Thus, the combination of enhanced catalysis in the mixed-metal catalysis solutions, the change in selectivities, and the differences in IR spectra indicate that the rhodium/iron and ruthenium/iron catalyst solutions are novel forms of cluster catalysis. In light of recent proposals by Ugo[10] and Muetterties,[11] these cluster-catalyzed reactions may be of use in modeling heterogeneous catalysis.

(10) R. Ugo, *Catal. Rev.-Sci. Eng.*, 11, 225 (1975).
(11) E. L. Muetterties, *Science (Washington, DC)*, 196, 839 (1977).

Acknowledgment. We thank one referee for his exceptional interest in our work. This work was supported in part by National Science Foundation Chemical Engineering Grants 77-21246 and 78-25069

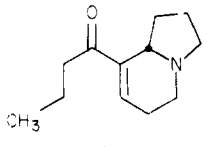
Registry No. Piperidine, 110-89-4; 1-pentene, 109-67-1; hexanal, 66-25-1; 2-methylpentanal, 123-15-9; *N*-hexylpiperidine, 7335-01-5; *N*-(2-methylpentyl)piperidine, 16627-38-6; piperidine formamide, 2158-03-4; $Co_2(CO)_8$, 10210-68-1; $Os_3(CO)_{12}$, 15696-40-9; $Ir_4(CO)_{12}$, 11065-24-0; $Fe_3(CO)_{12}$, 17685-52-8; $Ru_3(CO)_{12}$, 15243-33-1; $[(C_6H_5)_3P]Rh(CO)Cl$, 41988-66-3; $Rh_6(CO)_6$, 28407-51-4.

Communications

Total Synthesis of Elaeokanine A

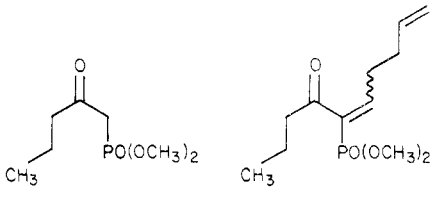
Summary: A new general approach to synthesis of *Elaeocarpus* alkaloids is discribed which utilizes the intramolecular imino Diels–Alder reaction as the key ring-forming step. The methodology has been applied to total synthesis of the alkaloid Elaeokanine A.

Sir: The *Elaeocarpus* alkaloids are a group of compounds isolated from the leaves of a few species of trees of the *Elaeocarpaceae* family, found mainly in tropical rain forests in several areas of the world.[1] We have developed a novel general strategy for construction of this class of natural products using the intramolecular imino Diels–Alder reaction as the pivotal step in formation of the bicyclic indolizidine ring system. Described below is the total synthesis of a typical *Elaeocarpus* alkaloid, elaeokanine A (**1**),[2] which exemplifies our new approach.[3]

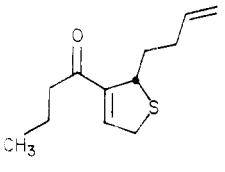


1

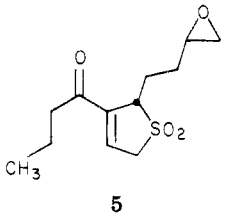
Keto phosphonate **2**[4] was condensed with 4-pentenal[5] with piperidine/acetic acid as catalyst[6] (benzene, reflux) to afford **3** in 76% yield as a 1:1 mixture of geometrical isomers which was used directly in the next step. Treatment of **3** with mercaptoacetaldehyde (generated in situ from its dimer, *p*-dithiane-2,5-diol) and triethylamine (CH_2Cl_2, reflux, 4–6 h) gave dihydrothiophene **4** in 56% yield.[7] Oxidation of **4** with excess *m*-CPBA in methylene chloride (room temperature, 24 h) afforded epoxy sulfone **5** (90%). Cleavage of the epoxide group of **5** to the carboxylic acid **6** was effected in a single step with a mixture of CrO_3/H_5IO_6 in aqueous acetone (room temperature, 3–4 h; 92%; IR (film) 3600–2800, 1710, 1680 cm^{-1}).[8] This carboxylic acid was converted to the corresponding amide **7** by treatment with ethyl chloroformate/triethylamine followed by anhydrous ammonia (58%; mp 76–78 °C; IR ($CHCl_3$) 3525, 3400, 1680, 1320, 1130 cm^{-1}; NMR ($CDCl_3$) δ 7.1 (1 H, br t), 6.2 (br s, NH_2)).



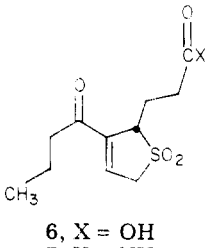
2 **3**



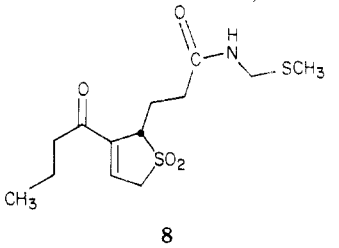
4



5



6, X = OH
7, X = NH_2



8

Several attempts were made to convert **7** into the derived *N*-(hydroxymethyl)amide with formaldehyde and

(1) Johns, S. R.; Lamberton, J. A. In "The Alkaloids"; Manske, R., Ed.; Academic Press: New York, 1973; Vol. 14, p 325.
(2) (a) Hart, N. K.; Johns, S. R.; Lamberton, J. A. *J. Chem. Soc. D* **1971**, 360; (b) *Aust. J. Chem.* **1972**, *25*, 817.
(3) For previous synthetic approaches to the *Elaeocarpus* alkaloids, see: (a) ref 2b; (b) Onaka, T. *Tetrahedron Lett.* **1971**, 4395; (c) Tanaka, T.; Ijima, I. *Tetrahedron* **1973**, *29*, 1285; (d) Howard, A. S.; Meerholz, C. A.; Michael, J. P. *Tetrahedron Lett.* **1979**, 1339. (e) A total synthesis of elaeokanine A has just been reported: Tufariello, J. J.; Ali, Sk. A. *Ibid.* **1979**, 4445.
(4) Cf. Dauben, W. G.; Beasley, G. H.; Broadhurst, M. D.; Muller, B.; Peppard, D. J.; Pesnelle, P.; Suter, C. *J. Am. Chem. Soc.* **1975**, *97*, 4793.
(5) Montgomery, L. K.; Matt, J. W. *J. Am. Chem. Soc.* **1967**, *89*, 6556.
(6) McIntosh, J. M.; Sieler, R. A. *Can. J. Chem.* **1978**, *56*, 226.
(7) McIntosh, J. M.; Sieler, R. A. *J. Org. Chem.* **1978**, *43*, 4431.
(8) This combination of reagents has been used to cleave a 1,2-diol to the diacid: Perold, G. W.; Pachler, K. G. R. *J. Chem. Soc. C* **1966**, 1918. To our knowledge it has not previously been utilized for epoxide cleavage.

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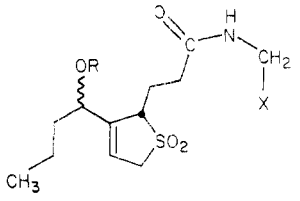
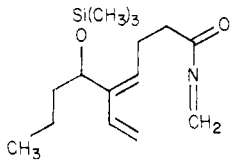
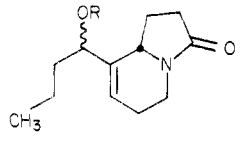
various bases.[9] However, base deprotonation occurred very readily in the dihydrothiophene dioxide ring, and a number of C-alkylation products were detected. Alternatively, amide **7** was combined with chloromethyl methyl sulfide in TFA[10] to give the (thiomethyl)amide **8** (62%; IR (film) 3450, 1680 cm^{-1}; NMR ($CDCl_3$) δ 4.3 (2 H, d), 2.2 (3 H, s)). Reduction of **8** with sodium borohydride/$CeCl_3$ in methanol (room temperature, 5 min) gave the allylic alcohol **9** as a mixture of diastereomers (90%; IR (film)





9, X = SCH_3; R = H
10, X = OAc; R = H
11, X = OAc; R = $Si(CH_3)_3$

12

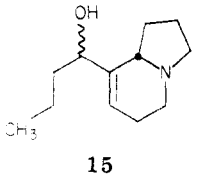


13, R = $Si(CH_3)_3$
14, R = H

3400, 1660 cm^{-1}).[11] The thiomethyl group of **9** could be smoothly exchanged with mercuric acetate in glacial acetic acid to afford acetate **10** (82%; IR (film) 3300, 1740, 1680 cm^{-1}). The alcohol functionality of **10** was silylated (Me_3SiCl, pyridine, hexamethyldisilazane) to give **11** which was used without purification.

A dilute toluene solution of **11** was slowly passed through a 15-cm column of glass helices maintained at 370–390 °C, providing bicyclic lactam **13** in 68% yield as a mixture of diastereomers (IR (film) 1680 cm^{-1}; NMR ($CDCl_3$) δ 5.8 (1 H, m), 4.3 (3 H, m)). This cyclization probably occurs via the unisolable diene–acylimine **12**.[9,12]

Hydrolysis of the silyl-protecting group of **13** (methanol/H_2O/HCl) led to alcohol **14** (IR (film) 3400, 1680 cm^{-1}) which upon reduction with a solution of Dibal-H in THF gave amino alcohol **15** (91%).[13] Oxidation of the allylic



15

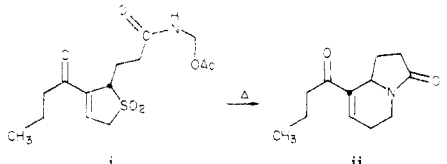
alcohol group of **15** with Me_2SO/trifluoroacetic anhydride (CH_2Cl_2, −78 °C) gave racemic elaeokanine A (62%) having IR, ^1H NMR, UV, and mass spectra identical with those of natural material.[14]

We expect that the approach outlined above can be used for the synthesis of many different *Elaeocarpus* alkaloids. Also, we are currently applying the intramolecular imino Diels–Alder reaction to preparation of several other classes of alkaloids.

Acknowledgment. We are grateful to the National Cancer Institute for support of this work (CA 25145), to Dr. R. Minard for mass spectra, and to A. Freyer for FT NMR spectra.

Registry No. (±)-**1**, 73971-21-8; **2**, 65921-74-6; *E*-**3**, 73971-22-9; *Z*-**3**, 73971-23-0; (±)-**4**, 73971-24-1; **5**, 73971-25-2; (±)-**6**, 73971-26-3; (±)-**7**, 73971-27-4; (±)-**8**, 73971-28-5; (±)-**9** (isomer 1), 73971-29-6; (±)-**9** (isomer 2), 73971-30-9; **10**, 73971-31-0; **11**, 73971-32-1; (±)-**13** (isomer 1), 73971-33-2; (±)-**13** (isomer 2), 73971-34-3; **14**, 73971-35-4; **15**, 33023-02-8; 4-pentenal, 2100-17-6; mercaptoacetaldehyde, 4124-63-4; chloromethyl methyl sulfide, 2373-51-5.

(9) Weinreb, S. M.; Khatri, N. A.; Shringarpure, J. *J. Am. Chem. Soc.* **1979**, *101*, 5073.
(10) Bernardi, L.; DeCastiglione, R.; Scarponi, U. *J. Chem. Soc., Chem. Commun.* **1975**, 320.
(11) Luche, J. L.; Rodriques-Hahn, L.; Crabbe, P. *J. Chem. Soc., Chem. Commun.* **1978**, 601.
(12) Direct pyrolysis of i, prepared by treatment of **8** with $Hg(OAc)_2$/HOAc, did produce some ii, but the yield was generally poor and the cyclization route via **11** was preferable. Pyrolysis of alcohol **10** gave **14** in low yield.



i ii

(13) Elaeokanine B has been found to have the planar structure shown in **15**.[2] However, the stereochemistry of this alkaloid has not been established.
(14) We are indebted to Dr. J. A. Lamberton for providing copies of the IR, UV, and NMR spectra of natural elaeokanine A. Dr. Lamberton has informed us that an authentic sample of this alkaloid is unfortunately no longer available.
(15) A. P. Sloan Foundation Fellow, 1975–1979; Recipient of a NIH Research Career Development Award, 1975–1980 (HL-00541).

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Thallium in Organic Synthesis. 56. A Novel Oxidative Intramolecular Cyclization/Rearrangement of 5-Norbornene-*trans*-2,3-dicarboxylic Acid with Thallium(III) Trifluoroacetate (TTFA)

Summary: Treatment of 5-norbornene-*trans*-2,3-dicarboxylic acid (**5**) with thallium(III) trifluoroacetate (TTFA) and BF_3·Et_2O results in oxidative intramolecular cyclization, accompanied by rearrangement, to give the previously unknown 5,7-dihydroxy-2,3-norbornanedicarboxylic acid di-γ-lactone (**9**).

Sir: The reaction of thallium(III) acetate (TTA) and other electrophiles with norbornene mono- and dicarboxylic acids and various derivatives to form norbornane lactones is well-documented.[1-3] The products obtained from TTA-induced oxidative lactonization are dependent upon the reaction conditions employed. At room temperature, it is possible to isolate, in high yield, the intermediates **2**, **4**, and **6** which result from oxythallation/lactonization,[2] whereas at elevated temperatures the initially formed organothallium compound, e.g., **2**, decomposes to the acetate **7** (Scheme I). The lactones **2**, **4**, and **6** may be stored at room temperature for several days and thus are among the

(1) (a) R. M. Moriarty and H. Gopal, *Tetrahedron Lett.*, 347 (1972); (b) R. M. Moriarty, H. Gopal, J. L. Flippen, and J. Karle, *ibid.*, 351 (1972).
(2) A. McKillop, M. E. Ford, and E. C. Taylor, *J. Org. Chem.*, **39**, 2434 (1974).
(3) S. Uemura, H. Miyoshi, M. Okano, I. Morishima, and T. Inubushi, *J. Organomet. Chem.*, **165**, 9 (1979).

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