Short Communication

The Absolute Configurations of Marmelo Lactones

Masakazu ISHIHARA, Tomoyuki TSUNEYA,
Haruyasu SHIOTA, Minoru SHIGA
and Yasushi YOKOYAMA*

Shiono Koryo Kaisha, Ltd.,
Niitaka, Yodogawa-ku, Osaka 532, Japan

*Department of Materials Chemistry,

Faculty of Engineering,

Yokohama National University,

Tokiwadai, Hodogaya-ku, Yokohama 240, Japan

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In the previous paper,¹⁾ we identified a pair of monoterpenic γ -lactones (2,7-dimethyl-4-hydroxy-5(*E*),7-octadienoic acid lactone) from the essential oil of quince (*Cydonia oblonga* Mill., marmelo in Japanese), and named them marmelo lactone-A and -B, respectively.

This paper describes the assignment of the *trans* form to marmelo lactone-A (**1**), $[\alpha]_D^{17} + 103^\circ$ ($c=3.5$, MeOH), and the *cis* form to marmelo lactone-B (**2**), $[\alpha]_D^{19} - 20^\circ$ ($c=4.0$, MeOH), and the elucidation of their absolute configurations by studies on their chiroptical data.

In the 1H -NMR of **2**, the signal of H_β -C(3) (at δ 1.62) was shifted to a higher field compared with that of **1** (at δ 2.08), because of shielding by the substituents on C(2) and C(4). Both substituents of **2** can be presumed to be situated at *cis* configuration with respect to H_β -C(3). The epimerization experiments of synthesized $(\pm)$ -**1** and $(\pm)$ -**2** also suggested the above assignment. The enolate of $(\pm)$ -**1**, prepared with lithium diisopropylamide in THF at $-78^\circ C$, was quenched with water to give a mixture of $(\pm)$ -**1** and $(\pm)$ -**2** in a 1:4

ratio. $(\pm)$ -**2** also gave a mixture of $(\pm)$ -**1** and $(\pm)$ -**2** in a 1:4 ratio by this same manner. These results can be explained by the proposal that each of the enolates was attacked by the electrophile (H^+) from the sterically unhindered site to afford the *cis* form as a major product.²⁾ Therefore, **1** was confirmed to be the *trans* form and **2** was the *cis* form.

Since each **1** and **2** showed very complex CD and ORD features at 200~240 nm by the influence of the conjugated diene groups, in order to remove this obstruction, they were transformed to the corresponding tetrahydro-derivatives **3** and **4** by catalytic hydrogenation. Each **3**, $[\alpha]_D^{21} + 36.5^\circ$ ($c=0.31$, MeOH), and **4**, $[\alpha]_D^{21} - 24.0^\circ$ ($c=0.13$, MeOH), showed a negative Cotton effect at 211 and 221 nm in the $n-\pi^*$ transition region of the lactone chromophore as listed in Table I.

TABLE I. CD SPECTRAL DATA OF γ -LACTONES (in MeOH)

Compound	λ_{max} (nm)	Sign	$[\theta] (\times 10^{-3})$
1	213	+	5.5
2	231	+	12.6
	212	-	25.1
3	211	-	5.3
4	221	-	4.2
7	212	+	3.1

The absolute configuration of **3** was established by its chiroptical correlation with (2*S*, 4*S*)-(-)-2,7-dimethyl-4-hydroxyoctanoic acid lactone (**7**) synthesized from (*R*)-(-)-4-hydroxy-7-methyl-6-octenoic acid lactone (**5**), $[\alpha]_D^{22} - 24.2^\circ$ ($c=1.32$, MeOH).^{3,4)} Catalytic hydrogenation of **5** gave **6**, $[\alpha]_D^{20} - 38.6^\circ$ ($c=0.26$, MeOH). Stereospecific methylation of the enolate of **6** gave **7**, $[\alpha]_D^{18} - 34.5^\circ$ ($c=0.43$, MeOH), as a single product. The 1H - and ^{13}C -NMR, IR and MS spectra of **7** were identical with those of **3**, but the specific rotation and CD spectrum of **7** showed quite opposite features. From this interrelation, the absolute configuration of **3** could be clearly assigned as (2*R*, 4*R*).

On the other hand, from application of the Beecham lactone rule,⁵⁾ the negative Cotton effect indicated that **4** was (2*R*,4*S*)-2,7-dimethyl-4-hydroxyoctanoic acid lactone, because both substituents can be presumed to adopt favorable quasi-equatorial conformations.⁶⁾ The Snetzke lactone rule⁷⁾ also supported the above assignment, because each substituent had a negative contribution to the sign of the Cotton effect. Furthermore, the spectral data (¹H- and ¹³C-NMR, IR and MS) of the mixed **8** and **7** (85:15, calculated from its ¹H-NMR integral values), obtained by the protonation of the enolate **7**, were identical in the most part with those of **4**, and the specific rotation of this mixture, $[\alpha]_D^{21} -23.8^\circ$ ($c=1.59$, MeOH), showed a similar value to that of **4**.⁸⁾

Consequently, the absolute configurations of marmelo lactone-A and -B could be determined as (2*R*,4*S*)-(+)-2,7-dimethyl-4-hydroxy-5(*E*),7-octadienoic acid lactone (**1**) and (2*R*,4*R*)-(–)-2,7-dimethyl-4-hydroxy-5(*E*),7-octadienoic acid lactone (**2**), respectively.⁹⁾

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- 8) This mixture was not separable by HPLC or GC (on PEG or Apiezon-L), so we could not obtain a pure sample of **8**, and the CD spectrum of this mixture showed a complex feature.
- 9) We previously reported on the absolute configurations of marmelo lactone-A and -B at the 25th TEAC Symposium in 1981, and assigned (2*R*,4*R*) to marmelo lactone-A and (2*R*,4*S*) to -B. However, we reinvestigated the structures of these lactones to reach the conclusion described in this paper.