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CONVERSION OF AILANTHONE INTO SHINJUDILACTONE, A BACKBONE-REARRANGED PICRASANE

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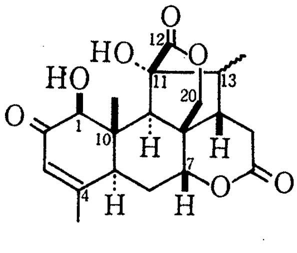
On heating with sodium hydrogencarbonate in aqueous methanol, ailanthone (2) afforded 13(12 → 11α)*abeo*-picrasanes [or 9(11 → 12α) *abeo*-picrasanes], shinjudilactone (1) and its 13-epimer (3), in a ratio of 1:1 in good yields. The reaction is likely to proceed through isomerization of 2 into an α-diketone (6), followed by benzilic acid rearrangement. Under the same conditions, norquassin (4) gave the rearrangement product, norquassinic acid (5).

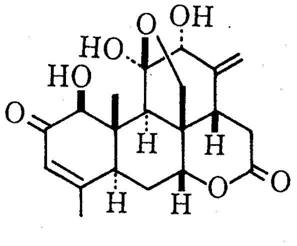
KEYWORDS —— benzilic acid rearrangement; quassinoids; shinjudilactone; ailanthone; norquassin; norquassinic acid; Simaroubaceae

Recently we have isolated three new quassinoids with modified picrasan skeletons: shinjudilactone (1)1) and shinjulactones B2) and C3) from *Ailanthus altissima* SWINGLE (= *A. glandulosa* DESF., Japanes name: Shinju or Niwaurushi, Simaroubaceae), together with several known quassinoids, and determined the structures of these new quassinoids by single crystal X-ray diffraction analysis.1-3) The structure elucidation has revealed that shinjudilactone (1) has a new migrated picrasane skeleton, 13(12 → 11α)*abeo*-picrasane [or 9(11 → 12α)*abeo*-picrasane], in which we are very interested from the biogenetical viewpoint. This communication describes a chemical conversion of ailanthone (2),4) a main quassinoid of this plant, into shinjudilactone (1) and its 13-epimer (3), and a transformation of norquassin (4) into norquassinic acid (5).5)



1 13α-CH_3

3 13β-CH_3



2

Two biogenetic routes from ailanthone (2) to shinjudilactone (1) are conceivable: a) protonation to $\Delta^{13(21)}$-double bond6) and a hydride migration give a cation at $C_{(12)}$, which could undergo reconstruction of a hemiacetal bridge to afford an intermediate cation carrying a positive ion at $C_{(11)}$, followed by ring contraction from one of the two cations and deprotonation; b) isomerization into an α-diketone (6) followed by benzilic acid rearrangement gives a hydroxy carboxylic acid, which is subjected to lactonization. Since the hydroxide ion is accessible to either $C_{(12)}$ or $C_{(11)}$ of the α-diketone (6), it could be suggested that 13(12 → 11α)*abeo*-type skeletal rearrangement or 9(11 → 12α)*abeo*-type rearrangement to give 1 takes place (Chart 1).

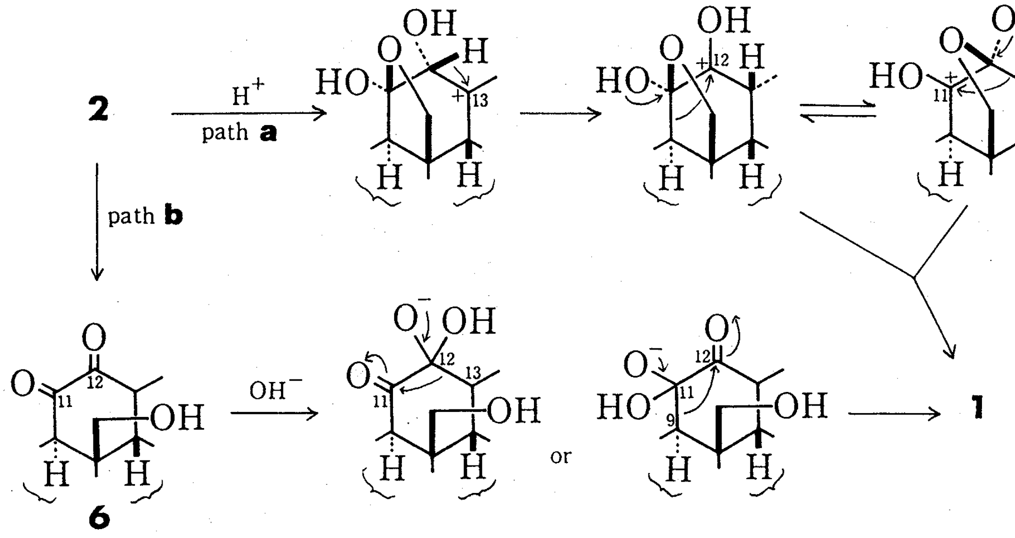


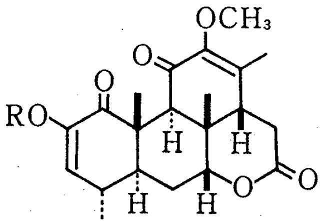
Chart 1

According to these considerations, chemical conversion of ailanthone (2) into shinjudilactone (1) was investigated. The reaction did not occur under acidic conditions using *p*-TsOH, HCl, HCl-AcOH, or $FeCl_3$-HCl, while a very complex mixture was obtained in the reaction of 2 with $BF_3 \cdot Et_2O$; shinjudilactone (1) was not detectable in the reaction mixture by TLC examination.

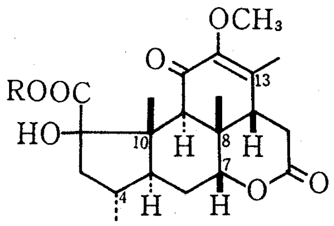
Alkaline conditions under reflux, such as $NaOH/H_2O$, KOH/MeOH, and $Ba(OH)_2/C_5H_5N$, gave extremely polar products. However ailanthone (2; 21 mg) in a mixture of methanol (2 ml) and water (2 ml) was heated with sodium hydrogencarbonate[7] (5 mg) under reflux for 30 min, and the reaction mixture was acidified with hydrochloric acid to give a mixture (20 mg); separation of this mixture by preparative TLC (SiO_2) developed with chloroform-methanol (19:1) afforded shinjudilactone (1; 10 mg) and 13-epishinjudilactone (3; 10 mg). Shinjudilactone (1) was completely identical with a natural specimen. 13-Epishinjudilactone (3), mp 263-266 °C (from methanol-ethyl acetate), $[\alpha]_D^{23}$ +48° (c 0.57, pyridine), showed a lower Rf value than that of 1 on a TLC plate and the following spectral data: IR (KBr) *ca*. 3300, 1745, 1675, 1620, 1250, and 1180 cm^{-1}; UV (ethanol) λ_{max} 239 nm (ε 10300); ^1H NMR (pyridine-d_5) δ 1.19 (3H, d, J=6 Hz; $C_{(13)}-CH_3$), 1.20 (3H, s; $C_{(10)}-CH_3$), 1.77 (3H, br s; $C_{(4)}-CH_3$), 4.22 (1H, s; $C_{(1)}$-H), 4.25 and 4.66 (each 1H, A and B parts of an AB-type quartet, J=12 Hz; $C_{(20)}-H_2$), 4.65 (1H, t; J=2 Hz; $C_{(7)}$-H), and 6.06 (1H, m; $C_{(3)}$-H); ^{13}C NMR (pyridine-d_5) δ 9.8, 11.4, 22.2, 27.0, 29.3, 41.9, 42.5, 42.8, 44.5, 48.3, 51.0, 74.3, 76.0, 76.6, 83.5, 126.3, 161.8, 170.9, 175.7, and 196.7; MS m/e (%) 376 (M^+; 8), 358 (6), 347 (8), 340 (10), 312 (45), 294 (40), 268 (100), and 253 (60); Found: m/e 376.1532. Calcd. for $C_{20}H_{24}O_7$: M 376.1520.

Shinjudilactone (1) was thus obtained from ailanthone (2). The conversion reaction proceeds through benzilic acid rearrangement (path b)[8] rather than through proton-induced rearrangement (path a). It seems likely that shinjudilactone (1) would be derived biogenetically from ailanthone (2) or its equivalent through a pathway similar to benzilic acid rearrangement.

Benzilic acid rearrangement, however, requires generally strongly basic conditions.[9,10] Since the rearrangement of a 1,2-diketone catalyzed by sodium hydrogencarbonate has not been described in the literature,[11] a rearrangement of norquassin (4) was examined under these conditions. Norquassin (4) undergoes benzilic acid rearrangement on treatment with boiling 10% aqueous sodium hydroxide solution to give norquassinic acid (5) as a hydrate.[5] Norquassin (4; 97 mg), prepared from quassin (7),[5] was heated with sodium hydrogencarbonate (*ca.* 10 mg) in 50% aqueous methanol (6 ml) under reflux for 5 h. The usual work-up afforded a crude acid (5), which was treated with diazomethane to give methyl norquassinate (8; 58 mg). The melting point and spectral data of the methyl ester (8)[12] were identical with those of a specimen prepared by sodium hydroxide-catalyzed rearrangement and also with those of an authentic sample.[5]



4 R=H
7 R=CH_3



5 R=H
8 R=CH_3

These conversions are the first examples of benzilic acid rearrangement catalyzed by a weak-base sodium hydrogencarbonate. Further investigation of the structural demand for the rearrangement is now in progress.

REFERENCES AND NOTES

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4) H. Naora, T. Furuno, M. Ishibashi, T. Tsuyuki, T. Takahashi, A. Itai, Y. Iitaka, and J. Polonsky, Chem. Lett., 1982, 661.
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6) Numbering of picrasane refers to the nomenclature described in the Chemical Abstracts.

7) Reaction catalyzed by sodium carbonate also gave the same mixture, but was accompanied by a formation of a small amount of by-products.

8) Whether formation of **1** is through 13(12 → 11α)*abeo*-type or 9(11 → 12α)*abeo*-type rearrangement remains undetermined.

9) *e.g.*, S. Selman and J. F. Eastham, Quart. Rev., **14**, 221 (1960); C. J. Collins and J. F. Eastham, "Rearrangements involving the carbonyl group," in "The Chemistry of the Carbonyl Group," ed by S. Patai, Interscience Publishers, London, 1966, p. 783.

10) When benzil was treated with $NaHCO_3/H_2O$-MeOH-THF (5:5:1) under reflux for 5.5 h, the starting material was recovered quantitatively.

11) Benzilic acid rearrangement of ethyl α,β-dioxobutyrate catalyzed by a saturated $KHCO_3/K_2CO_3$ solution has been described: H. Rodé-Gowal and H. Dahn, Helv. Chim. Acta, **56**, 2070 (1973).

12) IR (KBr) 3420, 1735, 1665, 1285, 1265, and 1040 cm^{-1}; ^1H NMR (chloroform-*d*) δ 1.01 (3H, d, J=5.5 Hz; $C_{(4)}$-CH_3), 1.12 (3H, s; $C_{(10)}$- or $C_{(8)}$-CH_3), 1.23 (3H, s; $C_{(8)}$- or $C_{(10)}$-CH_3), 1.93 (3H, s; $C_{(13)}$-CH_3), 2.56 (1H, s; $C_{(9)}$-H), 3.63 and 3.66 (each 3H, s; -OCH_3), and 4.29 (1H, t, J=2.5 Hz; $C_{(7)}$-H); MS m/e (%) 406 (M^+; 22), 391 (5), 388 (4), 347 (100), 333 (2), and 329 (9).

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