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ARNOTTIANAMIDE AND ISOARNOTTIANAMIDE THE STRUCTURAL ESTABLISHMENT DUE TO CHEMICAL CONVERSION FROM THE KNOWN BENZO[C]PHENANTHRIDINE ALKALOIDS BY THE NOVEL BAEYER-VILLIGER LIKE OXIDATION OF AN IMMONIUM GROUP

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In the course of our studies on the chemical constituents of Rutaceous plants, we[1] had recognized the presence of two structurally isomeric constituents containing a nitrogen atom in their molecules in the bark of *Xanthoxylum cuspidatum* Champ (*Fagara cuspidata* Engl), a Formosan Rutaceous plant But the contents of these components were so minute that we could not perform chemical establishments of their structures Fortunately, in the recent investigation, we could isolate a relatively large amount of one of these constituents from the bark of *X. arnottianum* Maxim (Japanese name Iwa-Zansho) and designated as arnottianamide (1) We wish to report here structural establishments of atnottianamide (1) and its structurally isomeric one, isoarnottianamide (2), due to conversions of chelerythrine (3) and nitidine (4) to these products by the novel Baeyer-Villiger like oxidation of their immonium groups, respectively

Arnottianamide (1) was obtained as colourless prisms, mp 267-269°, $C_{21}H_{19}O_6N$** (M^+ at m/e 381) from *X. arnottianum* in 0 1583 % yield and from *X cuspidatum* in 0 0020 % yield It shows following spectral data [IR ν(Nujol) cm^{-1} 3200-3450(OH), 1663(C=O), UV λ(EtOH) nm (log ε)· 236(4.73), 280(4.01)sh, 321(3.63)sh, 324(3 65), 332(3 81)]

Isoarnottianamide (2) was obtained as colourless prisms, mp 254-257°, $C_{21}H_{19}O_6N$** (M^+: at m/e 381) from only *X cuspidatum* in 0 00094 % yield It shows following spectral data [IR ν(KBr) cm^{-1}· 1670(C=O) UV λ(MeOH) nm(log ε) 237.5(4.73), 290(4 00), 332(3 86)]

Treatment of arnottianamide (1) with $LiAlH_4$ in THF gave deoxoarnottianamide (5) as colourless prisms, mp 200-202°, $C_{21}H_{21}O_5N$** (M^+ at m/e 367) [IR ν(Nujol) cm^{-1}: 3390(OH); NMR($CDCl_3$) δ· 2.72(6H, s, $N(CH_3)_2$), 3 91, 3.95(3H, s, OCH_3), 5.99(2H, s, OCH_2O), 6.51, 6 81, 7.18, 7.43(1H, d, J=8 5 Hz, arom H), 6.77(1H, s, OH), 7.09, 7.52(1H, s, arom H)] In the NMR spectrum of (5), there is not observed a signal corresponding to that which appeared in rather lower field in the NMR spectrum of (1), but a newly born signal due to an N,N-dimethyl group, indicating that (1) has an $N(CH_3)CHO$ group in its molecule

Treatment of (5) with Rodinow reagent[2] afforded methyl deoxoarnottianamide (6), as colourless prisms, mp 166.5-168 5°, $C_{22}H_{23}O_5N$** (M^+ at m/e 381). [NMR($CDCl_3$) δ· 2 63(6H, s, $N(CH_3)_2$), 3 85(3H, s, OCH_3), 3 90(6H, s, OCH_3×2), 5 98(2H, s, OCH_2O), 6 67, 6 83, 7.06, 7.37

Table 1 NMR Spectra of Arnottianamide (1) and Isoarnottianamide (2)

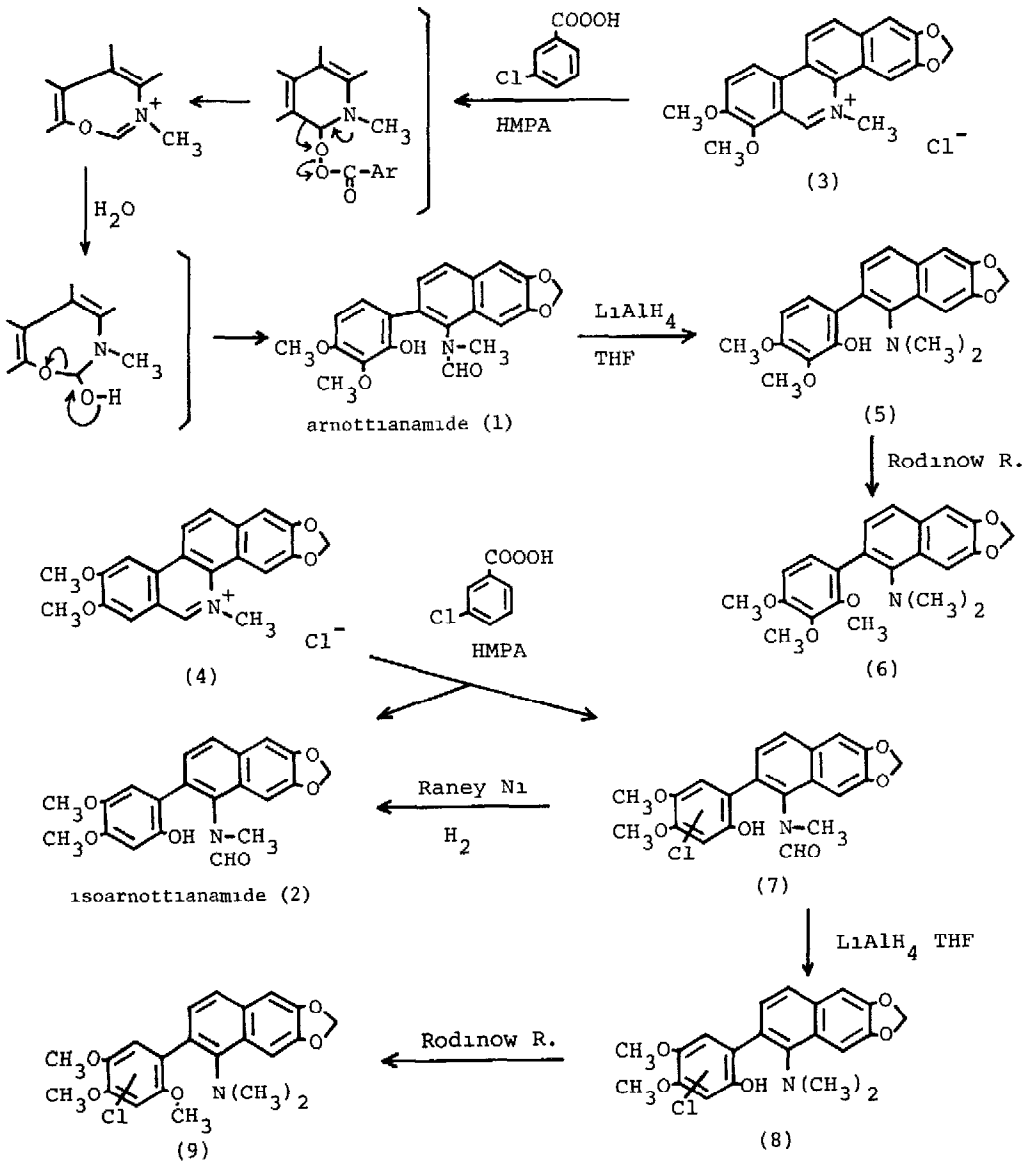
(CF_3COOH; δ)

		Arnottianamide (1)	Isoarnottianamide (2)
Common Signals	NCH_3	3.27 (3H, s)	3.26 (3H, s)
	OCH_3	4.04 (3H, s) 4.09 (3H, s)	3.97 (6H, s)
	OCH_2O	6.09 (2H, s)	6.08 (2H, s)
	NCHO	8.50 (1H, s)	8.50 (1H, s)
	Arom. Hs	7.03 (1H, s) 7.28 (1H, s) 7.36 (1H, d, J=8.5 Hz) 7.87 (1H, d, J=8.5 Hz)	7.02 (1H, s) 7.27 (1H, s) 7.35 (1H, d, J=9.0 Hz) 7.88 (1H, d, J=9.0 Hz)
Characteristic Signals	Arom. Hs	6.81 (1H, d, J=8.5 Hz) 7.06 (1H, d, J=8.5 Hz)	6.78 (1H, s) 6.88 (1H, s)

(1H, d, J=8.5 Hz, arom H), 7 08, 7 55(1H, s, arom H)]. This chemical evidence indicates the presence of a phenolic group in the molecule of arnottianamide (1)

The above functionalization of arnottianamide (1) and comparison between the NMR spectrum of arnottianamide (1) and that of isoarnottianamide (2) gave a clue to a speculation on formation of these constituents In the NMR spectrum, these two alkaloids show four common and two characteristic signals due to aromatic protons as shown in Table 1 In the case of (1), these characteristic signals were observed as two doublets having the same J value (8 5 Hz), indicating that two aromatic protons should be located at ortho-positions of a tetra-substituted benzene ring to each other. On the other hand, those protons of (2) would be allocated to para-positions of a corresponded benzene ring to each other because those signals appeared as two singlets The natural occurrence of such a pair of positional isomers[3] is widely known in the Rutaceous alkaloids, in particular, belonged to the benzylisoquinoline group, for example chelerythrine-nitidine (the ring A), berberine-xylopine type (the ring D), and laurifoline-xanthoplanine (the ring D) etc This observation allowed us to imagine that both alkaloids might be derived from benzo[c]phenanthridine alkaloids through some oxidative process in plant body Formation of phenol and $N(CH_3)CHO$ groups of arnottianamide can be rationally explained by supposing that its immonium groups of benzo[c]phenanthridine alkaloids were subjected to a Baeyer-Villiger like oxidation *in vivo* We, therefore, examined the possibility of this type of reaction *in vitro*

Treatment of chelerythrine (3) chloride with m-chloroperbenzoic acid in hexamethylphosphoric triamide (HMPA) at 40° gave arnottianamide in 70.1 % yield This chemical evidence established the structure of arnottianamide as formula (1)



The present success strongly supported the hypothesis that isoarnottianamide (2) might come from nitidene (4) *in vivo*. According to this hypothesis, the above oxidative reaction was also applied to nitidine (4) chloride In this trial, the main product was a chlorinated compound (7), mp 256-260°, $C_{21}H_{18}O_6NCl$** [IR ν(Nujol) cm^{-1} 3100-3400(OH), 1673(C=O), NMR($CDCl_3$) δ· 2 99 (3H, s, NCH_3), 3.77, 3.91(3H, s, OCH_3), 5.40(1H, s, OH), 6 02(2H, s, OCH_2O), 6.57, 7.03, 7 15 (1H, s, arom. H), 7.23, 7.70(1H, d, J=8 5 Hz, arom H), 8.10(1H, s, CHO)] in 33.6 % yield and (2) was also obtained as a minor product in 3 8 % yield Removal of the chlorine atom from (7) by catalytic hydrogenation on Raney nickel gave (2) in 27.3 % yield

Reduction of (7) with $LiAlH_4$ in THF gave N,N-dimethyl derivative (8), mp 151-153°, $C_{21}H_{20}O_5NCl$** [IR ν(Nujol) cm^{-1} 3450(OH), NMR($CDCl_3$) δ 2 81(6H, s, $N(CH_3)_2$), 3.82, 3 94(3H, s, OCH_3), 6 02(2H, s, OCH_2O), 6 66, 7 11, 7 46(1H, s, arom H), 7 13, 7 47(1H, d, J=8.5 Hz, arom. H)], in 63 7 % yield, indirectly indicating the presence of an $N(CH_3)CHO$ group in its molecule of (2)

Treatment of (8) with Rodinow reagent[2] afforded O-methyl N,N-dimethyl product (9), mp 158 5-159 5°, $C_{21}H_{22}O_5NCl$** [NMR($CDCl_3$) δ 2.69(6H, s, $N(CH_3)_2$), 3.51, 3 83, 3 94(3H, s, OCH_3), 6 01(2H, s, OCH_2O), 6 65, 7 10, 7 53(1H, s, arom H), 7 11, 7 40(1H, d, J=8 5 Hz, arom. H)], in 67 7 % yield, demonstrating the presence of a phenolic group in (7).

These chemical evidences are enough to establish the structure of isoarnottianamide as structure (2) The chlorine atom of (7) is seemed to come from chloride anion of nitidine (4) chloride and its position would be located to a ring A of a benzo[c]phenanthridine skeleton because we could find only one signal which was assignable to an aromatic proton of the ring A in the NMR spectra of all of the chlorinated derivatives However, the mechanism of chlorination and a precise location of the chlorine atom were remained obscure.

As mentioned above, we succeeded in correlating two natural amide derivatives with the known benzo[c]phenanthridine alkaloids by using a novel Baeyer-Villiger like oxidation on an immonium salt The studies on the extension and limitation of this novel reaction are now under progress in our laboratory

References

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** The compound gave satisfactory elemental analysis for the formula given

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