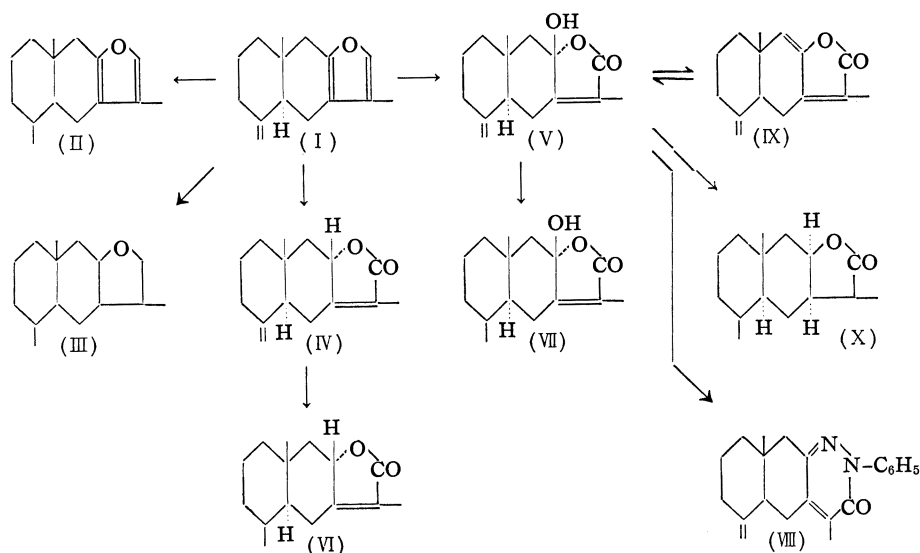


Structure and Autoxidation of Atractylon

The crystalline sesquiterpenoid, atractylon, was first isolated from the crude drug "Sō-jutsu"¹⁾ and later from *Atractylodes japonica* KOIDZUMI²⁾ and its related plant.³⁾ The present communication contains evidence which permits the assignment of expression (I) to atractylon and expressions (IV) and (V) to its autoxidation products.

Atractylon (I), $C_{15}H_{20}O$, m.p. 38° , $[\alpha]_D +40.0^\circ$,^{*1} had infrared spectrum which exhibited no band associated with hydroxyl or carbonyl grouping but a band at 1134 cm^{-1} assigned to ether mode. The presence of the furan system in (I) was indicated from the positive color reactions for furan ring such as vanillin-HCl, pine stick, Ehrlich, Liebermann-Burchard reactions and from ultraviolet spectrum ($\lambda_{\text{max}}^{\text{EtOH}}$ 220 m μ) as well as from the formation of maleic anhydride adduct, $C_{19}H_{22}O_4$, m.p. 118° . The third ethylenic bond as in exocyclic was revealed by infrared absorption (bands at 3077 , 1639 , 886 cm^{-1}) and by ozonolysis to give formaldehyde. Catalytic hydrogenation of (I) over PtO_2 in MeOH resulted in the saturation of the exocyclic double bond to afford the dihydro-derivative (II), $C_{15}H_{22}O$, b.p. 101° , $[\alpha]_D -44.0^\circ$. The retention of the furan system in (II) was indicated by the coloration given with reagents described above and by UV: $\lambda_{\text{max}}^{\text{EtOH}}$ 221 m μ . On catalytic hydrogenation in AcOEt using Pd-C, (I) took up three moles of H_2 with the formation of a saturated oxide (III), $C_{15}H_{26}O$, b.p. $120\sim 122^\circ$, $[\alpha]_D -51.4^\circ$, which was identified (IR spectra) with octahydrodesoxylinderene.⁴⁾ In agreement with the proposed structure, nuclear magnetic resonance spectrum of (I), measured at 40 Mc. in CCl_4 vs. H_2O as external reference, showed the following peaks: singlet (3H) at $+160\text{ c.p.s.}$, doublet (3H) at $+114\text{ c.p.s.}$ (J 1 c.p.s.), doublet (2H) at $+1\text{ c.p.s.}$ (J 5 c.p.s.) with additional fine splitting, unresolved band (1H) at -87 c.p.s.



*1 All analytical values are in good agreement with the molecular formula shown. $[\alpha]_D$ s refer to CHCl_3 solutions.

1) S. Takagi, G. Hongo: *Yakugaku Zasshi*, **44**, 539 (1924).

2) I. Yosioka, H. Hikino, Y. Hikino: unpublished data.

3) I. Yosioka, S. Takahashi, H. Hikino, Y. Sasaki: *Yakugaku Zasshi*, **80**, 1564 (1960).

4) H. Kondo, K. Takeda: *Ibid.*, **59**, 504 (1939).

(I) suffered remarkably rapid autoxidation on standing in air to give two crystalline products, (IV), $C_{15}H_{20}O_2$, m.p. 125° , $[\alpha]_D +266.1^\circ$, and (V), $C_{15}H_{20}O_3$, m.p. $197\sim197.5^\circ$, $[\alpha]_D +281.4^\circ$. The presence of a α,β -butenolide system in both (IV) and (V), was confirmed by the spectral properties in ultraviolet (λ_{max}^{EtOH} 220 m μ) and infrared region (bands at 1733, 1672 and 1736, 1695 cm^{-1} , respectively). (IV) and (V) showed also infrared bands at 900 and 897 cm^{-1} (vinylidene) and yielded formaldehyde on ozonolysis. On hydrogenation with Pd-C in AcOMe, (IV) and (V) gave dihydro-derivatives, (VI), $C_{15}H_{22}O_2$, m.p. $114\sim115^\circ$, $[\alpha]_D +130.8^\circ$, and (VII), $C_{15}H_{22}O_3$, m.p. $178\sim179.5^\circ$, $[\alpha]_D +299.0^\circ$, respectively, which retained the spectral properties due to α,β -butenolide but disclosed no $>C=CH_2$ absorption. That the last oxygen in (V) was the hydroxyl group situated as hemiketal lactone form in the α,β -butenolide system was established from the following observations: (V), UV: $\lambda_{max}^{NaOH-EtOH}$ 264 m μ , IR: ν_{Nujol} 3333 cm^{-1} , exhibited the weakly acidic properties, reacted with phenylhydrazine to give a product (VIII), $C_{21}H_{24}ON_2$, m.p. $210\sim212^\circ$, and was easily dehydrated to afford an anhydroderivative (IX), $C_{15}H_{18}O_2$, m.p. $106\sim108^\circ$, UV: λ_{max}^{EtOH} 275 m μ , from which (V) was regenerated by dissolution in alkali followed by acidification. Hydrogenation of (V) over PtO_2 in AcOH in the presence of HCl led to a saturated lactone (X), $C_{15}H_{24}O_2$, m.p. $141\sim143^\circ$, $[\alpha]_D +15.2^\circ$, which was identified (m.p., mixed m.p. and IR spectra) with tetrahydroalantolactone. It is very probable that (IV) is the desoxy-compound of (V). (VI) was proved to be identical (m.p., mixed m.p. and IR spectra) with the butenolide⁵⁾ derived from alantolactone. Although the autoxidation process from (I) to (V) has a few examples,⁶⁾ that from (I) to (IV) seems to have no precedence.

The authors are indebted to Dr. K. Takeda, Research Laboratory, Shionogi & Co., Ltd., who prepared a specimen of octahydrodesoxylinderene, and to Drs. I. Iwai and K. Tanabe, Takamine Research Laboratory, Sankyo Co., Ltd., who provided specimens of tetrahydroalantolactone and the butenolide (VI). Two of the authors (H.H. and Y.H.) also express their deep thanks to Professor T. Takemoto, Pharmaceutical Institute, Faculty of Medicine, Tohoku University, for continual interest and encouragement and for facilities in his laboratory to do a part of this work.

Pharmaceutical Institute,
Faculty of Medicine,
Tohoku University,
Kita-4-bancho, Sendai.

Hiroshi Hikino (ヒキノ ヒロシ)
Yasuko Hikino (曳野 靖子)

Faculty of Pharmacy,
University of Osaka,
Toneyama, Toyonaka,
Osaka-fu.

Itiro Yosioka (吉岡 一郎)

April 30, 1962.

5) H. Matsumura, I. Iwai, E. Ohki: *Ibid.*, **74**, 1029 (1954).

6) G. O. Schenck: *Ber.*, **77**, 661 (1944); *Angew. Chem.*, **60A**, 224 (1948); R. B. Woodward, R. H. Eastman: *J. Am. Chem. Soc.*, **72**, 399 (1950); A. Melera, K. Schaffner, D. Arigoni, O. Jeger: *Helv. Chim. Acta*, **40**, 1420 (1957).