

FURTHER STUDIES ON ISOASATONE

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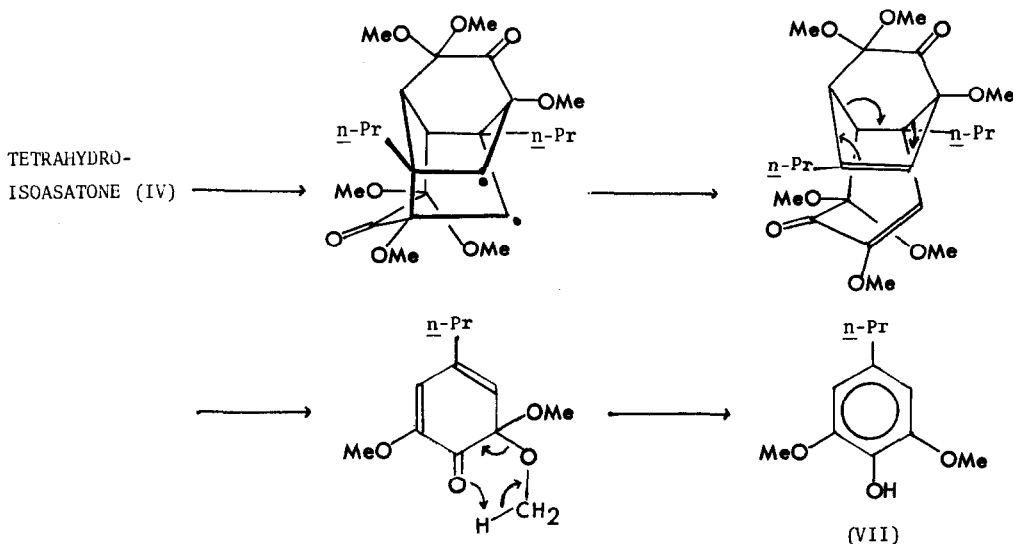
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As described in the preceding paper,¹ the carbon skeleton of isoasatone (I) consists of two C₆-C₃ units. From a biogenetic point of view, it is quite reasonable that 2,6-dimethoxy-4-allylphenol (II) or its further oxygenated compound (III) is regarded as the original precursor for isoasatone. In the present paper, we wish to describe some interesting reactions of isoasatone (I), which must support the above-mentioned idea.

Catalytic hydrogenation of isoasatone (I) has been known to afford tetrahydroisoasatone (IV).¹ Further treatment of IV with LiAlH₄ in THF (room temp., 3hr.) gave the corresponding dihydroxy-compound (V), m.p. 166-167°; C₂₄H₄₀O₈ [m/e 425 (M⁺- 31) and 228]; ν_{\max} (Nujol) 3500cm⁻¹. In the mass spectra of I, IV, V and the known dihydroxyisoasatone (VI)¹, each base peak was observed at the position corresponding to half of the molecular weight [I, 224(C₁₂H₁₆O₄); IV, 226(C₁₂H₁₈O₄); V, 228(C₁₂H₂₀O₄); VI, 226(C₁₂H₁₈O₄)]. Clearly, a highly strained bicyclo[2.2.0]hexane system of each compound was thermally decomposed in stepwise manner, and then retro-Diels-Alder reaction took place to give the corresponding dienones (For example, I→III). When heated in a sealed tube at 290-300° for 30min., tetrahydroisoasatone

(IV) afforded 2,6-dimethoxy-4-propylphenol (VII) in ca. 55% yield.

Probably, VII is produced in the same manner as that of the fragmentation reaction on electron impact, as shown below.



When stirred with active zinc powder in 6N-HCl-MeOH (3 : 10) at room temperature for 2hr., isoasatone (I) was converted to 2,6-dimethoxy-4-allylphenol (II) and a biphenyl-type compound (VIII) in 46 and 12% yields, respectively. The structures of these compounds were confirmed by the physical and chemical evidences, as follows.

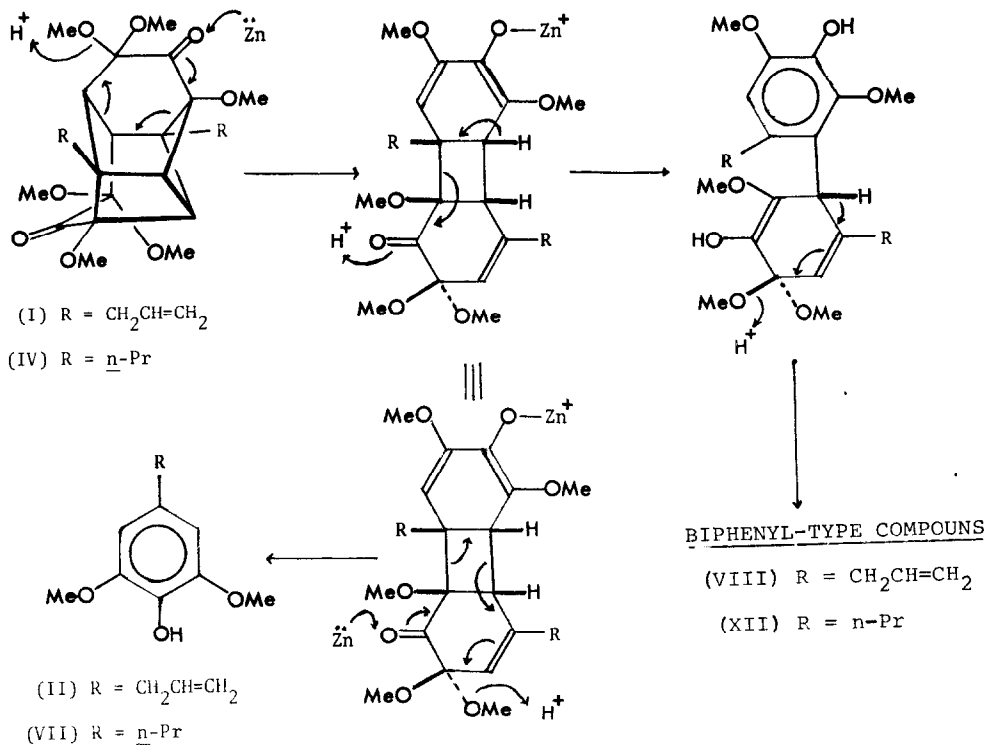
A colourless liquid (II): $C_{11}H_{14}O_3$ (m/e 194 (M^+)); ν_{\max} (film) 3510, 3080, 1635, 1615 and 1513cm^{-1} ; δ (CDCl_3) 3.30 (2H, d, $J = 6.0\text{Hz}$), 3.82 (6H, s), 4.80-5.25 (2H, m), 5.39 (1H, br., OH), 5.55-6.25 (1H, m) and 6.40ppm (2H, s).

A colourless viscous liquid (VIII): $C_{22}H_{26}O_6$ (m/e 386 (M^+)); ν_{\max} (film) 3460, 1640, 1613, 1585 and 1495cm^{-1} ; δ (CDCl_3) 3.00 (4H, d, $J = 6.0\text{Hz}$), 3.61 (6H, s), 3.90 (6H, s), 4.70-5.15 (4H, m), 5.52 (2H, br., OH), 5.45-6.20 (2H, m) and 6.60ppm (2H, s).

Acetylation of II with Ac_2O -pyridine (room temp., overnight) followed by catalytic hydrogenation over 10% Pd-C in EtOAc afforded the known compound (IX) in almost quantitative yield.² Acetylation of VIII also afforded the

corresponding acetate (X), m.p. 125-125.5°; $C_{26}H_{30}O_8$ (m/e 470 (M^+)); ν_{max} (Nujol) 1775, 1600 and 1585cm^{-1} ; λ_{max} (MeOH) 277 and 227nm (ϵ , 2160 and 17750, respectively); δ ($CDCl_3$) 2.36 (6H, s), 3.10 (4H, d, $J = 6.7\text{Hz}$), 3.58 (6H, s), 3.90 (6H, s), 4.75-5.10 (4H, m), 5.45-6.10 (2H, m) and 6.70ppm (2H, s). Further catalytic hydrogenation of X over 10% Pd-C in EtOAc also gave the known diacetate (XI)².

In the case of tetrahydroisoasatone (IV), 2,6-dimethoxy-4-propylphenol (VII) and the known biphenyl-type compound (XII)² both were obtained in 65 and 13.5% yields, respectively. These compounds may be produced according to the following path-way.

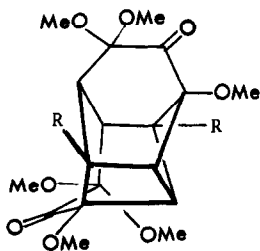


These experiments strongly suggest that isoasatone (I) must be reconstructed from 2,6-dimethoxy-4-allylphenol (II).

All compounds gave satisfactory physical data and elemental analyses.

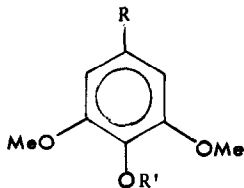
The authors wish to thank Drs. Hirokichi Harada and Hisatoyo Yazawa (Fuji-

sawa Pharmaceutical Co. Ltd.) for measurements of high resolution mass spectra.



(I) $R = \text{CH}_2\text{CH}=\text{CH}_2$

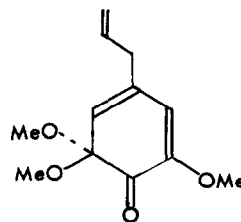
(IV) $R = \underline{n}\text{-Pr}$



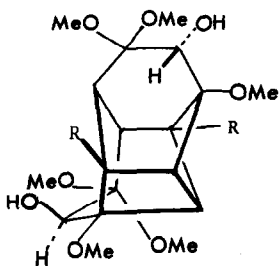
(II) $R = \text{CH}_2\text{CH}=\text{CH}_2$, $R' = \text{H}$

(VII) $R = \underline{n}\text{-Pr}$, $R' = \text{H}$

(IX) $R = \underline{n}\text{-Pr}$, $R' = \text{Ac}$

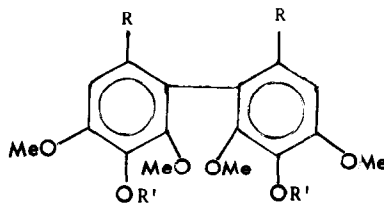


(III)



(V) $R = \underline{n}\text{-Pr}$

(VI) $R = \text{CH}_2\text{CH}=\text{CH}_2$



(VIII) $R = \text{CH}_2\text{CH}=\text{CH}_2$, $R' = \text{H}$

(X) $R = \text{CH}_2\text{CH}=\text{CH}_2$, $R' = \text{Ac}$

(XI) $R = \underline{n}\text{-Pr}$, $R' = \text{Ac}$

(XII) $R = \underline{n}\text{-Pr}$, $R' = \text{H}$

REFERENCES

1. Submitted to Tetrahedron Letters (1973).
2. Y. Chen, M. Hong, H. Hsu, S. Yamamura and Y. Hirata, Tetrahedron Letters, 1607 (1972).