A SHORT ROUTE TO THE 8,13-DIOXO-14-METHOXYBERBINES

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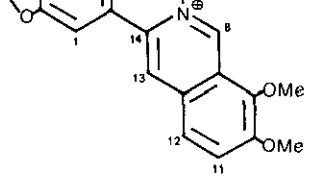
Pyridinium chlorochromate oxidation of oxyprotoberberines, followed by methanol work-up, leads to 8,13-dioxo-14-methoxyberbines.

It has previously been demonstrated that oxidative dimerization of berberine (1) using potassium ferricyanide provides the dimer oxybisberberine.[2] Cleavage of this dimer with pyridine hydrochloride in pyridine followed by methanol work-up leads to 8,13-dioxo-14-methoxycanadine (2).[3] Compound 2 or its hydroxy analog 2a are useful intermediates for the preparation of such heterocycles as the aporhoeadane 3, the γ-lactol 4, and the lactam 5.[2-4]

We have now found that compound 2 can be obtained in over 50% yield directly from the known and readily available oxyberberine (6)[5] by simple oxidation with pyridinium chlorochromate[6] at room temperature, followed by methanol work-up. This procedure thus obviates the need for oxybisberberine as a precursor to compound 2.

In like fashion, pyridinium chlorochromate oxidation of oxypseudopalmatine (7)[7] provided the hitherto unknown and highly oxidized tetrahydropalmatine derivative 8 in 42% yield. Treatment of 8 with concentrated hydrochloric acid produced a deep violet solution due to the formation of the cation 9. Dilution with water and methylene chloride extraction then led to the crystalline homoannular α-ketocarbinolamide 8a which had not previously been described in the literature.



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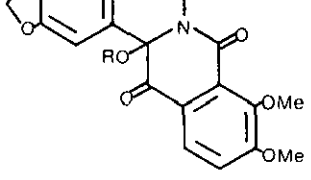

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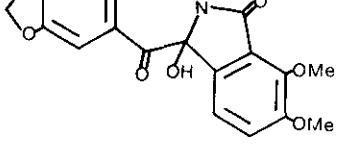
2a, R = H



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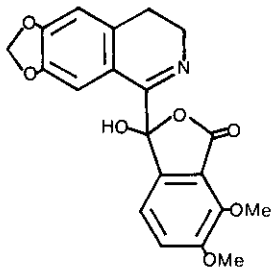

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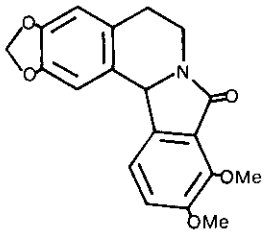

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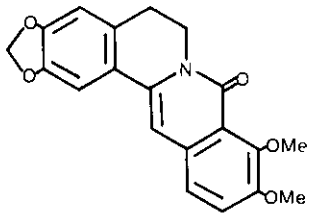

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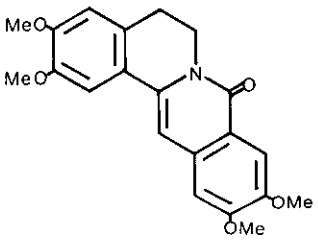

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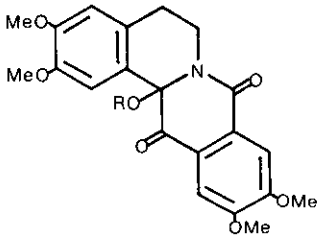
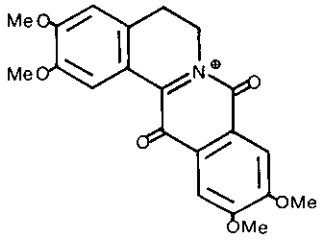


8, R = CH_3
8a, R = H



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Experimental

General Procedures:- Melting points are uncorrected. IR spectra were obtained on a Perkin Elmer 267 grating spectrophotometer. NMR spectra were taken on a FT 200 MHz instrument. All tlc was on Merck 254 precoated silica gel plates.

8,13-Dioxo-14-methoxycanadine (2):- A mixture of oxyberberine (6) (100 mg, 0.285 mmol) and pyridinium chlorochromate (125 mg, 0.58 mmol) in methylene chloride (10 ml) was stirred at room temperature for 12 h. Water was added, and the solution was extracted with methylene chloride. The organic layer was dried over sodium sulfate and concentrated in vacuo to leave a brown residue. Methanol (50 ml) was added, and the mixture stirred at room temperature for 6 h. Evaporation of the solvent left a residue which was purified by preparative tlc using CH_2Cl_2:MeOH (96:4). The product was obtained as a band of R_f 0.63, 60 mg (53%). Alternatively, column chromatography on silica gel using the same solvent system could be used to purify the product, mp 125-126° C.[3]

8,13-Dioxo-14-methoxytetrahydropseudopalmatine (8):- Oxidation of oxypseudopalmatine (7) by the above procedure yielded 8 in 42% yield as colorless crystals, $C_{22}H_{23}NO_7$, mp 147-148° C (MeOH); $\nu_{max}^{CHCl_3}$ 1650 and 1683 cm^{-1}; nmr ($CDCl_3$) δ 2.66-4.96 (m, 4H, CH_2CH_2), 3.25 (s, 3H, aliph. OCH_3), 3.85, 3.91, 4.01 and 4.04 (4s, 4x3H, arom. OCH_3), 6.62 (s, 1H, H-4), 7.29 (s, 1H, H-1), 7.52 (s, 1H, H-9) and 7.73 (s, 1H, H-12). MS chemical ionization m/e 414 (M + 1) in CH_4.

8,13-Dioxo-14-hydroxytetrahydropseudopalmatine (8a):- The deep violet solution obtained by treating 8 with conc. hydrochloric acid was diluted with water and extracted with methylene chloride. The organic layer was dried, filtered and evaporated. The residue was recrystallized from ether to yield colorless crystals (70% yield), $C_{21}H_{21}NO_7$, mp 160-161° C (ether), ν_{max}^{KBr} 1632, 1672 and 3330 br cm^{-1}, nmr ($CDCl_3$) δ 2.67-4.90 (m, 4H, CH_2CH_2), 3.85, 3.87, 4.01 and 4.04 (4s, 4x3H, arom. OCH_3), 6.64 (s, 1H, H-4), 7.07 (s, 1H, H-1), 7.49 (s, 1H, H-9) and 7.70 (s, 1H, H-12). MS chemical ionization m/e 400 (M + 1) in CH_4.

References

1. Permanent address: Department of Chemistry, Presidency College, Madras, India.
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