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TOTAL SYNTHESIS OF 8-DESOXY-ISOCAESPITOL, A NEW POLYHALOGENATED SESQUITERPENE FROM LAURENCIA CAESPITOSA1)

A.G. González, J.D. Martín, C. Pérez, M.A. Ramírez and F. Ravelo

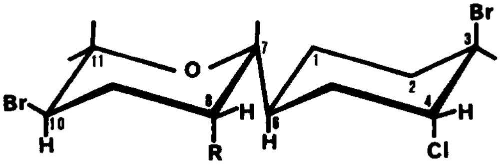
Departamento de Química Orgánica . Universidad de La Laguna
Instituto de Productos Naturales Orgánicos . CSIC . Tenerife . SPAIN

SUMMARY: The structure of a new polyhalogenated bisabolene-type sesquiterpene, 2 , isolated from *Laurencia caespitosa* has been elucidated by chemical and spectral means and confirmed by a three-step synthesis starting from commercial farnesol.

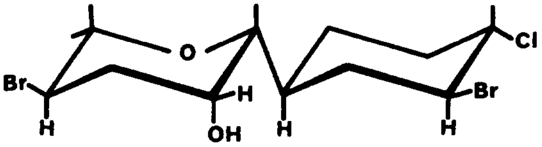
While isocaespitol (1)2) and caespitol (3)3) were the more plentiful of the halogenated sesquiterpenes isolated in our studies of the marine alga *L. caespitosa* Lamx (Rhodomelaceae), repeated silica gel fractionation of the petroleum ether extract yielded 0.0015% (based on dried seaweed weight) of a new polyhalogenated sesquiterpene, 8-desoxy-isocaespitol (2), mp 95-96º, $(\alpha)_D$ -27 . The molecular formula of 8-desoxy-isocaespitol (2), $C_{15}H_{25}Br_2ClO$, was established by elemental analysis and mass spectrometry [m/e 405, 403, 401, 399 (M^+-15); high resolution m/e 398.9727 ($C_{14}H_{22}{}^{79}Br_2{}^{35}ClO$ requires 398.9728)] . The PMR spectrum ($CDCl_3$, δ-value) exhibited signals for four quaternary Me groups (1.20, 1.29, 1.30 and 1.91) and two protons deshielded by halogens, 3.81 (dd, J=12 & 6 Hz) and 4.45 (t, J=3.5 Hz). Treatment of 8-desoxy-isocaespitol (2) with Zn/AcOH at r.t. gave the compound 4 4) as an oil in 94% yield.

The structure of 2 was confirmed by synthesis. N-Bromosuccinimide oxidation of commercial farnesol acetate in aqueous tetrahydrofuran5) provided the terminal bromohydrin 6, which, on treatment with $LiClO_4 \cdot 3H_2O$-Ac_2O-AcOH6) at r.t. for 48 hrs, gave the racemic mixture of compounds, 4 (9%), 8 (20%) and 9 (15%). When anhydrous $LiClO_4$ was used, the diacetate 7 was obtained in 95% yield.

Treatment of the synthetic racemate 4 with bromine chloride7) at -78º gave a 1:2 mixture of (±)-8-desoxy-isocaespitol (2) and its isomer 5 in 54% overall yield. (±)-8-Desoxy-isocaespitol was successfully isolated as the less soluble component by fractional crystallization from n-hexane, mp 94-96º, and proved identical (except for optical rotation) with natural 2, (TLC, IR, PMR and MS comparison). The racemate 5 was undoubtedly produced8) although we could not isolate it from the mixture.



1 R=OH
2 R=H



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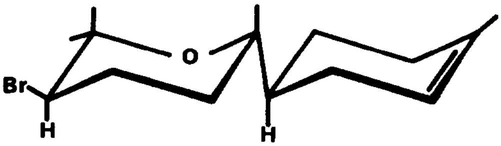

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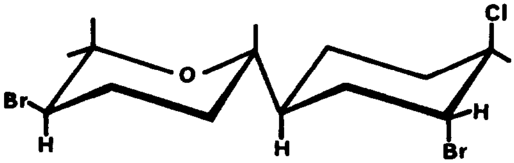

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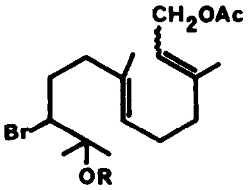
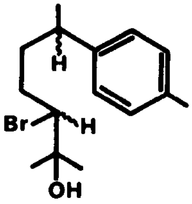


6 R=H
7 R=Ac



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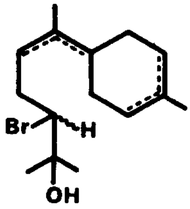

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4) Compound 4, oil, $(\alpha)_D$-9, $C_{15}H_{25}BrO$, M^+ at m/e 302, 300; PMR, 1.16, 1.27, 1.30 and 1.62 (s, 3H each), 3.90 (dd, 1H, J=16 & 6 Hz) and 5.40 (bs, 1H, $W_{1/2}$=7 Hz).

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