

SELECTIVE METHYL AND METHYLENE MIGRATION IN THE EPOXY  
DERIVATIVES DERIVED FROM 1-ABIETIC ACID<sup>1</sup>

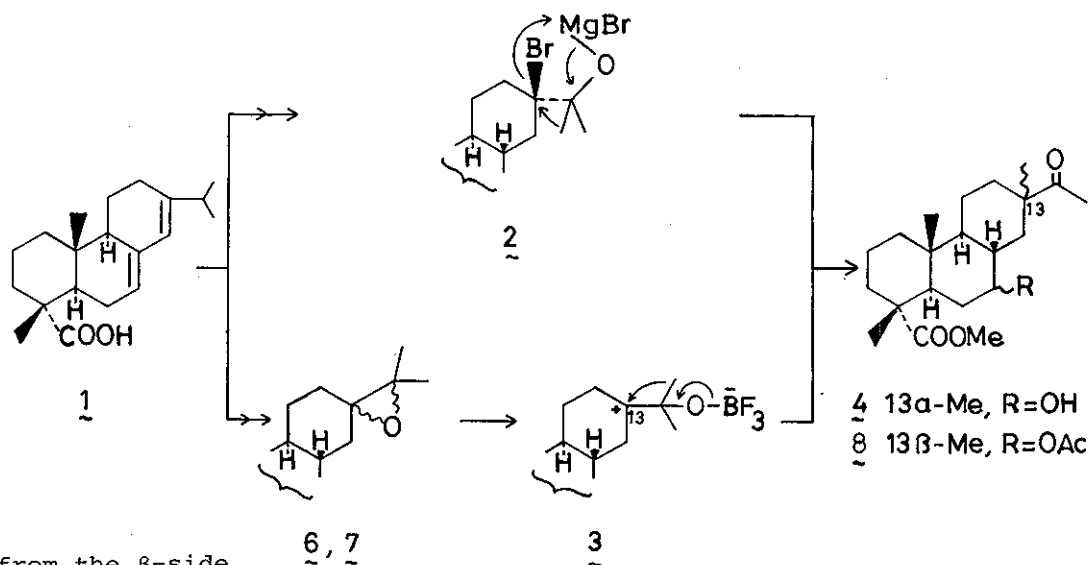
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The  $\alpha$ -epoxide (6) derived from 1-abietic acid (1) caused a stereoselective methyl migration to its 13 $\beta$ -position giving 8 in 54.2 % yield on  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  treatment in benzene. On the other hand, the  $\beta$ -epoxide (7) gave rise to a methylene migration to give 9 or 10 in 63.5 % yield. The 13 $\beta$ -methyl derivative (8) was converted to isohibane (13).

Resently, we reported a stereoselective migration of isopropyl-methyl group to the 13 $\alpha$ -position in a concerted manner via a magnesium salt of the bromohydrin (2) derived from 1-abietic acid (1) (1  $\rightarrow$  2  $\rightarrow$  4).<sup>2</sup> However, this method cannot be applicable to the synthesis of steroidal skeletons because the 13-methyl group thus introduced possesses the opposite configuration to that of steroids.

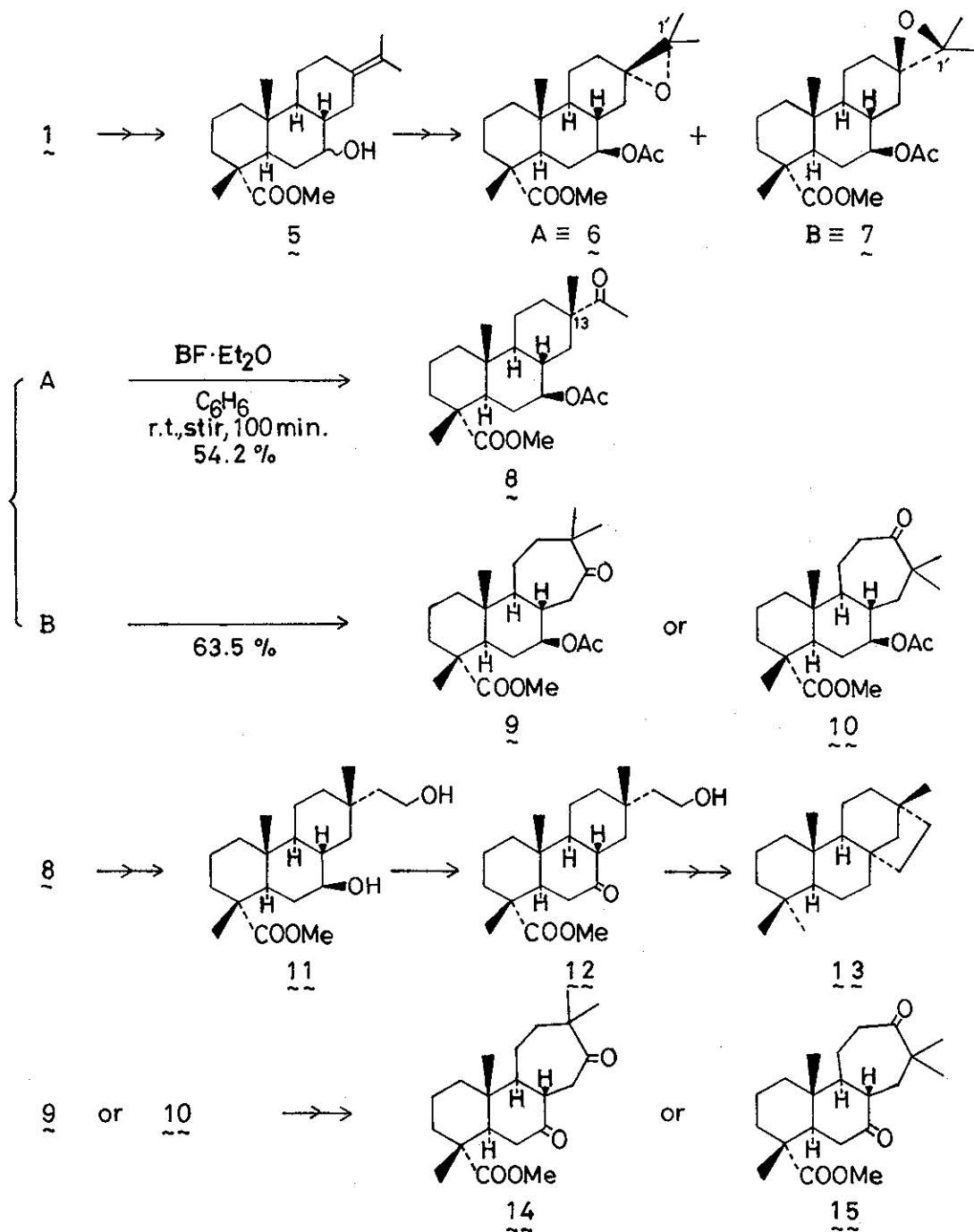
Now, we examined the reaction of epoxides (6, 7) derived from 1 with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  expecting the formation of a carbonium ion (cf. 3) and the subsequent migration of the methyl group to the C-13 position<sup>3</sup>



The tetrasubstituted olefin (5), the same intermediate as used in the formation of the 13 $\alpha$ -methyl derivative (4),<sup>2</sup> was acylated with Ac<sub>2</sub>O-pyridine and oxidized with *m*-chloroperbenzoic acid to give two epoxides, (A) ( $\delta$ : 1.32, 1.32 (s, 1'-Me), 4.55 (m, W/2=13 Hz, 7 $\alpha$ -H), M<sup>+</sup>: 392) and (B) ( $\delta$ : 1.28, 1.28 (s, 1'-Me), 4.55 (m, W/2=13 Hz, 7 $\alpha$ -H), M<sup>+</sup>: 392).

The former (A) was treated with BF<sub>3</sub>·Et<sub>2</sub>O in benzene for 100 min. giving exclusively the methyl migration product (8) (bp 110° (0.0005 mmHg),  $\delta$ : 1.10 (s, 13-Me), 2.09 (s, COCH<sub>3</sub>),  $\nu_{\text{max}}$ : 1740 (shoulder), 1735, 1710) in 54.2 % yield. On the other hand, the same treatment of the latter (B) gave only the methylene migration product (9 or 10) (mp 162-163°,  $\delta$ : 1.03, 1.04 (each s, 13- or 14-(Me)<sub>2</sub>),  $\nu_{\text{max}}$ : 1740, 1730, 1710) in 63.5 % yield. It is noticeable that the two isomeric epoxides afforded completely different products on BF<sub>3</sub>·Et<sub>2</sub>O treatment.

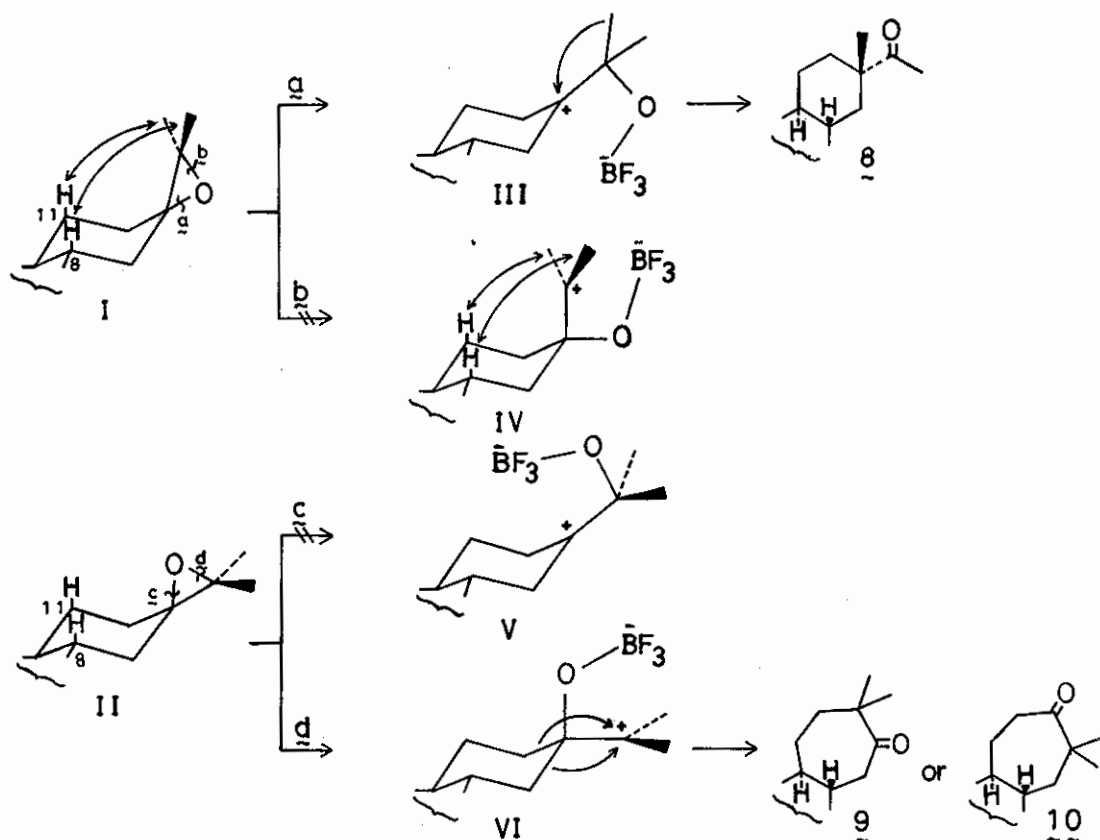
In order to determine the configuration of the 13-methyl group, a conversion of 8 into isohibane (13) of a known structure was carried



out. The methyl ketone (**8**) was treated successively with  $\text{NaBH}_4$ ,  $\text{MsCl}$ -pyridine,  $\text{KOH-MeOH-H}_2\text{O}$  and  $\gamma$ -collidine and the resulting vinyl derivative was subjected to hydroboration to give **11** containing 2/3 molar equivalent of crystal water (mp  $115-116^\circ$ ,  $\delta$ : 3.73 (t,  $J=7.5$  Hz, 2'-H),  $\nu_{\text{max}}^{\text{nujol}}$ : 3540, 3340 (b), 1705).<sup>4</sup> The diol (**11**) was oxidized with NBS in  $t\text{-BuOH-H}_2\text{O}$  to give **12** ( $\delta$ : 3.75 (t,  $J=8$  Hz, 2'-H),  $\nu_{\text{max}}$ : 3630, 3400 (b), 1730, 1710; 2,4-DNP: mp  $178-179^\circ$ , mixed mp  $178-179^\circ$ ). The physical data of **12** were identical with those of the authentic sample<sup>5</sup> having the  $13\beta$ -methyl group. The  $\beta$ -configuration of the 13-methyl group was thus confirmed and the methyl migration of A was found to proceed stereoselectively. As the conversion of **12** to **13** has already been accomplished,<sup>5</sup> the present synthesis of **12** means the stereoselective synthesis of isohibane (**13**) from 1-abietic acid (**1**) via the isopropyl-methyl migration.

The presence of the seven membered ring in **9** or **10** was confirmed by its conversion to the known compound (**14** or **15**).<sup>2</sup> In order to examine whether this ketone has the structure **9** or **10**, an introduction of a double bond adjacent to the carbonyl group by bromination-dehydrobromination or oxidation by DDQ or  $\text{SeO}_2$  was attempted but no desired product was obtained.

The structures of A and B were determined based on the mechanistic consideration concerning the formation of **8** and **9** or **10** from the  $\alpha$ - and  $\beta$ -epoxides (I and II), respectively. In the  $\alpha$ -epoxide (I), the cleavage should proceed through route a affording **8** since a steric interaction between the 8- and 11-hydrogens and the *gem*-dimethyl group was expected to be released when carbonium ion (III) was produced in the transition state. On the other hand, an interaction between these groups would be



seriously increased when the cleavage of I occurred at  $b$  (cf. IV).

The fact that the migration of methyl group took place exclusively from the  $\beta$ -side affording **8** suggests that the intermediate involves a tight ion pair such as III or proceeds through a concerted mechanism. In the  $\beta$ -epoxide (II), a steric interaction between two hydrogens at C-8 and C-11 and the epoxide oxygen is assumed to be not so serious than that in the  $\alpha$ -isomer and thus the reaction pathway would be governed by the stability of the intermediary carbonium ion. Since the carbonium ion (VI) is expected to be more stable than V, it is reasonable that a migration took place through route d to afford the seven membered ketone, **9** or **10**. Based on the above consideration, the compound A to

afford **8** was assigned as the  $\alpha$ -epoxide (**6**), and the compound B to afford **9** or **10**, the  $\beta$ -isomer (**7**).

It is noteworthy that the  $13\alpha$ -<sup>2</sup> and  $13\beta$ -methyl derivatives were obtained stereoselectively from the same intermediate (**5**). The present reaction would be extended to the syntheses of sandaracopimaric acid and steroids.

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#### REFERENCES

- 1 New compounds indicated by mp or bp gave satisfactory analytical values. NMR ( $\delta$ ) and IR ( $\nu_{\max}$ ) spectra, when not mentioned, were measured at 100 MHz in  $\text{CDCl}_3$  vs.  $\text{Me}_4\text{Si}$  as internal reference and in  $\text{CCl}_4$ , respectively.
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- 4 The compound **11** recrystallized from  $\text{EtOH-H}_2\text{O}$  contains 2/3 molar equivalent of crystal water and thus its melting point (115-116°) is different from that of the compound synthesized by another route.<sup>5</sup>
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