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A NOVEL PARTIAL SYNTHESIS OF (-)-WARBURGANAL

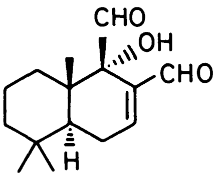
Iván RAZMILIC, Jorge SIERRA, José LOPEZ, and Manuel CORTES*
Facultad de Química, Pontificia Universidad Católica de Chile, Casilla 6177, Santiago, Chile

A short synthesis of (-)-Warburganal, from (+)-confertifoline through the α-epoxide is described.

Warburganal (**1**) is a natural product isolated from the East African tree *Warburgia ugandensis*.[1)] This sesquiterpene has attracted considerable synthetic interest because of its potent biological properties[2,3)] and several efficient routes to racemic **1** have been reported.[4)] However, the only synthesis of optically active Warburganal (**1**) has been described by Okawara et al.[5)] starting from ℓ-abietic acid, in fourteen steps.

We now wish to report a novel partial synthesis of (-)-**1**, in four steps using (+)-confertifoline (**2**)[6)] as starting material.

The lactone **2** was reduced with lithium aluminium hydride in ether at room temperature to give the olefinic diol **3**[7)] almost quantitatively. Epoxidation of diol **3** with m-chloroperbenzoic acid in methylene chloride solution at 0 °C gave a mixture of α and β epoxides in a ratio of about 7:3, which was separated by column chromatography (Silica gel). The major and less polar compound was the α epoxide **4**[8)] (67% yield from **3**; mp 86-87 °C; $[\alpha]_D^{24}$ +56° (c 0,5, $CHCl_3$)). The C7-C8 double bond was introduced next by reaction of **4** in diethyl ether at -20 °C with lithium diethylamide[9)] for 24 h, from which the allylic alcohol **5** was obtained in 30% yield. The optical rotation and spectral data of compound **5** were identical with those of the chiral triol previously obtained in this laboratory[10)] from (-)-drimenol. Oxidation of triol **5** with DMSO-trifluoracetic anhydride according to the known procedure[4)] gave (-)-Warburganal (**1**) (64% yield; mp 106-107 °C, $[\alpha]_D^{24}$ -260° (c 0.22, $CHCl_3$)). The spectral data are in good agreement with natural warburganal[2)], and the value of the optical rotation was almost indentical with those reported by Okawara.[5)]



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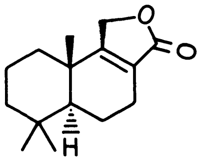

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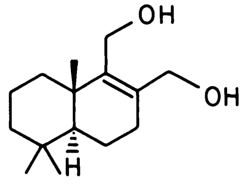

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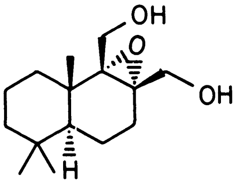

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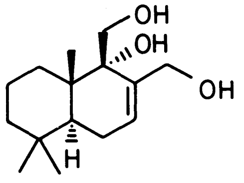

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Although the overall yield of this sequence is 13%, we have developed a short synthesis of (-)-Warburganal, starting with a substrate previously synthesised as chiral form.[11]

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