# A Biomimetic Approach to the *Elaeocarpus* Alkaloids. Syntheses of (±)-Elaeokanine A, (±)-Elaeokanine C, (±)-Elaeocarpidine, and (±)-Tarennine

Gordon W. Gribble,* Frank L. Switzer, and Richard M. Soll

*Department of Chemistry, Dartmouth College, Hanover, New Hampshire 03755*

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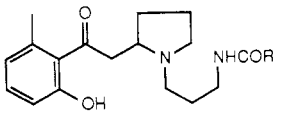
Convergent, biomimetically patterned syntheses of the *Elaeocarpus* alkaloids (±)-elaeokanine A (1), (±)-elaeokanine C (2), and (±)-elaeocarpidine (3) and the *Tarenna* alkaloid (±)-tarennine (17) are described in which the indolizidine ring is formed via a tandem Mannich–aldol condensation between 3-(1-$\Delta^1$-pyrroliniumyl)propanal (7) and benzyl 3-oxohexanoate (30c), in the case of 1 and 2, and via a Pictet–Spengler reaction between 7 and tryptamine (28), in the case of 3. Acid-promoted reduction of 3 with sodium cyanoborohydride gives 17. The key presumed intermediate 7 is generated in situ from amine bisacetal 15, which is synthesized in four steps from commercially available materials.

The majority of *Elaeocarpus* alkaloids represent a group of about 20 structurally similar indolizidine natural products (e.g., 1–6) in which the ring system is functionalized only at positions C-7 and C-8 (Scheme I).[1]

Their common plant source and similar structures imply that these alkaloids have a common biogenesis. Indeed, Onaka has suggested 3-(1-$\Delta^1$-pyrroliniumyl)propanal (7) as the universal intermediate in the formation of these *Elaeocarpus* alkaloids (Scheme I).[2] Furthermore, one can speculate that a plant diamine oxidase enzyme transforms spermidine (8) into the putative intermediate 7.[3] In fact, aminal 9 has been isolated from the reaction of 8 with pea seedling diamine oxidase (PSDO),[3d,e] and the related pyrrolinium aldehyde 11, implicated in the biooxidation of homospermidine (10), has led to a synthesis of the pyrrolizidine alkaloid trachelanthamidine (12) (Scheme II).[3c]

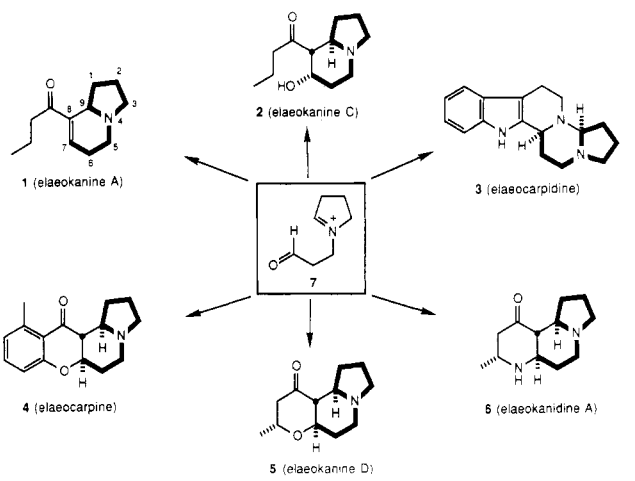
Onaka's biosynthetic hypothesis is reinforced by the recent isolation of the *Peripentadenia* alkaloids 13 and 14, which are more obviously derived from spermidine (8) than are the *Elaeocarpus* alkaloids.[4]



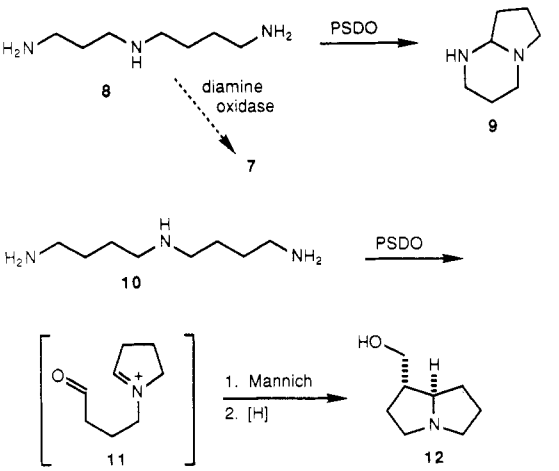

13, R = $(CH_2)_4CH_3$
14, R = $(CH_2)_2CH_3$

Thus, it became our goal in this research effort to develop a potentially general synthetic strategy to the *Elaeocarpus* alkaloids via (a) the generation of Onaka's pyrrolinium aldehyde 7 from an appropriate amine bisacetal (15) and (b) the subsequent trapping in situ of 7 with suitable nucleophiles (Scheme III).

**Scheme I**




**Scheme II**




The viability of this strategy was demonstrated in preliminary form for a synthesis of (±)-elaeocarpidine (3).[5] We now describe the full details of this methodology in the context of total syntheses of the alkaloids (±)-elaeokanine A (1),[1a] (±)-elaeokanine C (2),[1a] (±)-elaeocarpidine

(1) For reviews and leading references, see: (a) Johns, S. R.; Lamberton, J. A. *The Alkaloids*; Manske, R. H. F., Ed.; Academic: New York, 1973; Vol. 14, pp 325–346. (b) Saxton, J. E. *The Alkaloids* (Specialist Periodical Reports); Saxton, J. E., Ed.; The Chemical Society: London, 1971; Vol. 1, pp 76–81. (c) Herbert, R. B. *The Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1985; Vol. 3, pp 262–271. (d) Rajeswari, S.; Chandrasekharan, S.; Govindachari, T. R. *Heterocycles* **1985**, *25*, 659. (e) Howard, A. S.; Michael, J. P. *The Alkaloids*; Brossi, A., Ed.; Academic: New York, 1986; Vol. 28, pp 210–218.

(2) Onaka, T. *Tetrahedron Lett.* **1971**, 4395.

(3) For the oxidation of spermidine and related polyamines with diamine oxidase enzymes, see: (a) Hasse, K.; Schuhrer, K. *Biochem. Z.* **1962**, *336*, 20. (b) Leete, E. *J. Am. Chem. Soc.* **1982**, *104*, 1403. (c) Robins, D. J. *J. Chem. Soc., Chem. Commun.* **1982**, 1289. (d) Croker, S. J.; Loeffler, R. S. T.; Smith, T. A.; Sessions, R. B. *Tetrahedron Lett.* **1983**, *24*, 1559. (e) Brandänge, S.; Eriksson, L.-H.; Rodriguez, B. *Acta Chem. Scand., Ser. B.* **1984**, *38*, 526.

(4) (a) Lamberton, J. A.; Gunawardana, Y. A. G. P.; Bick, I. R. C. *J. Nat. Prod.* **1983**, *46*, 235. (b) Bick, I. R. C.; Gunawardana, Y. A. G. P.; Lamberton, J. A. *Tetrahedron* **1985**, *41*, 5627.

(5) Gribble, G. W., Soll, R. M. *J. Org. Chem.* **1981**, *46*, 2433.

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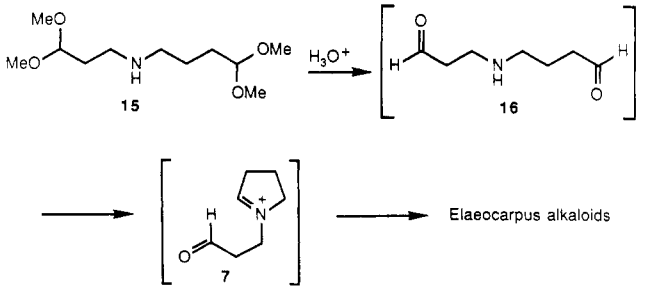
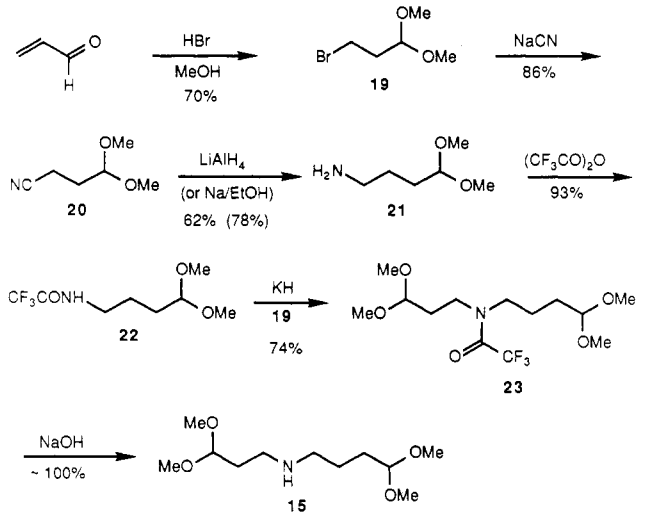
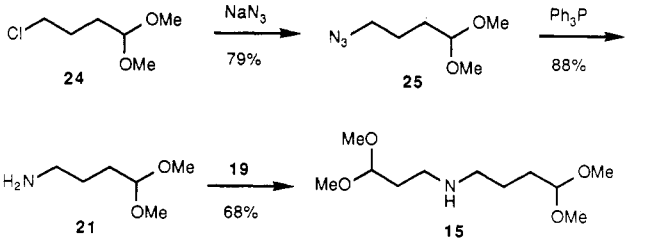
**Scheme III**



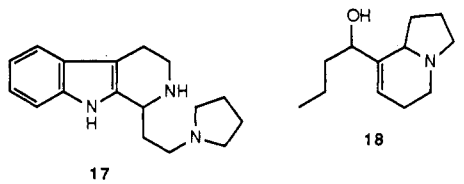

**Scheme IV**




**Scheme V**




(3),[1a] (±)-tarennine (17),[6] and, formally, (±)-elaeokanine B (18).[1a]

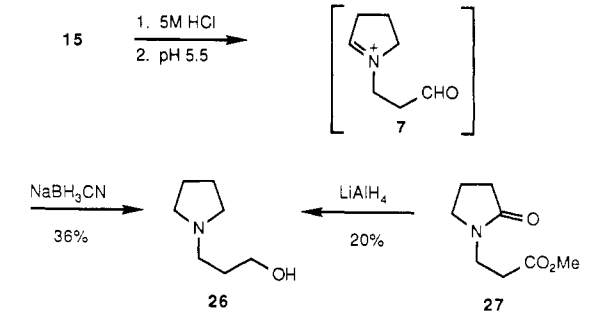



Beginning with the classical Robinson–Schöpf synthesis of tropinone, our projected Mannich–aldol sequence has ample precedent.[7]

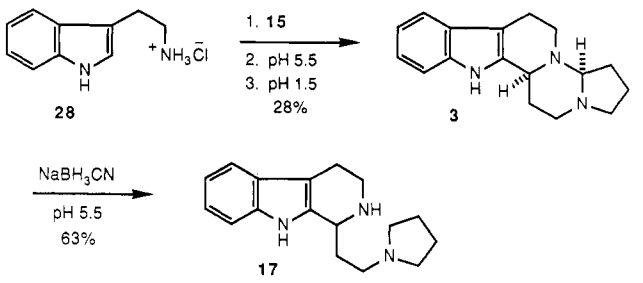
## Results and Discussion

The requisite amine bisacetal **15** was prepared by the two different methods summarized in Schemes IV and V.

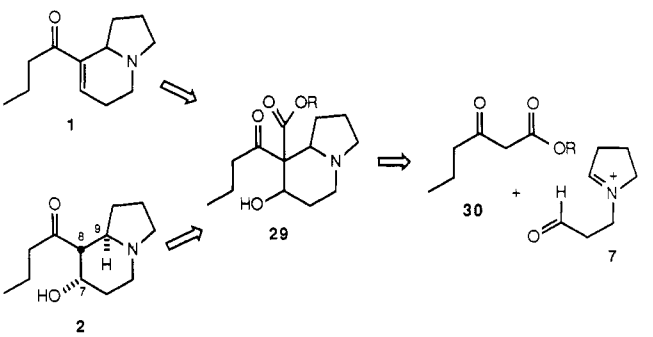
**Scheme VI**




**Scheme VII**




**Scheme VIII**




Of the two routes that we developed, the shorter one described in Scheme V was more suitable for large-scale runs, especially with the commercial availability of chloro acetal **24**. These syntheses of amine bisacetal **15** are fully described in the Experimental Section.

We initially examined the acidic hydrolysis of amine bisacetal **15** and subsequent[8] cyclization to pyrrolinium aldehyde **7** (Scheme III) in the presence of a reducing agent, whereby we could trap **7** as an N-substituted pyrrolidine. After some experimentation with different acidic conditions,[9] we found that treatment of amine bisacetal **15** with 5 M hydrochloric acid at room temperature (presumably generating the hydrochloride of amine dialdehyde **16**), followed by buffering to pH 5.5 with citrate–phosphate buffer (presumably generating pyrrolinium aldehyde **7**), and then followed by the addition of sodium cyanoborohydride gave pyrrolidine **26** (Scheme VI). The structure of **26** was confirmed by its independent synthesis from the known lactam ester **27**[10] by reduction of the latter with lithium aluminum hydride. Although the yield of **26** from

(6) Boissier, J. R.; Combes, G.; Effer, A. H.; Klinga, K.; Schlittler, E. *Experientia* **1971**, *27*, 677.

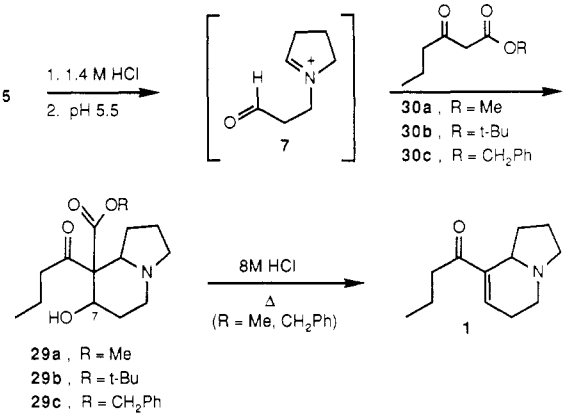
(7) (a) Robinson, R. *J. Chem. Soc.* **1917**, *111*, 762, 872. (b) Schöpf, C. *Angew. Chem.* **1937**, *50*, 779, 797. (c) Babor, K.; Ježo, I.; Kaláč, V.; Karvaš, M. *Chem. Zvesti* **1959**, *13*, 163; *Chem. Abstr.* **1959**, *53*, 20107. (d) Leonard, N. J.; Blum, S. W. *J. Am. Chem. Soc.* **1960**, *82*, 503. (e) Herbert, R. B.; Jackson, F. B.; Nicolson, I. T. *J. Chem. Soc., Chem. Commun.* **1976**, 450. (f) Stevens, R. V.; Lee, W. M. *J. Am. Chem. Soc.* **1979**, *101*, 7032. (g) Takano, S.; Ogawa, N.; Ogasawara, K. *Heterocycles* **1981**, *16*, 915.

(8) The acid hydrolysis (pH 5.83) of 4-amino-1,1-diethoxybutane proceeds without nitrogen assistance: Anderson, E.; Capon, B. *J. Chem. Soc., Perkin Trans 2* **1972**, 515.

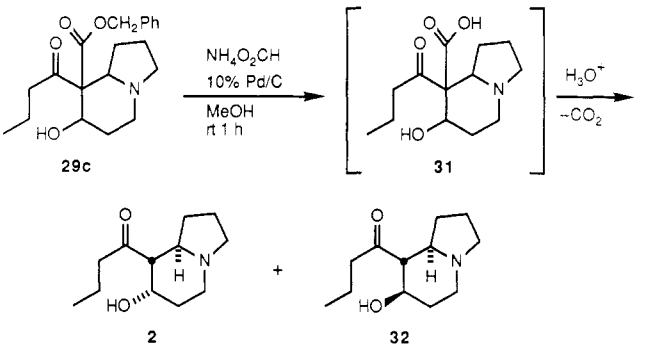
(9) In addition to exploring aqueous hydrochloric acid and varying pH, we examined acetic acid, trifluoroacetic acid, and *p*-toluenesulfonic acid under various conditions with **15**, but with much less success than as described in the text.

(10) Gribble, G. W. *J. Org. Chem.* **1970**, *35*, 1944.

**Scheme IX**




**Scheme X**




**15** was only fair, this experiment clearly established the feasibility of generating pyrrolinium aldehyde **7** from amine bisacetal **15** under acidic conditions.

The application of this chemistry to a synthesis of (±)-elaeocarpidine (**3**) and the related *Tarenna* alkaloid (±)-tarennine (**17**) is shown in Scheme VII. Thus, allowing tryptamine hydrochloride (**28**) to condense with pyrrolinium aldehyde **7**, as generated from amine bisacetal **15** according to Scheme VI, followed by stronger acid treatment to effect a Pictet–Spengler cyclization[11] gave (±)-elaeocarpidine (**3**) in 28% yield after purification by column chromatography and recrystallization. The overall condensation is stereoselective because the unknown trans isomer of elaeocarpidine, if formed, would presumably undergo rapid acid-catalyzed equilibration of the aminal linkage to afford the more stable cis isomer **3**.[12] Indeed, consistent with this notion is our observation that treatment of (±)-elaeocarpidine (**3**) at pH 5.5 with sodium cyanoborohydride gave (±)-tarennine (**17**) in 63% yield after recrystallization. Both alkaloids were identified by direct comparison with known material (cf. Experimental Section).

We envisioned that (±)-elaeokanine A (**1**) and (±)-elaeokanine C (**2**) could be fashioned from the same indolizidine intermediate **29** that would arise by a tandem Mannich–aldol condensation between pyrrolinium aldehyde **7** and a β-keto ester **30** as shown retrosynthetically in Scheme VIII.

On the basis of an observation made by Tufariello during the course of a synthesis of (±)-elaeokanine C (**2**) that featured an ultimate aldol cyclization step,[13] we were hopeful that the (correct) axial-hydroxyl configuration would obtain in indolizidine **29** and, thence, in (±)-elaeokanine C (**2**).

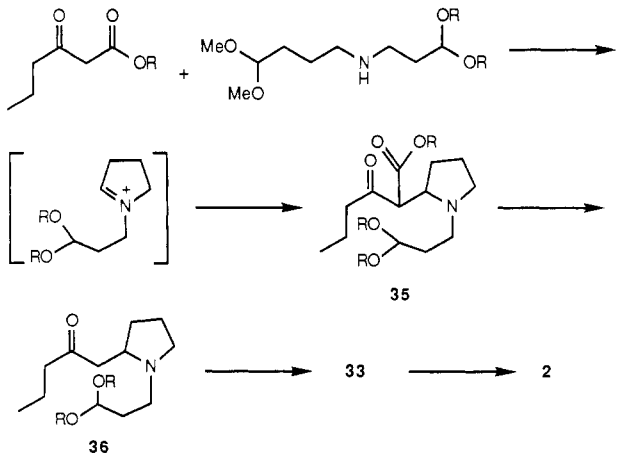
The synthesis of (±)-elaeokanine A (**1**) was achieved as follows (Scheme IX). Treatment of amine bisacetal **15** with 1.4 M aqueous hydrochloric acid followed by buffering the reaction mixture at pH 5.5 in the presence of the readily available 3-oxohexanoate esters (**30**, R = methyl, *tert*-butyl, benzyl)[14,15] afforded the desired indolizidines **29a–c** (42–62% yield) in which two major diastereomers predominate (by $^{13}C$ NMR). These mixtures display strong infrared Bohlmann bands[16] at 2940 and 2805 $cm^{-1}$ as expected for trans-fused indolizidines. By comparison of the $^{13}C$ NMR spectra of **29a–c** with those reported for (±)-elaeokanine C (**2**)[16] and (±)-7-epielaeokanine C (**32**),[17] we conclude that each mixture is epimeric at C-7 (i.e., C-7 axial OH at δ 69 and C-7 equatorial OH at δ 76). No attempt was made to separate and identify the isomers, but, rather, the crude mixture of **29** was either chromatographed (**29a**) or concentrated in vacuo to remove residual ester **30** prior to the subsequent reaction. In the event, treatment of either **29a** or **29c** with 8 M hydrochloric acid (reflux, 16 h) gave (±)-elaeokanine A (**1**) in 91% and 72% yield, respectively. Since (±)-elaeokanine A has previously been converted to (±)-elaeokanine B (**18**),[16] this route constitutes a formal synthesis of the latter alkaloid.

Our initial plan was to synthesize (±)-elaeokanine C (**2**) by effecting the decarboalkoxylation sans dehydration of **29**. However, several such reaction attempts (wet NaCl/DMF; $Et_4NCl$/HMPA; TMS-I; $MgCl_2$/HMPA; NaH/HMPA/NaCN) with **29a** resulted mainly in its decomposition. In some cases, traces of (±)-elaeokanine A (**1**) were detected by TLC. Likewise, attempts to decarboalkoxylate the *tert*-butyl ester **29b** to (±)-elaeokanine C (**2**) failed. Indeed, acidic hydrolysis of this ester was extremely sluggish and, for example, was only partially accomplished in concentrated hydrochloric acid at room temperature, but this gave only (±)-elaeokanine A (**1**). However, the benzyl ester **29c** proved to be a viable precursor to the target alkaloid **2** (Scheme X). Thus, catalytic transfer hydrogenation of **29c** with ammonium formate and 10% palladium/carbon (MeOH, room temperature, 1 h)[18] followed by mild acid treatment (HOAc, room temperature) afforded a mixture of (±)-elaeokanine C (**2**) and (±)-7-epielaeokanine C (**32**) in a ratio of 1:3 (60% yield from amine bisacetal **15**). These epimers could be separated by preparative TLC and were identified by comparison with the known compounds (cf. Experimental Section).

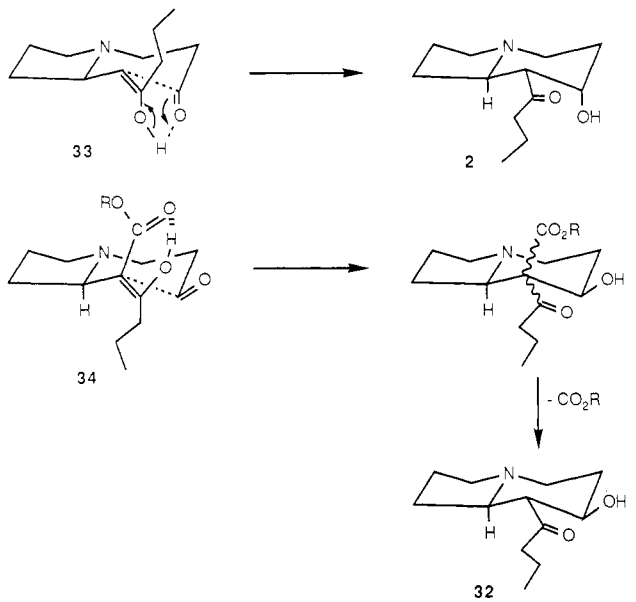
Unfortunately, other hydrogenation conditions did not improve the yield of the reaction. Likewise, attempts to epimerize **32** to **2** led primarily to (±)-elaeokanine A (**1**). It seems evident that the stereochemical control observed by Tufariello[13] (cf. **33**), leading exclusively to the axial-hydroxyl configuration present in (±)-elaeokanine C (**2**), is not a factor in our β-keto ester aldol cyclization transition state. In fact, the isolated of (±)-7-epielaeokanine C (**32**) as the major product is consistent with transition state **34**, in which an equatorial hydroxyl group would be the expected result. This rationale assumes that the β-keto

(11) Whaley, W. M.; Govindachari, T. R. *Org. React.* **1951**, *6*, 151.
(12) For an example of aminal isomerization, see: Thorsett, E. D.; Harris, E. E.; Patchett, A. A. *J. Org. Chem.* **1978**, *43*, 4276.
(13) Tufariello, J. J.; Ali, S. A. *Tetrahedron Lett.* **1979**, 4445.
(14) (a) Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082. (b) Weiler, L. *J. Am. Chem. Soc.* **1970**, *92*, 6702.
(15) Oikawa, Y.; Sugano, K.; Yonemitsu, O. *J. Org. Chem.* **1978**, *43*, 2087.
(16) Hart, N. K.; Johns, S. R.; Lamberton, J. A. *Aust. J. Chem.* **1972**, *25*, 817 and references cited therein.
(17) Otomasu, H.; Takatsu, N.; Honda, T.; Kametani, T. *Heterocycles* **1972**, *19*, 511; *Tetrahedron* **1982**, *38*, 2627.
(18) (a) Anwer, M. K.; Spatola, A. F. *Synthesis* **1980**, 929. (b) For a recent review, see: Ram, S.; Ehrenkaufer, R. E. *Synthesis* **1988**, 91.

**Scheme XI**

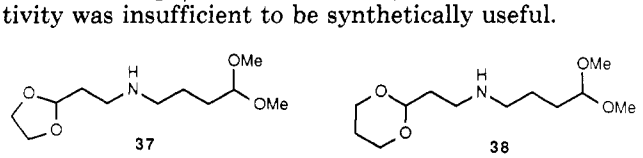


ester exists as the intramolecular hydrogen-bonding tautomer shown in **34**.



Finally, we made an attempt to carry out the stepwise indolizidine synthesis shown in Scheme XI. Our reasoning was that, if the aldol condensation could be delayed until after decarboalkoxylation of **35**, then the stereochemistry of the cyclization product would be controlled as for **33** → **2**.

Accordingly, we synthesized the mixed amine bisacetals **37** and **38** from amine acetal **21** and the appropriate bromo acetal. Although we found that the dimethyl acetal moiety in **37** and **38** was indeed hydrolyzed more rapidly than either the ethylene or propylene acetals under acidic conditions ($D_2O$/DCl, monitored by $^1H$ NMR), the selectivity was insufficient to be synthetically useful.



In conclusion, we have described biomimetically designed syntheses of *Elaeocarpus* alkaloids that are convergent and reasonably efficient, although the diastereoselection leading to (±)-elaeokanine C (**2**) is low. The readily availability of amine bisacetal **15** and its demonstrated applicability in the present methodology make the strategy proposed in Scheme III attractive for the synthesis of other, more complex *Elaeocarpus* alkaloids.

## Experimental Section

Melting points were determined in open capillaries with either a Mel-Temp Laboratory Devices apparatus or a Büchi 510 apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 599, 257, or 137 spectrometer. $^1H$ NMR spectra were determined at 60 MHz with a Hitachi Perkin-Elmer R-24 or a Varian EM-360A spectrometer or at 300 MHz with a Varian XL-300 spectrometer. $^{13}C$ NMR spectra were determined at 15 MHz with a JEOL FX60Q spectrometer or at 75 MHz with a Varian XL-300 spectrometer. Chemical shifts are reported in ppm downfield from internal tetramethylsilane. Low-resolution mass spectra were recorded on a Finnigan 4000 mass spectrometer. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA. The purity of those purified compounds that could not be analyzed due to their lability (**23**, **29a–c**) was estimated to be ≥90% by TLC and $^{13}C$ NMR spectroscopy.

**3-Bromo-1,1-dimethoxypropane (19).** This was prepared by using a combination of Ayer's procedure[19] and Büchi's synthesis of 2-(2-bromoethyl)-1,3-dioxolane.[20] Into an Erlenmeyer flask containing MeOH (18.2 g, 0.568 mol) at 0 °C was bubbled HBr gas until saturation was complete (~26 g of HBr). This solution was transferred to an ice-cooled 250-mL three-neck round-bottom flask equipped with a magnetic stir bar, dropping funnel, condenser, and drying tube. To this solution at 0 °C was added dropwise over 10 min freshly distilled acrolein (19.8 g, 0.353 mol) while HBr gas was bubbled into the solution. A brilliant violet coloration developed during the addition of acrolein. After additional HBr (49.8 g, 0.615 mol) had been absorbed by the solution, the lower layer was separated, dried ($CaCl_2$), and distilled in vacuo to afford 1,3-dibromo-1-methoxypropane (60.9 g, 74%): bp 90–100 °C/20 Torr (lit.[19] bp 60–80 °C/16 torr); $^1H$ NMR ($CDCl_3$) δ 2.60 (q, 2 H), 3.62 (s, 3 H), 3.62 (t, 2 H), 6.02 (t, 1 H).

Methanol (150 mL) was slowly poured into ice-cold 1,3-dibromo-1-methoxypropane from above, and the solution was stirred under $N_2$ for 2 h. An aliquot showed only **19** by $^1H$ NMR (absence of the triplet at δ 6.02 and appearance of a triplet at δ 4.55). The red solution was carefully poured into an ice-cold solution of saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$ (4 × 50 mL). The combined organic extract was washed with saturated aqueous NaCl (2 × 100 mL), dried ($K_2CO_3$), and concentrated in vacuo to give an orange oil. Distillation gave **19** (45.5 g, 70%) as a colorless oil: bp 76–85 °C/25 torr (lit.[21] bp 59 °C/12 torr); IR (neat) 2950, 2840, 1450, 1375, 1190, 1120, 1055, 975, 920, 870 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.55 (t, 1 H), 3.43 (t, 2 H), 3.36 (s, 6 H), 2.10 (q, 2 H). This NMR spectrum was identical with that reported.[19]

**3-Cyano-1,1-dimethoxypropane (20).** The general method of Reeves and White was used.[22] A mixture of NaCN (0.98 g, 0.020 mol), $H_2O$ (2 mL), bromo acetal **19** (1.0 g, 0.0055 mol), and tri-*n*-butylamine (0.05 g, 0.0002 mol) was refluxed for 2 h. The mixture was allowed to cool, diluted with $H_2O$ (10 mL), and extracted with $CH_2Cl_2$ (3 × 10 mL). The combined extract was washed with saturated aqueous NaCl, dried ($K_2CO_3$), and concentrated in vacuo to give an orange oil (0.65 g). Vacuum distillation afforded **20** (0.61 g, 86%) as a colorless oil: bp 110 °C/20 Torr; IR (neat) 2250, 1195, 1125, 1065, 975, 905 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 2.4 (m, 2 H), 2.0 (m, 2 H), 3.9 (s, 6 H), 4.5 (t, 1 H). These physical and spectral data were identical with those of a commercial sample of **20**.[23]

**4-Amino-1,1-dimethoxybutane (21) via Lithium Aluminum Hydride Reduction of 20.** The procedure of Lukeš and Trojánek was used.[24] To a mechanically stirred suspension of $LiAlH_4$ (10.2 g, 0.269 mol) in dry $Et_2O$ (500 mL) was slowly added a solution of cyano acetal **20** (30.0 g, 0.233 mol) in dry $Et_2O$ (40 mL) at a rate such that gentle reflux was maintained (~45 min). The

(19) Ayer, W. A.; Dawe, R.; Eisner, R. A.; Furuichi, K. *Can. J. Chem.* **1976**, *54*, 473.
(20) Büchi, G.; Wuest, H. *J. Org. Chem.* **1969**, *34*, 1122.
(21) Pineau, R. *Chem. Abstr.* **1952**, *46*, 416*h*.
(22) Reeves, W. P.; White, M. R. *Synth. Commun.* **1976**, *6*, 193.
(23) ROC/RIC Corp., Belleville, NJ. However, **20** is no longer commercially available.
(24) Lukeš, R.; Trojánek, J. *Chem. Listy* **1952**, *46*, 383; *Chem. Abstr.* **1953**, *47*, 4282.

mixture was stirred at reflux for 14 h and then cooled to 0 °C. The excess hydride was cautiously destroyed by the slow addition of 25% aqueous NaOH (100 mL). The $Et_2O$ layer was decanted, filtered through a filter cell, and saved. The remaining sludge was suspended in 25% aqueous NaOH (~450 mL) and filtered through the bed of a filter cell. The filter cell was extracted with several portions of 25% aqueous NaOH and $CH_2Cl_2$ (200 mL). The organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$ (5 × 100 mL). The combined $CH_2Cl_2$ extract was washed with saturated aqueous NaCl and dried ($K_2CO_3$). The $Et_2O$ extract from above was washed with saturated aqueous NaCl and dried ($K_2CO_3$). The $Et_2O$ and $CH_2Cl_2$ extracts were combined and concentrated in vacuo to give a pale yellow oil. Vacuum distillation gave **21** (19.1 g, 62%) as a colorless oil: bp 83–85 °C/22 Torr (lit.[25] bp 76–77 °C/18 Torr); IR (neat) 3400, 3320, 2950, 2825, 1600, 1450, 1385, 1195, 1125, 1055, 950, 810 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.35 (t, 1 H), 3.28 (s, 6 H), 2.68 (t, 2 H), 1.58 (m, 4 H), 1.38 (s, 2 H).

**4-Amino-1,1-dimethoxybutane (21) via Sodium Reduction of 20.** The procedure of Manske was used.[26] To an ice-cooled solution of cyano acetal **20** (10.0 g, 0.077 mol) in MeOH (150 mL) (efficient cooling is necessary) was added Na metal (16.6 g, 0.72 mol) in one portion. After the initial vigorous reaction had subsided, the mixture was refluxed and additional Na (~5.8 g, 0.25 mol) was added over 2 h until a gelatinous mixture resulted and no more Na dissolved. Methanol (15 mL) was added to the mixture to dissolve any remaining Na. After being cooled to room temperature, the reaction mixture was diluted with saturated aqueous NaCl (300 mL) and $H_2O$ (75 mL) and extracted with $CH_2Cl_2$ (4 × 100 mL). The combined $CH_2Cl_2$ extract was washed with saturated aqueous NaCl (2 × 100 mL), dried ($K_2CO_3$), and concentrated in vacuo to give a cloudy oil. Vacuum distillation afforded **21** (8.0 g, 78%) as a colorless oil (bp 100–103 °C/30 Torr), the spectral properties of which were identical with those of the material prepared by the previous procedure.

**4-Azido-1,1-dimethoxybutane (25).** The general method of Reeves and Bahr was used.[27] A stirred mixture of $NaN_3$ (47.9 g, 0.737 mol), 4-chloro-1,1-dimethoxybutane (**24**) (55.2 g, 0.362 mol), and tetra-*n*-octylammonium chloride (8.6 g, 0.017 mol) in $H_2O$ (150 mL) was refluxed for 6 h. The resulting red solution was cooled to room temperature and extracted with $CH_2Cl_2$ (4 × 100 mL). The extract was washed with saturated aqueous NaCl (200 mL), dried ($K_2CO_3$), and concentrated in vacuo. The crude product was distilled at reduced pressure to afford azide **25** (45.6 g, 79%) as a colorless oil: bp 75–87 °C/10 Torr; IR (neat) 2955, 2842, 2110, 1470, 1455, 1390, 1370, 1355, 1290, 1265, 1200, 1185, 1130, 1070, 960 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.3–4.6 (m, 1 H), 3.36 (s, 8 H), 1.5–2.0 (m, 4 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 104.0, 52.8, 51.2, 26.6, 24.0.

Anal. Calcd for $C_6H_{13}N_3O_2$: C, 45.27; H, 8.23; N, 26.40. Found: C, 45.46; H, 8.17; N, 26.50.

**4-Amino-1,1-dimethoxybutane (21) via Reduction of Azide 25.** The general method of Vaultier was used.[28] To a stirred solution of azide **25** (30.1 g, 0.189 mol) in THF (200 mL) at room temperature was added a dry THF solution (100 mL) of triphenylphosphine (49.5 g, 0.189 mol) in small portions (*Caution*: induction period) while maintaining the solution temperature below 40 °C. This addition was complete in 3 h and the resulting clear solution was then stirred for 1 h at room temperature. Water (4.5 mL, 0.25 mol) was then added and stirring was continued at room temperature for 16 h. The resulting solution was concentrated and the residue was extracted with $Et_2O$ (4 × 125 mL). The combined extract was dried ($K_2CO_3$) and concentrated in vacuo. The residue was distilled at reduced pressure to give amine **21** (22.1 g, 88%) as a colorless oil (bp 78–86 °C/14 Torr), the spectral properties of which were identical with those of the material prepared by the previous procedures.

**4-(Trifluoroacetamido)-1,1-dimethoxybutane (22).** To an ice-cooled solution of amine acetal **21** (10.0 g, 0.0751 mol), $Et_3N$ (63 g, 0.62 mol), and dry $Et_2O$ (100 mL) under $N_2$ with stirring was added dropwise over 5 min trifluoroacetic anhydride (21 mL, 0.15 mol). The mixture was stirred for 2 h at room temperature, then slowly poured into saturated aqueous $NaHCO_3$, and extracted with $Et_2O$ (2 × 100 mL). The extract was washed with $H_2O$ (2 × 100 mL) and saturated aqueous NaCl, dried ($K_2CO_3$), and concentrated in vacuo to give an oil. Vacuum distillation gave **22** (16.1 g, 93%) as a pale yellow oil, bp 110–118 °C/2.5 Torr. A second distillation gave an analytical sample: bp 87 °C/0.65 Torr; IR (neat) 3320, 2950, 2840, 1715, 1560, 1450, 1375, 1180, 720 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.50 (br s, 1 H), 4.38 (br t, 1 H), 3.38 (m, 2 H), 3.38 (s, 6 H), 1.68 (m, 4 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 104.3, 53.4, 39.7, 30.0, 23.1; mass spectrum, *m/e* 229 ($M^+$), 198, 166, 138, 126, 85, 75, 61, 58, 55, 52.

Anal. Calcd for $C_8H_{14}NO_3F_3$: C, 41.92; H, 6.16; N, 6.11. Found: C, 41.99; H, 6.14; N, 6.09.

**4-(*N*-(3,3-Dimethoxypropyl)trifluoroacetamido)-1,1-dimethoxybutane (23).** The general method of Nordlander was used.[29] Settled KH (Alfa, 23.6% oil dispersion) was placed in a tared 25-mL three-neck round-bottom flask (equipped with a dropping funnel and condenser) such that as little oil as possible was transferred. To the KH was added dry hexane (5 mL), and the suspension was vigorously stirred until a fine dispersion resulted. The dispersion was allowed to settle, and the hexane was removed by pipet and then discharged into MeOH. This washing procedure was repeated several times. The resulting oil-free KH was dried under a stream of $N_2$ to give a highly pyrophoric powder (0.17 g, 0.0042 mol). To this dry KH powder was added dry tetrahydrofuran (THF) (10 mL), and to the ice-cooled suspension was added dropwise a solution of amide acetal **22** (0.78 g, 0.0034 mol) in THF (2 mL). The mixture was stirred at 0° C for 5 min and then treated with 18-crown-6 ether (0.99 g, 0.0037 mol). The solution was slowly heated to reflux while a solution of bromo acetal **19** (0.80 g, 0.0044 mol) in THF (2 mL) was added dropwise over 10 min. The mixture was refluxed for 14 h, allowed to cool, and concentrated in vacuo to half of the original volume. The mixture was diluted with $H_2O$ (50 mL) and extracted with $CH_2Cl_2$ (3 × 25 mL). The extract was washed with $H_2O$ (3 × 25 mL) and saturated aqueous NaCl (25 mL), dried ($K_2CO_3$), and concentrated in vacuo to give a colorless oil (1.39 g). Column chromatography on silica gel (hexane/$Et_2O$ gradient elution) gave 1.33 g of an oil that contained 18-crown-6 by NMR. The oil was dissolved in $CH_2Cl_2$ (50 mL), washed with aqueous KCl (50 mL), dried ($K_2CO_3$), and concentrated in vacuo to give a yellow oil (0.90 g). The $^1H$ NMR indicated this to be a mixture of **22** and **23** in a ratio of 1:9.5 (74% yield, 80% conversion).

In a separate run, the crude product was purified by medium-pressure LC (EtOAc/hexane, 1:1) to give **23** as a pale yellow oil: IR (neat) 2950, 1690, 1450, 1360, 1240, 1195, 1125, 1070 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.38 (br t, 2 H), 3.35 (m, 4 H), 3.35 (s, 12 H), 1.5–2.2 (m, 6 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 104.2, 104.0, 102.6, 102.3, 53.3, 53.1, 48.0, 47.7, 47.6, 47.3, 46.8, 43.1, 32.0, 29.9, 29,8, 29.6, 23.8, 22.0 (partial); precise mass calcd for $C_{13}H_{23}NO_5F_3$ ($M^+$ – H) 330.1528, found 330.1540.

**4-((3,3-Dimethoxypropyl)amino)-1,1-dimethoxybutane (15) from 23.** A solution of amide bisacetal **23** (4.74 g, 0.0143 mol), MeOH (50 mL), and 25% aqueous NaOH (20 mL) was stirred at room temperature under $N_2$ for 2 h. The pale yellow solution was diluted with $H_2O$ (250 mL) and extracted with $CH_2Cl_2$ (4 × 50 mL). The extract was washed with $H_2O$ (2 × 100 mL) and saturated aqueous NaCl, dried ($K_2CO_3$), and concentrated in vacuo to give **15** (3.63 g, ~100%) as a pale yellow oil. The analytical sample was prepared by distillation: bp 120 °C/1.1 Torr; IR (neat) 3320, 2920, 2820, 1445, 1370, 1115, 1050 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.40 (t, 1 H), 4.32 (br t, 1 H), 3.22 (s, 12 H), 2.3–2.8 (m, 4 H), 1.25–1.9 (m, 6 H), 1.15 (br s, 1 h); $^{13}C$ NMR ($CDCl_3$) $\delta$ 104.3, 103.4, 52.7, 52.5, 49.5, 45.2, 32.7, 30.2, 25.0; precise mass calcd for $C_{10}H_{22}NO_3$ ($M^+$ – OMe) 204.1600, found 204.1618.

Anal. Calcd for $C_{11}H_{25}NO_4$: C, 56.14; H, 10.71; N, 5.95. Found: C, 56.15; H, 10.73; N, 5.93.

**4-((3,3-Dimethoxypropyl)amino)-1,1-dimethoxybutane (15) from 21.** To stirred amine **21** (27.7 g, 0.208 mol) at 80 °C was

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(26) Manske, R. H. F. *Can. J. Res.* **1931**, *5*, 598.
(27) Reeves, W. P.; Bahr, M. L. *Synthesis* **1976**, 823.
(28) Vaultier, M.; Knouzi, N.; Carrié, R. *Tetrahedron Lett.* **1983**, *24*, 763.
(29) Nordlander, J. E.; Catalane, D. B.; Eberlein, T. H.; Farkas, L. V.; Howe, R. S.; Stevens, R. M.; Tripoulas, N. A. *Tetrahedron Lett.* **1978**, 4987.

added 3-bromo-1,1-dimethoxypropane (**19**) (16.1 g, 0.088 mol) dropwise over 1 h. The resulting yellow mixture was stirred at 80 °C for an additional 3 h, cooled, and diluted with $CH_2Cl_2$ (200 mL). The mixture was washed with 5% aqueous NaOH (400 mL), and the aqueous phase was back-extracted with $CH_2Cl_2$ (2 × 100 mL). The combined $CH_2Cl_2$ extract was washed with saturated aqueous NaCl (200 mL), dried ($K_2CO_3$), and concentrated in vacuo to give a yellow oil. Distillation at $H_2O$ aspirator pressure gave some amine **21**. Continued distillation under higher vacuum gave amine **15** (14.0 g, 68%) as a colorless oil (bp 90–110 °C/0.15 Torr), the spectral properties of which were identical with those of the material prepared above.

***N*-(3-Hydroxypropyl)pyrrolidine (26) from *N*-(-2-Carbomethoxyethyl)pyrrolidin-2-one (27).** The lactam ester **27**[10] (2.00 g, 0.0117 mol) was added dropwise at room temperature with stirring to a suspension of $LiAlH_4$ (1.75 g, 0.046 mol) in dry $Et_2O$ (15 mL) over 30 min. The mixture was refluxed for 11 h under $N_2$, cooled to room temperature, and carefully treated with $H_2O$ (~30 mL). The organic layer was separated by decantation and the aqueous layer was extracted with $Et_2O$ (3 × 40 mL). The combined $Et_2O$ extract was dried ($K_2CO_3$) and concentrated in vacuo to give a yellow oil (0.5 g). Vacuum distillation gave **26** (0.30 g, 20%) as a colorless oil: bp 135 °C/80 Torr (lit.[30] bp 98 °C/18 Torr); IR (neat) 3350, 2950, 2880, 2800, 1700, 1460, 1355, 1135, 1060, 875 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.50 (br s, 1 H), 3.75 (t, 2 H), 2.55 (m, 6 H), 1.75 (m, 6 H); $^{13}C$ NMR ($CDCl_3$) δ 64.0, 55.9, 54.0, 29.3, 23.3.

***N*-(3-Hydroxypropyl)pyrrolidine (26) from Amine Bisacetal 15.** To 5 M HCl (5 mL) at room temperature under $N_2$ was added dropwise with stirring amine bisacetal **15** (0.50 g, 0.0021 mol). The solution was stirred at room temperature for 90 min and treated with 25% aqueous NaOH (~3.5 mL) and then with pH 5.5 citrate–phosphate buffer (30 mL). The solution was stirred at room temperature for 4 h and then treated with $NaBH_3CN$ (0.20 g, 0.0032 mol). The solution was stirred for an additional 70 min, basified with 25% aqueous NaOH, and extracted with $CH_2Cl_2$ (3 × 10 mL). The extract was dried ($K_2CO_3$) and concentrated in vacuo to give a yellow oil (0.15 g). Flash chromatography over silica gel (MeOH then MeOH/$Et_3N$, 95:5) gave **26** (0.10 g, 36%) as a yellow oil. This material was essentially identical ($^1H$ and $^{13}C$ NMR, IR) with that synthesized by the above procedure; precise mass calcd for $C_7H_{15}NO$ 129.1154, found 129.1172.

**(±)-Elaeocarpidine (3).** A solution of tryptamine hydrochloride (**28**) (0.90 g, 0.0046 mol), amine bisacetal **15** (1.00 g, 0.00426 mol), MeOH (40 mL), and a pH 5.5 citrate–phosphate buffer (100 mL) was stirred at room temperature for 5 h and then at 70 °C for 4 h. The pH was lowered to 1.5 by the addition of concentrated HCl, and the mixture was stirred and heated at 60–70 °C for 40 h. The orange solution was cooled, diluted with $H_2O$, basified with 25% aqueous NaOH, and extracted with $CH_2Cl_2$ (4 × 50 mL). The extract was washed with $H_2O$ (2 × 100 mL) and saturated aqueous NaCl, dried ($K_2CO_3$), and concentrated in vacuo to give an orange solid (1.51 g). Chromatography over basic alumina (activity III) ($CH_2Cl_2$/EtOAc gradient) gave a yellow solid (1.10 g), which was recrystallized from hexane/$CH_2Cl_2$ to give (±)-elaeocarpidine (**3**) (0.32 g, 28%) as a colorless solid (mp 209–210 °C (lit.[31] mp 213–215 °C), mixture mp 208–210 °C), identical with known material (IR, TLC, $^{13}C$ NMR, mass spectrum).[10]

**(±)-Tarennine (17).** A suspension of (±)-elaeocarpidine (**3**) (0.054 g, 0.20 mmol) and $NaBH_3CN$ (0.010 g, 0.16 mmol) in pH 5.5 citrate–phosphate buffer (2 mL) was stirred at 80 °C for 2 h. The mixture was cooled, basified with 25% aqueous NaOH, and extracted with EtOAc (3 × 10 mL). The extract was washed with saturated aqueous NaCl, dried ($K_2CO_3$), and concentrated in vacuo to give **17** as a colorless gum (0.045 g, 84%). Crystallization from acetone provided **17** (0.034 g, 63%) as tiny colorless needles (mp 123–123.5 °C (lit.[10] mp 123–124 °C)), identical with known material (TLC, IR).[10]

**Methyl 3-Oxohexanoate (30a).** This was prepared in 67% yield by the procedure of Weiler;[14] bp 100–109 °C/15 Torr (lit.[14] bp 77–79 °C/14 Torr).

***tert*-Butyl 3-Oxohexanoate (30b).** This was prepared in 77% yield by the procedure of Yonemitsu:[15] bp 55–69 °C/0.6 Torr, IR (neat) 2990, 2945, 2885, 1740, 1715, 1370, 1325, 1260, 1155 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 3.37 (s, 2 H), 2,55 (t, 2 H, $J$ = 8 Hz), 1.65 (t of q, 2 H, $J$ = 8, 8 Hz), 1.48 (s, 9 H), 0.93 (t, 3 H, $J$ = 8 Hz).

**Benzyl 3-Oxohexanoate (30c).** This was prepared in 78% yield by the procedure of Yonemitsu:[15] bp 100–112 °C/0.2 Torr; IR (neat) 2960, 2935, 2875, 1745, 1715, 1635, 1455, 1410, 1375, 1315, 1260, 1225, 1150, 745, 700 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.37 (s, 5 H), 5.17 (s, 2 H), 3.46 (s, 2 H), 2.50 (t, 2 H, $J$ = 8 Hz), 1.61 (t of q, $J$ = 8, 8 Hz), 0.89 (t, 3 H, $J$ = 8 Hz); $^{13}C$ NMR ($CDCl_3$) δ 202.5, 167.0, 135.2, 128.5, 128.3, 128.2, 66.9, 49.1, 44.8, 16.8, 13.4; mass spectrum, $m/e$ 220 ($M^+$), 192, 108, 107, 91 (100%), 86, 71.

**8-Carbomethoxy-7-hydroxy-8-(1-oxobutyl)indolizidine (29a).** To stirring 5 M HCl (21 mL) at room temperature under $N_2$ was added dropwise amine bisacetal **15** (2.0 g, 0.0085 mol). After 90 min, the reaction mixture was treated with 25% aqueous NaOH (~15 mL), and the solution was buffered at pH 5.5 (120 mL of citrate–phosphate buffer). At this point, β-keto ester **30a** (1.1 g, 0.0076 mol) was added and stirring was continued for 18 h. The orange solution was basified with 25% aqueous NaOH and extracted with $CH_2Cl_2$ (3 × 30 mL). The extract was washed with $H_2O$ (50 mL) and saturated aqueous NaCl (2 × 50 mL), dried ($K_2CO_3$), and concentrated in vacuo to give a red oil (1.65 g). Flash chromatography on silica gel (EtOAc to 2% MeOH/EtOAc elution) gave **30a** (0.30 g) and indolizidine **29a** (1.10 g). A second flash chromatography of **29a** on silica gel (hexane/EtOAc, 1:1, to EtOAc) gave **29a** (0.92 g, 62% based on recovered **30a**) as a yellow orange viscous oil, which showed two spots on TLC (EtOAc/$Et_3N$, 95:5): IR (neat) 3520, 2970, 2800, 2730, 1745, 1720, 1460, 1440, 1380, 1245, 1205, 1155, 1085, 870, 795 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.55 (m, 1 H), 3.75 and 3.85 (s, 3 H), 1.2–3.2 (m, 15 H), 1.92 (t, 3 H); $^{13}C$ NMR ($CDCl_3$) δ 206.2, 205.1, 172.6, 169.7, 75.7, 74.3, 69.2, 67.9, 67.2, 66.2, 61.1, 60.1, 54.5, 54.2, 54.0, 52.1, 51.7, 50.9, 50.1, 47.4, 45.7, 44.3, 42.8, 40.6, 32.0, 30.9, 30.5, 27.0, 26.2, 25.7, 22.9, 22.3, 21.1, 20.7, 16.7, 16.3, 14.0, 13.4; mass spectrum, $m/e$ 269 ($M^+$), 252, 238, 226, 225, 210, 198, 192, 180, 166, 150, 126, 97; precise mass calcd for $C_{14}H_{23}NO_4$ 269.1627, found 269.1648.

**8-Carbobenzoxy-7-hydroxy-8-(1-oxobutyl)indolizidine (29c).** Amine **15** (1.60 g, 6.80 mmol) was added to 1.5 M aqueous HCl (40 mL) at room temperature, and the mixture was stirred at room temperature for 1 h. To the resulting solution was added ice (~100 g), and the mixture was neutralized to ~pH 5 with 50% aqueous NaOH. Citrate–phosphate pH 5.5 buffer (100 mL) was then added followed directly by excess keto ester **30c** (3.0 g, 14 mmol), and the resulting solution was stirred at room temperature for 16 h. Ice (~100 g) was then added and the light yellow solution was acidified to pH 1 with concentrated HCl. The acidified solution was then extracted with $CH_2Cl_2$ (2 × 100 mL). The extract was dried ($K_2CO_3$) and concentrated in vacuo to recover excess **30c**. The aqueous phase was then basified with 50% aqueous NaOH to pH 10, and the resulting suspension was extracted with EtOAc (3 × 150 mL). The extract was dried ($K_2CO_3$) and concentrated in vacuo to give crude indolizidine **29c**. Flash chromatography (hexane/EtOAc/$Et_3N$, 75:20:5) over silica gel gave indolizidine **29c** as a yellow oil (1.35 g, 58%): IR (neat) 3530, 3400, 2965, 2940, 2805, 1742, 1715, 1460, 1380, 1365, 1200, 1080, 1020, 980, 755, 742, 703 $cm^{-1}$; $^{13}C$ NMR ($CDCl_3$) δ 206.4, 205.3, 172.2, 169.0, 135.0, 134.8, 128.5, 128.4, 128.1, 128.0, 76.0, 69.2, 68.1, 67.9, 67.2, 67.2, 67.1, 67.0, 66.8, 66.4, 61.2, 54.6, 54.3, 54.1, 51.0, 47.6, 43.1, 40.8, 32.1, 30.9, 26.2, 25.7, 23.8, 23.0, 21.2, 16.6, 16.4, 13.4, 13.4; mass spectrum, $m/e$ 345 ($M^+$), 274, 256, 192, 166, 126, 107, 97, 96, 91 (100%).

**8-Carbo-*tert*-butoxy-7-hydroxy-8-(1-oxobutyl)indolizidine (29b).** Indolizidine **29b** was prepared in a manner directly analogous to the preparation of **29c** from amine **15** (1.06 g, 4.50 mmol) and β-keto ester **30b** (2.05 g, 11.0 mmol) to give **29b** as a viscous amber syrup (0.58 g, 42%) that contained some triethylamine: IR (neat) 3500, 2960, 2935, 2870, 2790, 1740, 1710, 1460, 1435, 1370, 1270, 1255, 1165, 1150, 1090, 845 $cm^{-1}$; $^{13}C$ NMR ($CDCl_3$) δ 207.2, 205.5, 171.3, 168.2, 82.5, 81.5, 75.9, 68.8, 68.0, 67.7, 64.4, 61.2, 54.6, 54.4, 50.9, 47.5, 43.0, 40.6, 32.1, 31.0, 29.9, 27.9, 26.1, 25.7, 23.3, 21.3, 16.9, 16.6, 13.7, 13.5.

**(±)-Elaeokanine A (1).** A solution of indolizidine **29a** (0.20 g, 0.00074 mol) in 8 M HCl (3 mL) was heated at 100–110 °C under $N_2$ for 13 h. The solution was cooled, diluted with $H_2O$ (2 mL),

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(31) Gribble, G. W.; Switzer, F. L. *Synth. Commun.* **1985**, *17*, 377.

basified with 25% aqueous NaOH, and extracted with $CH_2Cl_2$ (4 × 10 mL). The extract was washed with $H_2O$ (2 × 10 mL) and saturated aqueous NaCl (10 mL), dried ($K_2CO_3$), and concentrated in vacuo to give (±)-elaeokanine A (1) (0.13 g, 91%) as a pale orange oil. This material was identical (IR, TLC) with a sample of the alkaloid and the mass spectrum matched that reported.[16]

Identical acid treatment of indolizidine **29c** gave upon workup a brown oil. Flash chromatography over silica gel (EtOAc/$Et_3N$, 95:5) yielded (±)-elaeokanine A (1) (43% from amine bisacetal **15**) as a yellow oil: IR ($CCl_4$) 2970, 2885, 2805, 2740, 1674, 1635, 1462, 1425, 1395, 1385, 1278, 1205, 1046, 911, 850, 728 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 6.88 (d of t, 1 H, $J$ = 4.2, 1.8 Hz), 3.46 (t, 1 H, $J$ = 8.5 Hz), 2.26–2.97 (m, 8 H), 1.67–1.92 (m, 4 H), 1.36 (t of q, 2 H, $J$ = 8, 8 Hz), 0.92 (t, 3 H, $J$ = 8 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 200.6, 141.9, 136.8, 58.6, 52.6, 45.0, 39.1, 29.3, 25.4, 22.3, 18.0, 13.7; mass spectrum, $m/e$ 193 ($M^+$), 192, 178, 165, 164, 150 (100%), 123, 122, 120, 95. These spectral data were identical with those for (±)-elaeokanine A (1) as prepared from **29a**.

**(±)-Elaeokanine C (2) and (±)-7-Epielaeokanine C (32).** Indolizidine **29c** was prepared as previously described from amine **15** (1.11 g, 4.74 mmol) and β-keto ester **30c** (2.37 g, 10.8 mmol). Crude **29c** was added to a stirred solution of ammonium formate (5.0 g, 79.4 mmol) in MeOH (100 mL) at room temperature. Palladium (10%) on activated carbon (0.68 g, 0.64 mmol) was added to this solution and the resulting suspension was stirred at room temperature for 1 h. The catalyst was then removed by filtration under argon. The recovered catalyst was extracted with methanol (3 × 50 mL), and the combined filtrate and extract were concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (100 mL) and extracted with 5% aqueous HCl (3 × 100 mL). Ice (~100 g) was added to the aqueous layer and the mixture was basified to pH 10 with 50% aqueous NaOH. The resulting sodium was then extracted with EtOAc (4 × 150 mL). The extract was dried ($K_2CO_3$) and concentrated in vacuo to give 0.30 g (30%) of a 1:1 mixture of **2** and **32**, which was separated by preparative TLC (hexane/triethylamine, 4:1, developed ~15 times) into **2** (oil) and **32** (oil). An additional 0.30 g (30%) of **32** (which is apparently more $H_2O$ soluble than **2**) was obtained by NaCl saturation of the aqueous layer followed by additional extraction with EtOAc (3 × 150 mL). Thus, overall, there were obtained 0.15 g (15%) of **2** and 0.45 g (45%) of **32** (yields based on **15**).

(±)-Elaeokanine C (2): IR ($CHCl_3$) 3400, 2960, 2935, 2875, 2810, 1708, 1460, 1373, 1163, 1040 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.26 (br s, 1 H), 3.80 (br s, 1 H), 3.06 (t, 1 H, $J$ = 8.8 Hz), 2.87 (d, 1 H, $J$ = 11.0 Hz), 2.40–2.62 (m, 5 H), 2.22 (q, 1 H, $J$ = 9.8 Hz), 1.70–2.00 (m, 5 H), 1.63 (t of q, 2 H, $J$ = 8, 8 Hz), 1.4 (m,1 H), 0.93 (t, 3 H, $J$ = 8 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 213.6, 65.1, 58.3, 58.0, 53.0, 46.0, 45.0, 32.0, 28.8, 20.4, 16.5, 13.4; mass spectrum, $m/e$ 211 ($M^+$), 182, 168, 167, 152, 150, 140, 124, 97 (100%), 96; these spectral data were identical with authentic spectra provided by Professor Shono. The methiodide of **2** was prepared in benzene at 40 °C with excess iodomethane (4 h). The crude methiodide was collected by filtration and recrystallized from EtOAc to yield the pure derivative as white needles; mp 207–208 °C (lit.[16] mp 203–205 °C).

(±)-7-Epielaeokanine C (**32**): IR ($CHCl_3$) 3615, 3400, 2965, 2940, 2880, 2805, 1708, 1463, 1377, 1160, 1043, 1002 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.33 (br s, 1 H), 3.81 (d of t, 1 H, $J$ = 4.5, 10.5 Hz), 3.00–3.10 (m, 2 H), 2.42–2.62 (m, 3 H), 1.38–2.14 (m, 11 H), 0.92 (t, 3 H, $J$ = 7.9 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 212.7, 71.1, 64.6, 61.4, 52.5, 49.4, 47.7, 34.0, 28.1, 21.4, 16.1, 13.4; mass spectrum, $m/e$ 211 ($M^+$), 182, 168, 167, 152, 140, 126, 124, 100, 97 (100%), 96; precise mass calcd for $C_{12}H_{21}NO_2$ 211.1572, found 211.1554. These spectral data were identical with those sent to us by Professor Kametani for (±)-7-epielaeokanine C (**32**).

**2-[2-((4,4-Dimethoxybutyl)amino)ethyl]-1,3-dioxolane (37).** Amine **37** was prepared from amine **21** (5.0 g, 38 mmol) and 2-(2-bromoethyl)-1,3-dioxolane (2.3 g, 13 mmol) in a manner directly analogous to the preparation of amine **15** (110 °C, 2 h). This procedure afforded **37** (1.65 g, 54%) as a light yellow oil: bp 125–130 °C/0.65 Torr; IR (neat) 3590, 3340, 2950, 2890, 2840, 1470, 1460, 1410, 1390, 1365, 1195, 1090, 950, 910 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.93 (t, 1 H, $J$ = 4.7 Hz), 4.38 (t, 1 H, $J$ = 5.5 Hz), 3.82–4.00 (m, 4 H), 3.31 (s, 6 H), 2.75 (t, 2 H, $J$ = 6.8 Hz), 2.62 (t, 2 H, $J$ = 7.0 Hz), 1.87 (d of t, 2 H, $J$ = 4.7, 6.8 Hz), 1.51–1.65 (m, 4 H), 1.35 (br s, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 104.3, 103.7, 64.7, 52.6, 49.7, 44.8, 33.9, 30.2, 25.1; mass spectrum, $m/e$ 218 (M – $CH_3$), 202 (M – $OCH_3$), 130, 114, 101, 87 (100%), 85, 84, 75, 73.

Anal. Calcd for $C_{11}H_{23}NO_4$: C, 56.63; H, 9.94; N, 6.00. Found: C, 56.46; H, 9.96; N, 5.93.

**2-[2-((4,4-Dimethoxybutyl)amino)ethyl]-1,3-dioxane (38).** Amine **38** was prepared from amine **21** (7.1 g, 53 mmol) and 2-(2-bromoethyl)-1,3-dioxane (4.5 g, 23 mmol) in a manner directly analogous to the preparation of amine **15** (90 °C, 2 h). This procedure afforded **38** (3.1 g, 54%) as a light yellow oil: bp 113–114 °C/0.1 Torr; IR (neat) 3600, 3350, 2960, 2850, 1470, 1382, 1248, 1197, 1130, 1090, 1055, 1010, 980, 950 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.72 (t, 1 H, $J$ = 5 Hz), 3.5–4.5 (m, 5 H), 3.33 (s, 6 H), 2.5–2.9 (m, 4 H), 1.35–2.0 (m, 9 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 104.3, 101.3, 66.8, 52.5, 49.6, 44.7, 35.3, 30.2, 25.7, 25.1; mass spectrum, $m/e$ 232 (M – $CH_3$), 216 (M – $OCH_3$), 144, 130, 114, 101 (100%), 84.

Anal. Calcd for $C_{12}H_{25}NO_4$: C, 58.27; H, 10.19; N, 5.66. Found: C, 57.78; H, 10.18; N, 5.50.

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# Yuehchukene Analogues

Ernest Wenkert,* Peter D. R. Moeller, and Serge R. Piettre

*Department of Chemistry (D-006), University of California—San Diego, La Jolla, California 92093*

Andrew T. McPhail*

*Paul M. Gross Chemical Laboratory, Department of Chemistry, Duke University, Durham North Carolina 27706*

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Yuehchukene and the bisnoryuehchukenes have been synthesized by the dimerization of β-(dehydroprenyl)indole and its demethyl derivative, respectively. Several routes of preparation of the monomers were developed. These β-indolyl dienes were used in Diels–Alder reactions, the products of one of which served as intermediates in the synthesis of some seconoryuehchukenes.

Yuehchukene, a chemical constituent of *Murraya paniculata* (L.) Jack present in small amount in the roots of the rutaceous Chinese plant *Yueh-Chu*, has been reported to possess potent antiimplantation activity in the rat.[1] In

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