

SELECTIVE METHYL AND METHYLENE MIGRATION IN THE EPOXY
DERIVATIVES DERIVED FROM *l*-ABIETIC ACID¹

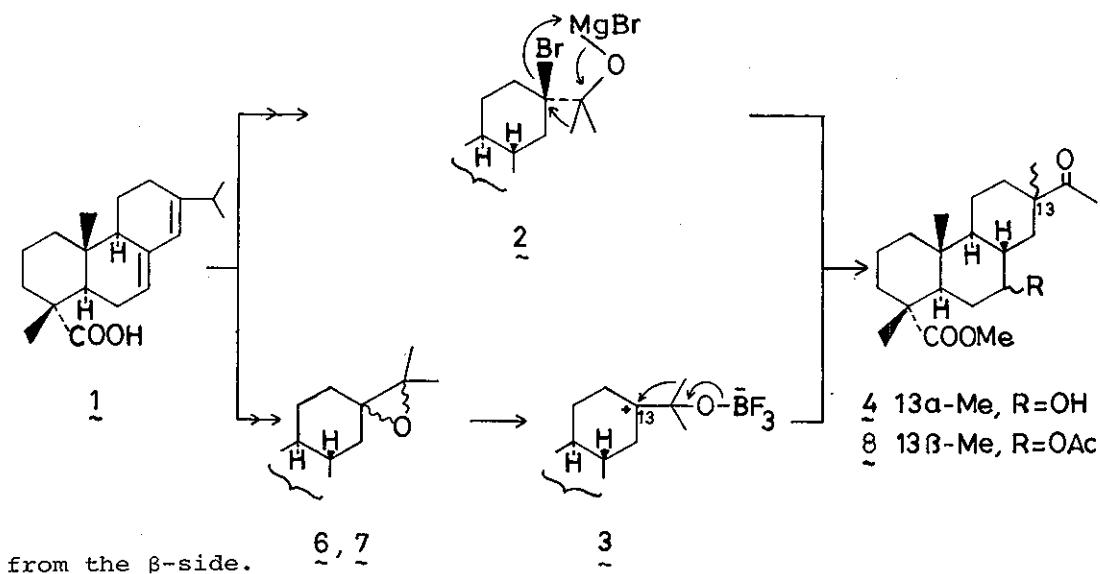
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The α -epoxide (δ) derived from *l*-abietic acid (l) caused a stereoselective methyl migration to its 13β -position giving δ in 54.2 % yield on $BF_3 \cdot Et_2O$ treatment in benzene. On the other hand, the β -epoxide (γ) gave rise to a methylene migration to give γ or $\lambda\delta$ in 63.5 % yield. The 13β -methyl derivative (δ) was converted to isohibane (l_3).

Recently, we reported a stereoselective migration of isopropyl-methyl group to the 13α -position in a concerted manner via a magnesium salt of the bromohydrin (γ) derived from *l*-abietic acid (l) ($l \rightarrow \gamma \rightarrow \delta$).² However, this method cannot be applicable to the synthesis of steroid skeletons because the 13 -methyl group thus introduced possesses the opposite configuration to that of steroids.

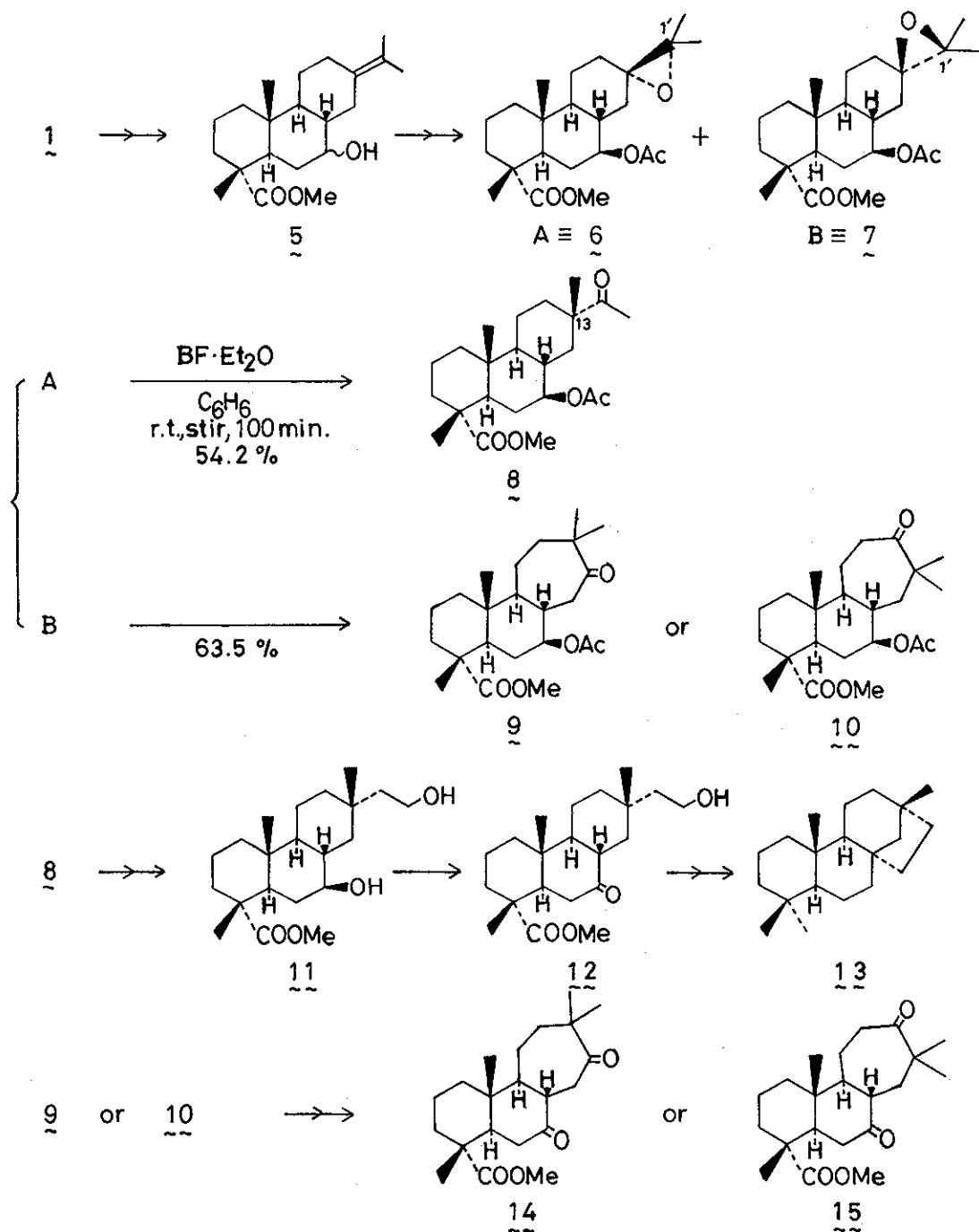
Now, we examined the reaction of epoxides (δ , γ) derived from l with $BF_3 \cdot Et_2O$ expecting the formation of a carbonium ion (cf. β) and the subsequent migration of the methyl group to the C-13 position³



The tetrasubstituted olefin (δ), the same intermediate as used in the formation of the 13α -methyl derivative (4),² was acylated with Ac_2O -pyridine and oxidized with *m*-chloroperbenzoic acid to give two epoxides, (A) (δ : 1.32, 1.32 (s, $1'\text{-Me}$), 4.55 (m, $W/2=13$ Hz, $7\alpha\text{-H}$), M^+ : 392) and (B) (δ : 1.28, 1.28 (s, $1'\text{-Me}$), 4.55 (m, $W/2=13$ Hz, $7\alpha\text{-H}$), M^+ : 392).

The former (A) was treated with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in benzene for 100 min. giving exclusively the methyl migration product (8) (bp 110° (0.0005 mmHg), δ : 1.10 (s, 13-Me), 2.09 (s, COCH_3), ν_{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° , δ : 1.03, 1.04 (each s, 13- or $14\text{-}(\text{Me})_2$), ν_{max} : 1740, 1730, 1710) in 63.5 % yield. It is noticeable that the two isomeric epoxides afforded completely different products on $\text{BF}_3 \cdot \text{Et}_2\text{O}$ treatment.

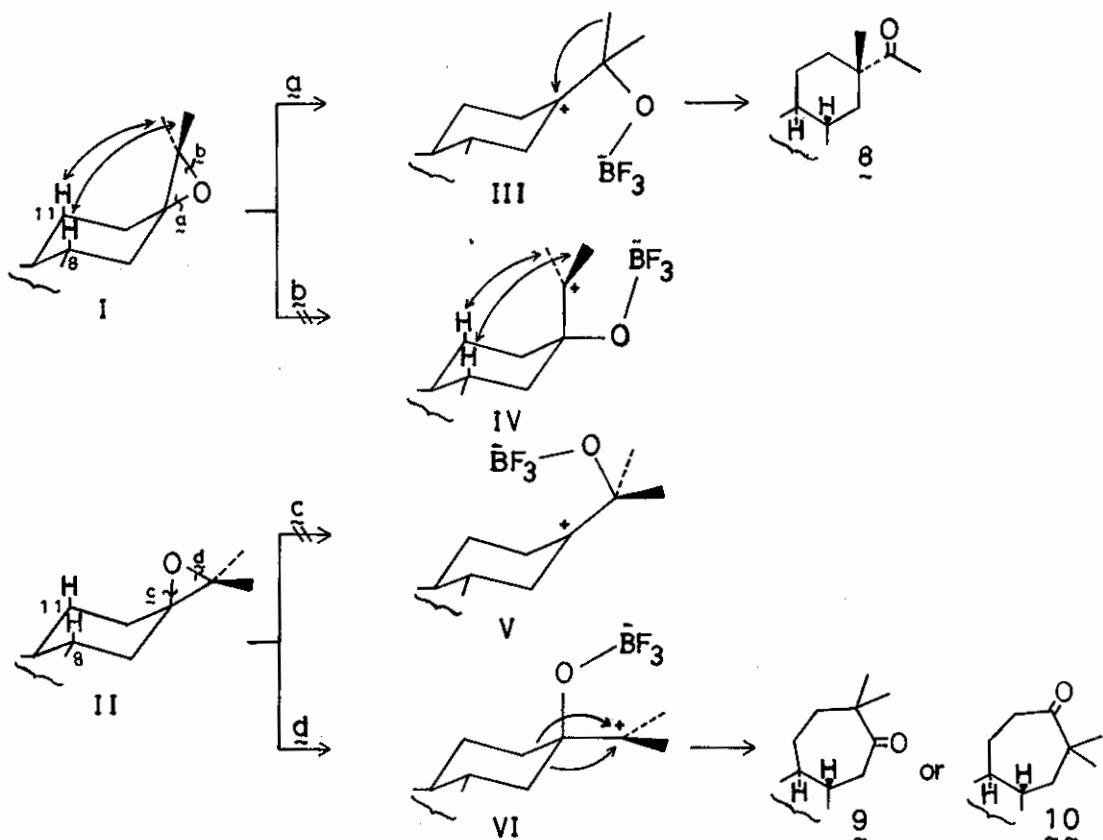
In order to determine the configuration of the 13 -methyl group, a conversion of 8 into isohibane (13) of a known structure was carried



out. The methyl ketone (8) was treated successively with NaBH_4 , MsCl -pyridine, $\text{KOH-MeOH-H}_2\text{O}$ and γ -collidine and the resulting vinyl derivative was subjected to hydroboration to give 11 containing 2/3 molar equivalent of crystal water (mp 115-116°, δ : 3.73 (t, $J=7.5$ Hz, 2'-H), $\nu_{\text{max}}^{\text{nujol}}$: 3540, 3340 (b), 1705).⁴ The diol (11) was oxidized with NBS in $t\text{-BuOH-H}_2\text{O}$ to give 12 (δ : 3.75 (t, $J=8$ Hz, 2'-H), ν_{max} : 3630, 3400 (b), 1730, 1710; 2,4-DNP: mp 178-179°, mixed mp 178-179°). The physical data of 12 were identical with those of the authentic sample⁵ having the 13β -methyl group. The β -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,⁵ the present synthesis of 12 means the stereoselective synthesis of isohibane (13) from *l*-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).² 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 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 α - and β -epoxides (I and II), respectively. In the α -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 β -side affording 8 suggests that the intermediate involves a tight ion pair such as III or proceeds through a concerted mechanism. In the β -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 α -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 δ was assigned as the α -epoxide (6), and the compound B to afford γ or δ , the β -isomer (7).

It is noteworthy that the 13α -² and 13β -methyl derivatives were obtained stereoselectively from the same intermediate (5). The present reaction would be extended to the syntheses of sandaracopimamic acid and steroids.

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REFERENCES

- 1 New compounds indicated by mp or bp gave satisfactory analytical values. NMR (δ) and IR (ν_{max}) spectra, when not mentioned, were measured at 100 MHz in $CDCl_3$ vs. Me_4Si as internal reference and in CCl_4 , respectively.
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- 4 The compound $\lambda\beta$ recrystallized from $EtOH-H_2O$ 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.⁵
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