

The Reduction of a Natural Diterpene Containing α , β -Unsaturated Keto Group

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Abstract: Hedychenone (**1**), a diterpene containing α , β -unsaturated keto group, was reduced by aluminum-mercury alloy, and a dimerized product (**2**) was obtained as the major product. The coupling occurred at β position of the keto group.

Keywords: Hedychenone, *Hedychium yunnanense*, diterpene, reduction.

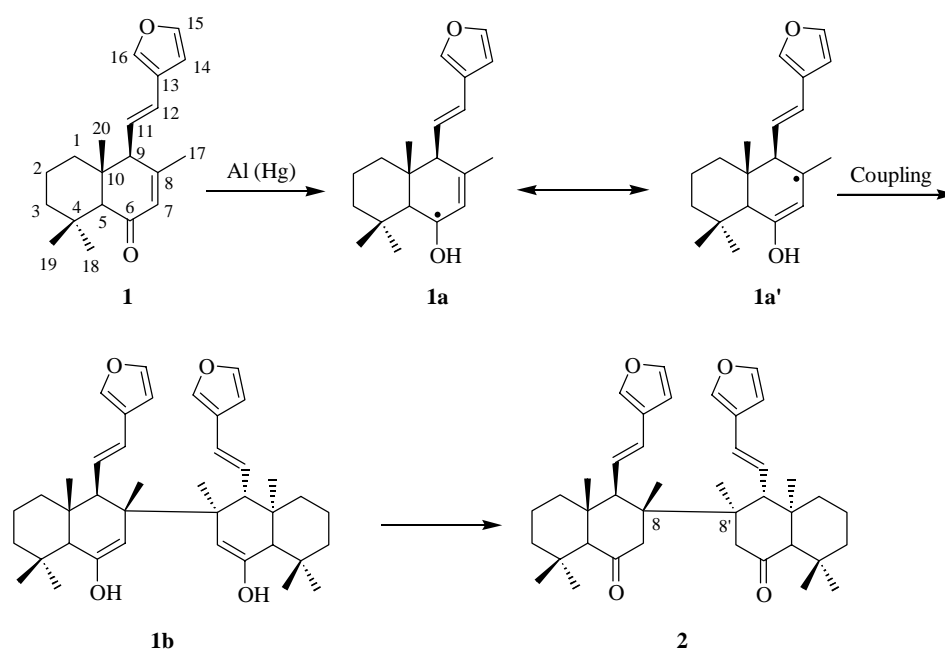
Hedychenone(**1**), a labdane-type diterpene, which showed cytotoxic activity against KB cells, was previously isolated from *Hedychium yunnanense*¹. It was found that the α , β -unsaturated ketone group of **1** showed significant inertness towards some reductants. For example, the $\Delta^{7(8)}$ group of **1** could be reduced by LiAlH_4 in THF while the keto group was not affected². Furthermore, both of the $\Delta^{7(8)}$ double bond and C-6 keto group of **1** could not be reduced by NaBH_4 in MeOH ³. In our recent studies, **1** was reduced by aluminum-mercury alloy in refluxed HCl-MeOH solution for 3 hours. After the reaction the alloy residue was removed through filtration and the solution was diluted with water and extracted with EtOAc . The EtOAc extract was subjected to column chromatography over silica gel eluted with petroleum ether- EtOAc (v/v 10:1) to produce a white powder **2** as the major product. On the basis of spectral data, **2** was determined to be an oddly dimerized product of **1**, and the mechanism of the dimer formation was deduced in **Scheme 1**.

Compound **2** was obtained as white powder. The HREIMS determined the molecular formula of **2** to be $\text{C}_{40}\text{H}_{58}\text{O}_4$, which was almost twice as that of **1**, indicating that **2** was a dimerized product. The ^{13}C NMR spectra of **2** showed only 20 signals, indicating that **2** had a symmetric structure. The IR data showed the presence of a keto group (1703 cm^{-1}) which was not conjugated with carbon-carbon double bond. The assignment of ^{13}C and ^1H NMR signals was supported by DEPT, ^1H - ^1H COSY, HMQC and HMBC spectral data. HMQC showed that the two protons at δ 3.04 and δ 2.07 were directly linked to the same carbon (C-7). The ROESY experiment revealed the cross peaks between δ 3.33 (H-9 α)

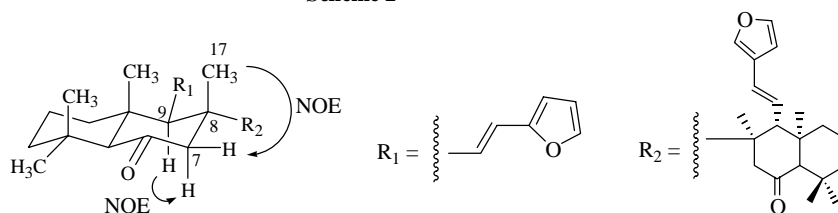
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and δ 3.04 (H-7 α), and between H-7 β and H-17 (CH₃), indicating the methyl group at C-17 was β -oriented (see **Scheme 2**).

Scheme 1



Scheme 2



The mechanism can be elucidated as follows: at first, **1** was reduced to a radical intermediate **1a**, which had a resonant structure **1a'**. The space hinderance effectively prohibited the coupling occurring at C6 and C6'. Therefore, the coupling at the less hindered positions, C8 and C8', was much more favorable. As a result, **1b** was formed as the major product, which underwent an isomerization process to get the final product **2**.

Table 1 ^{13}C NMR (125MHz) and ^1H NMR (500MHz) data of **2** ($\text{C}_5\text{D}_5\text{N}$, δ , ppm)

No.	^{13}C	^1H	No.	^{13}C	^1H
1	42.4		11	128.9	6.29 (dd, 10.5, 16.0)
2	18.8		12	125.5	6.84 (d, 16.0)
3	43.0		13	125.2	
4	32.7		14	108.3	6.99 (s)
5	65.8	2.09 (s)	15	141.1	7.69 (s)
6	212.1		16	145.0	8.01 (s)
7	54.0	3.04 (d, 12.2), 2.07 (d, 12.2)	17	18.5	0.91 (s)
8	49.2		18	32.0	0.76 (s)
9	57.7	3.33 (d, 10.5)	19	22.1	1.32 (s)
10	43.6		20	18.4	0.93 (s)

Coupling constants (Hz) in parentheses.

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