(2S,3R)-2-Amino-3-benzyl-1,5-pentanedioic acid, Hydrochloride (3). A suspension of diester **9b** (335 mg, 0.92 mmol) in 6 N aqueous HCl (10 mL) was refluxed. After ca. 2 h, the mixture became homogeneous. The solvent was then evaporated. The solid residue was suspended in Et_2O. The suspension was filtered, and the solid that was collected was dried to yield **3** (75%) as white crystals: mp 117 °C; $[\alpha]_D$ +13.5° (*c* 1.2, H_2O);[20] ^1H NMR (400 MHz, D_2O) δ 2.52 (dd, *J* = 5, 13.5 Hz, 1 H), 2.86 (dd, *J* = 4, 13.5 Hz, 1 H), 2.70 (dd, *J* = 6, 17.5 Hz, 1 H), 2.85 (m, 1 H), 3.05 (dd, *J* = 3, 17.5 Hz, 1 H), 3.95 (m, 1 H), 7.24-7.45 (m, 5 H); ^{13}C NMR (TFA) δ 35.3, 38.1, 39.9, 58.6, 128.3, 130.1, 130.6, 139.9, 175.9.

Anal. Calcd for $C_{12}H_{15}O_4N\cdot HCl\cdot H_2O$: C, 49.40; H, 6.22; N, 4.80. Found: C, 49.50; H, 6.12; N, 4.88.

Acknowledgment. We thank Sanofi Recherche for a grant to I.J. and the DRET for funding this research. Thanks are extended to Prof. H. Shirahama for providing us with the ^1H NMR spectrum of the cis isomer of lactone **7b** and to Prof. M. Goeldner for helpful discussions.

Supplementary Material Available: Tables of coordinates, anisotropic temperature factors, distances, and angles and ORTEP drawings for **7b** (8 pages). Ordering information is given on any current masthead page.

(20) The corresponding TFA salt[11] has the following physical properties: mp 155 °C; $[\alpha]_D$ +15.7° (*c* 0.2, H_2O).

Carboxyl-Mediated Pictet-Spengler Reaction. Improved Synthesis of 2,3,5,6,11,11b-Hexahydro-3-oxo-1*H*-indolizino[8,7-*b*]indoles from Tryptamine-2-carboxylic Acids

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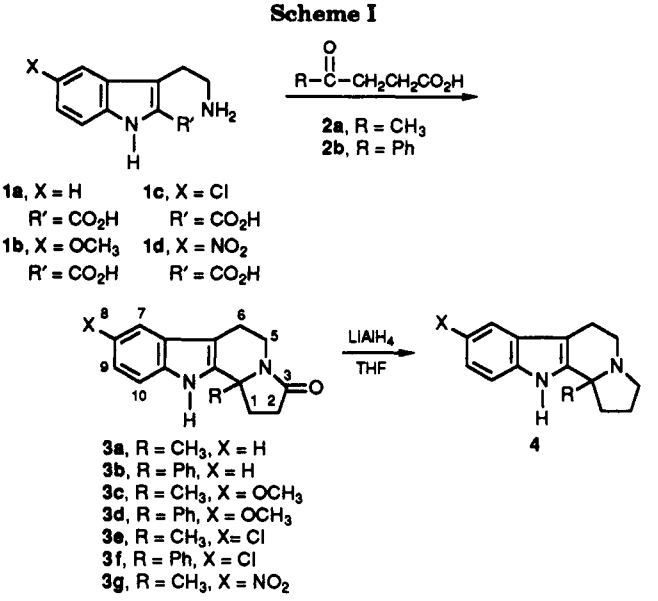
Indolizino[8,7-*b*]indoles are important intermediates in the pharmaceutical industry.[1-3] A number of these indoles have been shown to exhibit analgesic and antiinflammatory activity;[2,3] moreover, some of these compounds have been converted into indoloazonine or indolazecine derivatives, which exhibit diuretic activity.[3,4] A wide variety of indoles of the general formula **3** have been prepared by the Pictet-Spengler reaction of ring A substituted tryptamines **1** (R′ = H) with keto esters **2**, as illustrated in Scheme I. Reduction of the amide function, according to the published procedure,[2-4] provides the parent indolizino[8,7-*b*]indoles **4**. The sequence, however, depicted in Scheme I suffers from the limited availability of the required tryptamines when R′ = H.

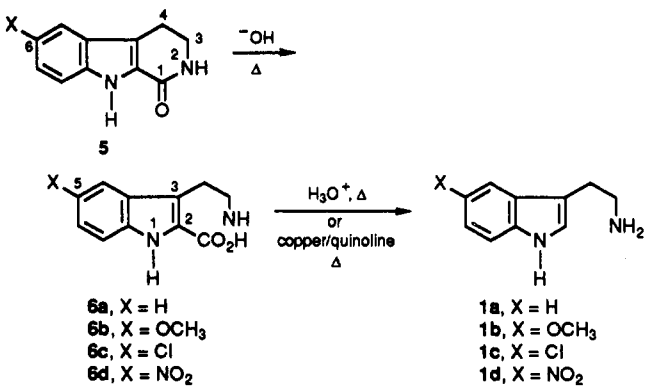
Recently, a modification of the Pictet-Spengler reaction has been developed[8] that permits direct use of tryptamine-2-carboxylic acids **1** (R′ = CO_2H) in this condensation. This improved synthesis of 11_b-substituted indolizino[8,7-*b*]indoles forms the subject of this paper.

One of the most versatile routes to ring A substituted tryptamines is the Abramovitch-Shapiro process[5] wherein

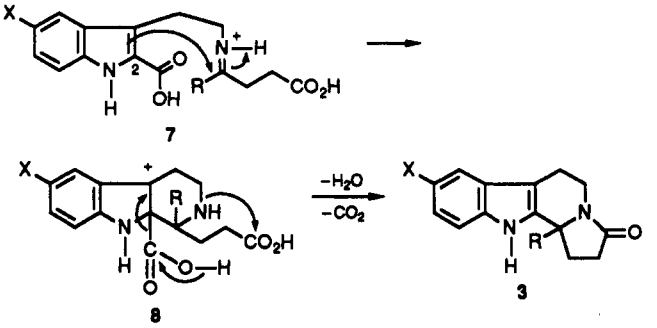
Scheme I



Scheme II



Scheme III

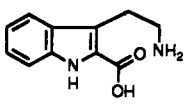
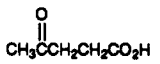
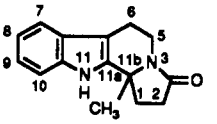
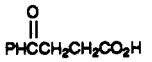
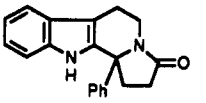
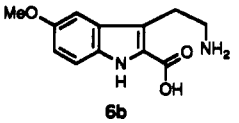
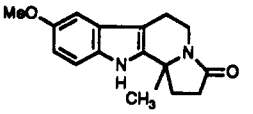
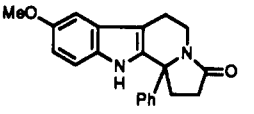
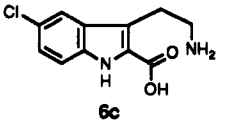
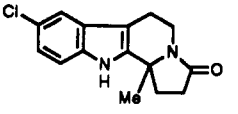
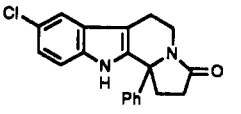
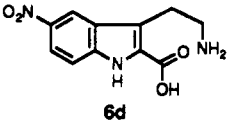
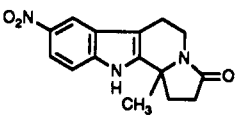
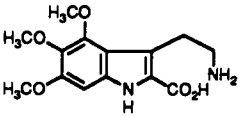
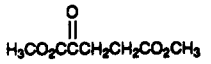
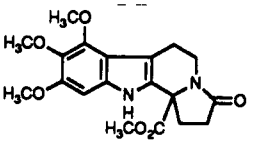


the Japp-Klingemann and Fischer indole[6] reactions are combined to furnish ring A substituted 1-oxo-1,2,3,4-tetrahydro-β-carbolines **5**. Although the hydrolysis of **5** to provide the tryptamine-2-carboxylic acid **6** proceeds in high yield,[6] the decarboxylation step to generate the desired tryptamine **1** often fails[5,7,8] under acidic conditions or even under the conditions of copper/quinoline (Δ).[9] For example, 5-chlorotryptamine-2-carboxylic acid (**6c**)

(1) Wawzonek, S.; Nordstrom, J. D. *J. Org. Chem.* **1965**, *30*, 265.
(2) Herbst, D. R. German Patent 2,033,631 (C1. C07d) 1971; *Chem. Abstr.* **1972**, *76*, 113061h.
(3) Herbst, D. R.; Smith, H. German Patent 2,004,356 (C1,C07d) 1971; *Chem. Abstr.* **1971**, *75*, 118297d.
(4) Herbst, D. R.; Smith, H. S. African Patent 70 00,530, 1971; *Chem. Abstr.* **1972**, *77*, P 34373d.
(5) Abramovitch, R. A.; Shapiro, D. J. *J. Chem. Soc.* **1956**, 4589.
(6) Robinson, B. *Fischer Indole Synthesis*, John Wiley and Sons: New York, 1982; 479.
(7) Phillips, R. R. *Organic Reactions*; John Wiley and Sons: New York, 1959; Vol. X, Chapter 2, p 143.
(8) Narayanan, K.; Schindler, L.; Cook, J. M. *J. Org. Chem.* **1991**, *56*, 359.
(9) Wiley, R.; Smith, N. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, 731.

0022-3263/91/1956-5733$02.50/0

Table I. Synthesis of 2,3,5,6,11,11b-Hexahydro-3-oxo-1*H*-indolizino[8,7-*b*]indoles from Tryptamine-2-carboxylic Acids

entry	tryptamine 2-acid	carbonyl component	product (% yield)[11]
1	 **6a**	 **2a**	 **3a** (85)
2	**6a**	 **2b**	 **3b** (67)
3	 **6b**	**2a**	 **3c** (90)
4	**6b**	**2b**	 **3d** (73)
5	 **6c**	**2a**	 **3e** (50)
6	**6c**	**2b**	 **3f** (60)
7	 **6d**	**2a**	 **3g** (52)
8	 **9**	 **10**	 **3h** (66)

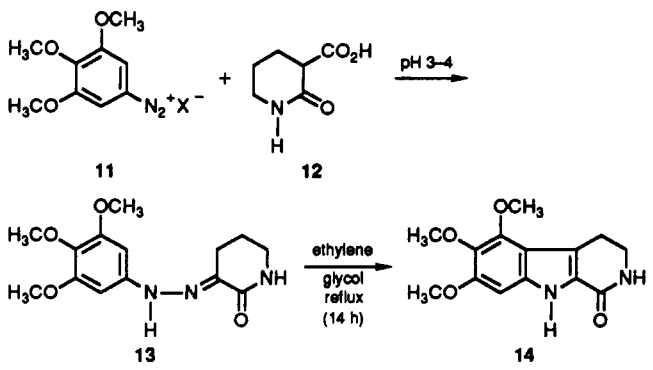
underwent decarboxylation only under vigorous conditions (30% aqueous HCl, Δ, 20 h) while 5-nitrotryptamine-2-carboxylic acid (**6d**) failed to undergo the decarboxylation reaction under a variety of conditions (Scheme II).[5,6] In addition, many ring A oxygen substituted tryptamine 2-acids failed to undergo the decarboxylation.[8]

In order to circumvent this problem, the synthesis of 1,2,3,4-tetrahydro-β-carbolines and indolizino[8,7-*b*]indoles by a carboxyl-mediated Pictet–Spengler reaction has been developed.[8] Examination of the intermediates in Scheme III provides an explanation for this phenomenon. Condensation of the tryptamine 2-acid **1** with the γ-keto carboxylic acid **2** would provide the Schiff base **7**. Intramolecular attack of the π-electrons from C-2 of intermediate **7** on the iminium ion would provide the carbocation **8**, as illustrated. Loss of the elements of CO_2 and H_2O from **8** would furnish the indolizino[8,7-*b*]indole **3**, negating the need for the tedious decarboxylation reaction (**6** → **1**). The proposed mechanism of this process has been described in detail in ref 8. In summary, the Pictet–Spengler reaction can be executed with the tryptamine 2-acids **6** in place of the corresponding tryptamines **1**, significantly streamlining the process.

The ring A substituted tryptamine-2-carboxylic acids **6a–d** required for this investigation were prepared by the method previously reported by Abramovitch and Shapiro.[5-7] When the tryptamine-2-carboxylic acids **6a–d** were heated, individually, with either levulinic acid **2a** or 3-benzoylpropionic acid **2b** in benzene/dioxane in the presence of trifluoroacetic acid, the corresponding 3-oxoindolizino[8,7-*b*]indoles **3a–g** were obtained, respectively. The yields of this process ranged from 50 to 90%, and the details are summarized in Table I. Of particular interest are the yields of the 8-chloro- and 8-nitroindolizinoindoles **3e**, **3f**, and **3g**, respectively. The carboxyl-mediated Pictet–Spengler reaction employed herein represents a considerable improvement over the previously reported synthesis of **3e–f**.[2,3] Since this modification obviates the need to remove the 2-carboxylic acid function from **6** prior to the condensation, it also constitutes a much improved route to indoles **3a–d** (see Table I).

In regard to the preparation of highly oxygenated ring A substituted indolizinoindoles for biological screening, the 4,5,6-trimethoxytryptamine-2-carboxylic acid **9** has recently been condensed with dimethyl 2-oxoglutarate (**10**) to furnish the 7,8,9-trimethoxy-2,3,5,6,11,11b-hexahydro-

Scheme IV



3-oxo-11b-(methoxycarbonyl)-1*H*-indolizino[8,7-*b*]indole (**3h**, entry 8, Table I). The preparation of the 2-carboxylic acid **9** from the diazonium salt **11** of 3,4,5-trimethoxyaniline is depicted in Scheme IV. Although no attempts to maximize the yields of this process have been made to date, the Fischer indole cyclization (**13** → **14**) was effected under thermal conditions,[6,10] which oftentimes provides much higher yields of the 1-oxotetrahydro-β-carbolines than the classical cyclization medium (HCO_2H, Δ).[5,6] The details of the synthesis of the oxotetrahydro-β-carboline **14**, as well as the conversion of the 2-carboxylic acid **9** into indolizinoindole **3h** are described in the Experimental Section.

In conclusion, the carboxyl-mediated Pictet–Spengler reaction[8] provides improved access to indolizinoindoles for biological evaluation as analgesics and antiinflammatory agents[1-4] even when the tryptamine-2-carboxylic acids are substituted in ring A with electron-withdrawing groups. This modification enhances the use of the Abramovitch–Shapiro method[5] for the synthesis of highly functionalized ring A substituted 1,2,3,4-tetrahydro-β-carbolines and indolizino[8,7-*b*]indoles.

Experimental Section

Microanalyses were performed on a F and M Scientific Corp. Model 185 carbon, hydrogen, and nitrogen analyzer. Melting points were taken on a Thomas-Hoover melting point apparatus and are reported uncorrected. Proton NMR spectra and ^{13}C NMR spectra were recorded on a Bruker 250-MHz spectrometer. Infrared spectra were taken on a Beckman Acculab-1 instrument, a Mattson Polaris R-10400, or a Nicolet Dx, while mass spectral data were obtained on a Hewlett-Packard 5855 GC–mass spectrometer.

All chemicals were purchased from Aldrich Chemical Co. unless otherwise stated. Analytical TLC plates used were E. Merck Brinkmann UV-active silica gel. Silica gel 60b for column chromatography was purchased from E.M. Laboratories. The TLC plates were visualized under UV light or developed with spray reagents. The 1,2,3,4-tetrahydro-β-carbolines were visualized by using a standard solution of ceric ammonium sulfate in 50% sulfuric acid.

Tryptamine-2-carboxylic acid (**6a**), 5-methoxytryptamine-2-carboxylic acid (**6b**), 5-chlorotryptamine-2-carboxylic acid (**6c**), and 5-nitrotryptamine-2-carboxylic acid were prepared according to published procedures.[5,7]

General Procedure for the Synthesis of 2,3,5,6,11,11b-Hexahydro-3-oxo-1*H*-indolizino[8,7-*b*]indoles. The tryptamine-2-carboxylic acid **6** (1 mmol) and the carbonyl component **2** (2 mmol) were taken up in a mixture of benzene/dioxane (2:1, 45 mL), and then trifluoroacetic acid (1 mL) was added. The reaction mixture was heated to reflux with a Dean-Stark trap to remove water. The reaction progress was monitored by TLC (EtOH/EtOAc (15:85)). After the reaction was deemed complete (1–2 days), the solvents were removed under reduced pressure. This was followed by partition of the residue between ethyl acetate and sodium bicarbonate solution. The organic layer was dried (Na_2SO_4) and the solvent removed in vacuo. The indolizino[8,7-*b*]indoles **3** were precipitated from the oil by the addition of ether and were purified by column chromatography on silica gel.

2,3,5,6,11,11b-Hexahydro-3-oxo-11b-methyl-1*H*-indolizino[8,7-*b*]indole (3a): mp 259–260 °C (lit.[1] mp 264–266 °C); ^1H NMR (DMSO-d_6) δ 1.55 (s, 3 H), 2.20–2.70 (m, 6 H), 3.10 (m, 1 H), 4.20 (m, 1 H), 7.00 (m, 2 H), 7.35 (m, 2 H), 10.95 (s, 1 H); IR (KBr) 3260, 1660 cm^{-1}; mass spectrum CI(CH_4) *m/e* 241 (MH^+, 100).

2,3,5,6,11,11b-Hexahydro-3-oxo-11b-phenyl-1*H*-indolizino[8,7-*b*]indole (3b): mp 259–261 °C (lit.[1] mp 263–264 °C); ^1H NMR (DMSO-d_6) δ 2.40–2.95 (m, 6 H), 3.50 (m, 1 H), 4.20 (m, 1 H), 6.90–7.70 (m, 9 H), 11.40 (bs, 1 H); IR (KBr) 3260, 1680 cm^{-1}; mass spectrum CI (CH_4) *m/e* 303 (MH^+, 100).

8-Methoxy-2,3,5,6,11,11b-hexahydro-3-oxo-11b-methyl-1*H*-indolizino[8,7-*b*]indole (3c): mp 197–198 °C (lit.[1] mp 200–201 °C); ^1H NMR ($DCCl_3$) δ 1.65 (s, 3 H), 2.20–3.00 (m, 6 H), 3.10 (m, 1 H), 3.85 (s, 3 H), 4.50 (m, 1 H), 6.80 (dd, *J* = 8.0, 2.0 Hz, 1 H), 7.20 (d, *J* = 8.0 Hz, 1 H), 9.40 (s, 1 H); IR (KBr) 3269, 1652 cm^{-1}; mass spectrum CI(CH_4) *m/e* 271 (MH^+, 100).

8-Methoxy-2,3,5,6,11,11b-hexahydro-3-oxo-11b-phenyl-1*H*-indolizino[8,7-*b*]indole (3d): mp 254–255 °C (lit.[1] mp 258–259 °C); ^1H NMR ($DCCl_3$) δ 2.50–3.10 (m, 7 H), 3.90 (s, 3 H), 4.40 (m, 1 H), 7.00 (m, 2 H), 7.40 (m, 6 H), 8.00 (s, 1 H); IR (KBr) 3265, 1680 cm^{-1}; mass spectrum CI(CH_4) *m/e* 333 (MH^+, 100).

8-Chloro-2,3,5,6,11,11b-hexahydro-3-oxo-11b-methyl-1*H*-indolizino[8,7-*b*]indole (3e): mp 224–225 °C (lit.[1] mp 229–230 °C); ^1H NMR ($DCCl_3$) δ 1.65 (s, 3 H), 2.20–3.20 (m, 6 H), 3.60 (m, 1 H), 4.50 (m, 1 H), 7.00–7.50 (m, 3 H), 8.00 (bs, 1 H); IR (KBr) 3250, 1660 cm^{-1}; mass spectrum CI (CH_4) *m/e* 276, 278 (MH^+, MH^+ + 2, 100, 31) chlorine isotopes.

8-Chloro-2,3,5,6,11,11b-hexahydro-3-oxo-11b-phenyl-1*H*-indolizino[8,7-*b*]indole (3f): mp 259–262 °C (lit.[1] mp 266–267 °C); ^1H NMR ($DCCl_3$) δ 2.40–3.00 (m, 6 H), 3.50 (m, 1 H), 4.45 (m, 1 H), 6.90–7.75 (m, 8 H), 8.50 (bs, 1 H); IR (KBr) 3260, 1680 cm^{-1}; mass spectrum CI (CH_4) *m/e* 337, 339 (MH^+, MH^+ + 2).

8-Nitro-2,3,5,6,11,11b-hexahydro-3-oxo-11b-methyl-1*H*-indolizino[8,7-*b*]indole (3g): mp 270–272 °C; ^1H NMR (DMSO-d_6) δ 1.50 (s, 3 H), 1.90–3.00 (m, 7 H), 4.20 (m, 1 H), 7.10 (d, *J* = 8.0 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 8.20 (s, 1 H), 11.00 (s, 1 H); IR (KBr) 3170, 1659 cm^{-1}; mass spectrum CI (CH_4) *m/e* 286 (MH^+, 100). Anal. Calcd for $C_{15}H_{16}N_3O_3 \cdot 1.25H_2O$: C, 58.06; 6.08; N, 13.46. Found: C, 58.09; H, 5.89; N, 13.21.

2,3-Dioxopiperidine 3-(3,4,5-Trimethoxyphenyl)hydrazone (13). The 3,4,5-trimethoxyaniline (7.20 g, 40 mmol) was treated with aqueous concd HCl (11 mL) and water (60 mL) and cooled to 0 °C. Sodium nitrite (3.6 g, in 10 mL of H_2O) was added dropwise to effect the diazotization (see **11**). This solution was added to the solution of 3-carboxy-2-piperidone (**12**) in water at 0 °C. (The piperidone **12** had been prepared from 3-carbethoxy-2-piperidone (6.80 g, 40 mmol) and potassium hydroxide (2.4 g in 80 mL H_2O) by stirring at 30 °C overnight.)[5,7] A saturated aqueous solution (50 mL) of sodium acetate was added to the reaction mixture to bring the pH to 4. The solution that resulted was stirred at 0 °C for 6 h, after which a precipitate formed that was filtered, washed with water, and dried (9.3 g, 79%). **13**: mp 200–202 °C; ^1H NMR ($CDCl_3$) δ 2.00 (m 2 H), 2.80 (m, 2 H), 3.50 (m, 2 H), 3.80 (s, 3 H), 3.90 (s, 6 H), 6.35 (s, 1 H), 7.10 (s, 1 H), 7.20 (s, 1 H); IR (KBr) 3670–3030, 1659, 1130 cm^{-1}; mass spectrum CI (CH_4) *m/e* 294 (MH^+). Anal. Calcd for $C_{14}H_{19}N_3O_4$: C, 57.34; H, 6.48; N, 14.33. Found: C, 58.05; H, 6.28; N, 14.07. This material was employed directly in the next step.

4,5,6-Trimethoxytryptamine-2-carboxylic Acid (9). The above hydrazone **13** (9.0 g, 30 mmol) was dissolved in ethylene glycol (100 mL) and heated to reflux under nitrogen overnight. The solution was cooled, and the solvent was distilled off under vacuum using a standard straight takeover distillation setup and an oil bath at 120 °C. The residue, which contained a little ethylene glycol, was taken up in ethyl acetate and washed with water. The aqueous layer was reextracted with ethyl acetate (4

(10) Crooks, P. A.; Robinson, B. *Chem. Ind.* **1967**, 547.

(11) Since many of the tryptamine-2-acids **6** (Scheme II) underwent the decarboxylation reaction in low yield, it was not practical to compare the yields directly with those cited in refs 3 and 4.

× 100 mL), and the combined ethyl acetate layers were dried (Na_2SO_4). The solvent was removed under reduced pressure. The residue was treated with $CHCl_3$/MeOH/ether and on reevaporation furnished a solid 14, which was directly subjected to alkaline hydrolysis (5.40 g): mp 180 °C; ^1H NMR ($DCCl_3$) δ 3.25 (t, J = 6.0 Hz, 2 H), 3.70 (m, 2 H), 3.80 (s, 6 H), 4.00 (s, 3 H), 6.70 (s, 1 H), 7.20 (s, 1 H), 11.10 (s, 1 H); IR (KBr) 3212, 2945, 1659, 1237 cm^{-1}; mass spectrum CI(CH_4) m/e 277 (MH^+, 100).

The ketocarboline 14 from above was added to potassium hydroxide (9.5 g) and water (100 mL) and the mixture heated to reflux for 24 h.[5,7] The reaction mixture was filtered and the filtrate brought to pH 5 with glacial acetic acid. The mixture was then cooled to precipitate the trimethoxytryptamine-2-carboxylic acid **9** (3.40 g, 40% overall): mp 208–210 °C; ^1H NMR (DMSO-d_6–CF_3COOD) δ 3.10 (m, 2 H), 3.50 (m, 2 H), 3.80 (s, 3 H), 3.85 (s, 3 H), 4.10 (s, 3 H), 6.75 (s, 1 H), 11.40 (s, 1 H); IR (KBr) 3430, 3268–2277, 1630, 1567, 1532 cm^{-1}; mass spectrum CI(CH_4) m/e 277 (MH^+ – 18, 100). Anal. Calcd for $C_{14}H_{18}N_2O_5 \cdot 0.25H_2O$: C, 56.28; H, 6.20; N, 9.38. Found: C, 56.02; H, 6.11; N, 9.02. Additional quantities of **9** can be obtained from the mother liquor.

7,8,9-Trimethoxy-2,3,5,6,11,11b-hexahydro-3-oxo-11b-(methoxycarbonyl)-1*H*-indolizino[8,7-*b*]indole (3h). The trimethoxytryptamine-2-carboxylic acid **9** (2.90 g, 10 mmol) and dimethyl 2-ketoglutarate (**10**; 2.70 g, 15 mmol) were added to a solution of benzene/dioxane (300:150 mL). This was followed by addition of TFAA (5 mL), and the mixture was heated to reflux under a Dean-Stark trap. After 36 h, the reaction mixture was cooled and the solvents were removed under reduced pressure. The residue was taken up in ethyl acetate, washed with aqueous sodium bicarbonate solution, and dried (Na_2CO_3). The solvent was removed under reduced pressure. The oil that remained was chromatographed by flash chromatography (silica gel) using EtOAc/EtOH (8:2) as the eluent to provide **3h** (2.5 g, 66%): mp 187 °C; ^1H NMR ($DCCl_3$) δ 2.20–3.20 (m, 7 H), 3.80 (s, 3 H), 3.90 (s, 6 H), 4.00 (s, 3 H), 6.65 (s, 1 H), 8.25 (s, 1 H); IR (KBr) 3248, 2938, 1736, 1680 cm^{-1}; mass spectrum CI(CH_4) m/e 375 (MH^+). Anal. Calcd for $C_{19}H_{22}N_2O_6$: C, 60.96; H, 5.88; N, 7.49. Found: C, 60.82; H, 5.88; N, 7.14.

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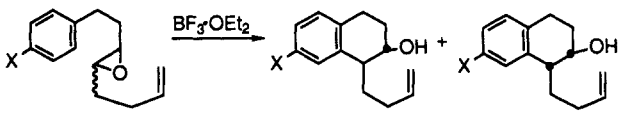
Registry No. **2a**, 123-76-2; **2b**, 2051-95-8; **3a**, 727-45-7; **3b**, 741-25-3; **3c**, 734-15-6; **3d**, 744-79-6; **3e**, 960-07-6; **3f**, 902-77-2; **3g**, 135663-91-1; **3h**, 135663-92-2; **6a**, 5956-86-5; **6b**, 52648-13-2; **6c**, 103795-47-7; **6d**, 96735-00-1; **9**, 92293-88-4; **10**, 13192-04-6; **12**, 41888-21-5; **13**, 5376-33-0; **14**, 5565-75-3; 3,4,5-trimethoxyaniline, 24313-88-0; 3-carbethoxy-2-piperidone, 3731-16-6.

Additions and Corrections

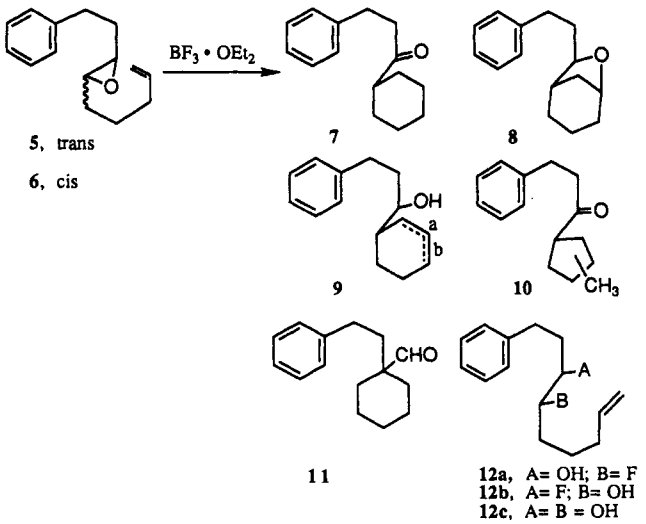
Vol. 55, 1990

Stephen K. Taylor,* David S. Bischoff, Curtis L. Blankespoor, Paul A. Deck, Suzanne M. Harvey, Patricia L. Johnson, Ariane E. Marolewski, Steven W. Mork, Douglas H. Morty, and Ronald Van Eenenaam. Competitive Intramolecular Cyclizations of Epoxides to Aromatic and Double Bond Positions.

Page 4202, Table I, compounds 1 and 2, and Scheme I, compounds 5 and 6, had extra bonds incorrectly drawn from the epoxide positions to the aromatic rings. The corrected figures are as shown



Scheme I



Vol. 56, 1991

Daniel E. Schaufelberger,* Gwendolyn N. Chmurny, John A. Beutler, Mary P. Koleck, A. Belinda Alvarado, Brigitte W. Schaufelberger, and Gary M. Muschik. Revised Structure of Bryostatin 3 and Isolation of the Bryostatin 3 26-Ketone from *Bugula neritina*.

Page 2895. The affiliation of John A. Beutler was listed erroneously with the Laboratory of Drug Discovery Research & Development DTP, NCI due to author error. The correct affilitation should have been listed as PRI/DynCorp. Dr. Beutler is currently affiliated with the LDDRD.

Paul A. Keifer, Robert E. Schwartz, Moustapha E. S. Koker, Robert G. Hughes, Jr., Dan Rittschof, and Kenneth L. Rinehart*. Bioactive Bromopyrrole Metabolites from the Caribbean Sponge *Agelas conifera*.

Page 2974, column 2, line 15, should read "...washed and filtered with acetone...".