

upfield. Comparison of the  $V_2W_4O_{19}^{4-}$  spectrum discussed above with the spectrum of the  $HV_2W_4O_{19}^{3-}$  anion<sup>22</sup> measured at 0 °C (see Figure 1d) reveals an upfield shift of only the  $OV_2$  resonance upon protonation. This pronounced change in chemical shift unambiguously identifies the  $OV_2$  oxygen in the  $V_2W_4O_{19}^{4-}$  cluster as the protonation site. Note that all resonances except the  $OV_2$  resonance in  $V_2W_4O_{19}^{4-}$  shift downfield upon protonation of the cluster. This downfield shift reflects a strengthening of metal-oxygen bonds and a concomitant reduction of negative charge on the oxygens in question.

When spectra of  $HV_2W_4O_{19}^{3-}$  are observed at elevated temperatures (see Figure 2e), two significant consequences of the reduced rate of  $^{17}O$  and  $^{51}V$  quadrupole relaxation are observed. First, the line widths of resonances for the OW oxygens are sufficiently narrowed as to allow resolution of the resonances for the two nonequivalent OW oxygen types. Their approximately equal intensities add support to the contention that the sample contains only the *cis*- $V_2$  isomer. Second, the OV, OVW, and  $OV_2H$  resonances are broadened owing to  $^{51}V$ - $^{17}O$  spin-spin coupling.<sup>23</sup> It is possible that reported failures<sup>6,12,13</sup> to observe resonances for OV, OVMO, and OVW resonances in other mixed-metal polyoxoanions were due to this line-broadening effect. We are currently attempting to measure vanadium-decoupled  $^{17}O$  NMR spectra in an effort to obtain more highly resolved spectra.

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- $[(n-C_4H_9)_4N]_2W_6O_{19}$  was obtained by refluxing  $[(n-C_4H_9)_4N]_4W_{10}O_{32}$  in  $CH_3OH/CH_3CN$ . Anal. ( $C_{32}H_{72}N_2O_{19}W$ ) C, H, N, W.
- $[(n-C_4H_9)_4N]_3VW_5O_{19}$  was obtained by refluxing  $[(n-C_4H_9)_4N]_4W_{10}O_{32}$  and  $[(n-C_4H_9)_4N]_4V_2O_7$  (1:1 mol ratio) in  $CH_3OH/CH_3CN$ , precipitating the product with ether, and recrystallizing in  $CH_3CN$ . Anal. ( $C_{48}H_{108}N_3O_{19}VW_5$ ) C, H, N, V, W.
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- $[(n-C_4H_9)_4N]_3HV_2W_4O_{19} \cdot H_2O$  was obtained by acidifying an aqueous solution of  $Na_2WO_4$  and  $NaVO_3$  (2:1 mol ratio) to pH 5 with HCl, obtaining a

crude precipitate by addition of  $(n-C_4H_9)_4NBr$ , and recrystallizing the precipitate from  $CH_3CN$ . Anal. ( $C_{48}H_{110}N_3O_{20}V_2W_4$ ) C, H, N, V, W.

- The resonances for oxygens bonded to one vanadium are presumably broadened much less than the resonance for the oxygen bonded to two vanadiums since, in the limit of slow  $^{51}V$  quadrupole relaxation at high temperature, the former should yield eight resolved components whereas the latter should yield fifteen components due to coupling to the two  $S = 7/2$   $^{51}V$  nuclei. Although line-shape simulations have not been calculated for a nucleus coupled to two  $S = 7/2$  quadrupolar nuclei as a function of quadrupole relaxation rate, results obtained for related systems<sup>24</sup> support this interpretation. Broadening of the  $OV_2H$  resonance cannot be due to rapid oxygen exchange with water since the water resonance is observed at 80 °C.
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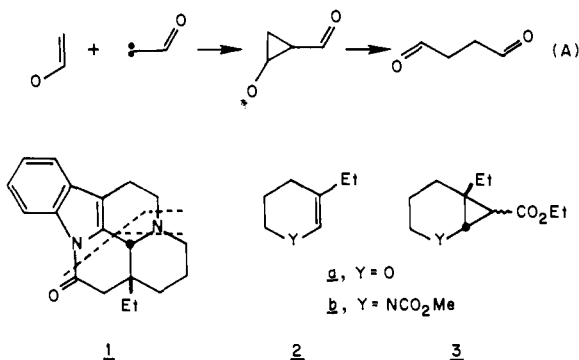
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#### Short Syntheses of Eburnamonine via $\beta$ -Oxycyclopropylcarbonyl and Related Intermediates

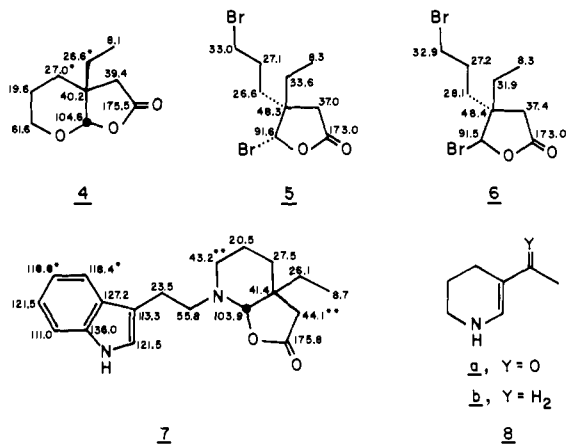
Sir:

The two-step construction of  $\gamma$  diketones outlined in sequence A has formed the basis of recent syntheses of cyclopentanoid terpenic and other natural products.<sup>1</sup> It seemed plausible that the scheme could be adapted to  $\gamma$ -imino ketone preparation by way of the introduction of nitrogen at some stage of the reaction sequence<sup>2</sup> and hence its applicability extended to the formation of alkaloids. The two syntheses of eburnamonine (**1**)<sup>3</sup> shown involve this concept in the production of the nonindole portion of the alkaloid (cf. dotted lines in **1**).

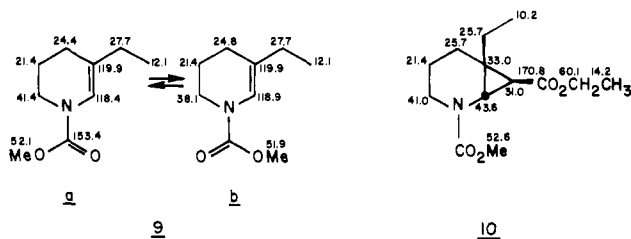


Dilute acid hydrolysis of esters **3a**, prepared previously by the copper-assisted decomposition of ethyl diazoacetate in dihydropyran **2a**,<sup>4</sup> yielded (93%) lactone **4**<sup>5</sup> (bp 82-84 °C (0.2 Torr); IR (neat) 5.58  $\mu$ ;  $^1H$  NMR  $\delta$  ( $CDCl_3$ ) 0.92 (t, 3,  $J = 7$  Hz), 1.3-1.8 (m, 6), 2.36 (s, 2), 3.5-4.0 (m, 2), 5.28 (s, 1)) whose treatment with boron tribromide in methylene chloride (room temperature, 14 h) gave (71%) dibromides **5** and **6** (mixture bp 121-124 °C (0.007 Torr); IR (neat) 5.52  $\mu$ ;  $^1H$  NMR ( $CDCl_3$ )  $\delta$  0.93, 0.96 (t each, total 3,  $J = 7$  Hz), 1.4-2.1 (m, 6), 2.41, 2.46 (s each, total 2), 3.2-3.6 (m, 2), 6.30, 6.31 (s each, total 1)). Hydrolysis (1% hydrochloric acid, dioxane, 80 °C, 20 h) of the mixture produced a bromo- $\gamma$ -lactol, whose interaction with tryptamine hydrochloride in anhydrous dimethyl sulfoxide (stirring 12 h with 3- $\text{\AA}$  sieves, 55 °C) led (78%) to carbinolamine lactone **7**:<sup>6</sup> IR ( $CHCl_3$ ) 2.87, 5.76  $\mu$ ;  $^1H$  NMR ( $CDCl_3$ )  $\delta$  0.78 (t, 3), 1.2-1.8 (m, 6), 2.1-2.5 (m, 2), 2.6-3.1 (m, 6), 5.07 (s, 1), 6.9-7.6 (m, 5), 8.39 (s, 1).

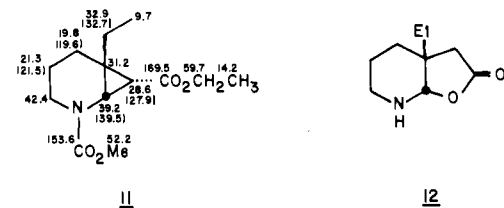
Reduction of 3-acetyl-1,4,5,6-tetrahydropyridine (**8a**)<sup>7</sup> with lithium aluminum hydride (refluxing dioxane, 8 h)<sup>8</sup> afforded (15%) 3-ethyl-2-piperidine (**8b**), whose immediate acylation



with methyl chlorocarbonate (tetrahydrofuran, triethylamine, 4 h) yielded (94%) of enamide **2b** (~4:1 **9a**–**9b** mixture in



deuteriochloroform solution): IR (neat) 5.87  $\mu$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.02 (t, 3,  $J = 7$  Hz), 1.8–2.2 (m, 6), 3.54 (m, 2), 3.73 (s, 3), 6.60 (s, 1). Decomposition of ethyl diazoacetate in the latter over copper bronze ( $\sim 135^\circ\text{C}$ ) gave (95%) esters **3b**, bp  $93\text{--}95^\circ\text{C}$  (0.008 Torr), in an  $\sim 2:1$  exo (**10**) to endo (**11**) ratio. Exo: IR (neat) 5.81, 5.86  $\mu$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  0.88,



1.26 (t, 3 each,  $J = 7$  Hz), 1.3–2.9 (m, 9), 3.35 (d, 1,  $J = 4$  Hz), 3.70 (s, 3), 4.15 (q, 2,  $J = 7$  Hz). Endo:<sup>9</sup> IR (neat) 5.81, 5.86  $\mu$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  0.97, 1.24 (t, 3 each,  $J = 7$  Hz), 1.9–2.2 (m, 7), 2.93, 3.00 (d each, total 1,  $J = 6$  Hz), 3.1–3.4 (m, 2), 3.67 (s, 3), 4.05 (q, 2,  $J = 7$  Hz). Alkaline hydrolysis (aqueous potassium hydroxide, diethylene glycol,  $100^\circ\text{C}$ , 12 h) of **3b** produced (88%) lactone **12** (mp  $72^\circ\text{C}$ ; IR ( $\text{CHCl}_3$ ) 2.94, 5.74  $\mu$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  0.90 (t, 3,  $J = 7$  Hz), 1.2–1.8 (m, 4), 1.81 (q, 2,  $J = 7$  Hz), 2.2–3.0 (m, 5), 5.12 (s, 1)) whose exposure to tryptophyl bromide (benzene, 30% sodium hydroxide, triethylbenzylammonium chloride,  $35^\circ\text{C}$ , 6 h) led (60%) to lactone **7**.

Thermolysis ( $250^\circ\text{C}$ , 0.01 Torr, 0.5 h) of lactone **7** yielded (60%) ( $\pm$ )-eburnamonine (**1**), mp  $200\text{--}201^\circ\text{C}$  (lit.<sup>3</sup> mp  $200\text{--}202^\circ\text{C}$ ) (spectrally identical with an authentic sample), completing two short syntheses of the alkaloid.

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- An early stage implies the replacement of an enol system by an enamine derivative. Since enamines themselves misbehave in the cyclopropanation step (E. Wenkert and C. A. McPherson, *J. Am. Chem. Soc.*, **94**, 8084 (1972); E. Wenkert, C. A. McPherson, E. L. Sanchez, and R. L. Webb, *Synth. Commun.*, **3**, 255 (1973)), an enamide was needed as starting material (cf. E. Wenkert, M. E. Alonso, H. E. Gottlieb, E. L. Sanchez, R. Pellicciari, and

P. Cogolli, *J. Org. Chem.*, **42**, 3945 (1977), and references cited therein; cf. also W. J. Welstead, Jr., H. F. Stauffer, Jr., and L. F. Sancilio, *J. Med. Chem.*, **17**, 544 (1974).

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- The numbers on the formulas represent carbon shifts in parts per million downfield from  $\text{Me}_4\text{Si}$ ;  $\delta$  ( $\text{Me}_4\text{Si}$ ) =  $\delta$  ( $\text{CDCl}_3$ ) + 76.9 ppm. Asterisked numbers may be interchanged.
- A sensitive solid whose melting point could not be observed because of thermal decomposition.
- E. Wenkert, K. G. Dave, F. Haglid, R. G. Lewis, T. Oishi, R. V. Stevens, and M. Terashima, *J. Org. Chem.*, **33**, 747 (1968).
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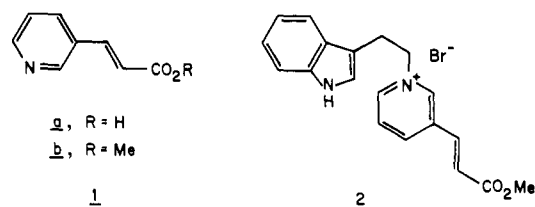
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## A Short Route to Pseudoyohimbine and Yohimbine

Sir:

Recently a short, new route of synthesis of the indoloquinolizidine skeleton characteristic of many indole alkaloids was introduced and applied to the total synthesis of a variety of ajmalicinoid bases.<sup>1</sup> The new method consists of  $\gamma$ -alkylation of *N*-alkyl- $\beta$ -acylpyridinium salts with carbon nucleophiles, acid-induced cyclization of the resultant 1,4-dihydropyridine product, and further elaboration of the thus-formed indoloquinolizidine. To test the generality of the reaction scheme, a study of similar reactions emanating from a  $\beta$ -acylpyridine vinyllogue was undertaken and, as shown below, turned into total syntheses of pseudoyohimbine and yohimbine.

Condensation of nicotinaldehyde with malonic acid in pyridine solution in the presence of piperidine yielded (96%)  $\beta$ -( $\beta$ -pyridyl)acrylic acid (**1a**), mp  $237\text{--}237.5^\circ\text{C}$ , whose es-



terification with methanolic sulfuric acid gave (95%) its ester **1b**, mp  $41\text{--}42^\circ\text{C}$ . Alkylation of the latter with tryptophyl bromide<sup>1</sup> afforded (98%) the salt **2**, mp  $195\text{--}197^\circ\text{C}$ .

Interaction of **2** with the sodio salt of dimethyl malonate in monoglyme, followed by treatment of the mixture with a saturated benzene solution of hydrogen bromide, yielded (10%) tetracycle **3a**:<sup>2</sup> mp  $220\text{--}221^\circ\text{C}$ ; IR (Nujol)  $3247, 1739, 1727, 1664\text{ cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{Me}_2\text{SO}-d_6$ )  $\delta$  3.58, 3.60, 3.81 (each s, 3), 4.78 (dm, 1,  $J = 11$  Hz), 5.21 (d, 1,  $J = 15$  Hz), 6.8–7.5 (m, 6). Exposure of the latter to lithium iodide trihydrate in  $\text{Me}_2\text{SO}^3$  at  $180^\circ\text{C}$  for 0.5 h led (82%) to diester **3b** (mp  $209\text{--}211^\circ\text{C}$ ; IR (KBr)  $3290, 1740, 1675\text{ cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.67, 3.73 (each s, 3), 4.56 (dm, 1,  $J = 12$  Hz), 5.41 (d, 1,  $J = 15$  Hz), 6.58 (s, 1), 6.9–7.6 (m, 5)) whose hydrogenation (platinum, glacial acetic acid, atmospheric pressure, room temperature, 5 h) produced (96%) diester **4a**<sup>2</sup> (hydrochloride mp  $234\text{--}235.5^\circ\text{C}$ ; IR ( $\text{CHCl}_3$ )  $3497, 1730\text{ cm}^{-1}$ ;  $^1\text{H}$