Alternative Synthesis of (±)-Eburunamenine *via* Cleavage of a Cyclic Dithioacetal of an α-Oxo-thione

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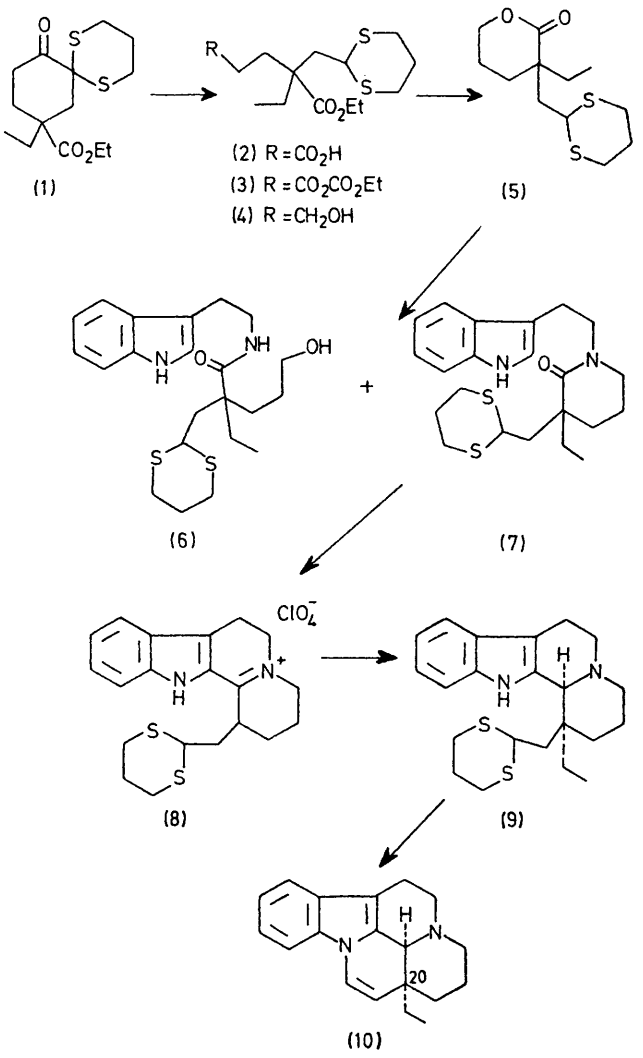
Summary An alternative synthesis of (±)-eburunamenine (**10**) is accomplished using the C-9 lactone (**5**) obtained by cleavage of the cyclic dithioacetal (**1**) as a building block of the non-tryptamine unit.

THE cyclic dithioacetal (**1**) is an efficient building block for the construction of the non-tryptamine unit of aspidosperma-type indole alkaloids.[1] We now describe a further application in which (**1**) serves as the non-tryptamine unit of eburunamine-type alkaloids.[2]

The dithioacetal (**1**)[1] was transformed into the oily C-9 lactone (**5**)† in 56% total yield by the following sequence. Treatment of (**1**) with sodium hydride in ether in the presence of water[3] gave (**2**) which, without purification, was converted into the mixed anhydride (**3**) with ethyl chloroformate in the presence of triethylamine. Crude (**3**) was then treated with sodium borohydride[4] in tetrahydrofuran (THF) to give (**4**) which on acid treatment afforded the lactone (**5**). Fusion of (**5**) with tryptamine at 160 °C afforded the secondary amide (**6**), an oil, in 82% yield and the lactam (**7**), m.p. 153–154 °C, in 6% yield. Cyclization of both compounds to the amorphous perchlorate (**8**) was carried out in refluxing acetonitrile containing phosphoryl chloride, followed by treating the crude reaction mixture with lithium perchlorate.[5,6] Stereospecific reduction of (**8**) to the tertiary amine (**9**), m.p. 185–186 °C, was carried out in 78·5% yield, using lithium tri-t-butoxyaluminium hydride in THF solution.[6] The final ring formation was accomplished by hydrolysing the dithioacetal group of the hydrochloride of (**9**) with an excess of methyl iodide in aqueous acetonitrile[1,7] at room temperature for 30 h‡ to give (±)-eburunamenine (**10**),§ amorphous, in 55% yield. Amorphous (±)-epieburunamenine (**10**; C-20 *epi*) could also be obtained stereospecifically in 50% overall yield from (**8**) by treatment of (**8**) with an excess of methyl iodide in aqueous acetonitrile, followed by reduction with sodium borohydride.



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† Satisfactory analytical and spectral data were obtained for all new compounds.

‡ A mixture of (±)-eburunamenine (**10**) (10%), (±)-eburunamine (**10**; 16,17-dihydro-16α-OH), m.p. 133—136 °C [lit. (K. H. Gibson and J. E. Saxton, *J. C. S. Perkin I*, 1972, 2776) 136—140 °C (34%), and (±)-isoburunamine (**10**; 16,17-dihydro-16β-OH) (3%) was obtained in a shorter reaction time (15 h).

§ Determined as dihydro-derivative: (±)-dihydroeburunamenine, m.p. 99—101 °C (lit. m.p. 100—104 °C). (±)-dihydro*epi*eburunamenine, m.p. 183—184 °C (lit. m.p. 183—184 °C) (see D. L. Coffen, D. A. Katonak, and F. Wong, *J. Amer. Chem. Soc.*, 1974, **96**, 3966).

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