

ISOLATION AND STRUCTURE OF ASATONE

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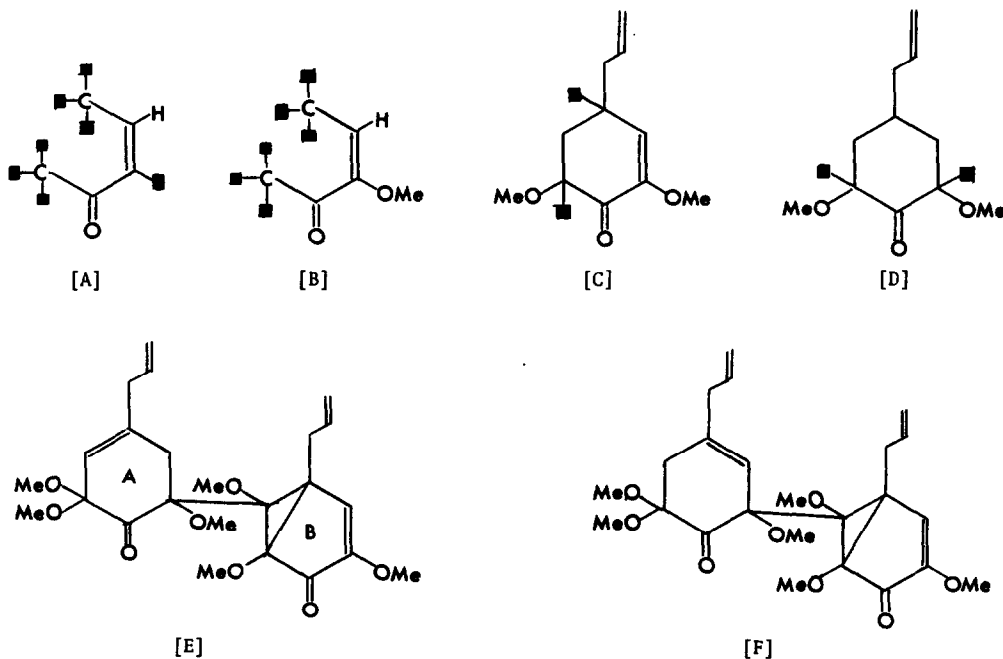
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Chemical constituents of many species of *Asarum* genus, *Aristolochiaceae*, have been investigated.¹ We wish to describe the isolation and structure of a novel compound, named "Asatone" obtained from *Asarum taitonense* Hayata. The carbon skeleton of this compound consists of two C₆-C₃ units.

A sample of pulverized material of the whole herb was refluxed with n-hexane for 3hr., and then filtered. The filtrates were concentrated under reduced pressure to give greenish yellow crude crystals which were chromatographed on silica gel and eluted with n-hexane-EtOAc (8 : 1) to give white crystals of asatone (I) in ca.0.2% yield, m.p. 101-2° (from n-hexane); $[\alpha]_D^{20} = \pm 0^\circ$ (in MeOH);² C₂₄H₃₂O₈ (m/e 448); λ_{\max} (MeOH) 278 and 229nm (ϵ , 5660 and 5100, respectively); ν_{\max} (KBr) 1740, 1720 and 1635cm⁻¹; δ (CDCl₃) 2.15(1H, q, J=7.5, 14.5Hz), 2.60-2.95(3H, m), 2.88(2H, br.s), 3.05(3H, s), 3.31(3H, s), 3.38(3H, s), 3.42(3H, s), 3.47(3H, s), 3.60(3H, s), 4.90-5.28(4H, m), 5.39(1H, s), 5.55(1H, q, J=1.9Hz) and 5.50-6.20(2H, m)ppm. The methyl singlets in δ 3.0-4.6 and IR spectrum(1740 and 1720cm⁻¹) indicate that I has six methoxyl and two carbonyl groups and all of them are in different environment to one another. The presence of two propenyl groups in I can be elucidated by its NMR signals [δ 4.90-5.28(4H, m) and 5.50-6.20(2H, m) coupled with the signals at δ 2.15(1H, q) and 2.60-2.95(3H, m)] coupled with catalytic hydrogenation which has been carried out over 10%Pd-C in EtOAc to afford tetrahydroasatone (II), m.p. 128-9°; m/e 452(M⁺); λ_{\max} (MeOH) 278 and 229nm (ϵ , 5100 and 3940, respectively); ν_{\max} (Nujol) 1745, 1720 and 1635cm⁻¹. The NMR spectrum of II has methyl triplet at δ 0.87(6H, J=6.5Hz) and the multiplets at δ 1.10-1.80 and 1.85-2.15 corresponding to four methylene groups instead of multiplets at δ 4.90-5.28 and 5.50-6.20 in I.³ The remaining signals are similar to each other.

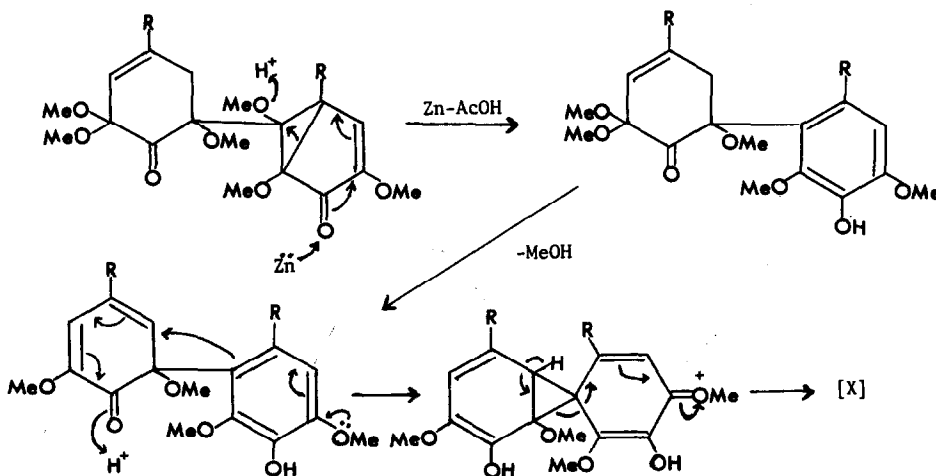
When treated with NaBH₄ in EtOH (room temp., 1.5hr.), I afforded a mixture of three reduction products(III, IV and V), as follows: hydroxyasatone A (III), m.p. 127-8°; C₂₄H₃₄O₈ (m/e 450); λ_{\max} (MeOH) 235sh and 218nm (ϵ , 2640 and 4500, respectively); ν_{\max} (Nujol) 3500, 1745, 1685, 1660(w) and 1640(w)cm⁻¹; δ 3.93(1H, s, -CH(OH)), 4.60(1H, s), 4.75-5.30(4H, m), 5.68(1H, q, J=1.8Hz) and 5.45-6.25(2H, m)ppm, and hydroxyasatone B (IV), m.p. 108-9°; C₂₄H₃₄O₈ (m/e 450); λ_{\max} (MeOH) 277 and 213nm (ϵ , 4390 and 2510, respectively); ν_{\max} (Nujol) 3510, 1715, 1660(w) and 1635cm⁻¹; δ 3.92(1H, s, -CH(OH)), 4.80-5.30(4H, m), 5.50(1H, q, J=1.8Hz), 5.60(1H, s) and 5.35-6.35(2H, m)ppm. It is noted that each NMR spectrum of III and IV has the singlet corresponding to one proton attached to the carbon atom bearing the resulting hydroxyl group, indicating that

the α - and β -positions of each carbonyl group must be fully substituted. Furthermore, the comparison of the UV, IR and NMR spectra between I and III indicates that I has an α,β -unsaturated carbonyl system [A] in which only one olefinic proton is located at the β -position, for the NMR singlet at δ 5.39 in I is shifted to δ 4.60 in III. In the case of the third compound (V), two carbonyl groups are completely reduced to hydroxyl groups. The partial structure [A] is further extended to [B] as follows. Catalytic hydrogenation of I in MeOH was carried out over 10%Pd-C (room temp. overnight) to afford a mixture of II and hexahydroasatone (VI) in ca. 70 and 10% yields, respectively. The IR and UV spectra of VI [m.p. 133-4°; $C_{24}H_{38}O_8$ (m/e 428 ($M^+ - 28$); λ_{max} (MeOH) 221nm (ϵ , 2817); ν_{max} 1750 and 1745 cm^{-1}] indicate that the conjugated double bond in the partial structure [A] has been hydrogenated. Furthermore, the NMR spectrum has the following signals: δ 0.82(3H, t, J=7.0Hz), 0.90(3H, t, J=7.0Hz), 1.15-1.84 (6H, m), 1.95(2H, t, J=7.0Hz), 2.31(2H, d, J=5.5Hz), 2.78(2H, s), 3.14(3H, s), 3.28(3H, s), 3.35(6H, s), 3.43(3H, s), 3.50(3H, s), 3.63(1H, t, J=5.5Hz) and 5.85(1H, q, J=1.9Hz)ppm. Irradiation at δ 2.31 caused the triplet at δ 3.63 to collapse to singlet. This finding strongly supports the presence of the partial structure [B] in I. On the other hand, catalytic hydrogenation of III and IV in EtOAc (10%Pd-C, room temp., overnight) yielded the corresponding tetrahydro-derivatives [VII, m.p. 162-3°; $C_{24}H_{38}O_8$ (m/e 454). VIII, m.p. 122-3°; $C_{24}H_{38}O_8$ (m/e 454)]. In the NMR spectrum of VIII, the AB-quartet centered at δ 2.55(2H) is observed instead of the broad singlet at δ 2.84 in II (or I), suggesting that the isolated carbonyl group must be present near the isolated methylene group in II (or I).



In general, I as well as II is very unstable for Lewis acids giving many degradation products. However, when treated with active zinc powder in acetic acid (under reflux, 6hr.), II gave

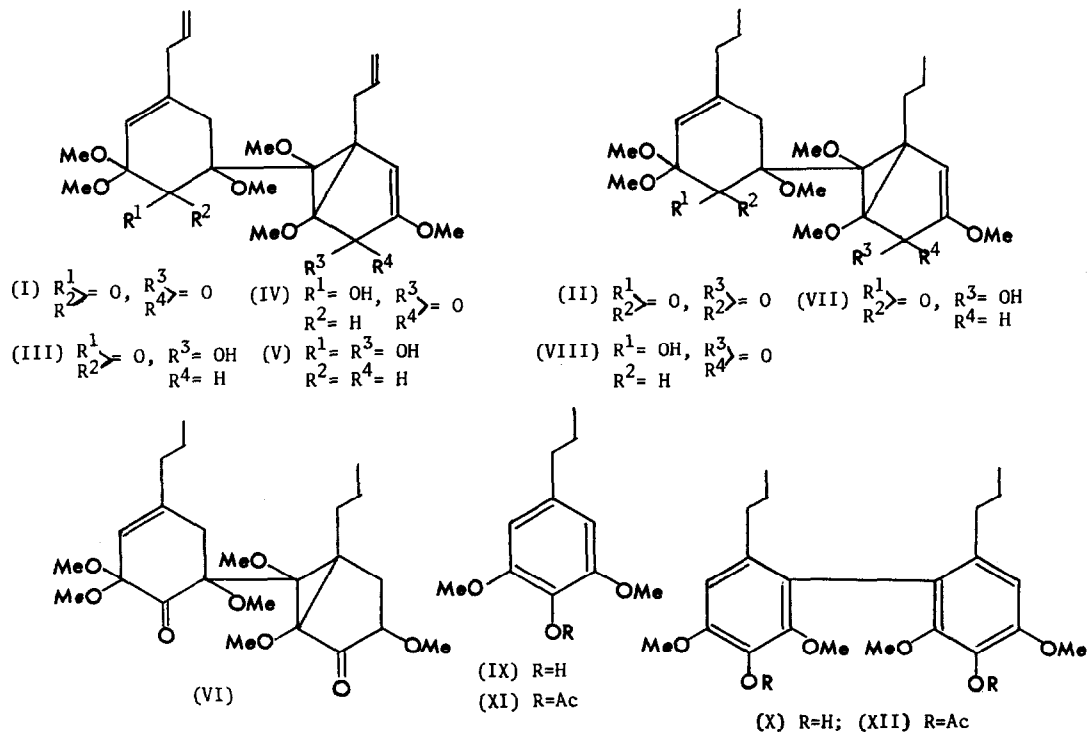
2,6-dimethoxy-4-propylphenol (IX) and a biphenyl-type compound (X), in 57(as 2eq.) and 23% yields, respectively. Further treatment of IX with acetic anhydride-pyridine afforded the corresponding acetate (XI), m.p. 88-88.5°(lit. 87°);⁴ m/e 238(M^+); ν_{\max} (Nujol) 1765, 1600, 1510sh and 1505 cm^{-1} ; δ 0.95(3H, t, $J=7.5Hz$), 1.57(2H, sextet, $J=7.5Hz$), 2.32(3H, s), 2.55 (2H, t, $J=7.5Hz$), 3.80(6H, s) and 6.42(2H, s)ppm. On the consideration of the formation of IX, the structure (X) can be deduced from its physical and chemical properties: $C_{22}H_{30}O_6$ (m/e 390); ν_{\max} (film) 3460, 1610, 1585 and 1495 cm^{-1} ; δ 0.81(6H, t, $J=7.0Hz$), 1.15-1.80(4H, m), 2.22 (4H, td, $J=7.0, 1.5Hz$), 3.60(6H, s), 3.95(6H, s) and 6.60(2H, br.s)ppm. Acetylation of X with acetic anhydride-pyridine afforded in quantitative yield the corresponding diacetate (XII), m.p. 117-8°(from EtOH); $C_{26}H_{34}O_8$ (m/e 474); λ_{\max} (MeOH) 279 and 232nm (ϵ , 2470 and 13750, respectively); ν_{\max} (Nujol) 1770, 1600 and 1585 cm^{-1} ; δ 2.34(6H, s)ppm. Formation of these aromatic compounds in high yields indicates that the carbon skeleton of I consists of two C_6-C_3 units, one of which includes the partial structure [B]. Accordingly, I should have two partial structures [C and D]. Furthermore, the UV absorption at 278nm in I (or II) and its disappearance in III can be explained only by further conjugation of cyclopropane ring with the chromophore [C],⁵ and the UV absorption at 221nm in VI can be assigned to the conjugated cyclopropane-ketone system.⁵ On the other hand, the remaining trisubstituted double bond (δ 5.55(1H, q, $J=1.9Hz$)) as well as the isolated methylene group (δ 2.88(2H, br.s)) in I must be included in [D]. Therefore, I should be represented by [E] or [F]. The biphenyl-type compound (X) may be produced as shown below.



Finally, the mass spectra of I and its derivatives satisfy the structure (I = E) rather than [F], as discussed below. The fragment peaks with the strongest intensity, which must be due to the bond fission between two rings A and B together with one proton transfer from the ring A to the ring B, are observed in their mass spectra: I, m/e 224.1034 for $C_{12}H_{16}O_4$; II, m/e 226.1236 for $C_{12}H_{18}O_4$; III, m/e 226.1201 for $C_{12}H_{18}O_4$; IV, m/e 226.1197 for $C_{12}H_{18}O_4$. The corresponding

fragment peaks are also found in V (m/e 226), VII (m/e 228) and VIII (m/e 228).

On a biogenetic point of view, asatone (I) seems to be quite interesting. All compounds gave satisfactory physical data and elementary analyses.



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