any pretreatment. Commercially available 2,3:6,7-dibenzotropone and benzophenone were recrystallized from hexane–ether mixtures.

All electrochemical measurements were carried out in anhydrous solvent containing 0.1 M tetraethylammonium tetrafluoroborate and 10^{-3} M ketone. A divided cell equipped with a platinum button (0.2 cm^2) working electrode and a NaCl calomel (0.01 M) reference electrode was used. The *iR* compensation used was 85–90% of oscillation. The instrumentation used was designed and constructed in these laboratories.[14]

The solutions used for product analyses were as above, except ca. 0.01 M ketone was used. The reactions were performed in a divided cell using a platinum gauze for the working electrode. The solutions were electrolyzed at 0.1 V past the E_{pc} value until 0.6 faraday/mol of ketone was consumed, ca. 35 min. During the electrolysis the solution became intensely colored. After the prescribed electrolysis time, the reaction vessel was left standing until the color faded, and then the solution was worked up. The reaction products were isolated by extraction between ethyl ether and water in the usual manner. The recovered yellow oil, 80–90% yield, was analyzed by TLC on Eastman no. 13252 alumina using either 3:1 ethyl ether–hexane or 1:1 ethyl ether–methanol. The analysis revealed the presence of the ketone as expected and a trace amount of carbinol plus a large unidentified peak, presumedly a dimeric product.

The IR and NMR spectra of this mixture were not informative because of their similarity to the spectra of the starting material.

When the reaction was repeated with the presence of 2 mol of $CoCl_2$, no difference was detected in the product mixture except for a possible lower reaction conversion.

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Registry No.—2,3:6,7-Dibenzotropone, 2222-33-5; benzophenone, 119-61-9; $CoCl_2$, 7646-79-9; $Ni(acac)_2$, 3264-82-2; $Fe(acac)_2$, 14024-17-0; $Al(acac)_3$, 13963-57-0.

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New Biogenetic-Type Approach to *Cephalotaxus* Alkaloids and the Mechanism of *Schelhammera*-Type Homoerythrinadienone Formation in Vitro

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Three monophenolic dibenz[*d,f*]azecines, **3b, 3c,** and **3d,** were synthesized by taking advantage of VOF_3–TFA/TFAA induced oxidative coupling of nonphenolic and monophenolic phenethyltetrahydroisoquinolines to homoneospirinedienones and homoproerythrinadienones. The oxidation of 2-hydroxydibenz[*d,f*]azecine **3b** with potassium ferricyanide yielded the cephalotaxine precursor **5b** (10%), which represents the first reported synthesis of such a compound along the biogenetic-type route. Similar oxidation of 3-hydroxydibenz[*d,f*]azecine **3c** gave naturally unknown homoerysodienone **6b** in 15% yield. However, when 12-hydroxydibenz[*d,f*]azecine **3d** was oxidized, no *Schelhammera*-type homoerythrinadienone **7b** was detectable. This implies that the diphenoquinone **4** may be an intermediate in the formation of the *Schelhammera*-type homoerythrinadienone.

Cephalotaxus is a genus of yew-like coniferous trees native to Japan and China and is the sole known source of the cephalotaxine family of alkaloids.[1] The tumor inhibitory activity of several esters of cephalotaxine (**1**) has generated considerable interest in both the synthesis of these alkaloids[2] and the elucidation of their biogenesis.[3]

In *Cephalotaxus harringtonia,* cephalotaxine (**1**; Scheme I) and its esters are accompanied by several *Schelhammera*-type alkaloids[4,5] such as 3-*epi*-schelhammericine (**2**). The presence of *Schelhammera*-type alkaloids in *Cephalotaxus* species has led some researchers[5a,6] to propose that both the *Schelhammera*-type and *Cephalotaxus* alkaloids are biogenetically related and may be classified as homoerythrina alkaloids. Marino and Samanen[6] have examined a unified approach to homoerythrina skeletons via the pivotal diphenolic dibenz[*d,f*]azecine **3a.** The compound **3a** seemed to be a common precursor of *Cephalotaxine*-type skeleton **5a,** homoerysodienone **6a,** and *Schelhammera*-type skeleton **7a,** and, indeed, **3a** was cleanly transformed into two cyclized homoerythrina skeletons using potassium ferricyanide in methylene chloride–sodium bicarbonate solution. The *Schelhammera*-type skeleton **7a** was isolated in 45% yield along with the homoerysodienone **6a** (15%) and the unreacted starting material (35%). That no cephalotaxine precursor **5a** was observed in the above oxidation is suggestive of the absence of either diphenoquinone intermediate **4** or a suitably disposed *p*-hydroxy group. The *Cephalotaxine*-type skeleton such as **5b** should also be obtainable via oxidation of monophenolic dibenz[*d,f*]azecine **3b,** and valuable information regarding the mechanism of homoerythrinadienone formation

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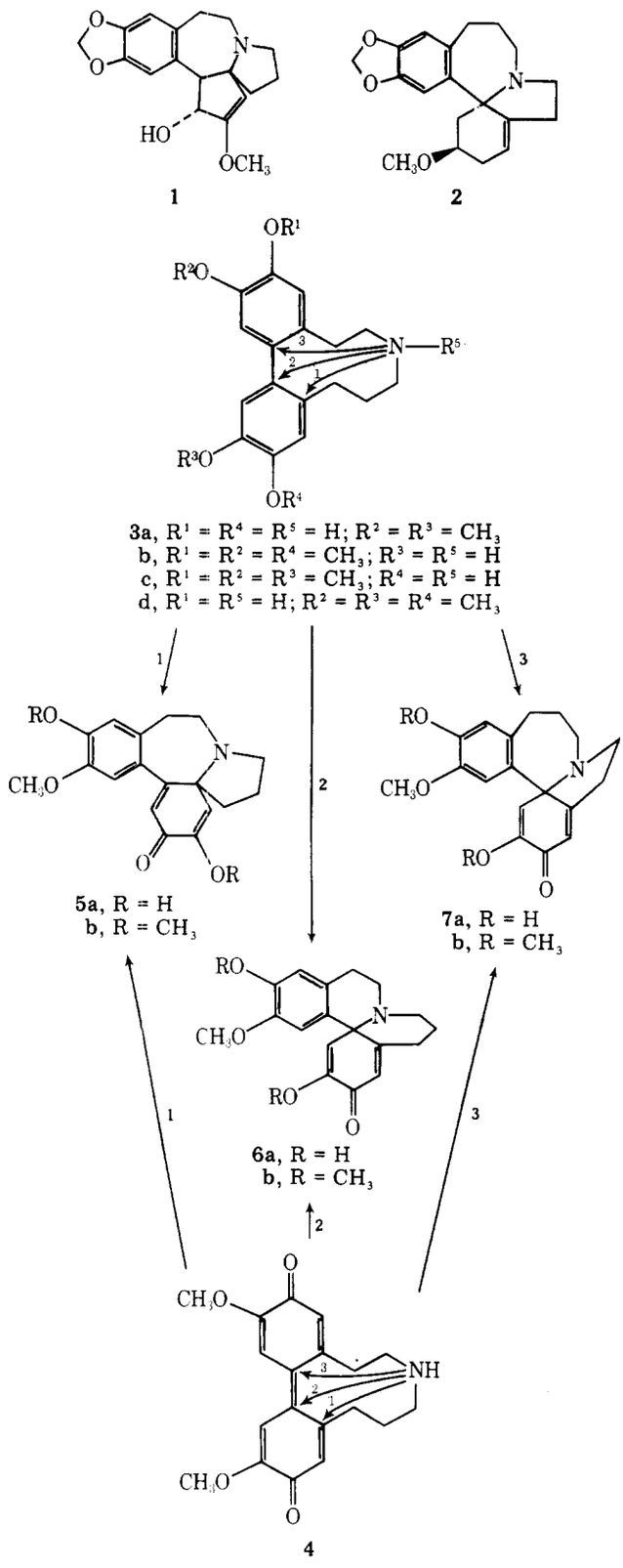
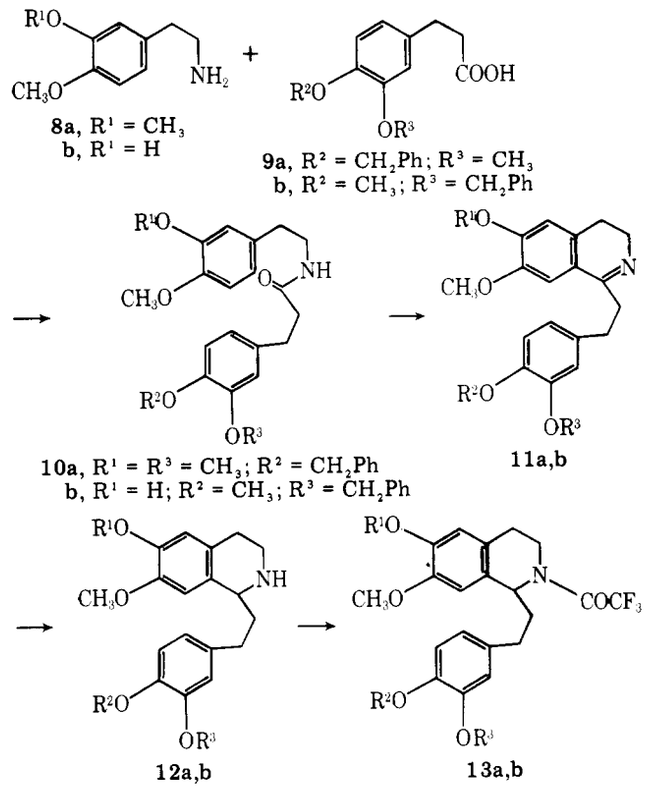
Scheme I



would result from studies on the oxidation of monophenolic dibenz[*d*,*f*]azecines **3c** and **3d**. This report[7b] details the preparation of the monophenolic dibenz[*d*,*f*]azecines **3b, 3c,** and **3d** and the results of the attempted oxidative transformation into the dienones **5b, 6b,** and **7b,** respectively.

The method used for the preparation of monophenolic dibenz[*d*,*f*]azecines **3b–d** is outlined in Scheme III. This scheme demonstrates the synthetic utility of homoneospirenedienones, obtained efficiently by VOF_3–TFA/TFAA induced oxidative coupling of nonphenolic and monophenolic phen-

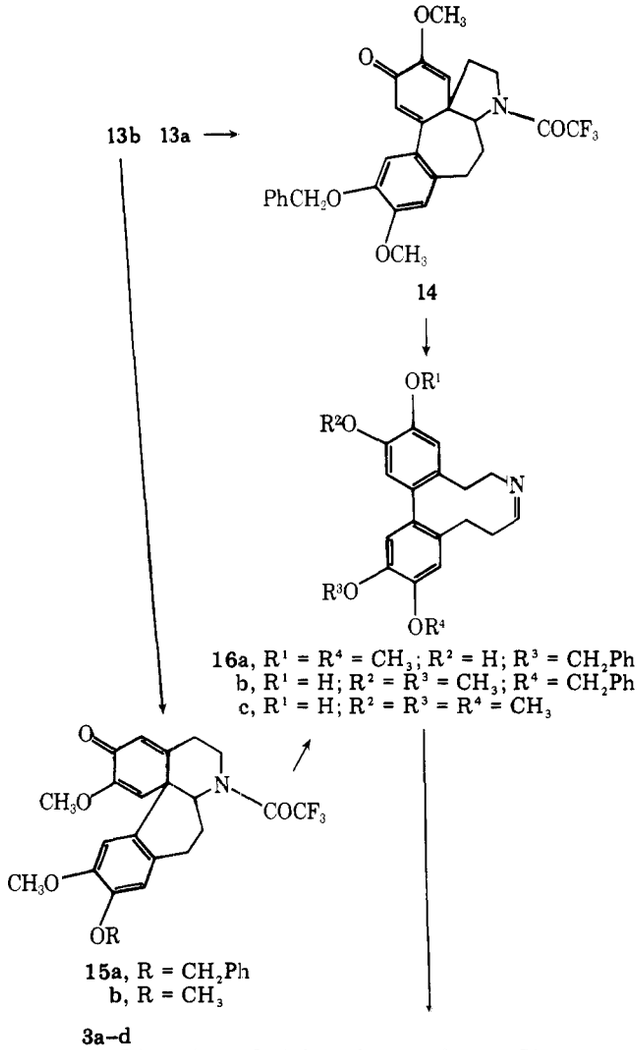
Scheme II



ethyltetrahydroisoquinolines.[7,8] The preparation of suitably substituted phenethyltetrahydroisoquinolines **13a,b** was achieved by the standard method shown in Scheme II. Nonphenol oxidative coupling[7] of the phenethyltetrahydroisoquinoline **13a** with VOF_3 in CH_2Cl_2 and TFA-TFAA yielded homoneospirinedienone **14** (Scheme III). Treatment of **14** with 1 N NaOH in methanol at 0 °C yielded the imine **16a,** which was converted into its hydrochloride salt with anhydrous hydrogen chloride in methanol. The imine hydrochloride was reduced with sodium borohydride in ethanol to give dibenz[*d*,*f*]azecine **3e,** which was treated without purification with trifluoroacetic anhydride (TFAA) and pyridine to yield **3f** in 70% overall yield from **14.** Methylation of **3f** with diazomethane gave **3g.** Debenzylation of **3g** by catalytic hydrogenation using 10% Pd/C gave **3h,** which was treated with potassium carbonate solution in aqueous methanol at room temperature to give the desired 2-hydroxydibenz[*d*,*f*]azecine **3b** (72% from **3f**). The 3-hydroxydibenz[*d*,*f*]azecine **3c** was prepared via a similar sequence of reactions from homoproerythrinadienone **15a,** which is readily available by monophenol oxidative coupling[8] of phenethyltetrahydroisoquinoline **13b.** Thus, treatment of **15a** with 1 N methanolic sodium hydroxide solution gave the imine **16b,** which was reduced with $NaBH_4$ to give dibenz[*d*,*f*]azecine **3i** in 88% yield. Acetylation of **3i** with TFAA and pyridine gave the trifluoroacetamide **3j** (75%). Methylation of **3j** with diazomethane gave **3k** (88%), and catalytic debenzylation of **3k** afforded **3l** (95%), which was hydrolyzed with 1 N methanolic sodium hydroxide solution to give the desired monophenolic dibenz[*d*,*f*]azecine **3c** in 82% yield. Finally the 12-hydroxydibenz[*d*,*f*]azecine **3d** was obtained by simple hydrolysis fragmentation of homoproerythrinadienone **15b**[8] to the imine **16c** followed by sodium borohydride reduction.

The 2-hydroxydibenz[*d*,*f*]azecine **3b** was treated with potassium ferricyanide in methylene chloride–sodium bicarbonate solution, and the *Cephalotaxine*-type compound **5b** was obtained in 10% yield. The IR (1695, 1687, and 1665 cm^{-1}) and UV spectra [λ_{max} 230 nm (log ϵ 4.16), 260 (3.90), 283 (3.79), and 326 (3.62)] showed the presence of a β-arylcyclohexadi-

Scheme III



enone system. The mass spectrum verified the formula $C_{20}H_{23}NO_4$. The NMR spectrum revealed two singlet aromatic protons (δ 6.68 and 6.59), two olefinic protons (δ 6.20 and 5.95), two aromatic methoxy signals (δ 3.89 and 3.86), and an olefinic methoxy signal (δ 3.72). The successful transformation of the dibenz[*d,f*]azecine **3b** into the *Cephalotaxine*-type skeleton **5b** represents the first reported synthesis of a potential *Cephalotaxus* alkaloid precursor along the biogenetic-type route, i.e., substituted phenethyltetrahydroisoquinolines → spirodienones → dibenz[*d,f*]azecines → cephalotaxine precursor.

Similarly the 3-hydroxydibenz[*d,f*]azecine **3c** was oxidized, and the naturally unknown homoerysodienone **6b** was obtained in 15% yield. However, when the 12-hydroxydibenz[*d,f*]azecine **3d** was oxidized and the isolated products were analyzed by TLC and IR, UV, NMR, and mass spectroscopy, no *Schelhammera*-type homoerythrinadienone **7b** was detectable. In comparing these results with those of the oxidation of the diphenolic dibenz[*d,f*]azecine **3a**,[6] it follows that both phenolic groups are required for the formation of the *Schelhammera*-type homoerythrinadienone **7b**, implying that the diphenoquinone **4** may be an intermediate in the reaction as was proposed in the *Erythrina* alkaloid series by Barton et al.[9]

Experimental Section

General. Melting points were determined on a Mettler FP2 melting point apparatus and are uncorrected. UV and IR spectra were determined on Beckman DK-2A and Perkin-Elmer 337 spectrophotometers, respectively. NMR spectra were recorded on a JEOL PS-100p FT NMR spectrometer interfaced to a Texas Instruments JEOL 980A computer with Me_4Si as an internal standard. Mass spectra were obtained on Hitachi Perkin-Elmer RMU-6E and AEI MS-902 spectrometers. All thin-layer chromatography was carried out on commercially prepared plates (E. M. Laboratories); silica gel 60 F-254 plates (2, 0.5, or 0.25 mm thickness, 20 × 20 cm) were used for preparative TLC. Visualization of the alkaloids was performed by means of ultraviolet light and/or by spraying the entire analytical plate, or the edges of the preparative plate, with an aqueous solution of iodoplatinic acid reagent (1.0 g in 250 mL of water containing 15 g of potassium iodide). Microanalyses were carried out by Atlantic Microlab, Inc., Atlanta, Ga. Column chromatography was carried out on silica gel 60 (70–230 mesh ASTM) obtained from E. M. Laboratories. Anhydrous sodium sulfate was used as a drying agent, exclusively. The phenethyltetrahydroisoquinolines **13a,b** were prepared by the standard procedure as described in the preceding paper.[7c]

***N*-(3,4-Dimethoxyphenethyl)-3-(4-benzyloxy-3-methoxyphenyl)propionamide (10a).** This was obtained in 95% yield from 3,4-dimethoxyphenethylamine (**8a**) and 4-benzyloxy-3-methoxyphenylpropionic acid (**9a**): mp 102.3–102.7 °C; IR ($CHCl_3$) 1665 cm^{-1}; NMR ($CDCl_3$) δ 7.35 (m, 5 H, **Ph**CH_2O), 6.70 (m, 6 H, ArH), 5.11 (s, 2 H, $PhCH_2O$), 3.85 (s, 9 H, OCH_3), 3.48–2.38 (m, 8 H, methylene protons).

Anal. Calcd for $C_{27}H_{31}NO_5$: C, 72.13; H, 6.95; N, 3.12. Found: C, 72.07; H, 6.95; N, 3.15.

1-(4-Benzyloxy-3-methoxyphenethyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (11a). The yield as the hydrochloride salt was 85%: mp 186–187.5 °C; NMR ($CDCl_3$) δ 7.37 (m, 5 H, **Ph**CH_2O), 7.04 and 6.77 (each s, 2 H, C-5 and C-8 protons), 6.94 (d, 1 H, C-2′ H, J = 1.7 Hz), 6.73 (d, 1 H, C-5′ H, J = 8.1 Hz), 6.53 (dd, 1 H, J = 8.1 and 1.7 Hz), 5.10 (s, 2 H, OCH_2), 4.00, 3.91, and 3.87 (all s, 9 H, OCH_3).

Anal. Calcd for $C_{27}H_{30}NO_4Cl{\cdot}0.5\ H_2O$: C, 67.98; H, 6.55; N, 2.94. Found: C, 68.05; H, 6.35; N, 2.91.

1-(4-Benzyloxy-3-methoxyphenethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (12a). The yield as the hydrochloride salt was 90%: mp 162.5–164.5 °C; NMR ($CDCl_3$) δ 7.38 (m, 5 H, **Ph**CH_2O), 6.98, 6.77, 6.58, and 6.47 (all s, 4 H, ArH), 5.10 (s, 2 H, OCH_2), 3.84 (s, 6 H, OCH_3), 3.79 (s, 3 H, OCH_3).

Anal. Calcd for $C_{27}H_{32}NO_4Cl$: C, 69.00; H, 6.86; N, 2.98. Found: C, 69.07; H, 6.86; N, 3.08.

1-(4-Benzyloxy-3-methoxyphenethyl)-6,7-dimethoxy-*N*-trifluoroacetyl-1,2,3,4-tetrahydroisoquinoline (13a). The yield was 97% as a colorless foam: IR ($CHCl_3$) 1692 cm^{-1} (C=O); NMR ($CDCl_3$) δ 7.35 (m, 5 H, **Ph**CH_2O), 6.70 (m, 5 H ArH), 5.56 (t, 1 H, CH, J = 7 Hz), 5.12 (s, 2 H, OCH_2), 3.88, 3.85, and 3.81 (each s, 9 H, OCH_3), 3.43–2.56 (m, 8 H, CH_2).

Anal. Calcd for $C_{29}H_{30}F_3NO_5$: C, 65.77; H, 5.71; N, 2.65. Found: C, 65.62; H, 5.77; N, 2.64.

***N*-(3-Hydroxy-4-methoxyphenethyl)-3-(3-benzyloxy-4-methoxyphenyl)propionamide (10b).** This was obtained in 75% yield from 3-hydroxy-4-methoxyphenethylamine (**8b**) and 3-benzyloxy-4-methoxyphenylpropionic acid (**9b**): mp 103.5–103.8 °C (from benzene–hexane); NMR ($CDCl_3$) δ 7.38 (m, 5 H, **Ph**CH_2O), 6.74 (m, 6 H, ArH), 5.69 (s, 1 H, OH), 5.11 (s, 2 H, OCH_2), 3.85 (s, 6 H, OCH_3), 3.38 (q, 2 H, $ArCH_2CH_2CO$), 2.83 (t, 2 H, $ArCH_2CH_2NH$, J = 7.5 Hz), 2.60 (t, 2 H, $ArCH_2CH_2CO$, J = 6.7 Hz), 2.31 (t, 2 H, $ArCH_2CH_2NH$, J = 7.5 Hz).

Anal. Calcd for $C_{26}H_{29}NO_5$: C, 71.70; H, 6.71; N, 3.22. Found: C, 71.58; H, 6.75; N, 3.20.

1-(3-Benzyloxy-4-methoxyphenethyl)-6-hydroxy-7-methoxy-1,2,3,4-tetrahydroisoquinoline (12b). Bischler–Napieralski cyclization of **10b** gave **11b** as an oil which without purification was converted to **12b**. The yield as the hydrochloride salt was 50%: mp 221.5–223 °C; NMR (CD_3OD–Me_2SO-d_6) δ 7.37 (s, 5 H, **Ph**CH_2O), 6.90 (brs, 3 H, ArH), 6.70 and 6.65 (both s, 2 H, ArH), 5.10 (s, 2 H, OCH_2), 3.82 (s, 6 H, OCH_3).

Anal. Calcd for $C_{26}H_{30}NO_4Cl{\cdot}0.5CH_3OH$: C, 67.02; H, 6.72; N, 2.99. Found: C, 67.23; H, 6.83; N, 2.96.

1-(3-Benzyloxy-4-methoxyphenethyl)-6-hydroxy-7-methoxy-*N*-trifluoroacetyl-1,2,3,4-tetrahydroisoquinoline (13b). The yield was 89%: mp 94.6–94.7 °C; NMR ($CDCl_3$) δ 7.42 (m, 5 H, **Ph**CH_2O), 6.77 (s, 3 H, ArH), 6.66 and 6.47 (both s, 2 H, ArH), 5.55

(broad s, 1 H, OH), 5.13 (s, 2 H, OCH_2), 3.85 and 3.82 (both s, 6 H, OCH_3), 3.64–2.5 (m, 8 H, CH_2).

Anal. Calcd for $C_{28}H_{28}NO_5F_3$: C, 65.23; H, 5.47; N, 2.72. Found: C, 65.28; H, 5.52; N, 2.75.

VOF_3 Oxidation of 13a. A solution of 2.7 g (5.10 mmol) of **13a** in 45 mL of dichloromethane and 8 mL of TFA–TFAA (20:1 by weight) was treated with a solution of 1.4 g (11.3 mmol) of VOF_3 in 4 mL of ethyl acetate and 8 mL of TFA–TFAA (20:1 by weight) for 20 min according to the procedure described earlier.[7b] After the usual workup and chromatography on silica gel, there was obtained 1.8 g of a yellow solid. Crystallization from methanol gave 1.66 g (63.5%) of **14** as yellow needles: mp 176.5–178 °C; UV (EtOH) λ_{max} (log ϵ) 342 (3.59), 285 (3.75), 258 (3.93), 235 (4.15) nm; IR ($CHCl_3$) 1725, 1700, 1675 cm^{-1}; NMR ($CDCl_3$) δ 7.36 (broad s, 5 H, **Ph**CH_2O), 6.66 (s, 2 H, ArH), 6.34 (s, 1 H, C-1 H), 5.70 (s, 1 H, C-4 H), 3.89 and 3.70 (both s, 6 H, OCH_3); mass spectrum, *m/e* 513 (M^+), 423

Anal. Calcd for $C_{28}H_{26}NO_5F_3$: C, 65.49; H, 5.10; N, 2.73. Found: C, 65.51; H, 5.06; N, 2.80.

5,6,9,10-Tetrahydro-2-benzyloxy-13-hydroxy-3,12-dimethoxydibenz[*d,f*]azecine (16a). A suspension of 150 mg (0.29 mmol) of **14** in 10 mL of 1 N methanolic sodium hydroxide was stirred at 0 °C under nitrogen for 8 h. The methanol was evaporated in vacuo, the residue suspended in water, the pH adjusted to ~8.0 with concentrated HCl, and the solution extracted with dichloromethane. The dichloromethane solution was washed with brine, dried, and evaporated to give 140 mg of a colorless glass. The glass was dissolved in 5 mL of methanol and the methanolic solution acidified with anhydrous methanolic HCl. The acidic solution was evaporated to dryness, and the residue crystallized from ethanol–ether to yield 127 mg (99.5%) of the hydrochloride salt of **16a:** mp 215–217 °C dec; NMR (Me_2SO-d_6) δ 9.23 (brs, 1 H, N^+H), 7.38 (s, 5 H, **Ph**CH_2O), 7.03, 6.99, 6.58, and 6.47 (each s, 4 H, ArH), 5.08 (s, 2 H, OCH_2), 3.84 (s, 6 H, OCH_3).

5,6,7,8,9,10-Hexahydro-2-benzyloxy-13-hydroxy-3,12-dimethoxy-*N*-trifluoroacetyldibenz[*d,f*]azecine (3f). A solution of 170 mg (0.375 mmol) of the imine hydrochloride (**16a**) in 10 mL of ethanol was cooled to 0 °C and treated with 50 mg of sodium borohydride, and the reaction mixture was stirred for 2 h. The ethanol was evaporated, the residue suspended in water, the pH adjusted to ~8.0 with concentrated HCl, and the solution extracted with dichloromethane. The dichloromethane solution was washed with brine, dried, and evaporated to yield 175 mg of **3e** as colorless glass. The glass was dissolved in 10 mL of dichloromethane and treated with 0.4 mL of trifluoroacetic anhydride and 4 drops of pyridine. The reaction mixture was stirred overnight at room temperature and worked up to give a yellow oil which was purified by preparative silica gel plates (chloroform) to afford an oil. Crystallization from ethanol gave 142 mg (70%) of **3f:** mp 81–82.5 °C; IR ($CHCl_3$) 3615 (OH), 1718 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 7.36 (brs, 5 H, **Ph**CH_2O), 6.82, 6.78, 6.64, and 6.62 (each s, 4 H, ArH), 5.59 (brs, 1 H, OH), 5.07 (s, 2 H, OCH_2), 3.92 (s, 6 H, OCH_3).

Anal. Calcd for $C_{28}H_{23}NO_5F_3$: C, 65.23; H, 5.47; N, 2.72. Found: C, 65.21; H, 5.23; N, 2.85.

5,6,7,8,9,10-Hexahydro-2-benzyloxy-3,12,13-trimethoxy-*N*-trifluoroacetyldibenz[*d,f*]azecine (3g). A solution of 580 mg (1.145 mmol) of **3f** in 10 mL of methanol was treated with an excess of an ether solution of diazomethane, and the solution was kept overnight at room temperature. The solvent was evaporated and the residue purified by preparative silica gel plates (chloroform) to give an oil which was crystallized from ether, yielding 550 mg (92%) of **3g** as white crystals: mp, 80.5–81.5 °C; IR ($CHCl_3$) 1722 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 7.37 (brs, 5 H, **Ph**CH_2O), 6.84 6.79, 6.63, and 6.54 (each s, 4 H, ArH), 5.09 (s, 2 H, OCH_2), 3.93, 3.91, and 3.80 (each s, 9 H, OCH_3).

Anal. Calcd for $C_{29}H_{30}NO_5F_3$: C, 65.77; H, 5.71; N, 2.65. Found: C, 65.86; H, 5.72; N, 2.69.

5,6,7,8,9,10-Hexahydro-2-hydroxy-3,12,13-trimethoxy-*N*-trifluoroacetyldibenz[*d,f*]azecine (3h). A solution of 590 mg (1.12 mmol) of **3g** in 20 mL of ethanol containing 135 mg of 10% Pd/C was hydrogenated at atmospheric pressure and temperature until the uptake of hydrogen ceased. The solution was filtered through Celite and evaporated to give 490 mg (100%) of **3h** as a white foam: IR ($CHCl_3$) 3618 (OH), 1715 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 6.79 (s, 2 H, ArH), 6.67 and 6.58 (both s, 2 H, ArH), 5.55 (s, 1 H, OH), 3.94, 3.92, and 3.82 (all s, 9 H, OCH_3); mass spectrum, *m/e* 439 (M^+), 424, 299, 285, 270, 257.

5,6,7,8,9,10-Hexahydro-2-hydroxy-3,12,13-trimethoxydibenz[*d,f*]azecine (3b). A mixture of 480 mg (1.09 mmol) of **3h,** 10 mL of methanol, and 10 mL of 15% aqueous potassium carbonate was stirred at room temperature for 30 h. The methanol was evaporated and the aqueous solution extracted with dichloromethane. The dichloromethane solution was washed with water, dried, and evaporated to leave 400 mg of a yellow foam which was crystallized from methanol, yielding 292 mg (78%) of **3b** as colorless crystals: mp 203.5–204 °C; IR ($CHCl_3$) 3620 cm^{-1} (OH); NMR ($CDCl_3$) δ 6.72, 6.71, 6.58, 6.54 (each s, 4 H, ArH), 3.90 (s, 6 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.46 (s, 3 H, CH_3OH of crystallization); mass spectrum, *m/e* 343 (M^+), 328, 311, 298, 285.

VOF_3 Oxidation of 13b. A solution of 1.03 g (2 mmol) of **13b** in 25 mL of dichloromethane and 5 mL of TFA–TFAA (20:1 by weight) was cooled to −10 °C (ice–salt bath). Following the addition of a solution of 640 mg (5.15 mmol) of VOF_3 in 2.0 mL of ethyl acetate and 2.0 mL of TFA–TFAA (20.1 by weight), the resulting blue solution was stirred for 6 min. The reaction mixture was worked up according to the procedure described earlier to give a yellow oil which was chromatographed on silica gel eluting with chloroform to give 1.1 g of a white foam. Crystallization from ether yielded 882 mg (86%) of **15a:** mp 107–107.4 °C; UV (EtOH) λ_{max} (log ϵ) 242 (4.36), 282 (3.73) nm; IR ($CDCl_3$) 1668, 1645, 1615 cm^{-1}; NMR ($CDCl_3$) ϵ 7.39 (br s, 5 H, **Ph**CH_2O), 6.69 and 6.47 (both s, 2 H, ArH), 6.33 and 5.29 (both s, 2 H, olefinic protons), 5.12 (s, 2 H, OCH_2), 3.73 (s, 3 H, aromatic OCH_3), 3.62 (s, 3 H, olefinic OCH_3); mass spectrum, *m/e* 513 (M^+), 485, 482, 422, 394.

Anal. Calcd for $C_{28}H_{26}NO_5F_3$: C, 65.49; H, 5.10; N, 2.73. Found: C, 65.48; H, 5.10; N, 2.72.

5,6,7,8,9,10-Hexahydro-3-benzyloxy-12-hydroxy-2,13-dimethoxydibenz[*d,f*]azecine (3i). A suspension of 300 mg (0.565 mmol) of **15a** in 35 mL of 1 N methanolic sodium hydroxide was stirred at 0 °C for 36 h to give the imine **16b.** Following the addition of 240 mg of sodium borohydride, portionwise, over 15 min, the reaction mixture was stirred for an additional 3 h. The methanol was evaporated, the residue dissolved in water, and the pH adjusted to ~8.0 with concentrated HCl. The basic solution was extracted with dichloromethane. The dichloromethane extract was washed with brine, dried, and evaporated to give 500 mg of a colorless glass which was crystallized from ethanol, yielding 362 mg (88.6%) of **3i** as colorless crystals: mp 166.1–166.5 °C; NMR ($CDCl_3$) δ 7.38 (m, 5 H, **Ph**CH_2O), 6.74 (s, 2 H, ArH), 6.58 and 6.55 (both s, 2 H, ArH), 5.18 (s, 2 H, OCH_3), 3.83 and 3.80 (both s, 6 H, OCH_3), 2.72–2.42 (m, 10 H, CH_2); mass spectrum, *m/e* 419 (M^+), 404, 387, 328, 300.

Anal. Calcd for $C_{26}H_{29}O_4N$: C, 74.43; H, 6.97; N, 3.34. Found: C, 74.19; H, 7.03; N, 3.33.

5,6,7,8,9,10-Hexahydro-3-benzyloxy-12-hydroxy-2,13-dimethoxy-*N*-trifluoroacetyldibenz[*d,f*]azecine (3j). A solution of 312 mg (0.744 mmol) of **3i** in 10 mL of dichloromethane was treated with 0.5 mL of trifluoroacetic anhydride and 5 drops of pyridine according to the procedure described for the preparation of **3f** to give 500 mg of a yellow glass which was crystallized from methanol, yielding 287 mg (75%) of **3j:** mp 148.5–152 °C; IR ($CHCl_3$) 3610 (OH), 1705 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 7.45 (m, 5 H, **Ph**CH_2O), 6.86 and 6.81 (both s, 2 H, ArH), 6.60 (s, 2 H, ArH), 5.19 (s, 2 H, OCH_2), 3.80 (s, 6 H, OCH_3).

Anal. Calcd for $C_{28}H_{28}NO_5F_3 \cdot 0.5\ H_2O$: C, 64.11; H, 5.31; N, 2.67. Found: C, 64.33; H, 5.31; N, 2.53.

5,6,7,8,9,10-Hexahydro-3-benzyloxy-2,12,13-trimethoxy-*N*-trifluoroacetyldibenz[*d,f*]azecine (3k). A solution of 260 mg (0.51 mmol) of **3j** in 5 mL of methanol was methylated according to the procedure described for the methylation of **3f** to give 235 mg (88%) of **3k** as colorless crystals: mp 147.5–149.5 °C (methanol); NMR ($CDCl_3$) δ 7.39 (m, 5 H, **Ph**CH_2O), 6.82 (s, 2 H, ArH), 6.61 (s, 2 H, ArH), 5.19 (s, 2 H, OCH_2). 3.92 (s, 3 H, OCH_3), 3.84 (s, 6 H, OCH_3), 3.45–2.4 (m, 10 H, CH_2).

Anal. Calcd for $C_{29}H_{30}NO_5F_3$: C, 65.77; H, 5.71; N, 2.65. Found: C, 65.79; H, 5.72; N, 2.63.

5,6,7,8,9,10-Hexahydro-3-hydroxy-2,12,13-trimethoxy-*N*-trifluoroacetyldibenz[*d,f*]azecine (3l). A solution of 200 mg (0.38 mmol) of **3k** in 15 mL of ethanol containing 100 mg of 10% Pd/C was hydrogenated according to the procedure described for the preparation of **3h** to give 180 mg of a colorless glass which was crystallized from methanol, yielding 159 mg (95%) of **3l** as colorless crystals: mp 189.6–190 °C; NMR ($CDCl_3$) δ 6.90, 6.83, 6.61, and 6.58 (all s, 4 H, ArH), 5.61 (s, 1 H, OH), 3.92, 3.85, and 3.84 (all s, 9 H, OCH_3), 3.52–2.44 (m, 10 H, CH_2).

Anal. Calcd for $C_{22}H_{24}NO_5F_3$: C, 60.13; H, 5.50; N, 3.19. Found: C, 60.09; H, 5.54; N, 3.15.

5,6,7,8,9,10-Hexahydro-3-hydroxy-2,12,13-trimethoxydibenz[*d,f*]azecine (3c). A solution of 140 mg (0.32 mmol) of **3l** in 10 mL of 1 N methanolic sodium hydroxide was stirred at room temperature for 18 h. The methanol was evaporated, the residue suspended in water, and the pH adjusted to ~8.0 with concentrated HCl. The solution was extracted with dichloromethane. The dichloromethane extract was washed with water, dried, and evaporated to afford a colorless oil which was crystallized from methanol, yielding

90 mg (82%) of **3c** as white crystals: mp 156.0–156.8 °C; NMR ($CDCl_3$) δ 6.78, 6.76, 6.59, and 6.51 (all s, 4 H, ArH), 5.30 (s, 1 H, OH), 3.92, 3.82, and 3.80 (all s, 9 H, OCH_3), 3.55–2.4 (m, 10 H, CH_2).

Anal. Calcd for $C_{20}H_{25}O_4N$: C, 69.94; H, 7.34; N, 4.08. Found: C, 69.80; H, 7.35; N, 4.05.

5,6,7,8,9,10-Hexahydro-12-hydroxy-2,3,13-trimethoxydibenz[*d,f*]azecine (3d). A suspension of 150 mg of (0.34 mmol) of **15b**[8] in 15 mL of 1 N methanolic sodium hydroxide was stirred at 0 °C for 36 h to give the imine **16c**. Following the addition of 100 mg of sodium borohydride, the reaction mixture was stirred for an additional 2 h and worked up according to the procedure described for the preparation of **3i** to give 120 mg of a colorless glass. Crystallization from methanol gave 83 mg (70%) of **3d** as white crystals: mp 179.8–181.2 °C; NMR ($CDCl_3$) δ 6.77 and 6.74 (both s, 2 H, ArH), 6.56 (s, 2 H, ArH), 5.30 (s, 1 H, OH), 3.91 (s, 3 H, OCH_3), 3.82 (s, 6 H, OCH_3), 3.51–2.5 (m, 10 H, CH_2).

Anal. Calcd for $C_{20}H_{25}O_4N$: C, 69.94; H, 7.34; N, 4.08. Found: C, 69.75; H, 7.30; N, 4.10.

Oxidation of 3b with Potassium Ferricyanide. A solution of 50 mg of the monophenolic dibenzazecine **3b** in 25 mL of dichloromethane was added to a rapidly stirred mixture of dichloromethane (125 mL) and 5% sodium bicarbonate (15 mL) containing potassium ferricyanide (100 mg) under nitrogen. After 2 h, the organic layer was separated and the aqueous solution extracted with dichloromethane. The combined organic layers were washed with brine, dried, and evaporated to leave a yellow glass which was applied to four 0.25 mm preparative silica gel plates and eluted with 5% methanol–chloroform. The band at R_f 0.65 was collected to give 7 mg of a yellow glass which was crystallized from ether to yield 5 mg (10%) of **5b** as yellow crystals: mp 149–152 °C; UV (EtOH) λ_{max} (log ε) 230 (4.16), 260 (3.90), 283 (3.79), 326 (3.62) nm; IR ($CHCl_3$) 1695, 1687, 1665 cm^{-1}; NMR ($CDCl_3$) δ 6.68 and 6.59 (both s, 2 H, ArH), 6.20 and 5.95 (both s, 2 H, olefinic protons), 3.89 and 3.86 (both s, 6 H, aromatic OCH_3), 3.72 (s, 3 H, olefinic OCH_3); high-resolution chemical ionization mass spectrum, *m/e* 342.1700 ($M^+ + 1$; calcd for $C_{20}H_{24}O_4N$, 342.1705).

Oxidation of 3c with Potassium Ferricyanide. A 25-mg sample of **3c** was treated with 50 mg of potassium hexacyanoferrate according to the procedure described for the oxidation of **3b** to give 30 mg of a yellow glass which was applied to 2 × 0.25 mm preparative silica gel plates and eluted with 5% methanol–chloroform. The band at R_f 0.65 was collected to give 5 mg of a colorless glass which was crystallized from ether to yield 4 mg (15%) of **6b** as colorless crystals: mp 160–163 °C; UV (EtOH) λ_{max} (log ε) 238 (4.46), 280 (3.69) nm; IR ($CHCl_3$) 1668, 1640, 1615 cm^{-1}; NMR ($CDCl_3$) δ 6.63 and 6.41 (both s, 2 H, ArH), 6.25 and 6.16 (both s, 2 H, olefinic protons), 3.87 and 3.70 (both s, 6 H, aromatic OCH_3), 3.62 (s, 3 H, olefinic OCH_3); high-resolution chemical ionization mass spectrum, *m/e* 342.1700 ($M^+ + 1$; calcd for $C_{20}H_{24}O_4N$, 342.1705).

Oxidation of 3d with Potassium Ferricyanide. A 25-mg sample of **3d** was treated with 50 mg of potassium ferricyanide according to the procedure described for the oxidation of **3b** to give 30 mg of a yellow glass. The infrared spectrum showed no dienone peaks at ca. 1668, 1640, and 1615 cm^{-1}.

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