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SYNTHESIS OF (24S)-ETHYL-CHOLESTA-5.22.25-TRIEN-3β-OL

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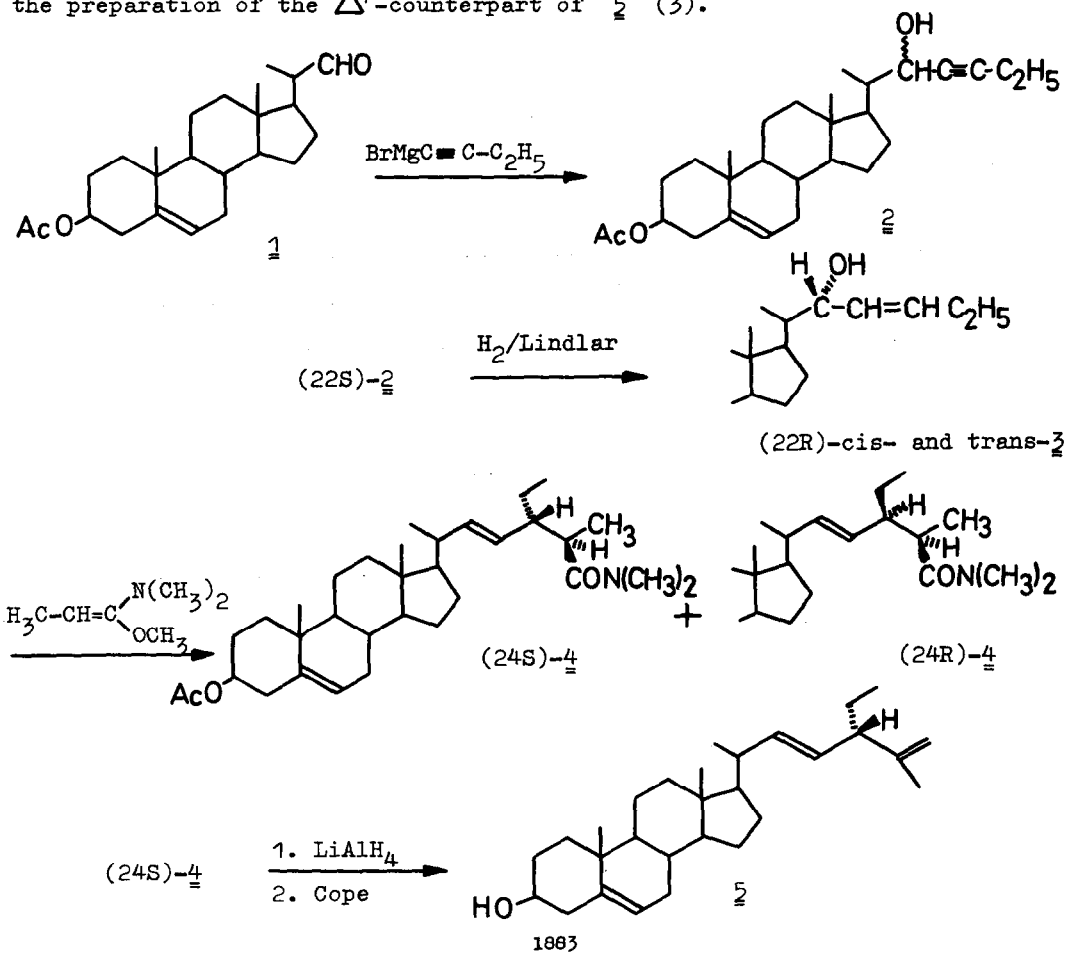
Recently, Bolger, Rees, Ghisalberti, Goad and Goodwin described the isolation of the title sterol 5 from Clerodendrum campbellii, its structure (1) and its biosynthesis from mevalonic acid (2). We wish to report a laboratory synthesis of 5 following the lines of our synthetic scheme for the preparation of the Δ^7-counterpart of 5 (3).



3ß-Acetoxy-22.23-dinor-chol-5-enaldehyde 1 on treatment with butynyl magnesium bromide gave the (22R,S)-carbinol 2. Although the separation of the 2-epimers was remarkably more difficult than in the Δ^7-series, the less polar epimer (22S by Horeau analysis) could be prepared in pure state. Unexpectedly, its hydrogenation with Lindlar catalyst resulted in a mixture of 23-cis- and trans-3 Claisen rearrangement of which with 1-dimethylamino-1-methoxy-prop-1-ene gave two epimeric amides 4. From our stereochemical studies in the Δ^7-series (4) we predict the (24S,25R)-configuration for 4 from 23-cis-3 and the undesired (24R,25R)-configuration for 4 from 23-trans-3. The 4-epimers were separated by thorough chromatography with cyclohexane/ether on alumina, the efficiency being controlled in GLC. The more polar epimer on alumina after reduction with lithium aluminum hydride to the amine and Cope degradation of the corresponding amine oxide gave synthetic 5 identical in all respects (spectra, GLC on two different columns, see also table) with the natural product. The data of compounds 2 - 4 and a detailed discussion of the stereochemistry will be given in the full paper.

Table - Melting points and rotation of natural and synthetic product

	reported (1,2)		found	
	m.p.	$[\alpha]_D$	m.p.	$[\alpha]_D$
5	146°	-37.8°	145.5°	-37.6°
			mixed m.p. 146°	
5-acetate	141°	-	140°	-34.7°

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