A New Diterpene Skeleton from a Boron Trifluoride–Diethyl Ether-catalysed Rearrangement of Methyl Isopimarate 8,9-Epoxide

Martine Taran and Bernard Delmond*

Institut du Pin, Université de Bordeaux I, 351 cours de la Libération, 33405 Talence Cedex, France

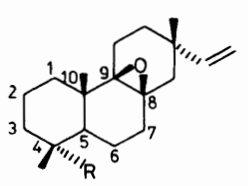
A backbone rearrangement, forming compounds with a new diterpene skeleton, is reported.

In previous papers dealing with the reactivity of trisubstituted diterpene epoxides towards boron trifluoride–diethyl ether[1] and active alumina[2] we have reported backbone rearrangements of isopimarane derivatives. In this paper we describe a rearrangement of a tetrasubstituted epoxide leading to a new tetracyclic diterpene skeleton.

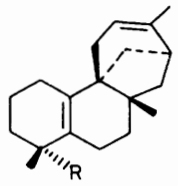
The 8,9β-epoxide of methyl isopimarate (**1**) on treatment with boron trifluoride–diethyl ether at room temperature yielded a mixture of carbonyl compounds (23%) and alkenes (74%) which were separated by chromatography. From the alkene component, compounds (**2**) (34%) and (**3**) (13%) were obtained *via* further chromatography over 10% $AgNO_3$-

impregnated silica gel. Their structures were assigned on the basis of spectral data.

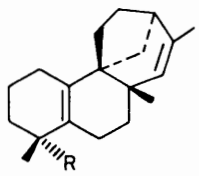
The most striking feature of the ^1H n.m.r. spectrum of compound (**2**) is the absence of any signal corresponding to a vinyl group (–CH=CH_2); the spectrum exhibited a multiplet at δ 5.17 ($w_{1/2}$ 8 Hz, 1 olefinic proton), a doublet (J 2 Hz, 3H) at δ 1.64 due to an olefinic methyl group, and three singlets at δ 1.02 (Me), 1.24 (Me) and 3.66 (–CO_2Me).



(1)

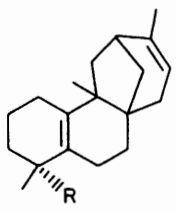


(2)

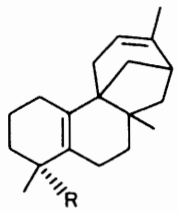


(3)

R = CO_2Me



(A)



(B)

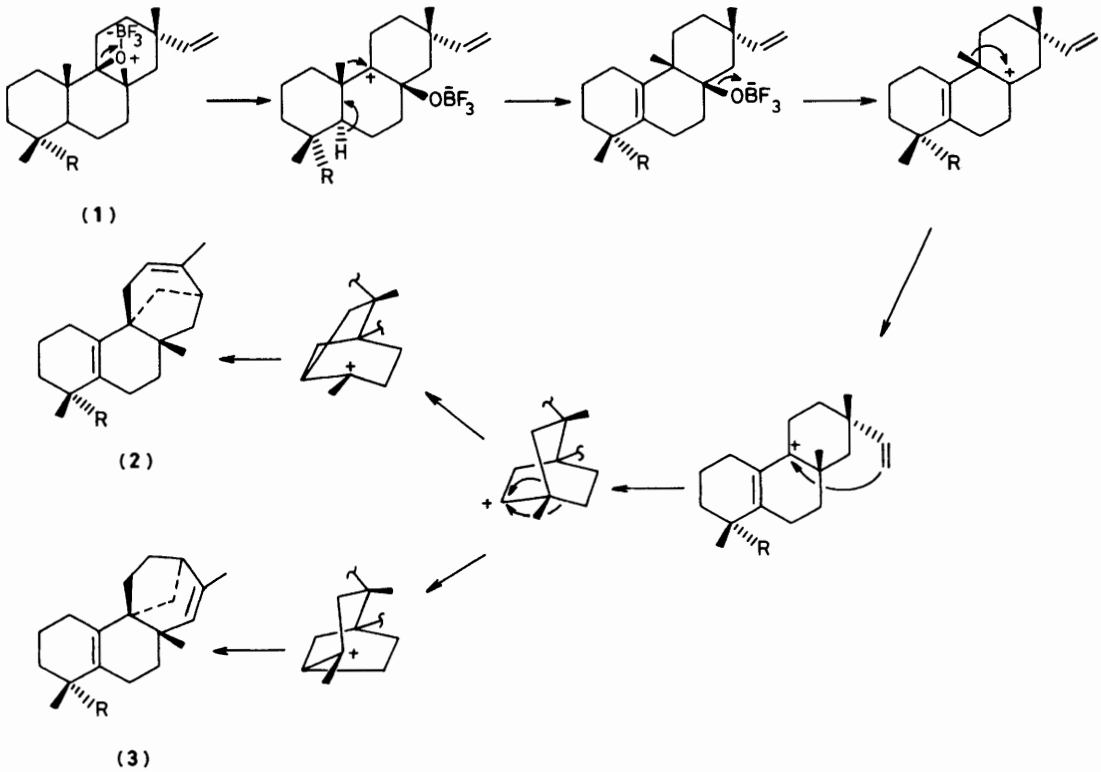
The ^{13}C n.m.r. spectrum revealed the presence of a tetrasubstituted double bond and therefore a tetracyclic structure for this compound is proposed. The tetrasubstituted double bond was shown to be at C-5–C-10 by mass spectroscopy. This assignment was supported by the chemical shift of the methyl group on C-10 (δ 24.4).[3] The spectral data are consistent with two possible structures, (A) and (B); a single-crystal X-ray analysis[4] established structure (B) in which the methyl group is located at C-8.

The ^1H n.m.r. spectrum of compound (**3**) indicated the absence of an ABX system (–CH=CH_2) and exhibited a singlet at δ 4.77 ($w_{1/2}$ 3 Hz) arising from a proton on a trisubstituted double bond and a doublet (J 2 Hz) at δ 1.64 due to an olefinic methyl group.

Analysis of the ^{13}C n.m.r. spectrum of (**3**) shows that it possesses a tetracyclic structure in which a tetrasubstituted double bond is located at C-5–C-10 (δ_{Me} 24.4). Furthermore, a low power off-resonance decoupling experiment indicated that quaternary carbons C-8 and C-9 exhibit long-range coupling (^2J and ^3J respectively) with the olefinic proton. The tetracyclic structure (**3**) assigned to this compound is supported by these spectral data.

The proposed mechanism (Scheme 1) by which (**2**) and (**3**) are produced involves a cyclisation by interaction of the vinyl group and cationic centre C-9, followed by rearrangement of a bridged ion intermediate.

This rearrangement of the isopimarate 8,9-epoxide (**1**) represents a new transformation of a diterpene skeleton. The nature of the bicyclo[3.2.1]octane moiety constituting the C/D ring system means that compounds (**2**) and (**3**) can be related to stemodane and stemarane diterpenes, including the antiviral and tumour-inhibitory aphidicolin.[5,6] This rearrange-



Scheme 1. Proposed mechanism of formation of compounds (**2**) and (**3**) from (**1**).

ment could provide a chemical test for the biosynthesis of aphidicolin.[7,8] As far as we know, there is only one recent report[9] in the literature of such a biomimetic method.

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