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SYNTHESIS OF THEASPIRONE, A COMPONENT OF TEA ESSENTIAL OIL

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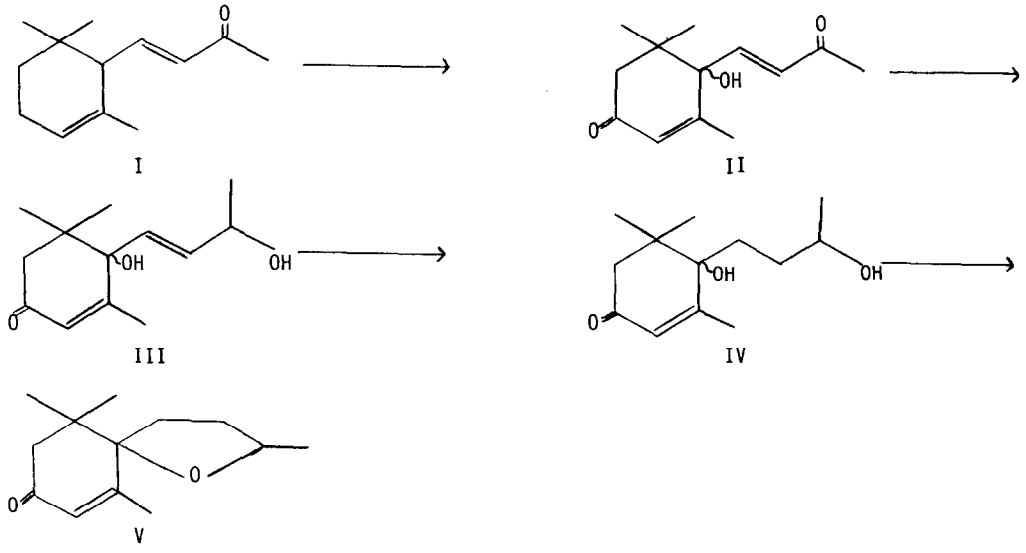
In a recent communication (1) Ina and Sakato described the isolation and structure elucidation of theaspirone (V), an important aroma constituent of tea essential oil. In order to confirm the structure proposed by Ina and Sakato, and to evaluate the flavor properties of this material, its synthesis was undertaken. An ideal starting material was available in the form of 1-hydroxy-4-keto-α-ionone (II) which was the key intermediate in our synthesis of abscisic acid (abscisin II) (2). We now wish to report the synthesis of structure V and its identity with theaspirone. The synthetic route also yielded the epimer of the natural product.*



In accordance with the above scheme 1-hydroxy-4-keto-α-ionone (II) was prepared by t-butyl chromate oxidation of α-ionone (I) using t-butyl alcohol as solvent in 23-27% yield (2).

*Theaspirone is evidently a single geometrical isomer. However, it was not divulged (1) whether or not the naturally-occurring material was optically active.

TABLE 1

SPECTRAL DATA FOR THEASPIRONE AND ITS PRECURSORS

	ir (μ) (nujol)	nmr (τ)[a]	mass spectrum (m/e)
IIIa mp 104-106°	3.04 10.18	9.05 (s, 6, $C(\underline{CH_3})_2$)	224 (M^+)
	6.02 10.26	8.70 (d, 3, J=7.0Hz, $CHOH\underline{CH_3}$)	
	6.20	8.10 (s, 3, $CH=C\underline{CH_3}$)	
	8.88	7.90 (s, 2, $\underline{OH}$)	
	9.30	7.68 (m, 2, $\underline{CH_2}CO$)	
	9.67	5.60 (m, 1, $\underline{CH}OHCH_3$)	
	9.76	4.15 (s, 3, vinyl protons)	
IIIb mp 111-113°	(nujol)	same as IIIa	224 (M^+)
	2.91 8.82		
	3.00 9.09		
	6.06 9.50		
	6.17 10.25		
IV	(liquid film)	8.97 (s, 3, $C(\underline{CH_3})_2$)	226 (M^+)
	2.93 9.78	8.90 (s, 3, $C(\underline{CH_3})_2$)	
	6.02	8.81 (d, 3, J=6.5Hz, $CHOH\underline{CH_3}$)	
	6.15	7.95 (s, 3, $CH=C\underline{CH_3}$)	
	8.13	7.65 (m, 2, $\underline{CH_2}CO$)	
	8.45	6.20 (m, 1, $\underline{CH}OHCH_3$)	
	9.00	6.10 (s, 2, $\underline{OH}$)	
	9.55	4.17 (s, 1, $\underline{CH}=CCH_3$)	
V bp 96-97° (0.05mm)	(liquid film)		208 (M^+), 152
	6.03	9.03, 8.99, 8.94 (6, $C(\underline{CH_3})_2$)	
	6.19	8.73 (d, 3, J=5.8Hz, $CHC\underline{H_3}O$)	
	9.13	8.03 (d, 3, J=1.5Hz, $CH=C\underline{CH_3}$)	
	9.27	7.7 (s, 2, $\underline{CH_2}CO$)	
	11.04	5.78 (m, 1, $\underline{CH}CH_3O$)	
	11.42	4.27 (q, 1, J=1.5Hz, $\underline{CH}=CCH_3$)	

[a]The nmr spectra were recorded using a Varian A-60A instrument in $CDCl_3$ with TMS as internal reference.

Compound II was reduced with one equivalent of sodium borohydride in methanol. Simple crystallization of the crude reduction product from ether-pentane afforded the two isomers, IIIa and IIIb, in 63% yield.

The hydrogenation of IIIa was carried out at ambient temperature and atmospheric pressure using pre-reduced platinum oxide in ethanol. As was expected, the conversion of III to IV by catalytic hydrogenation suffered from competing reactions such as saturation of the enone system and probably hydrogenolysis of the allylic hydroxyl groups. Purification of the syrupy keto diol IV was accomplished by chromatography on silicic acid using mixtures of 1-5% methanol in chloroform; the spectral data obtained for IV confirmed that the structure was 4-(1-hydroxy-4-keto-2,6,6-trimethyl-2-cyclohexen-1-yl)-2-butanol. Compound IV, obtained in 45% yield from the hydrogenation, was cyclized to the spiro ether V in 44% yield by heating in dimethyl sulfoxide (DMSO) according to the procedure of Gillis and Beck (3). Alternatively, the reaction was effected by the method of Reynolds and Kenyon (4) by treatment of IV with benzenesulfonyl chloride in boiling pyridine (46% yield). In both procedures the desired product (V) was conveniently extracted from reaction mixtures using pentane.

The spectral properties of theaspirone and its precursors are given in Table 1. As was previously reported, the mass spectrum of V shows a prominent peak at 152 mass units that is thought to arise from the parent ion by loss of isobutylene (1). The presence of three gem-methyl absorptions (relative intensities of 1:2:1) in the nmr spectrum* suggested the presence of two geometrical isomers.

That the final product obtained by the DMSO method (3) was a mixture of both of the possible isomers was confirmed through analysis by glpc (100 ft. polyphenyl ether capillary column, programmed from 50 to 85° at 10°/min.) which resulted in the complete resolution of V into two components in a ratio of 1:1 having retention times of 139 and 147.5 minutes. This distribution of isomers in the final product was also obtained when the synthetic scheme was completed using a mixture of IIIa and IIIb, regardless of the method used in the cyclization of IV. The stereochemical outcome of the pyridine-benzenesulfonyl chloride method of cyclization of IV, starting with the pure isomers (IIIa and IIIb), has not been investigated. The fact that further treatment of both IIIa and IIIb led to a 1:1 mixture of spiro ethers (V) suggests that the cyclization step is non-stereoselective. However, the possibility that these intermediates are epimerized

*The remainder of the nmr spectrum of V was essentially identical to that reported for the natural product (1).

during hydrogenation (5) has not been ruled out.

The synthetic theaspirone was readily purified for evaluation of its organoleptic properties by preparative glpc using a 10% OV-1 column.

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