was suggested that the optical impurity was due to a partial racemisation in the reduction step. Another explanation is that some reaction involving path A (Fig. 1) may have occurred.

The enantiomer of *4*, synthesised in five steps from methyl (*S*)-lactate,[7] has been of use in various connections,[7–9] including the synthesis [10] of chirally labelled valine.

Experimental. The isotopic purity of SBD (Merck Sharp & Dohme) was given as min. 98 % and that of LAD (Ciba) as min. 99 %. Analytical GLC was performed on a Porapak Q column (0.2 × 200 cm, 150 °C) and preparative GLC on a similar column (0.4 × 200 cm, 140 °C). The deuterated compounds were assumed to show the same response factors as the nondeuterated ones. Spinning-band column distillations were carried out using a Nester-Faust NFT-51 apparatus. Optical rotations were measured on a Perkin-Elmer 241 polarimeter and a linear relation between optical purity and enantiomeric composition was assumed. Specific rotations of deuterated compounds are not corrected for the small amounts of optically inactive nondeuterated species. NMR spectra were recorded on a JEOL JNM-FX 100 instrument.

Ethyl (S)-*lactate* (Merck-Schuchardt) was distilled at 59–60 °C (2.6 kPa) through the spinning-band column, > 99.9 % purity (GLC, 3 % JXR, 10 % Carbowax 20 M); $\alpha_D^{16.0}$ −10.95°; $\alpha_D^{25.0}$ −11.19°; $\alpha_D^{50.0}$ −11.79° (neat, $l = 1$ dm). Most values of α_D given in the literature are higher and the same applies to the values for samples obtained from two other suppliers. These higher rotations, persistent even after spinning-band column distillation, are due to the presence of ethyl (*S*)-2-ethoxypropionate which was isolated and characterised by ^{1}H NMR and optical rotations (*cf.* Ref. 11). Only the sample from Merck-Schuchardt gave a constant optical rotation for the middle fractions during the distillation. The tosylates prepared from samples of ethyl lactate from the three suppliers showed, however, identical specific rotations.

Tosylate 1 was prepared essentially as described.[12] The product was not distilled but rather crystallised by slow cooling (to −80 °C) of a solution of the crude product in a 1:9 mixture of ether–light petroleum (40–60 °C); colourless needles separated (70–75 % yield). After one recrystallisation they showed m.p. 33–33.5 °C; $\alpha_D^{40.0}$ −52.87°, $\alpha_{436}^{40.0}$ −106.1° (neat, $l = 1$ dm); $[\alpha]_D^{25.0}$ −34.77°, $[\alpha]_{365}^{25.0}$ −103.6° (*c* 1.0, $CHCl_3$); lit.[13] values: m.p. 31.5–32.5 °C; $[\alpha]_D^{20}$ −39.7°; lit. value for the enantiomer [12]: α_D^{40} +25.2° (neat, $l = 50$ mm).

Reduction with SBD. A stirred mixture of *1* (45.3 g, 0.167 mol) and SBD (3.5 g, 0.083 mol) was heated at 100 °C (48 h) under reduced pressure (*ca.* 10 Pa). The volatile products were continuously collected in a trap cooled with liquid nitrogen. The condensate (8.7 g) contained triethyl borate and *2* in the approximate mol ratio 1:2 (NMR), corresponding to a 34 % yield of *2*. One of the fractions taken in the spinning-band column distillation contained 1.65 g of *2* (10 % yield) and showed a purity > 98 % (NMR); $\alpha_D^{25.0}$ −0.63°, $\alpha_{365}^{25.0}$ −2.68° (neat, $l = 1$ dm). ^{1}H NMR ($CDCl_3$): δ 4.13 (q, 2H), 2.30 (1H, t of q, J_1 2.4 Hz, J_2 7.5 Hz), 1.26 (t) and 1.13 (t of d, J_1 1.0 Hz, J_2 7.5 Hz), in all 6H.

Sodium (R)-*(2-$^2H_1$) propionate* was prepared by hydrolysis of *2* with two mol equivalents of sodium hydroxide (0.6 M solution in H_2O–EtOH, 1:1, 25 °C, 25 min). After washing with ether and acidification with hydrochloric acid, the deuteriopropionic acid was extracted with ether. The ethereal extract was neutralised (pH 8) with aqueous sodium hydroxide solution. The solvents were removed and the sodium salt was then dried under high vacuum ($p < 10^{-4}$ Pa); $[\alpha]_D^{25.0}$ −0.88°; $[\alpha]_{365}^{25.0}$ −3.12°; $[\alpha]_{365}^{20.0}$ −3.19° (*c* 10, H_2O). A value of $[\alpha]_{365}^{20}$ −3.36° (*c* 1.9, H_2O) was measured for a sample with a deuterium content of 93 %.[1] The value calculated for the pure compound is thus −3.61°.[1] Vacuum distillation of the above ethereal extract afforded *(R)-(2-$^2H_1$)propionic acid* of approximately 99 % purity (NMR); $\alpha_D^{25.0}$ −0.59°, $\alpha_{546}^{25.0}$ −0.72°, $\alpha_{436}^{25.0}$ −1.41°, and $\alpha_{365}^{25.0}$ −2.68° (neat, $l = 1$ dm); $[\alpha]_D^{25.0}$ −0.93°,

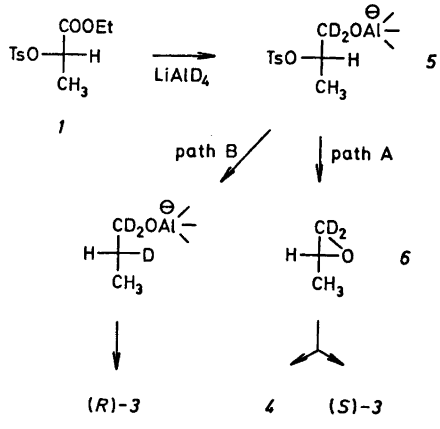

Fig. 1. Principal reaction paths in the reduction of ethyl (*S*)-2-tosyloxypropionate (*1*) with lithium aluminium deuteride.

$[\alpha]_{546}^{25.0}$ −1.13°, $[\alpha]_{436}^{25.0}$ −2.11°, and $[\alpha]_{365}^{25.0}$ −3.75° (*c* 25, H_2O); Measurements in D_2O gave the same values as in H_2O (*cf.* Ref. 3). Lit. values: α_{400} −1.54° (neat);[2] $[\alpha]_{364}^{20}$ −2.4° (neat, $l=1$ dm);[3] $[\alpha]_{365}^{20}$ −2.4° (*c* 25, D_2O);[3] for the enantiomer: $[\alpha]_{400}$ +2° (H_2O).[4]

Reduction with LAD. A solution of *1* (32.6 g, 0.12 mol) in THF (80 ml) was added during 1 h to a refluxing solution of LAD (5.0 g, 0.12 mol) in THF (100 ml) and the mixture was then refluxed for 22 h. After it had been allowed to cool, a mixture of THF (5 ml) and water (5 ml) was added under stirring. The resulting slurry was centrifuged and the solid residue was washed twice with THF containing conc. hydrochloric acid (1.5 ml). The combined THF layers were dried first with $MgSO_4$ then with molecular sieves (4 Å). GLC showed ethanol, *4*, and *3* to be present in the molar ratios 1.00:0.52:0.47. One spinning-band column distillation gave a partial separation of the components; 2.5 g of *4* containing 14 mol-% of ethanol was obtained and 1.5 g of *3* containing 8 mol-% of *4*. An analytical sample of *4* (> 99 % purity, GLC) was obtained by preparative GLC; α_D^{25} −0.068°, α_{546}^{25} −0.080°, α_{365}^{25} −0.234° (neat, $l=25$ mm); lit.[7] values for the enantiomer: α_D^{25} +0.27°, α_{546}^{25} +0.31°, α_{365}^{25} +0.98° (neat, $l=1$ dm). ^1H NMR ($CDCl_3$): δ 4.01 (q, 1H), 1.77 (s, 1H), 1.20 (d, 3H, J 6.1 Hz). Compound *3* was oxidised with Pt/O_2 in sodium hydrogen carbonate solution (23 °C, 70 h)[14] and the sodium salt was prepared as described above, $[\alpha]_{365}^{25}$ −1.13° (*c* 2.5, H_2O).

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