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CONVERSION OF AILANTHONE INTO SHINJULACTONE C THROUGH AN IONIC [4+2] CYCLOADDITION REACTION

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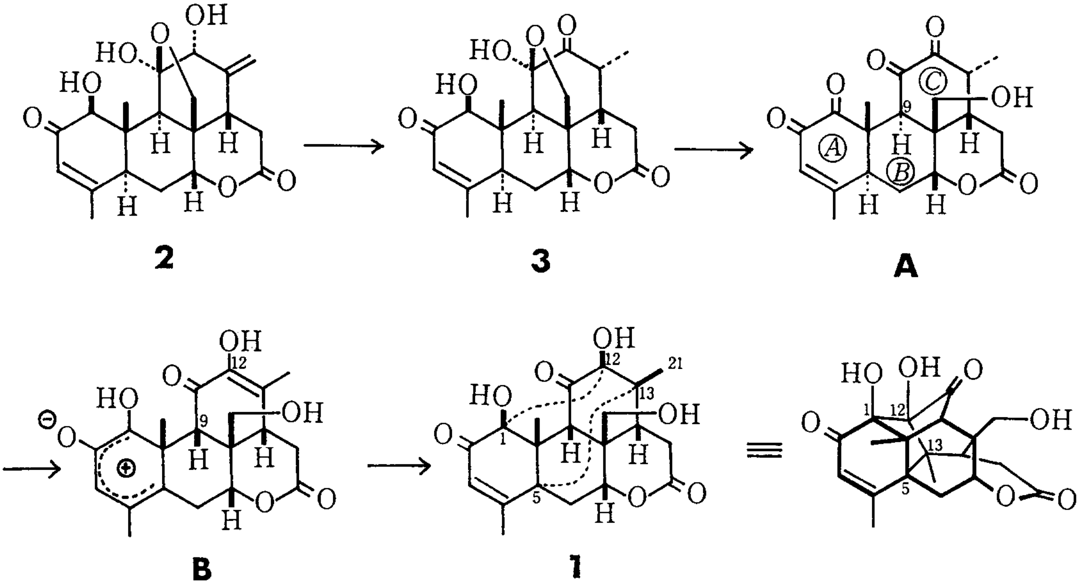
Summary: Ailanthone was converted into shinjulactone C with a 1α,12α:5α,13α-dicyclo-9β*H*-picrasane skeleton. The key reaction consists of an intramolecular ionic [4+2] cycloaddition between a pentadienyl cation and an olefin.

Recently we have isolated three new quassinoids with modified picrasane skeletons, shinjudilactone,1) shinjulactones B2) and C (1)3) from *Ailanthus altissima* SWINGLE and determined their structures by single crystal X-ray analysis. These migrated picrasane skeletons are interesting from the biogenetical view point, and we have reported a transformation of ailanthone (2),4) a main quassinoid of this plant, into shinjudilactone through benzilic acid rearrangement.5) This communication describes chemical conversion of ailanthone (2) into shinjulactone C (1) with a 1α,12α:5α,13α-dicyclo-9β*H*-picrasane skeleton.

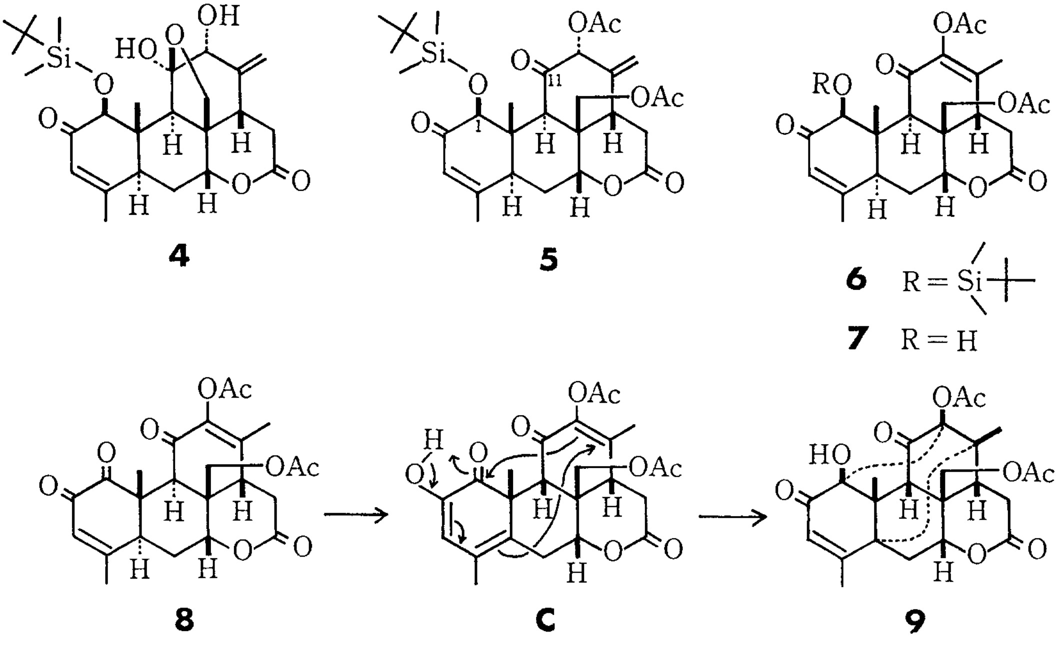
A conceivable biogenetic pathway from ailanthone (2) to shinjulactone C (1) *via* intermediates A and B is shown in Scheme 1. An inversion of a chiral center at C-9 position must occur prior to the cycloaddition of Δ^{12}-double bond in ring C with a pentadienyl cation in ring A. If the inversion of 9α-H into 9β-H occurs and both rings B and C adopt boat forms, rings A and C would be sterically very close to each other enough to overlap π-orbitals.

According to these considerations, chemical conversion of ailanthone (2) into shinjulactone C (1) was investigated. J. Polonsky *et al.*6) reported that when glaucanol was heated in pyridine, the inversion of 9α-H into 9β-H occurred. Ailanthone (2) was heated in pyridine under reflux for 9 h to afford isoailanthone (3) in 67% yield7); it was shown that the isomerization proceeded without inversion of the C-9 position. However the heating was continued for 15-20 h to afford a complex mixture, from which shinjulactone C (1) was obtained in 5-8% yield together with isoailanthone (3; yield 30-40%) and many unidentified by-products. Since the reaction was carried out in atmosphere, isoailanthone (3) or other intermediates must suffer auto-oxidation, which was supported by the following experiment; neither ailanthone (2) nor isoailanthone (3), on heating in argon atmosphere, yielded shinjulactone C (1) at all.

In order to elucidate the reaction mechanism, a stepwise conversion was investigated. Treatment of ailanthone (2) with *t*-butyldimethylsilyl chloride (5.0



Scheme 1



Scheme 2

equiv.) in the presence of imidazole(13 equiv.) in DMF at room temperature for 18 h afforded a monosilyl derivative (4; mp 234-236 °C, yield 94%),[8,9] which underwent acetylation with acetic anhydride in pyridine (70 °C, 18 h) to give a monosilyl diacetate (5; mp 182-184 °C, yield 92%).[10] On heating in pyridine under reflux for 11 h, 5 isomerized to a monosilyl enolacetate (6; mp 210-213 °C, yield 95%).[11] ^{1}H NMR of 6 showed a signal due to vinyl methyl protons (δ 1.79, 3H, s; 13-CH_3) instead of signals due to *exo*-methylene (δ 5.14 and 5.20, each 1H, s; 21-H) and a proton (δ 5.45, 1H, s; 12-H) attached to a carbon atom with an acetoxyl group for 5. Signals due to a proton attached to a carbon atom with a silyloxyl group appeared at δ 3.97 (1H, s; 1-H) in ^{1}H NMR spectra of both 5 and 6. ^{13}C NMR spectrum of 5 showed a signal at δ 198.9 due to a carbonyl carbon atom at C-11 position, while a signal due to a hemiacetal carbon atom was observed at δ 108.5 for 4. From these results the structure of the monosilyl diacetate (5) was firmly established. Although desilylation of the monosilyl enolacetate (6) with fluoride anion proceeded slowly, a treatment of 6 with AcOH-H_2O-THF (2:1:1) at room temperature afforded 1-hydroxy enolacetate (7; mp 173-175 °C, yield 85% based on the consumed 6),[12] which was subjected to Jones oxidation (0 °C, 30 min) to give an α-diketone (8; mp 160-164 °C, yield 80%).[13] This compound corresponds to a diacetate of the intermediate A.

Now the α-diketone (8) in hand was transformed into 12,20-di-*O*-acetylshinjulactone C (9) by heating in pyridine under reflux for 9 h in 22% yield, which was shown to be completely identical with a specimen (9) derived from natural shinjulactone C (1). The reaction from 8 to 9 could be explained by the same mechanism, the coexistence of an ionic [4+2] cycloaddition of class B[14] and a sigmatropic change of order [1,9], proposed for perezon-pipitzol transformation.[15] The reaction process from 8 to 9 through an intermediate C is depicted in Scheme 2. Alkaline hydrolysis of 9 with potassium methoxide in methanol afforded shinjulactone C (1) in *ca.* 90% yield.

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8) On the similar silylation conditions, chaparrin afforded 2,11-di-*O*-*t*-butyldimethylsilylchaparrin; A. J. Caruso, J. Polonsky, and B. S. Rodriguez, Tetrahedron Lett., 23, 2567 (1982).

9) 4: IR (KBr) 3450, 3250, 1730, 1685, 1660, and 840 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.15 and 0.16 (each 3H, s), 1.05 (9H, s), 1.25 (3H, s), 1.95 (3H, br s), 3.52 and 3.90 (each 1H, d, *J*=8 Hz), 4.01 (1H, s), 4.26 (1H, s), 4.50 (1H, t, *J*=2.5 Hz), 5.22 and 5.31 (each 1H, br s), and 5.99 (1H, m); ^{13}C NMR (CDCl$_3$) δ -4.1 q, -2.5 q, 10.1 q, 19.1 s, 22.4 q, 25.7 t, 26.7 q, 26.7 q, 26.7 q, 34.5 t, 43.0 d, 43.5 d, 45.2 s, 45.6 s, 47.2 d, 71.6 t, 78.0 d, 79.3 d, 86.0 d, 108.5 s, 120.7 t, 126.3 d, 143.4 s, 159.4 s, 169.3 s, and 195.1 s; MS m/e 490 (M$^+$), 475, 433, and 57; Found: m/e 490.2383. Calcd for $C_{26}H_{38}O_7Si$: M 490.2385.

10) 5: IR (Nujol) 1750, 1690, 1230 and 845 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ -0.10 and -0.14 (each 3H, s), 0.84 (9H, s), 1.14 (3H, s), 1.83 (3H, br s), 2.00 and 2.07 (each 3H, s), 3.97 (1H, s), 3.80 and 4.31 (each 1H, d, *J*=12 Hz), 4.57 (1H, br s), 5.14 and 5.20 (each 1H, s), 5.45 (1H, s) and 5.85 (1H, m); ^{13}C NMR (CDCl$_3$) δ -3.7, -3.3, 10.6, 18.8, 20.6, 21.0, 21.9, 25.9, 26.5, 26.5, 26.5, 30.7, 40.1, 41.6, 42.6, 46.4, 51.1, 65.0, 76.0, 77.9, 86.9, 114.5, 126.9, 140.5, 158.3, 168.9, 169.9, 170.1, 196.5, and 198.9; MS m/e 574 (M$^+$), 559, 517, 475, and 207; Found: m/e 574.2618. Calcd for $C_{30}H_{42}O_9Si$: M 574.2598.

11) 6: IR (Nujol) 1740, 1710, 1690, 1240, and 845 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ -0.12 and 0.07 (each 3H, s), 0.90 (9H, s), 1.24 (3H, s), 1.79 (3H, s), 1.93 (3H, br s), 2.18 and 2.20 (each 3H, s), 3.97 (1H, s), 4.60 (1H, t, *J*=2.5 Hz), 4.19 and 4.68 (each 1H, d, *J*=12 Hz), and 5.98 (1H, m); MS m/e 574(M$^+$), 559, 517, 475, 457, and 207; Found: m/e 574.2648. Calcd for $C_{30}H_{42}O_9Si$: M 574.2598.

12) 7: IR (KBr) 3430, 1740, 1675, 1220, and 1030 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.16 (3H, s), 1.86 (3H, s), 1.97 (3H, br s), 2.11 and 2.26 (each 3H, s), 3.30 (1H, s), 3.97 (1H, d, *J*=3.5 Hz), 4.47 (1H, d, *J*=3.5 Hz), 4.21 and 4.61 (each 1H, d, *J*=12 Hz), 4.59 (1H, br s), and 6.07 (1H, m); MS m/e 460 (M$^+$), 418, 400, 358, 151, and 60; Found: m/e 460.1741. Calcd for $C_{24}H_{28}O_9$: M 460.1734.

13) 8: IR (KBr) 2910, 1740, 1695, 1220, and 1040 cm^{-1}; UV (EtOH) λ_{max} 245 nm (ε 9100); ^{1}H NMR (CDCl$_3$) δ 1.41 (3H, s), 1.89 (3H, s), 2.04 (3H, br s), 2.11 and 2.25 (each 3H, s), 3.52 (1H, s), 4.56 (1H, t, *J*=2.5 Hz), 4.25 and 4.65 (each 1H, d, *J*=12 Hz), and 6.23 (1H, m); ^{13}C NMR (CDCl$_3$) δ 14.2, 16.0, 20.0, 20.6, 22.4, 25.6, 30.3, 38.5, 41.0, 43.1, 44.8, 51.5, 61.9, 76.9, 129.0, 141.4, 143.2, 164.1, 167.9, 168.5, 170.2, 185.5, 187.5, and 198.5; MS m/e 458 (M$^+$), 430, 416, and 151; Found: m/e 458.1586. Calcd for $C_{24}H_{26}O_9$: M 458.1576.

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