

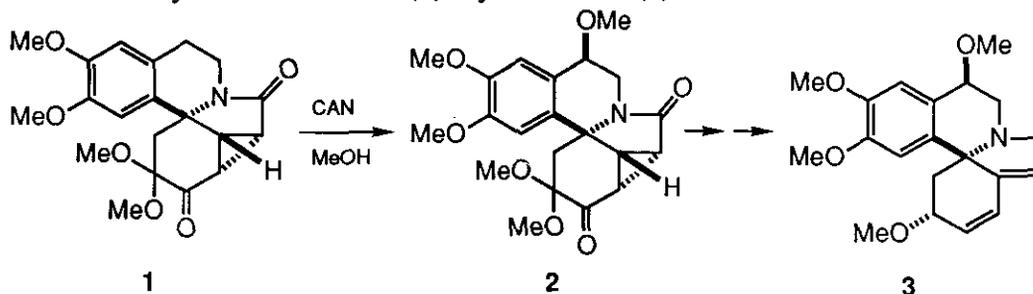
## SYNTHESIS OF 11 $\beta$ -HYDROXY *ERYTHRINA* ALKALOID, ERYTHRARTINE, AND ITS *O*-ACETATE (ERYTHRASCINE?)<sup>1</sup>

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**Abstract**— Oxidation of an erythrinan alkaloid erysotramidine (4) with CAN in AcOH-MeCN gave, in moderate yield, the 11 $\beta$ -acetoxy derivative (5b), which was transformed into erythartine (8). Its *O*-acetate (*O*-acetylerythartine) was not identical with erythrasine in the <sup>1</sup>H-nmr spectra, presenting an ambiguity on the reported structure of erythrasine.

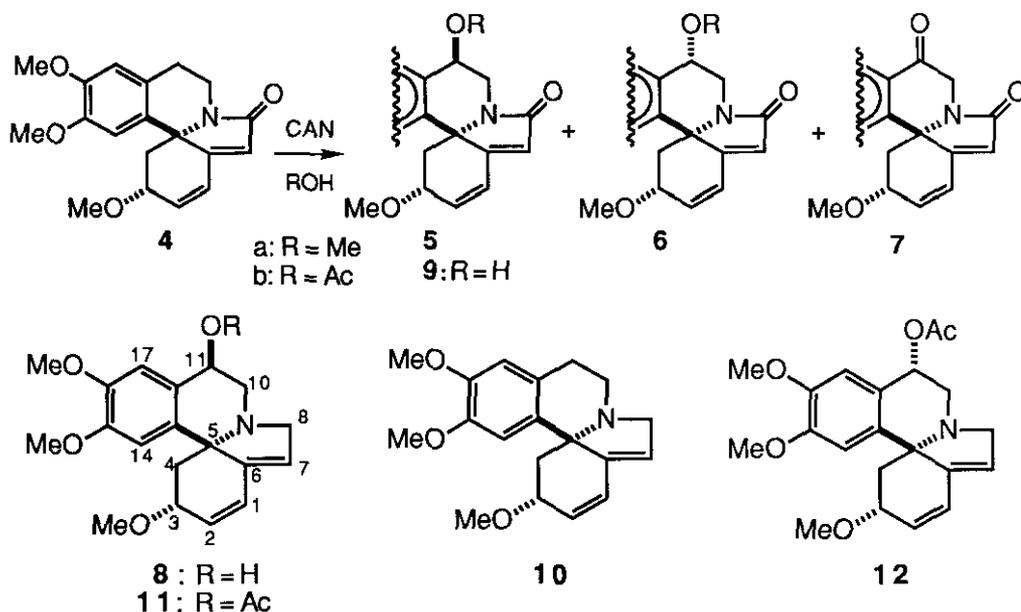
Oxidation of an erythrinan derivative (1) with ceric ammonium nitrate (CAN) in methanol results in stereoselective introduction of an OMe group at C-11 $\beta$  position to give 2, which was successively transformed into ( $\pm$ )-erythristemine (3).<sup>2</sup>



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 ( $\pm$ )-erysotramidine [( $\pm$ )-**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 ( $\pm$ )-8-oxoerythristemine previously reported.<sup>2</sup>

Oxidation of natural (+)-erysotramidine [(+)-**4**] with 2.2 mol eq. of CAN in AcOH-MeCN gave two 11-acetoxy products, the 11 $\beta$ -isomer (**5b**) (50%) and the 11 $\alpha$ -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 <sup>1</sup>H-nmr spectra ( $\delta$  5.82, dd,  $J=3.5, 2$  Hz for **5b**, and  $\delta$  6.16, dd,  $J=7.5, 2.5$  Hz for **6b**). Predominant formation of the  $\beta$ -isomer agrees with the stereochemical consideration previously suggested.<sup>2</sup> Compound (**5b**) was transformed into the natural alkaloid erythartine (**8**) and its *O*-acetyl derivative (**11**) as follows. Reduction of **5b** with LiAlH<sub>4</sub>-AlCl<sub>3</sub> (3:1) in THF gave **8** (47%) and **9** (10%) together with the deacetoxyated product, (+)-erysotrine (**10**) (24%). Compound (**8**) was identical with the natural alkaloid erythartine, reported by Ito *et al.*,<sup>3</sup> thus furnishing the first synthesis of 11 $\beta$ -hydroxy *Erythrina* alkaloid. Acetylation of **8** in a usual manner gave the *O*-acetate (**11**).



In 1972, Ghosal *et al.*<sup>4</sup> isolated an alkaloid named erythrasine from seeds of *Erythrina arborescens*, with proposing the structure of 11-acetoxyerysotrine. However, the <sup>1</sup>H-nmr spectrum of **11** was different from that of erythrasine,<sup>4</sup> particularly in the chemical shift of OMe groups. Comparison of the spectrum of erythartine (**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 11 $\alpha$ -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. <sup>1</sup>H-Nmr of 11-Acetoxyerysotrine Derivatives

	<b>5b</b>	<b>6b</b>	<b>11</b>	erythrascine <sup>4</sup>
ArHa	6.81	6.88	6.79	7.02
	7.02	6.96	6.88	7.05
OCH <sub>3</sub> <sup>a</sup>	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 <sub>3</sub> <sup>a</sup>	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	— <sup>b</sup>
	(dd, 3.5, 2)	(dd, 7.5, 2.5)	(m)	

<sup>a</sup>. Singlet. The other data for **5b**, **6b**, and **11** are indicated in the text.

<sup>b</sup>. 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<sub>2</sub>Cl<sub>2</sub> formed a yellow precipitate, which was removed by filtration. The filtrate was washed with saturated aqueous NaHCO<sub>3</sub> and water, dried over MgSO<sub>4</sub>, 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. [ $\alpha$ ]<sub>D</sub>: +44° (c=0.29 in CHCl<sub>3</sub>). Ir (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1727, 1683. <sup>1</sup>H-Nmr (CDCl<sub>3</sub>)  $\delta$ : 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.  $[\alpha]_D^{+157^\circ}$  ( $c=0.297$  in  $CHCl_3$ ). Ir ( $CHCl_3$ )  $cm^{-1}$ : 1733, 1679.  $^1H$ -Nmr ( $CDCl_3$ )  $\delta$ : 6.16 (1H, dd,  $J=7.5, 2.5$  Hz, H-11), 4.54 (1H, dd,  $J=14.5, 7.5$  Hz, H-10 $\beta$ ), 3.89 (1H, m, H-3), 3.57 (1H, dd,  $J=14.5, 2.5$  Hz, H-10 $\alpha$ ), 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.

### 11 $\beta$ -Hydroxyerysotrine (Erythartine) **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  $-15^\circ C$ ] 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.  $[\alpha]_D^{+136.4^\circ}$  ( $c=0.075$ ,  $CHCl_3$ ) [lit.  $[\alpha]_D^{+135^\circ}$  ( $c=0.5$ ,  $CHCl_3$ )].<sup>3</sup>  $^1H$ -Nmr ( $CDCl_3$ )  $\delta$ : 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-11 $\alpha$ ), 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 erythartine.<sup>3</sup>

### *O*-Acetylerythartine **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.  $[\alpha]_D^{+66^\circ}$  ( $c=0.05$ ,  $CHCl_3$ ). Uv  $\lambda_{max}$  nm ( $\epsilon$ ): 212 (23700), 233 (13400), 283 (3400). Ir ( $CHCl_3$ )  $cm^{-1}$ : 1714.  $^1H$ -Nmr ( $CDCl_3$ )  $\delta$ : 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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