551 (6.1), 591 (4.0), 647 (2.3); emission ($CHCl_3$) λ_{max}, nm (rel intens) 650.1 (9.85), 713.3 (1.0).

3-Pyridinesulfonyl chloride was obtained as previously described:[1c] white powder, mp 138–140 °C (lit.[4a] mp 141–144 °C); IR (Nujol) 1625 (m, C=C), 1590 (m, C=N), 1180–1190, 1100 (s, SO_2); ^{1}H-NMR (DMSO-d_6) δ 8.07 (t, 1 H, J = 8 Hz, H-5″), 8.67 (d, 1 H, J = 8 Hz, H-6″), 8.88 (s, 1 H, N-H), 9.08 (d, 1 H, J = 6 Hz, H-4″), 9.16 (s, 1 H, H-2″); ^{13}C-NMR (DMSO-d_6) δ 128.2, 138.7, 142.5, 143.2, 147.0.

3-Pyridinesulfonamide was prepared as previously described:[1c] yellow powder, mp 108–110 °C (lit.[4b] mp 110–111 °C); IR (KBr) 3320 (m, NH), 1590 (m, C=C), 1570 (w, C=N), 1180, 1120 (s, SO_2); ^{1}H-NMR (DMSO-d_6) δ 7.56 (br s, 2 H, NH), 7.62 (dt, 1 H, J = 7.3 Hz), 8.18 (dd, 1 H, J = 8.2 Hz), 8.78 (dd, 1 H, J = 6.1 Hz), 8.97 (d, 1 H, J = 2.5 Hz); ^{13}C-NMR (acetone-d_6) δ 123.4, 133.4, 146.3, 146.7, 152.0; FABMS 159 (calcd for $C_5H_6N_2O_2S$ [M + 1] m/z 159).

Reaction of 5,10,15-Tris(α-bromo-*m*-tolyl)-20-*m*-tolylporphyrin, 3, with *m*-Pyridinesulfonamide in the Presence of Excess Cesium Carbonate. Cesium carbonate (938 mg, 2.88 mmol) was added to a solution containing **3** (474 mg, 0.48 mmol) and *m*-pyridinesulfonamide (114 mg, 0.72 mmol) in dry DMF (480 mL). The reaction mixture was stirred at room temperature overnight and then evaporated to dryness. The purple solid obtained was dissolved in chloroform (50 mL), filtered, and evaporated. The resulting purple residue was subjected to flash chromatography using silica gel and eluting with chloroform. The nonpolar purple bands were collected, and the residue obtained was divided into eight fractions and each fraction was subjected to preparative TLC on a 0.5- × 200- × 200-mm silica plate eluting with chloroform. Two bands were collected and were treated with trifluoroacetic acid (1 mL). The resulting green solution of each of the bands was diluted with chloroform, washed with 5% aqueous ammonium hydroxide solution, water, and brine, dried over anhydrous Na_2SO_4, and evaporated to give a purple powder. The polar band gave 35 mg (7%) of **1a** as a purple solid and the nonpolar band gave 17 mg (3.4%) of **1b** as a purple powder. **1a**: ^{1}H-NMR ($CDCl_3$) δ −3.92 (s, 4 H, NH), 2.46, 2.53, 2.56 (s, 6 H, CH_3), 4.65, (m, 8 H, CH_2(R)), 4.85, (s, 4 H, CH_2(R′)), 7.00 (s, 6 H, H-2′), 7.42, 7.44 (s, s, 2 H, H-2‴), 7.47 (broad s, 2 H, H-4‴), 7.53 (broad s, 7 H, H-6″, H-5‴, H-5′(R′)), 7.59 (d, 2 H, J = 8 Hz, H-6‴), 7.65 (t, 4 H, J = 6.5 Hz, H-5′ (R)), 7.79 (broad s, 6 H, H-4′(R′), H-4′(R)), 8.19 (d, 4 H, J = 6 Hz, H-6′(R)), 8.22 (broad s, 7 H, H-5″, β-pyrrolic H), 8.30 (d, 2 H, J = 7.5 Hz, H-6′(R′)), 8.41 (s, 12 H, β-pyrrolic H), 8.77 (broad s, 3 H, H-4″), 9.07, 9.19 (broad s, s, 3 H, H-2″); ^{13}C NMR ($CDCl_3$) δ 21.44 (CH_3), 49.65 (CH_2), 118.18, 120.12 (meso), 123.55 (C6‴), 126.12, 126.65, (C2‴), 127.35 (C5′), 128.30 (C4‴), 128.66 (C4′), 130.23 (β-pyrrolic), 131.28, 131.63 (C5‴), 132.66 (C3′), 133.19 (C6′), 133.74 (C4′), 134.83 (C6‴, C5″, C6′), 135.23 (C-5′), 135.99 (C-3‴), 138.0 (C1‴), 141.23 (C1′), 142.13 (C1′), 148.17, 148.29 (C2″), 153.02, 153.19 (C4″); FABMS 1803.5 (calcd for $C_{111}H_{83}N_{14}O_6S_3$ [M + 1] m/z 1803.5); UV/vis ($CHCl_3$) λ_{max} ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1}) 406 (sh, 307), 414 (472), 515 (21.3), 550 (8.1), 590 (5.8), 648 (3.2); emission ($CHCl_3$) λ_{max}, nm (rel intens) 650.1 (8.25), 713.3 (1.0).

1b: ^{1}H-NMR ($CDCl_3$) δ −3.32 (s, 4 H, NH), 2.51, 2.72 (broad s, broad s, 6 H, CH_3) 3.67 (d, 2 H, J = 15 Hz, CH_2b(R_2), 3.87 (d, 2 H, J = 14.5 Hz, CH_2b(R_1A), 4.19 (d, 2 H, J = 15 Hz, CH_2b(R_1B), 4.82 (d, 2 H, J = 14.5 Hz, CH_2a(R_2), 4.99 (d, 2 H, J = 14.5 Hz, CH_2a(R_1A), 5.12 (d, 2 H, J = 15 Hz, CH_2a(R_1B), 6.27 (s, 2 H, H-2′R_2), 6.88 (s, 2 H, H-2′R_1A), 7.24 (sh of chloroform, H-2′R_1B), 7.44 (broad s, H-6‴), 7.45 (t, J = 7.5 Hz, H-5′R_1B), 7.46 (overlapped with H-5′, H-4′R_2B), 7.47 (t, J = 7.5 Hz, H-5′R_1A), 7.54 (td, J = 7.5, 1 Hz, H-5‴), 7.56 (s, H-2‴), 7.65 (overlapped with H-5′, H-4′R_2A), 7.66 (t, J = 7.5 Hz, H-5′R_2A), 7.69 (overlapped with H-4′ and H-5′, H-4‴), 7.80 (broad s, H-4′ R_1B, H-4′ R_1A, H-5′R_2B), 7.88 (broad s, H-6‴), 7.99, 8.00 (broad s, β-pyrrolic), 8.09 (d, J = 7.5 Hz, H-6′R_1B), 8.15 (broad s, H-6′R_1A), 8.34 (broad s, H-6′R_2A, β-pyrrolic), 8.56 (broad s, β-pyrrolic, H-6′R_2B), 8.67 (broad s, H-4″), 8.79 (broad s, H-5″), 9.02 (sh H-2′R_2), 9.04 (broad s, H-2′R_1); FABMS 1803.5 (calcd for $C_{111}H_{83}N_{14}O_6S_3$ [M + 1] m/z 1803.5); UV/vis ($CHCl_3$) λ_{max} ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1}) 408 (sh, 297), 416 (551), 516 (24.3), 552 (8.7), 591 (6.6), 647 (3.4); emission ($CHCl_3$) λ_{max}, nm (rel intens) 650.1 (8.58), 713.3 (1.0).

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Supplementary Material Available: ^{1}H-NMR and ^{13}C-NMR spectra of porphyrins **1a** and **3** and 2D ^{1}H–^{1}H (COSY) for **1b** (10 pages). Ordering information is given on any current masthead page.

A Convenient Method for Converting Saturated Aldehydes to α,β-Unsaturated Aldehydes Elongated by One Carbon Atom. The Pd(II)-Promoted Oxidation of Methyl Enol Ethers

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In the course of our ongoing research directed toward the synthesis of structurally complex indole alkaloids,[1] we found it necessary to evaluate the various currently available methods for transforming an aliphatic aldehyde, i.e., RCH_2CHO (**I**), into an α,β-unsaturated aldehyde, elongated by one carbon atom, i.e., RCH=CHCHO (**II**) (Scheme I). A number of such methods are, in fact, available. For example, the aldehyde **I** can first be converted into a methyl enol ether by reaction with (methoxymethylene)triphenylphosphorane ($CH_3OCH{=}PPh_3$).[2] Acidic hydrolysis of the methyl enol ether would give a saturated aldehyde whose chain is one unit longer than that of the parent aldehyde. The aldehyde thus obtained can then be converted into the corresponding α,β-unsaturated aldehyde by, for example, (i) introducing a suitable leaving group (e.g., halogen, SR, or SeR[3]) at the position α to the carbonyl group and then inducing β-elimination of the elements of HX, (ii) treating the corresponding trimethylsilyl enol ether or allyl enol carbonate with a Pd(II)[4] or Pd(0)[5] species, or (iii) directly dehydrogenating the aldehyde by treatment with Pd(0)/AgOTf.[6] Alternatively, trimethylsilyl cyanide can be added to the aldehyde **I**[7] and the resultant α,β-unsaturated nitrile can be converted to **II**, or the Shapiro reaction[8] can be applied to **I**. However, all these methods for preparing **II** from **I** require three or more steps and the imposition of relatively stringent reaction conditions. If a direct conversion of methyl enol ethers **III**, which can be easily obtained by the Wittig reaction of $CH_3OCH{=}PPh_3$ and aldehydes **I**, into α,β-unsaturated aldehydes **II** can be effected, then an expeditious method for achieving the desired transformation will have been found.

The belief that methyl enol ethers could be transformed into α,β-unsaturated aldehydes was inspired by the work of Saegusa et al.,[4] who found that the silyl enol ethers of saturated ketones could be dehydrosilylated to α,β-un-

(1) (a) Takayama, H.; Sakai, S. *J. Synth. Org. Chem. Jpn.* **1990**, *48*, 876–890. (b) Koike, T.; Takayama, H.; Sakai, S. *Chem. Pharm. Bull.* **1991**, *39*, 1677–1681.
(2) Wittig, G.; Schlosser, M. *Chem. Ber.* **1961**, *94*, 1373–1383.
(3) Williams, D. R.; Nishitani, K. *Tetrahedron Lett.* **1980**, *21*, 4417–4420.
(4) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011–1013.
(5) (a) Tsuji, J.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1983**, *24*, 5635–5638. (b) Shimizu, I.; Minami, I.; Tsuji, J. *Tetrahedron Lett.* **1983**, *24*, 1797–1800. (c) Tsuji, J.; Minami, I.; Shimizu, I.; Kataoka, H. *Chem. Lett.* **1984**, 1133–1136. (d) Baba, T.; Nakano, K.; Nishiyama, S.; Tsuruya, S.; Masai, M. *J. Chem. Soc., Chem. Commun.* **1989**, 1697–1699.
(6) Mukaiyama, T.; Ohshima, M.; Nakatsuka, T. *Chem. Lett.* **1983**, 1207–1210.
(7) Oda, M.; Yamamuro, A.; Watabe, T. *Chem. Lett.* **1979**, 1427–1430.
(8) Nativi, C.; Ravida, N.; Ricci, A.; Seconi, G.; Taddei, M. *J. Org. Chem.* **1991**, *56*, 1951–1955.

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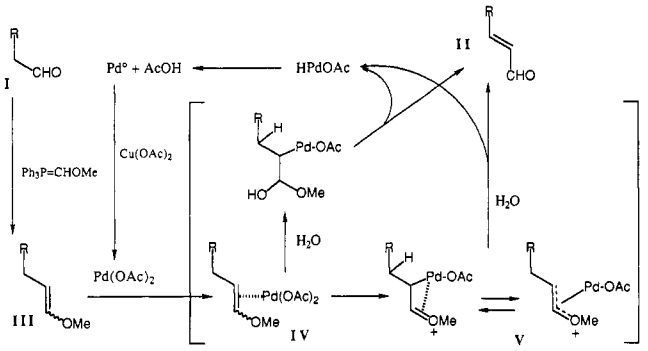
Scheme I



saturated ketones by treatment with $Pd(OAc)_2$ in acetonitrile. However, when Saegusa's conditions were applied to the methyl enol ether **2** (prepared from **1**), no reaction occurred. But, when water (1.2 equiv) was also added to the reaction mixture, a 56% yield of the α,β-unsaturated aldehyde **3** was obtained (Table I, entry 1). Furthermore, if instead of water, 5% aqueous $NaHCO_3$ was added, a smooth reaction (0 °C, 30 min), which afforded **3** in 88% yield (entry 2), occurred. The use of a combination of 5% aqueous $NaHCO_3$, $Pd(OAc)_2$ (0.5 equiv), and $Cu(OAc)_2 \cdot H_2O$ (1.0 equiv), of which the last may serve to oxidize Pd(0) back to Pd(II), in CH_3CN led to an improvement of the yield of the α,β-unsaturated aldehyde **3**, to 92% (entry 3). Under catalytic conditions [0.1 equiv of $Pd(OAc)_2$, 1.85 equiv of $Cu(OAc)_2 \cdot H_2O$] both the reaction rate and the yield of **3** decreased (entry 4). Treatment of **2** with $Pd(OAc)_2$ and $AcOH/H_2O$ (instead of 5% $NaHCO_3$) also produced **3**, in 72% yield (entry 5). The success that attended the application of the conditions described in entry 3 to other substrates (e.g., **5**, **8**, **11**, and **14**) indicated that this new reaction was general. In the case of the methyl enol ether **17**, which is unstable under the reaction conditions described in entries 2 and 3, 10-camphorsulfonic acid monohydrate ($CSA \cdot H_2O$) was employed as an additive in an attempt to stabilize the tetrahydro-β-carboline system. In the presence of $CSA \cdot H_2O$, **17** gave the desired α,β-unsaturated aldehyde **18** in 80% yield (entry 10). Thus, the method described here affords stable (*E*)-α,β-unsaturated aldehydes from mixtures of geometrically isomeric methyl enol ethers. That the products are trans isomers becomes evident from an inspection of their ^1H NMR spectra, which show large coupling constants ($J >$ 15 Hz) between the two vinylic protons. As to the mechanism of the reaction, it may involve the addition of water to the π-palladium complex **IV** or to the intermediate oxo(π-allyl)palladium complex **V** and the subsequent β-elimination of a palladium hydride species.

Experimental Section

General Comments. Compound **7** was prepared as previously described.[9] Compounds **4**, **10**, and **13** were purchased from Tokyo Kasei Kogyo Co., LTD. (Japan), and were used as received. THF and Et_2O were purified by distillation from sodium benzophenone ketyl before use. CH_3CN was distilled from CaH_2 and was stored over 4-Å molecular sieves. All reactions were performed under an atmosphere of Ar.

5-Phenylpentanal (1). A solution of (2-phenylethyl)magnesium bromide [prepared from (2-bromoethyl)benzene (10.18 g, 55 mmol), Mg turnings (1.28 g, 53 mmol), and dry THF (40 mL)] was added to a cold (0 °C) stirred solution of 2-(2-bromoethyl)-1,3-dioxolane[10] (9.05 g, 50 mmol) in dry THF (30 mL). A solution of Li_2CuCl_4[11] (33 mg, 0.15 mmol) in dry THF (1.5 mL) was then added. The mixture was stirred at 0 °C for 2 h and then at rt for 3 h. The mixture was concentrated under reduced pressure; then it was poured into cold saturated aqueous NH_4Cl. The whole was extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was dissolved in a mixture of THF (65 mL) and a 2 N aqueous HCl solution (65 mL). The two-phase mixture was refluxed for 3 h. THF was evaporated from the cooled mixture and the residue was diluted with saturated aqueous NH_4Cl. That mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was distilled in vacuo to give the title compound (**1**, 5.50 g, 68%): bp 112–117 °C (5 mmHg); ^1H NMR (270 MHz) δ 9.74 (1 H, t, J = 1.7 Hz), 7.31–7.15 (5 H, m); IR ($CHCl_3$) 1725 cm^{-1}; MS m/z (rel intensity) 162 (M^+, 36), 91 (100); HRMS calcd for $C_{11}H_{14}O_2$ 162.1044, found 162.1050.

Hirsutinal (16). A solution of hirsutine[12] (1104 mg, 3.00 mmol) in 1 N aqueous HCl was refluxed for 3 h. The mixture was cooled to rt, was made alkaline by adding 10% aqueous NH_3, and was extracted with $CHCl_3$. The extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography on alumina (Merck Al_2O_3 90, activity II–III, EtOAc) to give 679 mg (77%) of the aldehyde **16**: an amorphous powder; UV (MeOH) λ_{max} 224, 281 nm; ^1H NMR (500 MHz) δ 9.84 (1 H, s, CHO), 7.93 (1 H, br s, NH), 4.05 (1 H, m, H-3), 0.86 (3 H, t, J = 7.4 Hz); IR ($CHCl_3$) 3460, 1720 cm^{-1}; MS m/z (rel intensity) 296 (M^+, 99.9), 295 (100), 267 (31), 251 (79); HRMS calcd for $C_{19}H_{24}ON_2$ 296.1889, found 296.1888.

Preparation of Methyl Enol Ethers 2, 5, 8, 11, and 14. The preparation of 1-methoxy-6-phenyl-1-hexene (**2**) is typical. To a cold (0 °C) stirred suspension of (methoxymethyl)triphenylphosphonium chloride (2.54 g, 7.41 mmol) in dry Et_2O (30 mL) was added PhLi (7.41 mmol, 4.11 mL of a 1.8 M solution in cyclohexane/Et_2O). The mixture was stirred at rt for 30 min; then it was cooled to −15 °C. A solution of 5-phenylpentanal (**1**) (1.0 g, 6.17 mmol) in dry Et_2O (15 mL) was slowly added. The mixture was stirred at rt for 1.5 h and then was poured into cold saturated aqueous NH_4Cl. The whole was extracted with Et_2O. The extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography on silica gel (Merck silica gel 60, 230–400 mesh, CH_2Cl_2/hexane, 1:9) to give 1.10 g (94%) of **2**: an inseparable mixture of geometric isomers (*E*:*Z* = ca. 1:1); ^1H NMR (270 MHz) δ 6.27 (0.5 H, d, J = 12.5 Hz), 5.85 (0.5 H, dt, J = 7.0, 1.3 Hz), 4.70 (0.5 H, dt, J = 12.5, 7.2 Hz), 4.31 (0.5 H, ddd, J = 7.0, 7.0, 7.0 Hz), 3.56 (1.5 H, s), 3.48 (1.5 H, s); IR ($CHCl_3$) 1660, 1110 cm^{-1}; MS m/z (rel intensity) 190 (M^+, 38), 158 (25), 130 (53), 71 (100); HRMS calcd for $C_{13}H_{18}O$ 190.1357, found 190.1359.

1-Methoxy-4-phenyl-1-butene (5): 122 mg (75%); *E*:*Z* = ca. 2:1; ^1H NMR (270 MHz) δ 6.29 (0.67 H, d, J = 12.9 Hz), 5.86 (0.33 H, dt, J = 6.3, 1.3 Hz), 4.74 (0.67 H, dt, J = 12.9, 7.3 Hz), 4.35 (0.33 H, ddd, J = 6.3, 7.2, 7.2 Hz), 3.47 (2 H, s), 3.53 (1 H, s); IR ($CHCl_3$) 1655, 1105 cm^{-1}; MS m/z (rel intensity) 162 (M^+, 14), 91 (15), 71 (100); HRMS calcd for $C_{11}H_{14}O$ 162.1044, found 162.1051.

1-Methoxy-5,5-dicarbethoxy-1-heptene (8): 99 mg (73%); *E*:*Z* = ca. 2:1; ^1H NMR (270 MHz) δ 6.28 (0.67 H, d, J = 12.8 Hz), 5.86 (0.33 H, d, J = 6.0 Hz), 4.69 (0.67 H, dt, J = 12.8, 6.8 Hz), 4.30 (0.33 H, m), 4.18 (4 H, q, J = 7.3 Hz), 3.56 (1 H, s), 3.49 (2 H, s), 1.24 (6 H, t, J = 7.3 Hz), 0.83 (3 H, t, J = 7.7 Hz); IR ($CHCl_3$) 1730, 1665, 1110 cm^{-1}; MS m/z (rel intensity) 272 (M^+, 2), 227 (10), 188 (100), 173 (64), 142 (66); HRMS calcd for $C_{14}H_{24}O_5$ 272.1622, found 272.1638.

(12*Z*)-1-Methoxy-1,12-heptadecadiene (11): 290 mg (73%); *E*:*Z* = ca. 3:2; ^1H NMR (270 MHz) δ 6.27 (0.6 H, d, J = 12.5 Hz), 5.86 (0.4 H, dt, J = 6.3, 1.3 Hz), 5.35 (2 H, m), 4.72 (0.6 H, dt, J = 12.5, 7.3 Hz), 4.33 (0.4 H, ddd, J = 6.3, 7.3, 7.3 Hz), 3.57 (1.2 H, s), 3.50 (1.8 H, s); IR ($CHCl_3$) 1660, 1110 cm^{-1}; MS m/z (rel intensity) 266 (M^+, 22), 234 (9), 71 (100); HRMS calcd for $C_{18}H_{34}O$ 266.2640, found 266.2625.

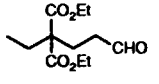
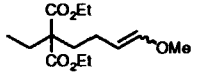
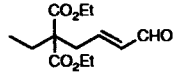
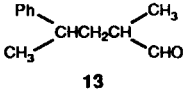
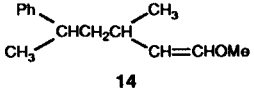
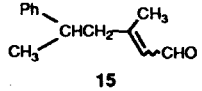
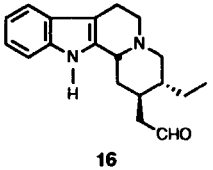
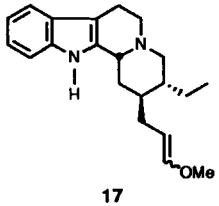
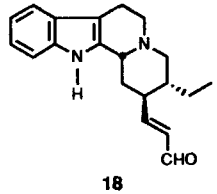
(9) (a) Yamanaka, E.; Nakayama, K.; Yanagishima, N.; Nagashima, K.; Yamauchi, M.; Sakai, S. *Chem. Pharm. Bull.* **1980**, *28*, 2527–2530. (b) Warner, D. T.; Moe, O. *J. Am. Chem. Soc.* **1948**, *70*, 3470–3472.

(10) Büchi, G.; Wüest, H. *J. Org. Chem.* **1969**, *34*, 1122–1123.

(11) Tamura, M.; Kochi, J. *Synthesis* **1971**, 303–305.

(12) (a) Southon, I. W.; Buckingham, J. *Dictionary of Alkaloids*; Chapman and Hall: New York, 1989; p 504. (b) Haginiwa, J.; Sakai, S.; Aimi, N.; Yamanaka, E.; Shinma, N. *Yakugaku Zasshi* **1973**, *93*, 448–452.

Table I. Conversion of Methyl Enol Ethers III Derived from Aldehydes I to α,β-Unsaturated Aldehydes II

				conditions for conversion of III into II[a]				
entry	aldehyde I	enol ether III	yield (I → III) (%)[b]	Pd-(O-Ac)$_2$, equiv	additive	temp (°C)/ time (h)	product α,β-unsaturated aldehyde II	yield (III → II) (%)[b]
1	$Ph(CH_2)_4CHO$ (1)	$Ph(CH_2)_4CH{=}CHOMe$ (2)	94	1.0	H_2O (1.2 equiv)	0/6	$Ph(CH_2)_3CH{=}CHCHO$ (3)	56
2				1.0	5% $NaHCO_3$	0/0.5		88
3				0.5	5% $NaHCO_3$, $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv)	0/1, 24/1		92
4				0.1	5% $NaHCO_3$, $Cu(OAc)_2{\cdot}H_2O$ (1.9 equiv)	0/0.5, 24/6		49[c]
5				1.0	H_2O, AcOH	0/0.5		72
6	$PhCH_2CH_2CHO$ (4)	$PhCH_2CH_2CH{=}CHOMe$ (5)	75	0.5	5% $NaHCO_3$, $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv)	0/0.5, 24/1	$PhCH_2CH{=}CHCHO$ (6)	83
7	 7	 8	73	0.5	5% $NaHCO_3$, $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv)	0/0.5, 24/1	 9	94
8	$CH_3(CH_2)_3CH{=}CH(CH_2)_8CHO$ (10)	$CH_3(CH_2)_3CH{=}CH(CH_2)_9CH{=}CHOMe$ (11)	73	0.5	5% $NaHCO_3$, $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv)	0/0.5, 24/1.5	$CH_3(CH_2)_3CH{=}CH(CH_2)_8CH{=}CHCHO$ (12)	96
9	 13	 14	80	0.5	5% $NaHCO_3$, $Cu(OAc)_2{\cdot}H_2O$ (1.0 equiv)	0/0.25, 24/3	 15	86[d]
10	 16	 17	80	1.0	CSA·H_2O (1.0 equiv)	−16/1.3	 18	80

[a] All reactions were performed in CH_3CN solution. [b] Isolated yield. [c] 37% of the starting material 2 was recovered. [d] Mixture (ca. 1:1) of cis and trans isomers.

1-Methoxy-3-methyl-5-phenyl-1-hexene (14): 820 mg (80%); a mixture of four diastereomers (*E*:*Z* = ca. 7:3); ^{1}H NMR (270 MHz) δ 6.24 (0.3 H, d, *J* = 13.0 Hz), 6.12 (0.4 H, d, *J* = 12.5 Hz), 5.85 (0.15 H, d, *J* = 6.3 Hz), 5.82 (0.15 H, d, *J* = 6.9 Hz), 4.58–4.48 (0.7 H, m), 4.18–4.10 (0.3 H, m), 3.50 (0.45 H, s), 3.47 (0.45 H, s), 3.55 (1.2 H, s), 3.52 (0.9 H, s); IR ($CHCl_3$) 1655, 1110 cm^{-1}; MS *m*/*z* (rel intensity) 204 (M^+, 70), 157 (39), 105 (37), 85 (100); HRMS calcd for $C_{14}H_{20}O$ 204.1514, found 204.1516.

Preparation of 17. To a cold (0 °C) stirred suspension of (methoxymethyl)triphenylphosphonium chloride (1.60 g, 4.68 mmol) in dry Et_2O (32 mL) was slowly added PhLi (4.68 mmol, 2.6 mL of a 1.8 M solution in cyclohexane/Et_2O). The mixture was stirred at rt for 30 min. A solution of hirsutinal (**16**) (1067 mg, 3.60 mmol) in dry Et_2O (5.5 mL) was then added drop by drop. After 5 min, an ethereal solution of (methoxymethyl)triphenylphosphorane (4.68 mmol), prepared in the manner described above, was added. The mixture was stirred at rt for 15 min; then it was poured into cold water. The whole was extracted with EtOAc. The extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography on silica gel (MeOH/$CHCl_3$, 1:9) to give 940 mg (80%) of **17**: a relatively unstable amorphous powder (*E*:*Z* = ca. 1:1); UV (MeOH) λ_{max} 225, 281 nm; ^{1}H NMR (500 MHz) δ 7.73 (1 H, br s, NH), 6.30 (0.5 H, d, *J* = 12.5 Hz), 6.00 (0.5 H, dt, *J* = 7.1, 1.3 Hz), 4.72 (0.5 H, ddd, *J* = 12.5, 7.6, 7.6 Hz), 4.36 (0.5 H, ddd, *J* = 7.1, 7.1, 7.1 Hz), 3.97 (1 H, m, H-3), 3.59 and 3.56 (3 H, s), 0.86 and 0.85 (3 H, t, *J* = 7.3 Hz); IR ($CHCl_3$) 3470, 1660 cm^{-1}; MS *m*/*z* (rel intensity) 324 (M^+, 32), 309 (45), 251 (100), 169 (13). HRMS calcd for $C_{21}H_{28}ON_2$ 324.2202, found 324.2191.

Preparation of the α,β-Unsaturated Aldehydes 3, 6, 9, 12, and 15. The preparation of (*E*)-6-phenyl-2-hexenal (**3**) is typical. To a stirred suspension of $Pd(OAc)_2$ (30 mg, 0.134 mmol) in CH_3CN (0.6 mL) at rt were added 5% aqueous $NaHCO_3$ (0.05 mL) and $Cu(OAc)_2 \cdot H_2O$ (54 mg, 0.268 mmol). The mixture was cooled to 0 °C; then a solution of the methyl enol ether **2** (51 mg, 0.268 mmol) in CH_3CN (0.35 mL) was added. The mixture was vigorously stirred at 0 °C for 1 h and then at rt for 1 h. The mixture was then poured into saturated aqueous NH_4Cl and the whole was extracted with $CHCl_3$. The extract was dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography on silica gel (EtOAc/hexane, 1:7) to give 43 mg (92%) of **3**: ^{1}H NMR (270 MHz) δ 9.50 (1 H, d, *J* = 8.1 Hz), 6.84 (1 H, dt, *J* = 15.4, 6.8 Hz), 6.12 (1 H, ddt, *J* = 15.4, 8.1, 1.2 Hz); UV (EtOH) λ_{max} 218 nm; IR ($CHCl_3$) 1690 cm^{-1}; MS *m*/*z* (rel intensity) 174 (M^+, 5), 130 (52), 91 (100); HRMS calcd for $C_{12}H_{14}O$ 174.1043, found 174.1040.

(*E*)-4-Phenyl-2-butenal (6): 45 mg (83%); ^{1}H NMR (270 MHz) δ 9.53 (1 H, d, *J* = 7.7 Hz), 6.97 (1 H, dt, *J* = 15.8, 6.4 Hz), 6.11 (1 H, ddt, *J* = 15.8, 7.7, 1.7 Hz), 3.65 (2 H, dd, *J* = 6.4, 1.7 Hz); UV (EtOH) λ_{max} 217 nm; IR ($CHCl_3$) 1690 cm^{-1}; MS *m*/*z* (rel intensity) 146 (M^+, 84), 117 (100), 115 (61), 91 (51). HRMS calcd for $C_{10}H_{10}O$ 146.0730, found 146.0730.

(*E*)-5,5-Dicarbethoxy-2-heptenal (9): 40 mg (94%); ^{1}H NMR (270 MHz) δ 9.50 (1 H, d, *J* = 7.7 Hz), 6.74 (1 H, dt, *J* = 15.8, 7.3 Hz), 6.14 (1 H, ddt, *J* = 15.8, 7.7, 1.3 Hz), 4.20 (4 H, q, *J* = 7.3 Hz), 2.88 (2 H, dd, *J* = 7.3, 1.3 Hz), 1.96 (2 H, q, *J* = 7.3 Hz), 1.26 (6 H, t, *J* = 7.3 Hz), 0.88 (3 H, t, *J* = 7.3 Hz); UV (EtOH) λ_{max} 216 nm; IR ($CHCl_3$) 1730, 1690 cm^{-1}; MS *m*/*z* (rel intensity) 256 (M^+, 7), 188 (66), 109 (100); HRMS calcd for $C_{13}H_{20}O_5$ 256.1309, found 256.1303.

(2*E*,12*Z*)-Heptadecadienal (12): 45 mg (90%); ^{1}H NMR (270 MHz) δ 9.51 (1 H, d, *J* = 8.1 Hz), 6.85 (1 H, dt, *J* = 15.4, 6.8 Hz), 6.11 (1 H, ddt, *J* = 15.4, 8.1, 1.3 Hz), 5.35 (2 H, m); UV (EtOH) λ_{max} 221 nm; IR ($CHCl_3$) 1690 cm^{-1}; MS *m*/*z* (rel intensity) 250 (M^+, 100), 232 (23), 193 (10), 166 (17), 134 (27), 109 (39), 95 (54), 81 (68); HRMS calcd for $C_{17}H_{30}O$ 250.2297, found 250.2290.

3-Methyl-5-phenyl-2-hexenal (15): *E*:*Z* = ca. 1:1, 42 mg (86%); ^{1}H NMR (270 MHz) δ 9.92 (0.5 H, d, *J* = 8.1 Hz), 9.73 (0.5 H, d, *J* = 8.1 Hz), 5.84 (0.5 H, dd, *J* = 8.1, 1.0 Hz), 5.80 (0.5 H, dd, *J* = 8.1, 1.0 Hz), 2.10 (1.5 H, d, *J* = 1.0 Hz), 1.90 (1.5 H, d, *J* = 1.0 Hz), 1.34 (1.5 H, d, *J* = 6.8 Hz), 1.27 (1.5 H, d, *J* = 6.8 Hz); UV (EtOH) λ_{max} 204, 237 nm; IR ($CHCl_3$) 1690, 1640 cm^{-1}; MS *m*/*z* (rel intensity) 188 (M^+, 7), 173 (9), 162 (8), 105 (100); HRMS calcd for $C_{13}H_{16}O$ 188.1201, found 188.1207.

Preparation of the α,β-Unsaturated Aldehyde 18. To a cold (−16 °C) stirred mixture of $Pd(OAc)_2$ (25.7 mg, 0.114 mmol), 10-camphorsulfonic acid monohydrate (27 mg, 0.108 mmol), and dry CH_3CN (1 mL) was added a solution of **17** (34.6 mg, 0.107 mmol) in dry CH_3CN (1 mL). After 80 min, the mixture was diluted with brine and was made alkaline by adding 10% aqueous NH_3. The whole was then extracted with $CHCl_3$. The extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography on silica gel (MeOH/$CHCl_3$, 1:6) to give 26.4 mg (80%) of **18**: an amorphous powder; ^{1}H NMR (270 MHz) δ 9.56 (1 H, d, *J* = 8.1 Hz), 7.93 (1 H, br s, NH), 6.81 (1 H, dd, *J* = 15.8, 8.1 Hz), 6.14 (1 H, dd, *J* = 15.8, 7.7 Hz), 4.27 (1 H, br s), 0.86 (3 H, t, *J* = 7.5 Hz); UV (EtOH) λ_{max} 224, 282 nm; IR ($CHCl_3$) 3460, 1685, 1630 cm^{-1}; MS *m*/*z* (rel intensity) 308 (M^+, 60), 307 (62), 279 (42), 184 (100); HRMS calcd for $C_{20}H_{24}O$ 308.1889, found 308.1885.

Supplementary Material Available: NMR spectra of new compounds (15 pages). Ordering information is given on any current masthead page.

A New Imidazole Alkaloid from the Marine Sponge *Leucetta microrhaphis*

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Imidazole alkaloids have recently been reported as antimicrobial constituents of the calcareous sponges *Leucetta chagosensis*[1,2] and *Clathrina clathrus*.[3] Among the more interesting of the imidazole alkaloids is clathridine, which was isolated from *C. clathrus* as a very stable zinc complex (**1**). As part of a continuing program to discover new bioactive metabolites from marine organisms, we examined a bright yellow sponge *Leucetta microhaphis* that was collected in Pohnpei in 1989. Nonpolar material from the methanolic extract of the frozen sponge tissue was chromatographed on silica gel followed by reversed-phase HPLC to obtain the known clathridine zinc complex (**1**, 0.01% dry wt), which was identified by comparison of physical and spectral data with literature values.[3] The more polar material was chromatographed on Sephadex LH-20 followed by reversed-phase HPLC to obtain a novel alkaloid, (9*E*)-clathridine 9-*N*-(2-sulfoethyl)imine (**2**, 0.018% dry wt).

(9*E*)-Clathridine 9-*N*-(2-sulfoethyl)imine (**2**) was isolated as yellow needles, mp 275–277 °C dec. The molecular formula, $C_{18}H_{20}N_6O_6S$, was determined by high-resolution mass measurement. The IR spectrum contained bands at 3410 (NH or OH), 1770 (carbonyl), and 1600 cm^{-1} (aromatic). In the ^{1}H NMR spectrum (1:5 $CDCl_3$/DMSO-d_6), the downfield signals at δ 7.01 (br s, 1 H), 6.91 (br d, 1 H, *J* = 7.9 Hz), and 6.84 (d, 1 H, *J* = 7.9 Hz) indicated the presence of a 1,2,4-trisubstituted benzene ring. The ^{13}C NMR signals due to the trisubstituted aromatic ring were assigned as shown in Table I by interpretation of the COLOC (*J* = 8 Hz) experiment. The chemical shifts of

(1) Carmely, S.; Kashman, Y. *Tetrahedron Lett.* **1987**, *28*, 3003.
(2) Carmely, S.; Ilan, M.; Kashman, Y. *Tetrahedron* **1989**, *45*, 2193.
(3) Ciminiello, P.; Fattorusso, E.; Magno, S.; Mangoni, A. *Tetrahedron* **1989**, *45*, 3873.
(4) Ciminiello, P.; Fattorusso, E.; Mangoni, A.; Di Blasio, B.; Pavone, V. *Tetrahedron* **1990**, *46*, 4387.

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