respective formylneospirinedienone products was based on the following assignment of the proton signals in the NMR spectrum (TFA) of 8a: $^{20-22} \delta$ 8.66 and 8.24 (s, s, 1 H, CHO), 7.28 and 7.22 (s, s, 1 H, C-12 H), 7.07 and 6.88 (s, s, 1 H, C-1 H), 6.84 and 6.82 (s, s, 1 H, C-9 H), 6.34 (s, 1 H, C-4 H), 3.99, 3.94, and 3.78 (all s, 9 H, C-11 OCH₃, C-10 OCH₃, C-3 OCH₃). The NMR spectrum of 8d (the oxidation product of 5d) lacked the signals attributable to the C-1 proton, and the spectrum of 8e (the oxidation product of 5e) lacked the signal attributable to the C-4 proton.

Evidence for the postulated facile acid-catalyzed rearrangement of the acylmorphinandienone 7a to the acylneospirinedienone 8a was adduced from a study of the chemistry of the N-formylmorphinandienone 3a. Electrooxidative coupling of 5a in HBF4⁴ yielded 3a (8%; mp 139-140°; uv $\lambda_{max}^{Me\bar{O}H}$ (log ϵ) 238 (4.23), 283 (3.89) nm; ir $\lambda_{max}^{CHCl_3}$ 5.93 (sh), 5.98, 6.07, 6.17 μ ; NMR (CDCl₃) δ 8.14 and 7.98 (s, s, 1 H, CHO), 6.80 (s, 1 H, ArH), 6.55 (s, 1 H, olefinic H), 6.32 and 6.30 (s, s, 1 H, C-8 H), 6.28 (s, 1 H, olefinic H), 3.84, 3.78, and 3.73 (all s, 9 H, 3-OCH₃); mass spectrum m/e 355 (M⁺)) along with 8a (2.5%).²³ The structure of 3a was proven by reduction with LiAlH₄ in THF to the oily N-methyldienol and oxidation of the dienol with MnO₂ to O-methylflavinantine (3b, 29%).²⁴ When 3a was treated with anhydrous methanolic HCl, rearrangement accompanied ketalization, and the dimethyl ketal⁷ of 8a was obtained (44%). Treatment of 3a with HBF_4 at room temperature for 30 min gave 8f ($R^1 = R^3 = R^4 = H$) (74%), and methylation of 8f with diazomethane gave 8a (31%).

Morphinandienones have been postulated to be precursors to dibenzazonine alkaloids such as protostephanine, via a pathway involving a neospirine intermediate.²⁵ Furthermore, biomimetic syntheses^{26,27} and the conversion of a labeled morphinandienone precursor to protostephanine in Stephania japonica²⁶ have been reported. The demonstrated sequence $5a \rightarrow 7a \rightarrow 8a$ and our facile conversion of neospirinedienones to dibenzazonine derivatives^{7,9} parallel the sequence of skeletal rearrangements proposed for dibenzazonine alkaloid biosynthesis in Stephania japonica.

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Facile Biomimetic Syntheses of Dibenzazonine and Aporphine Alkaloids^{1,2}

Sir:

Morphinandienones have recently been recognized as the primary products of chemical^{3,4} as well as anodic^{5,6} coupling of nonphenol benzylisoquinoline precursors. The ease of acid-catalyzed rearrangement of these spirodienones⁴ led us to explore their potential as in vitro alkaloid precursors. We report herein several facile and efficient syntheses of dibenzazonine and aporphine alkaloids via morphinandienone intermediates. In addition, the possible implications of these reactions for alkaloid biosynthesis are discussed.

Electrooxidative coupling of (\pm) -laudanosine $(5a)^5$ in HBF₄⁶ yielded (\pm) -O-methylflavinantine (1) in 94% yield. Treatment of 1 with boron trifluoride-etherate at room temperature for 26 hr, followed by hydrogenation over Pt in methanol gave erybidine (3),⁷ in 85% yield (Scheme I). By analogy with the demonstrated favored rearrangement of morphinandienones to neospirinedienones under the influence of strongly acidic catalysts,⁴ the conversion of 1 to 3 is presumed to proceed via the intermediacy of 2 and 4. The high-yield synthesis of 3 represents the most efficient reScheme I



ported route to dibenzazonine alkaloids, and, as noted earlier,⁴ parallels the sequence of skeletal rearrangements proposed for the biosynthesis of dibenzazonine alkaloids im *Stephania japonica*.

Chemical intramolecular coupling of (\pm) -N-formylnorlaudanosine (**5b**) with VOF₃-TFA gave, as a minor product (6%), (\pm) -N-formylnorglaucine (**7b**), and similar treatment of (\pm) -laudanosine (**5a**) gave (\pm) -glaucine (**7a**) in 43% yield.³ Furthermore, (\pm) -glaucine (**7a**) was also obtained, in 17% yield, by electrooxidative coupling of **5a** in TFA.⁸ In view of aforementioned observations concerning the formation of morphinandienones as the primary products of oxidative coupling of nonphenol benzylisoquinolines, we were led to speculate that the formation of aporphines may proceed via the route $5 \rightarrow 6 \rightarrow 8 \rightarrow 7$ (Scheme II). To evaluate the possible role of morphinandienones as aporphine precursors, (\pm) -O-methylflavinantine (**1**) was heated on the steam bath with concentrated hydrochloric acid for 90 min,



whereupon a precipitate separated. The product (89% yield) was (\pm) -1,2-dihydroxy-9,10-dimethoxyaporphine (10) as its hydrochloride salt:9 mp 197-198° (MeOH); uv λ_{max}^{EtOH} (log ϵ) 281 (4.19), 302 (4.18) nm; NMR (TFA) δ 8.02 (s, 1 H, H-11), 6.94 (s, 1 H, H-8), 6.70 (s, 1 H, H-3), 3.90, 3.88 (each s, 6 H, 2-OCH₃), 2.59 (d, 3 H, N-CH₃); mass spectrum m/e (%) 327 (95, M⁺), 326 (100), 312 (32), 310 (22), 296 (15), 284 (27), 269 (10), 253 (20); positive Quastel test for a catechol.¹⁰ Treatment of 10 with an excess of diazomethane gave (\pm) -glaucine (7a), isolated as the hydrobromide, mp 220-221° (79%).11 The facile and high-yield conversion from 5a to 1 and thence to 7a constitutes the most efficient reported route to 1.2.9.10-tetrasubstituted aporphines, and supports the proposed intermediacy of morphinandienones in the chemical and anodic oxidation of (\pm) -laudanosine (5a) to (\pm) -glaucine (7a). Furthermore, it is likely that the conversion of 1 to 10 proceeds via the intermediacy of proerythrinadienone 9. It is noteworthy that spirodienones similar to 9 have been proposed as biosynthetic intermediates to explain the incorporation of norprotosinomenine (5c) into aporphine alkaloids in Dicentra exi $mia.^{12}$



To evaluate the potential of the new aporphine synthesis for the preparation of 1,2,10,11-tetrasubstituted aporphines, (\pm) -N-ethoxycarbonylnorsalutaridine (11a) was prepared by the procedure of Schwartz and Mami.¹³ Methylation of 11a with $CH_3I-K_2CO_3$ in acetone gave $(\pm)-O$ methyl-*N*-ethoxycarbonylnorsalutaridine (**11b**, 89%): mp 161.5–162.5° (EtOH–Et₂O); uv λ_{max}^{EtOH} (log ϵ) 238 (4.48), 280 (3.87) nm; ir $\lambda_{max}^{CHCl_3}$ 5.93, 5.98, 6.09, 6.20 μ ; NMR (CDCl₃) δ 7.27 (s, 1 H, H-5), 6.84 (s, 2 H, H-1 and H-2), 6.35 (s, 1 H, H-8), 3.97, 3.87, 3.79 (each s, 9 H, 3-OCH₃); mass spectrum m/e (%) 399 (100, M⁺), 371 (22), 326 (20). Reduction of 11b with LiAlH₄ in THF under reflux gave a mixture of the epimeric (\pm) -O-methylsalutaridinols (80%) which was oxidized with MnO₂ in CHCl₃ to yield (\pm) -O-methylsalutaridine (11c, 60%): mp 70-73° (Et₂O); uv λ_{max}^{EtOH} (log ϵ) 239 (4.47), 280 (3.86) nm; ir $\lambda_{max}^{CHCl_3}$ 5.99, 6.09, 6.20 μ ; NMR¹⁴ (CDCl₃) δ 7.28 (s, 1 H, H-5), 6.84 (s, 2 H, H-1 and H-2), 6.33 (s, 1 H, H-8), 3.93, 3.86, 3.80 (each s, 9 H, 3-OCH₃), 2.45 (s, 3 H, N-CH₃); mass spectrum m/e (%) 341 (100, M⁺), 326 (39), 313 (25), 298 (31). Treatment of 11c with concentrated hydrochloric acid on the steam bath for 3 hr followed by methylation with an excess of diazomethane yielded (\pm) corydine (12a, 31%; mp 165-166.5° (lit. 148°,¹⁵ 165-167°16); mixture TLC, uv, NMR,¹⁵ and mass spectrum¹⁷ identical with those of naturally occurring (+)-corydine¹⁸). Also isolated were (\pm) -O-methylcorydine (12b) as the hydrochloride (11%, mp 234-235° dec, characterized as the methiodide of 12b, mp 248-250° dec, lit.¹⁹ 248° dec) and starting material (11c, 11%). The low conversion yield and long required reaction period may be attributable to the steric crowding in 1,2,10,11-tetrasubstituted aporphines.

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The acid-catalyzed rearrangements of morphinandienones thus follow two principal routes, one which leads to dibenzazonine derivatives (e.g., $1 \rightarrow 2 \rightarrow 4$), and a second which leads to aporphines (e.g., $1 \rightarrow 9 \rightarrow 10$). The rearrangement to aporphines appears to be favored in reactions involving substrates and conditions which may enhance the participation of the nitrogen free electron pair, possibly through the intermediacy of a species such as 13.20 Exami-



nation of the molecular model of 13 indicates that stereoelectronic factors favor migration of the arvl group, to yield a proerythrinadienone intermediate. In contrast, those acidcatalyzed rearrangements of morphinandienones whch involve minimal nitrogen participation (e.g., with boron trifluoride salts or amide derivatives) result in migration of the alkyl group, to yield neospirine derivatives.

Biosynthetic studies have demonstrated that (\pm) -reticuline (5d) is a precursor of the aporphine alkaloids (+)-bulbocapnine,²¹ (+)-isoboldine,²² and (+)-magnoflorine,²³ and these results have been interpreted as indicative of a "direct-coupling" mechanism. The in vivo conversion of (\pm) reticuline (5d) to morphinandienones has also been demonstrated.²⁴ In view of the newly discovered facile in vitro conversion of morphinandienones to aporphines, biosynthetic experiments are underway to explore the possibility that morphinandienones may as well be in vivo precursors of aporphine alkaloids.

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New Metalloorganic Compounds of Tungsten(III)

Sir:

The high stability and number of chromium(III) complexes have no counterpart in the chemistry of molybdenum and tungsten.¹ For example¹ the only pure halo compounds of tungsten(III) are $W_2 X_9^{3-}$ salts where X = Cl and Br. We wish now (i) to report a simple synthesis of tungsten-(III) dialkylamides and our characterization of these compounds and (ii) to indicate how these compounds afford synthetic routes to an extensive chemistry of tungsten(III) which was hitherto unknown.

Previously we reported² that the reaction of $LiNMe_2$ with a variety of tungsten halides led to either pure $W(NMe_2)_6$ or mixtures of $W(NMe_2)_6$ and $W_2(NMe_2)_6$. However, we were unable to isolate pure $W_2(NMe_2)_6$ from these W(III)-W(VI) mixtures by classical techniques. An examination of the mixed W(III)-W(VI) dimethylamides by X-ray diffraction techniques showed that the two dimethylamides cocrystallized. The unit cell contained two dimers, W₂(NMe₂)₆, and one monomer, W(NMe₂)₆. This study was significant in providing the first structurally characterized molecule with an unbridged triple bond between two tungsten atoms. However, W(III)-W(VI) dimethylamide samples were not amenable for the development of the chemistry of tungsten(III). Since $W(NMe_2)_6$ is an extremely sterically congested molecule, we thought that synthetic procedures which had formerly yielded the highest $W_2(NMe_2)_6$ to $W(NMe_2)_6$ ratio would further favor the formation of $W_2(NR_2)_6$ at the expense of $W(NR_2)_6$ if other lithium dialkylamides LiNR2 were employed (these are inherently more bulky than -NMe₂). We have now found that this is indeed the case. The reaction of decomposed $WCl_4(OEt_2)_2^3$ with LiNMeEt or LiNEt₂ (4 equiv) in THF-hexane leads to the isolation of the appropriate W(III) dialkylamides upon sublimation, 120-150°, 10⁻⁴ cm Hg, as pale-yellow crystalline solids. These compounds are oxygen and moisture sensitive, diamagnetic, and show