respective formylneospirinedienone products was based on the following assignment of the proton signals in the NMR spectrum (TFA) of **8a**:[20-22] δ 8.66 and 8.24 (s, s, 1 H, C*H*O), 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 OCH_3, C-10 OCH_3, C-3 OCH_3). 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 HBF_4[4] yielded **3a** (8%; mp 139–140°; uv λ_{max}^{MeOH} (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 ($CDCl_3$) δ 8.14 and 7.98 (s, s, 1 H, C*H*O), 6.80 (s, 1 H, Ar*H*), 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-OCH_3); mass spectrum *m/e* 355 (M^+)) along with **8a** (2.5%).[23] The structure of **3a** was proven by reduction with $LiAlH_4$ in THF to the oily *N*-methyldienol and oxidation of the dienol with MnO_2 to *O*-methylflavinantine (**3b**, 29%).[24] When **3a** was treated with anhydrous methanolic HCl, rearrangement accompanied ketalization, and the dimethyl ketal[7] 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 japonica*[26] have been reported. The demonstrated sequence **5a** → **7a** → **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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(12) All new compounds were characterized by concordant analytical and spectral data. The structural formulas containing asymmetric atoms refer to racemic compounds.
(13) T. Kametani, R. Charubala, M. Ihara, M. Koizumi, K. Takabashi, and K. Fukumoto, *J. Chem. Soc. C*, 3315 (1971); T. Kametani, K. Takabashi, T. Honda, M. Ihara, and K. Fukumoto, *Chem. Pharm. Bull.*, **20**, 1793 (1972).
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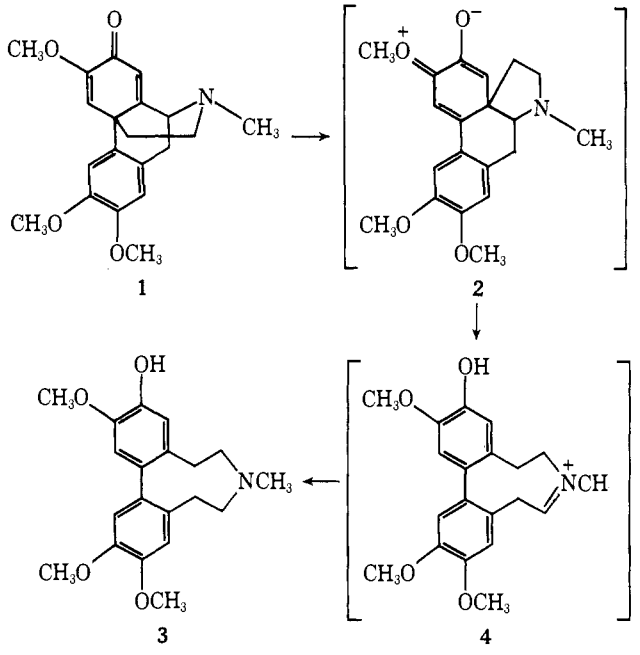
Facile Biomimetic Syntheses of Dibenzazonine and Aporphine Alkaloids[1,2]

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 spirodienones[4] 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 (±)-laudanosine (**5a**)[5] in HBF_4[6] yielded (±)-*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 re-

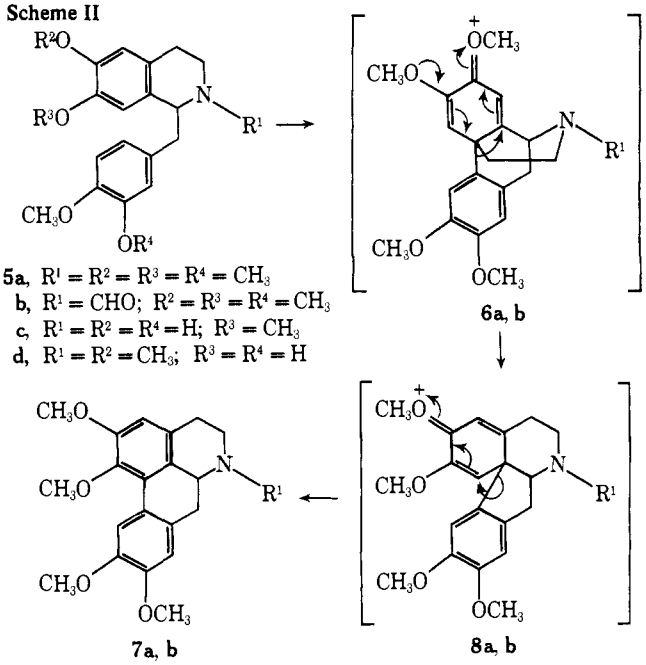
Scheme I



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

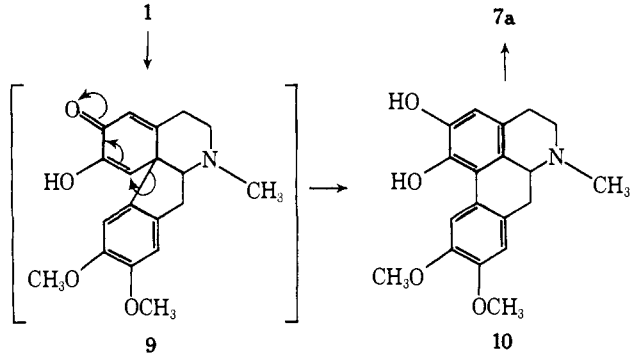
Chemical intramolecular coupling of (±)-*N*-formylnorlaudanosine (**5b**) with VOF_3–TFA gave, as a minor product (6%), (±)-*N*-formylnorglaucine (**7b**), and similar treatment of (±)-laudanosine (**5a**) gave (±)-glaucine (**7a**) in 43% yield.[3] Furthermore, (±)-glaucine (**7a**) was also obtained, 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** → **6** → **8** → **7** (Scheme II). To evaluate the possible role of morphinandienones as aporphine precursors, (±)-*O*-methylflavinantine (**1**) was heated on the steam bath with concentrated hydrochloric acid for 90 min,

Scheme II

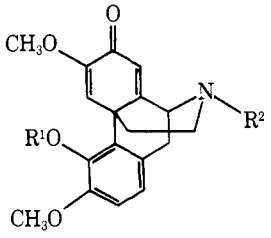


5a, $R^1 = R^2 = R^3 = R^4 = CH_3$
b, $R^1 = CHO$; $R^2 = R^3 = R^4 = CH_3$
c, $R^1 = R^2 = R^4 = H$; $R^3 = CH_3$
d, $R^1 = R^2 = CH_3$; $R^3 = R^4 = H$

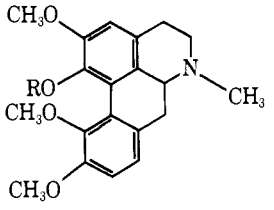
whereupon a precipitate separated. The product (89% yield) was (±)-1,2-dihydroxy-9,10-dimethoxyaporphine (**10**) as its hydrochloride salt:[9] mp 197–198° (MeOH); uv λ_{max}^{EtOH} (log ε) 281 (4.19), 302 (4.18) nm; NMR (TFA) δ 8.02 (s, 1 H, H-11), 6.94 (s, 1 H, H-8), 6.70 (s, 1 H, H-3), 3.90, 3.88 (each s, 6 H, 2-OCH_3), 2.59 (d, 3 H, N-CH_3); 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 (±)-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 (±)-laudanosine (**5a**) to (±)-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 eximia*.[12]



To evaluate the potential of the new aporphine synthesis for the preparation of 1,2,10,11-tetrasubstituted aporphines, (±)-*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 (±)-*O*-methyl-*N*-ethoxycarbonylnorsalutaridine (**11b**, 89%): mp 161.5–162.5° (EtOH–Et_2O); 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 ($CDCl_3$) 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-OCH_3); mass spectrum *m/e* (%) 399 (100, M^+), 371 (22), 326 (20). Reduction of **11b** with $LiAlH_4$ in THF under reflux gave a mixture of the epimeric (±)-*O*-methylsalutaridinols (80%) which was oxidized with MnO_2 in $CHCl_3$ to yield (±)-*O*-methylsalutaridine (**11c**, 60%): mp 70–73° (Et_2O); 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; NMR[14] ($CDCl_3$) 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-OCH_3), 2.45 (s, 3 H, N-CH_3); 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 (±)-corydine (**12a**, 31%; mp 165–166.5° (lit. 148°,[15] 165–167°[16]); mixture TLC, uv, NMR,[15] and mass spectrum[17] identical with those of naturally occurring (+)-corydine[18]). Also isolated were (±)-*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.

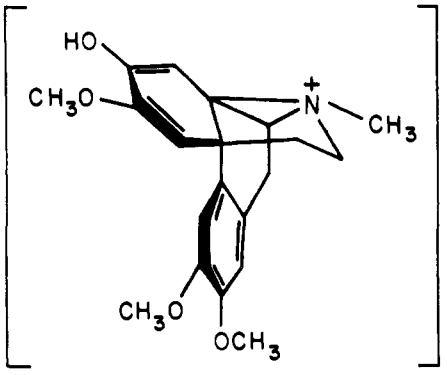


11a, $R^1 = H$; $R^2 = COOEt$
b, $R^1 = CH_3$; $R^2 = COOEt$
c, $R^1 = R^2 = CH_3$



12a, R = H
b, R = CH_3

The acid-catalyzed rearrangements of morphinandienones thus follow two principal routes, one which leads to dibenzazonine derivatives (e.g., **1** → **2** → **4**), and a second which leads to aporphines (e.g., **1** → **9** → **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-



13

nation of the molecular model of **13** indicates that stereoelectronic factors favor migration of the aryl group, to yield a proerythrinadienone intermediate. In contrast, those acid-catalyzed 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 (±)-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 (±)-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.

References and Notes

(1) Presented in part at a Meeting of the Heterocyclic Chemistry Group, The Chemical Society, London, Jan 6, 1975.
(2) This investigation was supported by grants from the National Cancer Institute (CA-12059) and from Hoffmann-La Roche Inc.
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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 example[1] the only pure halo compounds of tungsten(III) are $W_2X_9^{3-}$ 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 reported[2] 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, $W_2(NMe_2)_6$, and one monomer, $W(NMe_2)_6$. 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 $LiNR_2$ were employed (these are inherently more bulky than $^-NMe_2$). We have now found that this is indeed the case. The reaction of decomposed $WCl_4(OEt_2)_2$[3] with LiNMeEt or $LiNEt_2$ (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