SYNTHESIS OF 11β-HYDROXY *ERYTHRINA* ALKALOID, ERYTHRARTINE, AND ITS *O*-ACETATE (ERYTHRASCINE?)[1]

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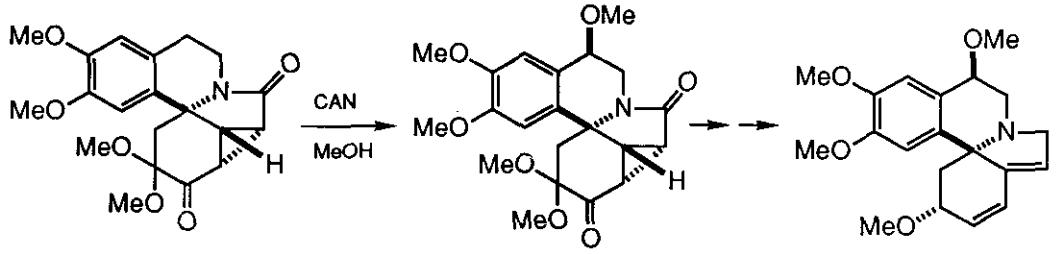
Abstract----- Oxidation of an erythrinan alkaloid erysotramidine (**4**) with CAN in AcOH-MeCN gave, in moderate yield, the 11β-acetoxy derivative (**5b**), which was transformed into erythrartine (**8**). Its *O*-acetate (*O*-acetylerythrartine) was not identical with erythrascine in the ^{1}H-nmr spectra, presenting an ambiguity on the reported structure of erythrascine.

Oxidation of an erythrinan derivative (**1**) with ceric ammonium nitrate (CAN) in methanol results in stereoselective introduction of an OMe group at C-11β position to give **2**, which was successively transformed into (±)-erythristemine (**3**).[2]

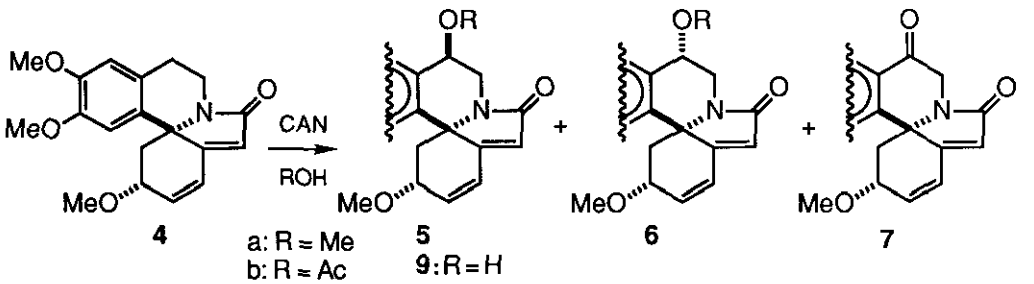


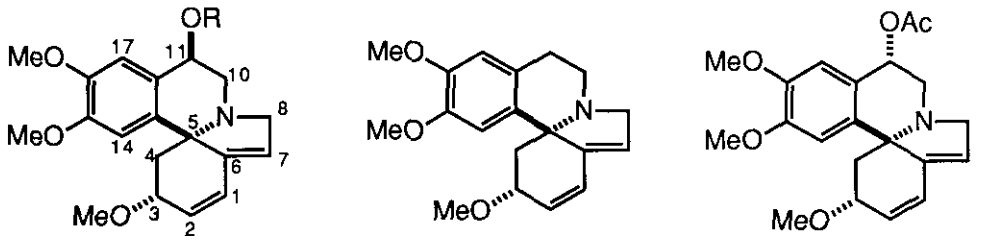
1 **2** **3**

This paper describes that the above oxidation method is also applicable to the erythrinan alkaloid, erysotramidine (**4**), which has a dienoid system in the molecule. Another application of this method is that, when the solvent in the oxidation is changed, this oxidation results in the alteration of oxygen functionality, producing alkaloids of different oxygen functionalities.

Oxidation of (±)-erysotramidine [(±)-**4**] with 2.2 mol eq. of CAN in methanol for 10 min at room temperature gave three oxygenated products, **5a** (41%), **6a** (11%), and **7** (31%). Compound (**5a**) was identical with (±)-8-oxoerythristemine previously reported.[2]

Oxidation of natural (+)-erysotramidine [(+)-**4**] with 2.2 mol eq. of CAN in AcOH-MeCN gave two 11-acetoxy products, the 11β-isomer (**5b**) (50%) and the 11α-isomer (**6b**) (33%). Configuration of the acetoxy group in each product was elucidated on the basis of the coupling pattern of 11-proton in the ^{1}H-nmr spectra (δ 5.82, dd, J=3.5, 2 Hz for **5b**, and δ 6.16, dd, J=7.5, 2.5 Hz for **6b**). Predominant formation of the β-isomer agrees with the stereochemical consideration previously suggested.[2] Compound (**5b**) was transformed into the natural alkaloid erythrartine (**8**) and its *O*-acetyl derivative (**11**) as follows. Reduction of **5b** with $LiAlH_4$-$AlCl_3$ (3:1) in THF gave **8** (47%) and **9** (10%) together with the deacetoxylated product, (+)-erysotrine (**10**) (24%). Compound (**8**) was identical with the natural alkaloid erythrartine, reported by Ito *et al.*,[3] thus furnishing the first synthesis of 11β-hydroxy *Erythrina* alkaloid. Acetylation of **8** in a usual manner gave the *O*-acetate (**11**).





In 1972, Ghosal *et al.*[4] isolated an alkaloid named erythrascine from seeds of *Erythrina arborescens*, with proposing the structure of 11-acetoxyerysotrine. However, the ^{1}H-nmr spectrum of **11** was different from that of erythrascine,[4] particularly in the chemical shift of OMe groups. Comparison of the spectrum of erythrartine (**8**) with that of the corresponding 8-oxo derivative (**9**) suggested that the chemical shift of the OMe groups would not be much

affected by introduction of an 8-oxo group. Therefore, although the 11α-acetoxy isomer (**12**) was not prepared, we anticipate that the OMe chemical shifts of **12** would be similar to those of the 8-oxo derivative (**6b**). However, the reported chemical shifts of OMe groups of erythrascine are again very much different from those of **6b**. Therefore, the reported structure of erythrascine is questionable (if the nmr data for OMe group are not erroneously reported).

Table 1. ^{1}H-Nmr of 11-Acetoxyerysotrine Derivatives

	5b	**6b**	**11**	erythrascine[4]
ArH[a]	6.81	6.88	6.79	7.02
	7.02	6.96	6.88	7.05
OCH_3[a]	3.38	3.36	3.35	3.22
	3.80	3.78	3.78	3.45
	3.86	3.87	3.85	3.48
$COCH_3$[a]	2.07	2.12	2.11	2.12
olefin H				
H-1	6.39	6.38	6.08	5.92
	(br d, 10)	(br d, 10)	(br d, 10)	(br d, 10)
H-2	6.94	6.91	6.61	6.46
	(dd, 10, 2.5)	(dd, 10, 2.5)	(dd, 10, 2)	(br dd, 10, 2.5)
H-7	6.06	6.04	5.76	5.68
	(br s)	(br s)	(br s)	(br s)
H-11	5.82	6.16	5.88	___[b]
	(dd, 3.5, 2)	(dd, 7.5, 2.5)	(m)	

[a]. Singlet. The other data for **5b**, **6b**, and **11** are indicated in the text.
[b]. Not reported in ref. 4.

EXPERIMENTAL

CAN Oxidation of (+)-Erysotramidine [(+)-4] in AcOH-MeCN

A solution of (+)-erysotramidine (36 mg, 0.11 mmol) and CAN (133 mg, 0.24 mmol) in AcOH (3 ml) and MeCN (0.4 ml) was stirred for 1 h at room temperature. Dilution of the reaction mixture with CH_2Cl_2 formed a yellow precipitate, which was removed by filtration. The filtrate was washed with saturated aqueous $NaHCO_3$ and water, dried over $MgSO_4$, and concentrated. The residue was purified by a preparative hplc (AcOEt : hexane = 4 : 1) to give **5b** (21 mg, 50%) and **6b** (14 mg, 33%). **5b**: Pale yellow oil. $[\alpha]_D$: +44° (c=0.29 in $CHCl_3$). Ir ($CHCl_3$) cm^{-1}: 1727, 1683. ^{1}H-Nmr ($CDCl_3$) δ: 5.82 (1H, dd, *J*=3.5, 2

Hz, H-11), 4.55 (1H, dd, *J*=15, 2 Hz, H-10), 4.14 (1H, m, H-3), 3.55 (1H, dd, *J*=15, 3.5 Hz, H-10), 2.76 (1H, dd, *J*=12, 5.5 Hz, H-4), 1.71 (1H, dd, *J*=12, 10 Hz, H-4). High-Ms *m/z*: Calcd for $C_{21}H_{23}NO_6$ (M^+): 385.1526. Found: 385.1518. **6b**: Pale yellow oil. $[\alpha]_D$: +157° (c=0.297 in $CHCl_3$). Ir ($CHCl_3$) cm^{-1}: 1733, 1679. ^{1}H-Nmr ($CDCl_3$) δ: 6.16 (1H, dd, *J*=7.5, 2.5 Hz, H-11), 4.54 (1H, dd, *J*=14.5, 7.5 Hz, H-10β), 3.89 (1H, m, H-3), 3.57 (1H, dd, *J*=14.5, 2.5 Hz, H-10α), 3.22 (1H, dd, *J*=11.5, 5 Hz, H-4), 1.76 (1H, dd, *J*=11.5, 10 Hz, H-4). High-Ms *m/z*: Calcd for $C_{21}H_{23}NO_6$ (M^+): 385.1526. Found: 385.1495.

11β-Hydroxyerysotrine (Erythrartine) 8

Compound (**5b**) (10 mg, 0.026 mmol) in dry THF (1 ml) was reduced with AlH_3 [prepared from 41 mg (1.1 mmol) of $LiAlH_4$ and 48 mg (0.36 mmol) of $AlCl_3$ in dry Et_2O (2 ml) at -15°C] for 1 h at room temperature. The solution was diluted with Et_2O and made basic with 28% NH_4OH. The ethereal layer was washed with water, dried over Na_2SO_4, and concentrated. Flush chromatography ($CHCl_3$:MeOH=9:1) of the product gave **8** (4 mg, 47%), and a mixture of **9** and **10** (2:5, 3 mg). **8**: Pale yellow oil. $[\alpha]_D$: +136.4° (c=0.075, $CHCl_3$) [lit. $[\alpha]_D$: +135° (c=0.5, $CHCl_3$)].[3] ^{1}H-Nmr ($CDCl_3$) δ: 6.99, 6.84 (each 1H, s, ArH), 6.60 (1H, dd, *J*=10, 2 Hz, H-2), 6.05 (1H, br d, *J*=10 Hz, H-1), 5.75 (1H, br s, H-7), 4.77 (1H, t, *J*=4 Hz, H-11α), 4.07 (1H, m, H-3), 3.91, 3.78, 3.32 (each 3H, s, OCH_3), 3.64, 3.21 (each 1H, dd, *J*=14.5, 4 Hz, H-10), 2.43 (1H, dd, *J*=11, 5.5 Hz, H-4), 1.92 (1H, t, *J*=11 Hz, H-4). The data are identical with those of erythrartine.[3]

***O*-Acetylerythrartine 11**

Acetylation of **8** (1.6 mg) with pyridine (12 drops) and acetic anhydride (6 drops) for 14 h at room temperature gave the acetate (**11**) (1.5 mg, 83%) as a pale yellow oil. $[\alpha]_D$: +66° (c=0.05, $CHCl_3$). Uv λ_{max} *nm* (ε): 212 (23700), 233 (13400), 283 (3400). Ir ($CHCl_3$) cm^{-1}: 1714. ^{1}H-Nmr ($CDCl_3$) δ: 4.20 (1H, m, H-3), 2.46 (1H, dd, *J*=11.5, 6 Hz, H-4). Ms *m/z* (%): 371 (M^+, 24), 340 (23), 311 (83), 296 (58), 280 (100). High-Ms *m/z*: Calcd for $C_{21}H_{25}NO_5$: 371.1731. Found: 371.1694.

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