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SYNTHESIS OF 1,4-DIMETHYL-6,7-(4'-METHYLFURANO-2',3')-AZULENE*
(LINDERAZULENE)

Ken'ichi Takeda, Hitoshi Minato and Makoto Ishikawa
Shionogi Research Laboratory,
Shionogi & Co., Ltd., Osaka, Japan

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THE structure of linderene, isolated from the root of <u>Lindera strychnifolia</u> Vill., has already been proposed to be as shown in formula (I) by Takeda.[1] On zinc-dust distillation of linderene, linderazulene[2] (II) was obtained. This azuelene was assumed to be 1,4-dimethyl-6,7-(4'-methylfurano-2',3')-azulene. We have effected the synthesis of linderazulene in order to further confirm its structure.

On the synthesis of linderazulene, we started from guaiol (III). When an α,β-unsaturated ketone (IV)[3] was catalytically hydrogenated in ethanol with 5% palladium-barium carbonate, a hydroxyketone (V), colourless prisms, m.p. 103-104°, $[\alpha]_D$ -59.9°, was obtained in 64% yield. On dehydration of V with phosphorus oxychloride-pyridine, a mixture of the double bond isomers (VI), a colourless oil, b.p. 92-94°/1.2 mm was

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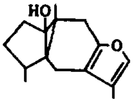
* Analysis of all the compounds described corresponded to the calculated values.

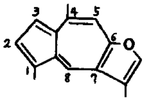
[1] K. Takeda, Chem. Pharm. Bull. (Japan) 1, 244 (1953).

[2] K. Takeda and W. Nagata, Chem. Pharm. Bull. (Japan) 1, 164 (1953).

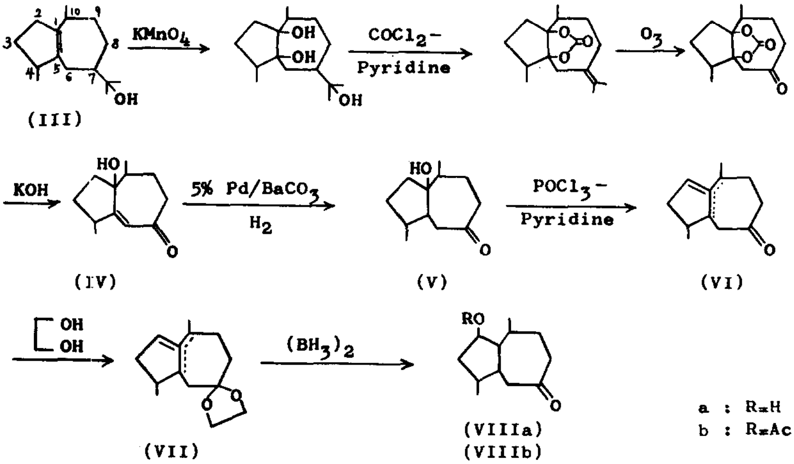
[3] K. Takeda and H. Minato, Tetrahedron Letters No. 22, 33 (1960); Chem. Pharm. Bull. (Japan) 9, 619 (1961).



(I)



(II)



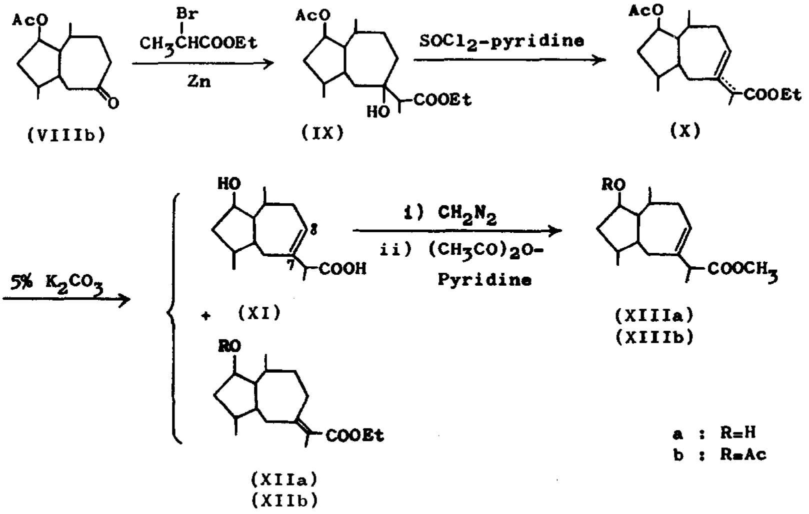
(III) (IV) (V) (VI) (VII) (VIIIa) (VIIIb)

a : R=H
b : R=Ac

obtained in 84% yield. A ethylene ketal derivative (VII) of VI, a colourless oil, b.p. 87-89°/0.5 mm afforded 2-hydroxyketone (VIIIa), colourless plates, m.p. 102-103°, $[\alpha]_D$ -59.9°, in 46% yield by hydroboration and following deketalisation with 80% acetic acid.

Reformatsky reaction of 2-acetoxyketone (VIIIb), colourless prisms, m.p. 58-60°, $[\alpha]_D$ -17.3°, with ethyl α-bromopropionate gave in 73% yield a colourless oil (IX), b.p. 140-149°/0.05 mm, $[\alpha]_D$ +38.6°, which was dehydrated with thionyl chloride-pyridine to give a mixture of the double bond isomers (X), a colourless oil, b.p. 121-125°/0.02 mm, $[\alpha]_D$ +11.5°, in 74% yield.

Separation of this mixture (X) into β,γ-unsaturated acid (XI) and α,β-unsaturated ester (XIIa) was achieved by hydrolysis with potassium carbonate. When X was refluxed with 5% potassium carbonate in methanol on a steam bath for 8 hr, β,γ-unsaturated acid (XI), colourless needles, m.p. 138-141°, λ_{max}^{alc} 206.5 mμ (ε 4910), $[\alpha]_D$ +29.8° and the unsaponified α,β-unsaturated ester (XIIa) were obtained in 43% and in 38% yield, respectively.



Acetoxy α,β-unsaturated ester (XIIb), a colourless oil, b.p. 162-163°/1.5 mm, $[\alpha]_D$ -26.7°, showed an absorption maximum at 230 mμ (ε 8900) corresponding to α,β-unsaturated ester, whereas XI showed a maximum at 206.5 mμ in the ultra-violet spectra. Thus, it is evident that XI is a β,γ-unsaturated acid.

Esterification of XI with diazomethane followed by acetylation afforded a β,γ-unsaturated ester (XIIIb), b.p. 120°/0.05 mm, $[\alpha]_D$ +54.1°. The NMR spectrum** of XIIIb shows a triplet centered at

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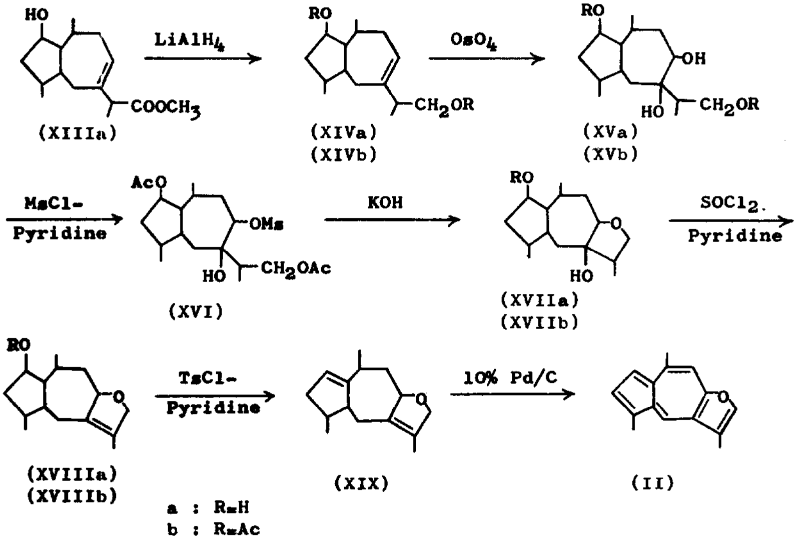
** Spectra were taken on deuterated chloroform solution with a Varian A-60 NMR Spectrometer.

4.31 τ (J=6.6 c.p.s.) corresponding to the hydrogen of a $>C=CH-$ group, and its intensity shows that there is only one such hydrogen atom in the molecule. The fact that the signal is split into a triplet indicates the existence of two protons on the adjacent carbon atom. This interpretation of the NMR spectrum leads to the conclusion that the situation of the double bond in XIIIb is at C 7-8.***



Lithium aluminum hydride reduction of XIIa followed by acetylation afforded a diacetoxy compound (XIVb), a colourless oil, b.p. 118-120°/0.002 mm in 96% yield. When XIVb was oxidized with osmium tetroxide, an oily dihydroxy derivative (XVb) was obtained in 74% yield (XVa, colourless plates, m.p. 153-154°, $[\alpha]_D$ +28.7°). Compound XVIIa, colourless prisms, m.p. 169-170°, $[\alpha]_D$ -26.1°, was obtained by mesylation of XVb with mesyl chloride-pyridine followed

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*** The position of the double bond in XIIIb was also confirmed by chemical degradation.

by the ring-closure of XVI with 5% potassium hydroxide in methanol in 50% yield. Its monoacetate (XVIIb), colourless prisms, m.p. 154.5-155.5°, was dehydrated with thionyl chloride-pyridine to give XVIIIb, a colourless unstable oil in ca. 97% yield. The thus obtained unsaturated acetate (XVIIIb) was saponified by 4% potassium carbonate in methanol in nitrogen atmosphere for 3 hr to yield XVIIIa, colourless needles, m.p. 92-94°. The position of the double bond in XVIIIa was established to be represented by formula XVIIIa by its NMR spectrum.

The tosylate of XVIIIa was heated in pyridine at 90-100° for 1 hr to give an unstable colourless oil (XIX), ν_{max}^{film} 3063 (=C-H), 1052 (C-O), 845 and 810 cm^{-1}. The NMR spectrum of XIX also satisfied this structure.

A mixture of XIX and 10% palladium charcoal (2:1) was heated in a metal bath at 300-310° for 3-5 min, a violet crude azulene was obtained in ca. 20% yield. The thus obtained 1,4-dimethyl-6,7-(4'-methylfurano-2',3')-azulene (II) was purified by the repetition of alumina chromatography and recrystallization of its 2,4,6-trinitrobenzene adduct as lustrous violescent-black plates, m.p. 106-107°; 2,4,6-trinitrobenzene adduct, violescent-black needles, m.p. 154-5°.

This synthesized azulene was established to be identical with linderazulene in all respects.