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# Modification of Norditerpenoid Alkaloids: Ⅱ. A Simple and Convenient Preparation of the Imine Derivatives of Norditerpenoid Alkaloids

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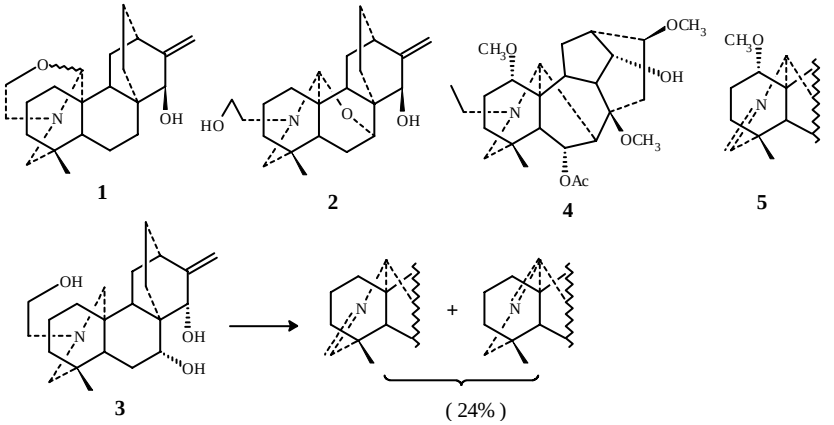
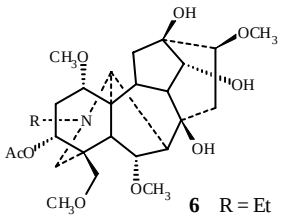
**Abstract**: Treatment of 3-acetylpseudaconie **6** and 3, 13-diacetylyunnaconitine **9** with NBS/acetone-$H_2O$ (2:1) at room temperature produced corresponding imine derivatives **8** and **10**, respectively, in good yields. This is a novel simple and convenient method for preparation of the imine compounds.

**Keywords**: Norditerpenoid alkaloids, imine.

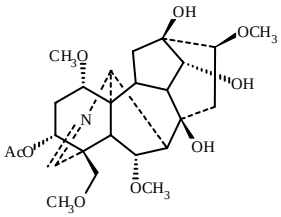
Interest the modification of the norditerpenoid alkaloids led us to preparation of the imine derivatives. Preparation methods of the imines have been summed, including oxidation with $CrO_3$/pyridine[2], rearrangement of chloroamines[3] and heating some oxazolidine-containing or having *O, N*-mixed norditerpenoid alkaloids such as isoatisine **1**[4] and ajaconine **2**[5], with $Ac_2O$-pyridine. In addition, oxidation of **3**[6] with Pb $(OAc)_4$ is also used for this purpose. In 1995, Fuente, *et al* prepared an imine **5** (21% ) starting from peregrine **4** by oxidation of $KMnO_4$/acetone-$H_2O$ (2:1)[7]. In the course of research of modification of the norditerpenoid alkaloids, we found surprisingly that treatment of 3-aceylpseudaconine **6**[8] with NBS/acetone-$H_2O$ (3:1) at room temperature gave the N-



deethyls **7**[9] and imine **8**[10] in 49% and 51% yields, respectively. This is a novel simple, convenient preparation for the imine derivatives of the norditerpenoid alkaloids. A number of experiments showed that the varieties and yields of the resultants were greatly dependent upon the reaction conditions. The main product **7** was produced when using the less than 2 mol NBS. In addition, the substrates having 3-hydroxyl group led to complex products.



**6** R = Et
**7** R = H



**8**

Compound **8**: a white amorphous powder, $C_{25}H_{37}NO_9$ (FABMS+$^{13}$C NMR). Its $^1$H-($^{13}$C-) NMR spectra showed the absence of the *N*-ethyl group and the presence of a characteristic imine moiety [$\delta_H$7.52 (1H,s); $\delta_C$ 165.0d]. In an analogous manner, treatment of 3, 13-diacetylyunnaconitine **9**[11] with NBS also afforded the imine **10**[12] and *N*-deethyl compound **11**[9] (**Figure 1**). A process of formation of the imines and the *N*-deethylation of the norditerpenoid alkaloids that shown in **Figure 2** was postulated.

**Figure 1**

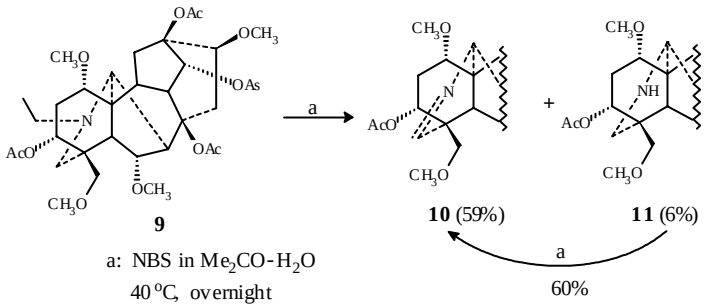
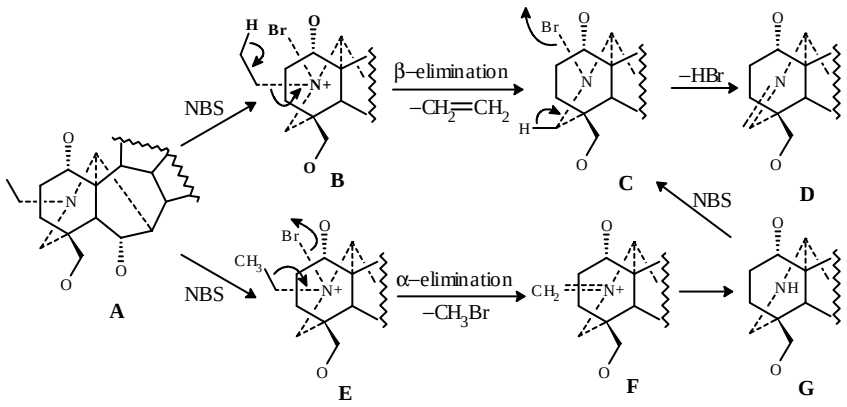
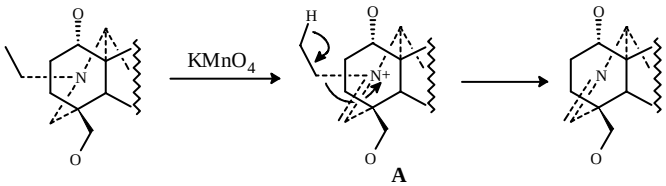



**Figure 2.**



This is evidently different from Fuente's method. In the latter, the imine **4** may be derived from the β-elimination of the intermediate A (**Figure 3**). Our method is simpler, more convenient and in better yield.

**Figure 3**

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**References and Notes**

1. Feng Peng WANG and Xiao Tian LIANG, Chemistry of the diterpenoid alkaloids, in "The Alkaloids: Chemistry and Pharmacology"(G. A. Cordell, ed.), vol. 42, pp.151-247, Academy Press, New York, 1992.
2. S. W. Pelletier, P. C. Pathasarathy, *J. Am. Chem. Soc*, **1965**, *87*, 777.
3. T. Yatsunami, T. Isona, I. Hayakawa, and T. Okamoto, *Chem. Pharm. Bull*, **1975**, ***23***, 3030.
4. D. Dvornik, O. E. Edwards, *Can. J. Chem*, **1957**, *35*, 860.
5. D. Dvornik, O. E. Edwards, *Chem. & Ind (London)*, **1957**, 952.
6. Jing Lei Nie, M.S. Thesis, *Kuming Institute of Botany*, **1996**, 20.
7. G. de La Fuente, L. Rwiz. Mesia, *Phytochem*, **1995**, ***39***, 1459.
8. **6**: white amorphous powder, $^{13}$C NMR (50MHz,$CDCl_3$) δ: 82.2 (1), 31.3 (2), 71.8 (3), 42.5 (4), 50.2 (5), 82.5 (6), 52.2 (7), 72.6 (8), 46.6 (9), 41.6 (10), 49.7 (11), 35.7 (12), 76.5 (13), 79.2 (14), 39.8 (15), 84.1 (16), 61.9 (17), 72.1 (18), 49.0 (19), 47.7 ($NCH_2$-), 13.5 ($NCH_2CH_3$), 56.2 (1'), 57.4 6'), 57.6 (16'), 58.7 (18'), 170.1, 21.0 (OAc).
9. Feng Peng WANG, Ju Zheng FAN, Zheng Bang LI, Jin Song YANG and Bo Gang LI, *Chin. hem. Lett*, submitted.
10. **8**: white amorphous powder, $C_{25}H_{37}NO_9$ (FABMS+$^{13}$C NMR). IR (KBr)cm$^{-1}$: 3435 (OH), 1736, 1250 (OAc), 1638 (C=N). $^1$H NMR (400MHz) δ: 2.05 (3H, s, OAc), 3.17, 3.23, 3.26, 3.41 (each 3H, s, 4×$OCH_3$), 5.00 (1H dd, J=7.2, 5.2Hz, 3β-H), 7.52 (1H, s, 19-H). $^{13}$C NMR (100MHz) δ: 81.6 (1), 31.4 (2),71.8 (3), 49.6 (4), 49.2 (5), 82.8 (6), 56.0 (7), 71.3 (8), 45.5 (9), 42.5 (10), 50.5 (11), 34.9 (12), 76.5 (13), 79.4 (14), 38.2 (15), 84.5 (16), 61.9 (17), 71.9 (18), 165.0 (19), 57.1 (1'), 57.3 (6'), 57.7 (16'), 59.0 (18'), 170.0, 20.9 (OAc). FABMS m/z (%): 496 (M+1, 100).
11. **9**: white amorphous powder, $^1$H NMR (200MHz, $CDCl_3$) δ: 1.09 (3H, t, J=7.0Hz, $NCH_2CH_3$), 1.29 (3H, s, 8-OAc), 2.02, 2.04 (each 3H, s, 2×OAc), 3.16, 3.17, 3.21, 3.36, 3.84 (each 3H, s, 5×OCH3), 4.86 (1H, dd, J=10.0, 8.0Hz, 3β-H), 5.05 (1H, d, J=5.0Hz, 14β-H), 6.90, 8.02 (each 2H, AA'BB' system, Ar-H). $^{13}$C NMR (50MHz) δ: 81.4 (1), 31.7 (2), 71.3 (3), 42.4 (4), 46.0 (5), 79.8 (6), 43.5 (7), 85.1 (8), 48.9 (9), 40.9 (10), 49.8 (11), 35.1 (12), 81.8 (13), 76.6 (14), 39.4 (15), 83.2 (16), 61.0 (17), 71.5 (18), 48.8 (19), 55.9 (1'), 57.9 (6'), 57.9 (16'), 58.6

(18'), 47.2 ($NCH_2$-), 13.2 ($NCH_2CH_3$), 169.6, 170.1, 170.1; 21.0, 21.4, 21.3 (3×OAc), 165.8 (O=C-OR), 122.3 (1"), 131.7 (2", 6"), 113.6 (3", 5"), 163.4 (4"), 55.2 (4"-$OCH_3$).

12. **10**: white amorphous powder, $C_{37}H_{43}NO_{12}$ (FABMS+$^{13}$C NMR). IR (KBr)($cm^{-1}$): 1728, 1250 (OAc), 1637 (C=N). $^1$H NMR (400MHz, $CDCl_3$) δ: 1.25 (3H, s, 8-OAc), 2.02, 2.04, 2.06 (each 3H, 3×OAc), 3.05, 3.18, 3.23, 3.36, 3.82 (each 3H, s, 5×$OCH_3$), 5.12 (1H, t, J=7.2Hz,3β-H), 7.34 (1H, s, 19-H), 6.88, 8.00 (each 2H, AA'BB' system, Ar-H). $^{13}$C NMR (100MHz) δ: 83.7 (1), 29.9 (2), 73.1 (3), 49.8 (4), 44.5 (5), 79.6 (6), 41.7 (7), 84.0 (8), 53.9 (9), 41.0 (10), 50.9 (11), 35.2 (12), 81.7 (13), 77.0 (14), 38.6 (15), 80.3 (16), 61.5 (17), 72.6 (18), 163.3 (19), 56.0 (1'), 58.4 (6'), 57.5 (16'), 59.1 (18'), 169.6, 169.6, 170.6, 21.2, 21.4, 21.6 (3×OAc), 166.0 (O=C-O), 122.3 (1"), 132.0 (2", 6"), 113.8 (3", 5"), 163.6 (4"), 55.5 (4"-$OCH_3$). FABMS m/z (%): 622 (M+1, 100).

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