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Modifications of Norditerpenoid Alkaloids: Ⅲ. Preparation of 7,17-seco Yunnaconitine Derivatives *via* Rearrangement of Chloroamine

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Abstract: Preparation of both 7,17-seco yunnaconitine derivatives **6** starting from yunnaconitine **3** *via* rearrangement of chloroamine **5** is described.

Keywords: Norditerpenoid Alkaloids; 7,17-seco ynnaconitine.

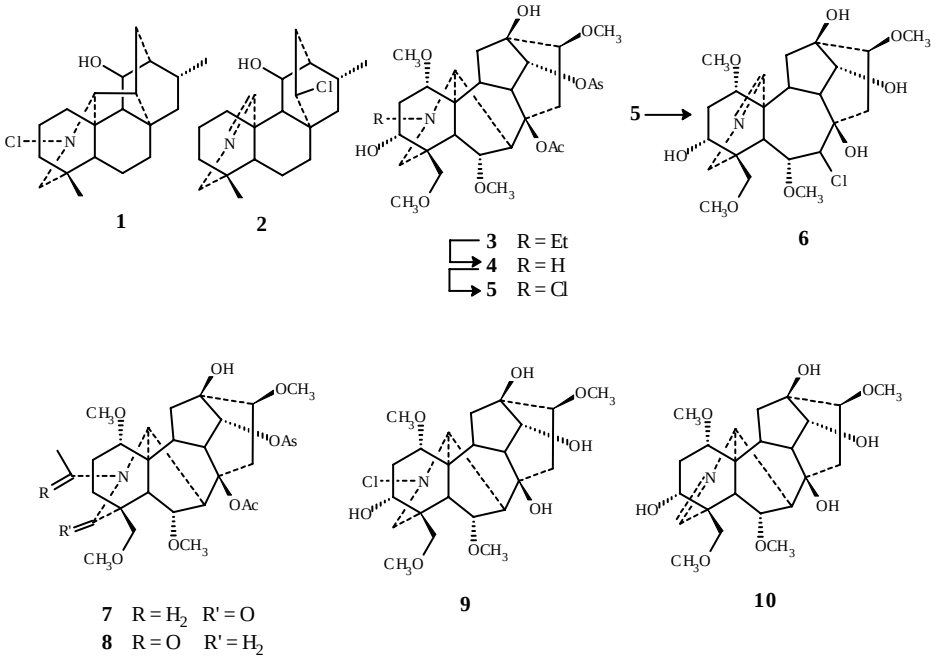
In our investigation of modification of the norditerpenoid alkaloids, cleavage of the C(17)-C(7) bonds is the key reaction. Ref. [1] gave a systematic summing-up about the cleavages, including pyrolysis of *N*-oxides[2], pyrolysis-reduction[3], photolysis-reduction[4], rearrangement-reduction[5], oxidation-reduction[3c,6] and neighboring group participation[7]. However, most of them led to the complicated products[5], with low yields or difficult purification. In this paper, we report in details on the cleavage of the C(17)-C(7) bonds in the aconitine-type norditerpenoid alkaloid yunnaconitine **3** *via* rearrangement of chloroaminine **5**.

In 1973, Yatsunami, *et. al* reported the successful cleavage of the C(17)-C(7) bond in kobusine into **2** *via* rearrangement of chloroamine **1**[8]. Examination of the Dreiding model shows that the C(17)-C(7) bond in **3** was stereochemically similar to the C(20)-C(14) bond in kobusine, leading to a route for cleavage of the C(17)-C(7) bond in **3** as showed in **Figure 1**. According to Ref. [9], treatment of **3** with $KMnO_4$ afforded compounds **7**[10] (20.5%), **8**[10] (30.5%), and the desired *N*-deethyls **4**. Reaction of **4** with NCS at rt. for 1 h gave chloroamine **5**[11] (85.7%). Refluxing **5** in 1.2 mol/L NaOMe solution. under N_2 for 24 h according to Ref. [8] gave complex products, which are not responsive to modified Dragendorff's reagent, suggesting a deamination to be happen during the reaction. Only an aminoalcohol **9**[12] was afforded when treatment of **5** at room temperature. under similar conditions.

Treatment of **5** in 1.2 mol/L NaOMe was under microwave irridation for 30 seconds gave a complex product, from which two components mixture was isolated. Its

^{13}C NMR spectra showed two sets of similar signals. The ^{1}H(^{13}C) NMR and IR spectra of this mixture also showed the presence of two types of imine moieties [-N=CH(17) and –N=CH(19)] [δ_H 8.0^9 (8.0^8) (1H,s); δ_C 162.2 (163.1) d; 1655 cm^{-1}]. This suggested that the mixture consisted of the desired product **6**[13] and compound **10**[13]. In addition, its mass spectrum displayed the molecular ion peak at m/z 489 and its isotopic ion peak at m/z 491 (two peak high ratio=3:1) for **6**, and the characteristic ion fragments at m/z 453 (M^+), 422 (M-31), 436 (M-17), 435 (M-18) for **10**. Finally, structures of **6** and **10** were deduced on the basis of careful assignments for their ^{1}H-(^{13}C-) NMR and DEPT spectra. This is a novel approach to cleavage of the C(17)-C(7) bonds in the norditerpenoid alkaloids. But, it is still necessary to promote the yields of the desired products.

Figure 1.



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References and Notes

1. F. P. Wang and X. T. Liang, Chemistry of the diterpenoid alkaloids, "*The Alkaloids*: *Chemistry and Pharmacology*"(G. A. Coedell, ed.),. *42*,.151-47, Academic Press, New York, **1992**.
2. a). K. Wiesner, M. Gotz, D. L. Sommons, L. R. Fowler, F. W. Bachelor, R. F. C. Brown, and G. Buchi, *Tet. Lett*, **1959**, *2*, 15;
   b). F. P. WANG and S. W. Pelletier, *Chin. Chem. Lett*, **1991**, *2*, 109.
3. a). O. E. Edwards, *Chem. Commun*, 1965, 319;
   b). K. Wada, H. Bando, T.Mori, R. Wada, Y. Kanaiwa, and T. Amiya, *Chem. Pharm. Bull*, **1985**, *33*, 3658;
   c). O. E. Edwards, L. Fonzes, and L. Marion, *Can. J. Chem*, **1966**, *44*, 583.
4. S. W. Pelltier, J. F. Moore, R. C. Desai, N. V. Mody, and H. K. Desai, *J. Am. Chem. Soc*, **1982**, *47*, 5290; K. Wiesner and T. Inaba, *J. Am. Chem. Soc*, **1969**, *91*, 1036.
5. T. Amiya and T. Shima, *Bull. Chem. Soc. Jpn*, **1967**, *40*, 1957; T. amiya, Y. Kanaiwa, N. Nakano, and T. Shima, *Chem. Soc. Jpp*, **1978**, *51*, 248.
6. O. E. Edwards, M. Los, and L. Marion, *Can. J. Chem*, **1959**, *37*, **1996**.
   Z. Valenta and I. G. Wright, *Tetrahedron*, **1960**, 284.
   O. E. Edwards, L. Marion, and D. K. R. Stenart, *Can. J. Chem*, **1956**, *34*, 1315.
7. R. Aneja and S. W. Pelletier, *Tet. Lett*, **1964**, 669.
   R.Aneja and S. W. Pelletier, *Tet. Lett*, **1965**, 215.
8. T. Yatsunami, T. Isono, I. Hayakawa, and T. Okamoto, *Chem. Pharm. Bull*, **1975**, *23*, 3030.
   T. Yatsunami, S. Furuya, and T. Okamoto, *Chem. Pharm. Bull*, **1978**, *26*, 3199.
9. F. P. WANG, J. Z. FU, J. S. YANG, Z. B. LI and B. G. LI , *Chin. Chem. Lett*, submitted.
10. **8**: white amorphous powder. ^{1}H NMR (200MHz, $CDCl_3$) δ: 1.29, 2.16 (each 3H, s, 2×OAc), 3.12, 3.12, 3.29, 3.29, 3.85 (each 3H, s, 5×OCH_3), 4.15 (1H, d, J=6.6Hz, 6β-H), 4.85 (1H, d, J=4.8Hz, 14β-H), 6.88, 8.01 (each 2H, AA'BB' system, Ar-H). FABMS m/z (%): 674 (M+1, 100).
11. **5**: white amorphous powder. $C_{33}H_{44}NO_{11}Cl$ (FABMS+^{13}C NMR) ^{1}H NMR (200MHz, $CDCl_3$) δ: 1.33 (3H, s, OAc), 3.16, 3.27, 3.27, 3.52, 3.85 (each 3H, s, 5×OCH_3), 4.09 (1H, d, J=6.4Hz, 6β-H), 4.84 (1H, d, J=5.0Hz, 14β-H), 6.89, 8.0 (each 2H, AA'BB' system, Ar-H). ^{13}C NMR (50MHz) δ: 81.2 (1), 34.6 (2), 70.1 (3), 46.8 (4), 50.8 (5), 82.1 (6), 46.2 (7), 84.8 (8), 44.7 (9), 41.1 (10), 49.5 (11), 34.9 (12), 74.6 (13), 78.0 (14), 38.9 (15), 83.1 (16), 70.1 (17), 75.4 (18), 56.8 (19), 56.4 (1'), 58.3 (6'), 57.7 (16'), 59.5 (18'), 169.5, 21.3 (OAc), 166.0 (O=C-OR), 122.3 (1"), 131.5 (2", 6"), 113.7 (3", 5"), 163.4 (4"), 55.4 (4"-OCH_3). FABMS m/z (%): 666 (M+1, 100). 632 (M-Cl+1, 46).
12. **9**: white amorphous powder. ^{1}H NMR (200MHz, $CDCl_3$) δ: 3.23, 3.29, 3.35, 3.40 (each 3H, s, 4×OCH_3), 4.24 (1H, d, J=7Hz, 6β-H).
13. **6**: white amorphous powder. $C_{23}H_{36}NO_8Cl$ (EIMS+^{13}CNMR). IR (KBr) cm^{-1}: 1720 [-N=C(17)]. ^{1}H NMR (200MHz, $CDCl_3$) δ: 3.17, 3.282, 3.322, 3.43 (each 3H, s, 4×OCH_3), 8.09 (1H, s, H-19). ^{13}C NMR (75MHz) δ: 80.6 (1), 34.4 (2), 70.5 (3), 41.9 (4), 52.4 (5), 81.5 (6), 71.5 (7), 71.7 (8), 49.3 (9), 41.7 (10), 57.1 (11), 38.8 (12), 76.6 (13), 79.1 (14), 43.5 (15), 84.2 (16), 162.7 (17), 77.0 (18), 75.5 (19), 55.7 (1'), 58.3 (6'), 57.2 (16'), 59.2 (18'). EIMS m/z (%): 492 (M_2+1, 53), 491 (M_2^+, 35), 490 (M_1+1, 100), 489 (M_1^+, 85), 460 (M_2-31, 58), 458 (M_1-31, 40), 456 (M_2-Cl, 36), 454 (M_1-Cl, 28).

10: white amorphous powder. $C_{23}H_{35}NO_8$ (EIMS+^{13}CNMR). IR (KBr) cm^{-1}: 1655 [-N=C(19)]. ^{1}H NMR (200MHz, $CDCl_3$) δ: 3.17, 3.288, 3.329, 3.40 (each 3H, s, 4×OCH_3), 8.08 (1H, s, H-19). ^{13}C NMR (75MHz) δ: 80.9 (1), 34.7 (2), 70.5 (3), 57.1 (4), 49.6 (5), 81.7 (6), 48.7 (7), 71.8 (8), 48.4 (9), 42.0 (10), 49.2 (11), 38.4 (12), 76.5 (13), 79.2 (14), 40.0 (15), 84.3 (16), 59.3 (17), 76.7 (18), 163.1 (19), 55.9 (1'), 57.8(6'), 57.5(16'), 59.1(18'). EIMS m/z (%): 453 (M^+, 16), 436 (M-17, 82), 435 (M-18, 88), 434 (100), 422 (M-31, 84).

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