Total Synthesis of Chaetomellic Anhydrides A and B via a Novel Succinate to Maleate Oxidation

Michael J. Kates and J. Herman Schauble*

Department of Chemistry, Villanova University, Villanova, Pennsylvania 19085

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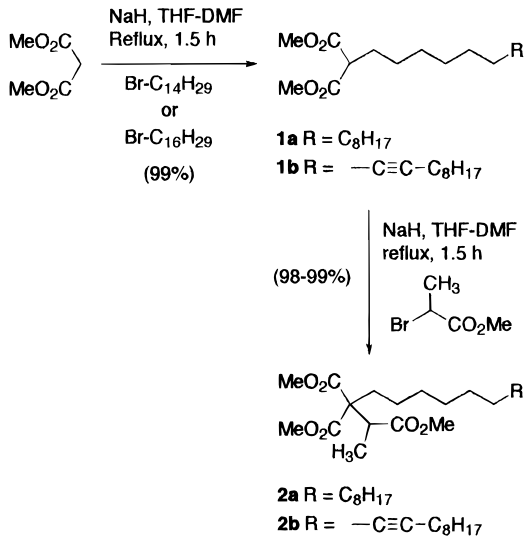
In a recent paper, we reported a facile two-step *in situ* process for oxidation of succinic to maleic-type anhydrides, thioanhydrides, and imides in excellent yields.[1] Herein, we report utilization of this sequence as the key steps for the synthesis of both Chaetomellic anhydrides A and B (**8a** and **9**, respectively). The latter have recently been isolated from fermentation extracts of the coelomycete *Chaetomella acutiseta* and (as the free acids) are found to be highly specific farnesyl pyrophosphate mimics of Ras farnesyl-protein transferase, exhibiting potent inhibitory activity.[2a−f] Two alternate syntheses of Chaetomellic anhydride A have recently been reported.[3]

Malonic ester-type syntheses[4] were used to construct the carbon skeletons of both Chaetomellic anhydrides. Thus, reaction of 1-bromotetradecane or 1-bromo-7-hexadecyne (**10**) with dimethyl malonate and sodium hydride (1:5:2 molar ratio, respectively) in THF−DMF under reflux afforded only the monoalkyl malonates **1a** and **1b** in essentially quantitative yields, relative to the starting bromides (Scheme 1).[5] Ensuing reaction of monoalkyl malonates **1a**,**b** with excess methyl 2-bromopropionate and sodium hydride in THF−DMF under reflux gave triesters **2a** and **3b**, in yields of 98−99%. It was requisite that alkylation of dimethyl malonate with the long chain bromides be carried out prior to alkylation with methyl 2-bromopropionate, since reaction in the reverse order afforded dimethyl 2-methyl-3-(methylcarboxy)succinate, which, however, failed to undergo further alkylation.

Hydrolysis and decarboxylation of the triesters **2a** and **2b**, effected by treatment with 3 M ethanolic potassium hydroxide/water (3:1 V/V) under reflux for 8−10 h, followed by acidification to pH ∼2, and heating under reflux for an additional 18 h, gave mixtures of the diastereomeric erythro (*S**,*S**; *R**,*R**) and threo (*R**,*S**; *S**,*R**) succinic acids (**3a**, **4a** and **3b**, **4b**, respectively), isolated in yields >90%, relative to the triesters (Scheme 2). Diastereomers **3a** and **4a** were easily separated by trituration of the oily crude product with 5% dichloromethane in pentane. The remaining insoluble white solid diacid, mp 126−127 °C, was assigned the erythro structures **3a**, since it underwent reaction with *N*-methylmorpholine and methyl chloroformate at 0 °C to give *cis*-anhydride **5a** ($J_{2,3}$ = 9.1 Hz). Evaporation of the dichloromethane−pentane extract gave a second white solid diacid, mp 95−96.5 °C, assigned as the threo isomers **4a**, since the latter gave only the corresponding *trans*-anhydride **6a** ($J_{2,3}$ = 7.5 Hz). The threo **3a** to erythro **4a** diastereoselectivity was 3:1 established by quantitative NMR analysis of the mixture of crude diacids.

Scheme 1



The diastereomeric succinic acids **3b** and **4b** were also separable due to their differential solubility in pentane. Trituration afforded a pentane-insoluble diacid **3b**, mp 97.5−99 °C, that reacted with *N*-methylmorpholine and methyl chloroformate at 0 °C to afford the *cis*-anhydride **5b** ($J_{2,3}$ = 9.1 Hz); thus, the diacid was assigned the erythro structures **5b**. Evaporation of the pentane extract resulted in the low-melting waxy solid threo diacids **4b**, identified by conversion to the *trans*-anhydride **6b** ($J_{2,3}$ = 7.5 Hz). The diastereoselectivity of threo **4b** to erythro **3b** diacids was 2.5:1, obtained by quantitative NMR analysis.

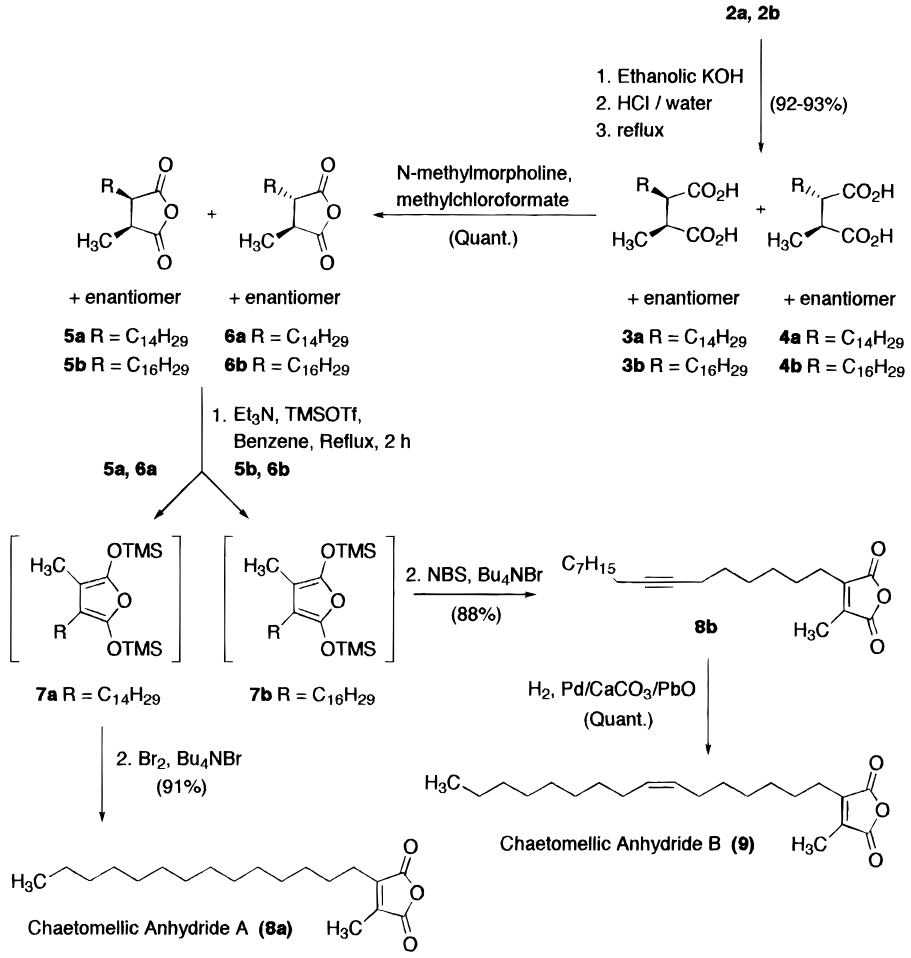
The vicinal coupling constants $J_{2,3}$ observed for the stereoisomeric anhydride pairs (**5a**, **6a** and **5b**, **6b**) are in agreement with those determined using a combination of MM2 and modified Karplus-type calculations.[6] Furthermore, as expected from the calculated differences in steric energies (≥1.5 kcal/mol), the cis-anhydrides **5a** and **5b** underwent facile conversion to the respective trans isomers **6a** and **6b** upon reaction with DBU in dichloromethane.

The oxidative sequence for conversion of succinic-type anhydrides **5a**, **6a** and **5b**, **6b** to maleic anhydrides **8a** and **8b**, was carried out by reaction of the anhydrides with Et_3N and TMSOTf (1:3:3 mol ratio) in benzene under reflux to give the corresponding 3-methyl-4-tetradecyl-2,5-bis((trimethylsilyl)oxy)furan (**7a**) and 3-(7-hexadecynyl)-4-methyl-2,5-bis((trimethylsilyl)oxy)furan (**7b**) respectively (Scheme 2).[1] Subsequent treatment of intermediate **7a** with 1 mol % pure tetra-*n*-butylammonium bromide in dry methylene chloride, followed by addition of pure bromine (1 mol equiv) at 0 °C gave

(1) Kates, M. J.; Schauble, J. H. *J. Org. Chem.* **1995**, *60*, 6676.
(2) (a) Singh, S. B.; Zink, D. L.; Liesch, J. M. et al. *Tetrahedron* **1993**, *49*, 5917. (b) Lingham, R. B.; Silverman, K. C.; Bills, G. F. et al. *Appl. Microbiol. Biotechnol.* **1993**, *40*, 370. (c) Gibbs, J. B.; Pompliano, D. L.; Mosser, S. D. et al. *J. Biol. Chem.* **1993**, *268*, 7617. (d) Singh, S. B. Merck & Co. Inc. Eur. Pat. Appl. 92203809.6, 1992. (e) Singh, S. B.; Bills, G. F.; Lingham, R. B.; Silverman, K. C.; Zink, D. L. Merck & Co. Inc. Eur. Pat. Appl. 92203808.8, 1992. (f) Gill, M. *Phytochemistry* **1981**, 21, 1786.
(3) (a) Singh, S. B. *Tetrahedron Lett.* **1993**, *34*, 6521. (b) Branchaud, B. P.; Slade, R. M. *Tetrahedron Lett.* **1994**, *35*, 4071.
(4) van Liemt, W. B. S.; Steggerda, W. F.; Esmeijer, R.; Lugtenburg, *J. Recl. Trav. Chem. Pays-Bas* **1994**, *113*, 153.
(5) Brillon, D.; Deslongchamps, P. *Can. J. Chem.* **1987**, *65*, 43.
(6) (a) MM2 calculations were performed using CSC Chem3D Plus, Cambridge Scientific Computing Inc, 875 Massachusetts Ave., Sixth Floor, Cambridge, MA 02139. (b) Modified Karplus-type calculations were performed using PCMODEL, Serena Software, Box 3076, Bloomington, IN 47402-3076.

S0022-3263(96)00197-1 CCC: $12.00

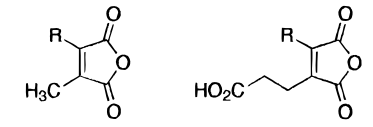
Scheme 2



Chaetomellic anhydride A (**8a**) in 91% isolated yield, accompanied by anhydride **6a** in 6% yield. The latter results via hydrolysis of **7a**.

Similarly, oxidation of 2,5-bis((trimethylsilyl)oxy)furan **7b**, using pure NBS rather than bromine as the oxidant, afforded anhydride B (**8b**) in 88% yield, accompanied by hydrolysis product **6b** in 9% yield. Reduction of **8b** with hydrogen on Lindlar catalyst in cyclohexane gave Chaetomellic anhydride B (**9**), quantitatively.[7]

Other naturally occuring 2,3-dialkylmaleic anhydrides have been reported. These include 2-ethyl-3-methylmaleic anhydride (**11**) (from the volatile oil of *Paederia foetida L.*[8] and from elderberry (*Sambucus nigra L.* fruit, Korsør cultivar),[9] 2-hexyl-3-methylmaleic anhydride (**12**) (from the essential oil of *Agropyrum repens* rhizome,[10] and tricarboxylic acid anhydrides **13**−**15** produced from stearic acid by *Pseudomonas cepacia* A-1419, isolated from soil.[11] Such maleic-type anhydrides should also be accessible from the corresponding succinic-type congeners, via two-step oxidative sequences of the type described herein for the syntheses of Chaetomellic anhydrides A and B.



11 R = C_2H_5 **13** R = C_6H_{13}
12 C_6H_{13} **14** C_8H_{17}
15 $C_{10}H_{21}$

Experimental Section

General Information. Melting points are uncorrected. Boiling points were obtained using short path vacuum distillation and are uncorrected. Starting materials, bromine (99.99+%), *N*-bromosuccinimide (99%), tetra-*n*-butylammonium bromide (99+%), and solvents were obtained from Aldrich Chemical Co. Solvent removal was performed by rotoevaporation, and solvents were dried with $MgSO_4$ unless otherwise indicated. GC analyses were performed using a 10M Hewlett-Packard HP-1 macrocapillary column. ^1H and ^{13}C NMR were recorded at 200 and 50.3 MHz, respectively. Full carbon assignments for all intermediates and Chaetomellic anhydrides A and B, including techniques used to determine long chain carbon assignments, will be published separately. Elemental analyses were provided by Robertson Microlit Laboratories, Inc., P.O. Box 927, Madison, NJ 07940.

1-Bromo-7-hexadecyne (10). To a stirred solution containing 20 g (0.145 mol) of 1-decyne, 3 mg of triphenylmethane, and 2.52 mL (0.0145 mol) of HMPA in 400 mL of THF under argon at −40 °C was added butyllithium (~58.0 mL, 0.145 mol) until the solution turned pink-red in color. At that temperature 177 g (0.725 mol) of 1,6-dibromohexane was added and the mixture heated under reflux for 44 h. The THF was removed *in vacuo* and the remaining solution distilled at 134 °C (3.4 torr) to remove excess dibromide. The residual liquid was dissolved in 150 mL of pentane, washed with 50 mL of water and 50 mL of brine, and then dried and solvent removed to afford 45.61 g of crude alkyne. Silica gel column chromatography, using pentane as eluant, afforded 38.35 g (88%) of **10** as a pale yellow oil: bp

(7) Brillon, D.; Deslongchamps, P. *Can. J. Chem.* **1987**, *65*, 56.
(8) Wong, K. C.; Tan, G. L. *Flavour Fragrance J.* **1994**, *9*, 25.
(9) Poll, L.; Lewis, M. J. *Lebensm.-Wiss. u.-Technol.* **1986**, *19*, 258.
(10) Boesel, R.; Schilcher, H. *Planta Med.* **1989**, *55*, 399.
(11) Itoh, S.; Esaki, N.; Masaki, K.; Blank, W.; Soda, K. *J. Ferment. Bioeng.* **1994**, *77*, 513.

176 °C (4.0 Torr); ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, $J_{15,16}$ = 6.7 Hz), 1.29−1.45 (18H, 2 × bs), 1.86 (2H, p, $J_{2,3}$ = 7.1 Hz), 2.09−2.15 (4H, cm), 3.49 (2H, t, $J_{1,2}$ = 6.9 Hz); ^{13}C NMR (CD_2Cl_2) δ14.28, 18.92, 19.01, 23.05, 28.08, 28.26, 29.21, 29.30, 29.51, 29.56, 29.63, 32.23, 33.16, 33.81, 79.89, 80.46.

Dimethyl Malonates 1a and 1b. A solution of 6.0 g (0.248 mol) of NaH in 550 mL of THF and 180 mL of DMF was prepared at 0 °C under argon. To this solution was added slowly, via syringe, 82.21 g (0.622 mol) of dimethyl malonate at 0 °C. The mixture was stirred at rt for 15 min, and then bromotetradecane (34.4 g, 0.124 mol) or 1-bromo-7-hexadecyne (**10**) (37.5 g, 0.124 mol) was added and the mixture heated under reflux for 1.5 h. The THF was removed *in vacuo* and the residue diluted with 100 mL water and extracted with 3 × 75 mL of pentane and 100 mL of pentane/ether (1:1). The combined extract was dried and concentrated, and excess dimethyl malonate, bp 68 °C (4.5 Torr), was removed by distillation. Alkylation using bromotetradecane gave 40.13 g (99%) of a colorless oil, which crystallized to white solid **1a**: mp 43−44 °C; ^{1}H NMR (CD_2Cl_2) δ 0.89 (3H, t, J = 6.7 Hz), 1.26 (24H, bs), 1.85 (2H, bq, J = 7.7 Hz), 3.33 (1H, t), 3.70 (6H, s); ^{13}C NMR (CD_2Cl_2) δ 14.26, 23.09, 27.70, 29.19, 29.66, 29.78, 29.82, 29.98, 30.07, 30.11, 30.12, 30.14, 30.15, 32.36, 51.88, 52.26, 169.88. Alkylation using bromide **10** gave 43.45 g (99%) of pale yellow oil **1b**: ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 7.0 Hz), 1.26−1.45 (16H, cm), 1.85 (2H, bq, J = 7.5 Hz), 2.11 (4H, cm), 3.34 (1H, t), 3.70 (6H, s); ^{13}C NMR (CD_2Cl_2) δ 14.13, 18.94, 19.00, 23.06, 27.58, 28.88, 29.13, 29.15, 29.26, 29.43, 29.56, 29.61, 29.68, 32.29, 51.86, 52.32, 80.05, 80.35, 169.87.

Triesters 2a and 2b. A solution of 5.45 g (0.226 mol) of NaH in 550 mL of THF and 180 mL of DMF was prepared at 0 °C under argon. To this solution was added, slowly via syringe, 37.0 g (113 mol) of **1a** or 40.0 g (0.113 mol) of **1b** at 0 °C and the mixture stirred at rt for 15 min. Methyl 2-bromopropionate 38.0 g (0.226 mol) was then added and the mixture heated under reflux for 1.5 h. The THF was removed in vacuo and the remaining mixture combined with 100 mL of water and extracted with 3 × 75 mL of pentane and 100 mL of pentane/ether (1:1). The combined extract was dried and concentrated and the excess methyl 2-bromopropionate removed by distillation at 56 °C (4.5 Torr) to leave crude **2a** or **2b**, respectively. Both compounds were chromatographed on silica gel using CH_2Cl_2 as eluant. **2a** was obtained as a pale yellow oil (45.8 g, 98%): ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.6 Hz), 1.24 (3H, d, J = 7.2 Hz), 1.26 (24H, bs), 1.84 (2H, bcm), 3.09 (1H, q, J =7.2 Hz), 3.64 (3H, s), 3.68 (3H, s), 3.70 (3H, s); ^{13}C NMR (CD_2Cl_2) δ 13.41, 14.24, 23.00, 24.98, 29.58, 29.70, 29.86, 29.94, 29.99 (2C's), 30.02 (2C's), 30.24, 32.25, 34.24, 44.02, 51.94, 52.30, 52.36, 59.94, 170.97, 171.27, 174.22. Compound **2b** was also obtained as a pale yellow oil (49.2 g, 99%): ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.7 Hz), 1.24 (3H, d, J = 7.2 Hz), 1.24−1.52 (20H, bcm), 1.85 (2H, cm), 2.11 (4H, cm), 3.09 (1H, q), 3.64 (3H, s), 3.69 (3H, s), 3.71 (3H, s); ^{13}C NMR (CD_2Cl_2) δ13.44, 14.26, 18.92, 18.98, 23.04, 24.94, 28.77, 29.24, 29.42, 29.53, 29.59, 29.65, 29.81, 32.25, 34.19, 44.08, 51.85, 52.21, 52.29, 59.92, 80.08, 80.34, 170.82, 171.07, 174.00.

Succinic Acids 3a, 4a and 3b, 4b. Solutions of triesters **2a** (32g, 0.079 mol) or **2b** (35 g, 0.079 mol) in 300 mL of freshly prepared 3 M ethanolic KOH and 100 mL of water were heated under reflux for 8−10 h (loss of methyl esters monitored by ^{1}H NMR). Additional water (100 mL) was added, and the resulting solutions were distilled (azeotropic removal of ethanol) until the temperature of the distillate was 100 °C and gave a negative response to Jones reagent. The aqueous solutions were acidified (pH = 2) with concd HCl and then refluxed for 18 h. The cooled solutions were saturated with NaCl and extracted with diethyl ether (3 × 75 mL), dried, and concentrated, affording **3a**, **4a** (24.11 g, 92%) or **3b**, **4b** (26.78 g, 93%). Both mixtures of succinic acids appeared to be reasonably pure by ^{1}H and ^{13}C NMR. Succinic acids **3a**, **4a** were separated by triturating with 100 mL of 5% CH_2Cl_2 in pentane. The insoluble white solid **3a** was isolated by filtration: mp 126−127 °C; ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.7 Hz), 1.45 (3H, d, J = 6.6 Hz), 1.25−1.61 (24H, cm), 1.81 (2H, bq), 2.56 (2H, cm, high order), 10.56 (2H, bs); ^{13}C NMR (CD_2Cl_2−DMSO) δ 14.12, 15.14, 22.67, 27.59, 29.34, 29.50, 29.52, 29.62, 29.64, 29.66, 29.68 (3C's), 30.68, 31.90, 41.98, 48.55, 175.75, 176.25. The filtrate was concentrated to afford **4a** as a white solid: mp 95−96.5 °C; ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.7 Hz), 1.20 (3H, d, J = 7.2 Hz), 1.26 (24H, bs), 1.59 (2H, bq), 2.60 (1H, dt, J = 6.2, 8.3 Hz), 2.74 (1H, dq), 10.06 (2H, bs); ^{13}C NMR (CD_2Cl_2−DMSO) δ 14.26, 14.42, 23.01, 27.26, 28.88, 29.69, 29.83, 29.97, 29.99, 30.00, 30.03 (4C's), 32.25, 40.97, 47.65, 177.62, 178.25. Anal. Calcd for $C_{19}H_{36}O_4$: C, 69.47; H, 11.04. Found (mixture of **3a**, **4a**): C, 69.20; H,10.94. Succinic acids **3b**, **4b** were separated by trituration with 100 mL of pentane. The insoluble white solid **3b** was removed by filtration: mp 97.5−99 °C; ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.7Hz), 1.91 (3H, d, J = 6.7Hz), 1.26−1.50 (22H, cm), 2.11 (4H, bt), 2.66 (2H, cm), 10.26 (2H, bs); ^{13}C NMR (CD_2Cl_2−DMSO) δ 14.25, 15.14, 18.94, 18.97, 22.98, 27.77, 28.97, 29.17, 29.32, 29.44, 29.47, 29.54 (2C's), 30.79, 32.17, 42.13, 48.67, 80.27, 80.42, 177.20, 178.02. The filtrate was concentrated to a dark yellow oil, which crystallized to a low melting white waxy solid (**4b**): ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.7 Hz), 1.27 (3H, d, J = 7.0 Hz)*, 1.27−1.47 (22H, cm), 2.12 (4H, bt), 2.60 (1H, ddd, J = 3.9, 8.0, 9.9 Hz), 2.75 (1H, dq), 10.23 (2H, bs), *determined by COSY; ^{13}C NMR (CD_2Cl_2) δ 14.18, 14.24, 18.95, 19.00, 23.02, 26.98, 28.88, 28.90, 29.21, 29.43, 29.46, 29.52, 29.57, 29.63, 32.23, 40.80, 47.32, 80.05, 80.31, 181.08, 181.63. Anal. Calcd for $C_{21}H_{36}O_4$: C, 71.55; H, 10.29. Found (mixture **3b**, **4b**): C, 71.71; H, 10.19.

General Procedure for Preparation of Cyclic Anhydrides 5a, 6a, 5b, and 6b. A solution of appropiate diacid (**3a**, **4a**, **3b**, or **4b**) and *N*-methylmorpholine (20 mmol each) in 50 mL of dry THF was prepared at 0 °C under argon. Methyl chloroformate (20 mmol) was added and the solution stirred for 15 min at rt. The *N*-methylmorpholine hydrochloride was filtered and the filtrate concentrated to afford quantitative yields of the corresponding succinic anhydrides. Compound **5a** was obtained as a pale yellow oil, crystallizing to a low-melting white waxy solid: ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.8 Hz), 1.27 (24H, bs), 1.29 (3H, d, J = 7.3 Hz), 1.87 (2H, cm), 3.07 (1H, dt, J = 6.9 Hz), 3.31 (1H, dq, J = 9.1 Hz); ^{13}C NMR (CD_2Cl_2) δ 11.19, 14.27, 23.04, 26.50, 27.52, 29.68, 29.72, 29.75, 29.94, 30.00, 30.05 (2C'S), 30.08 (2C's), 32.30, 39.13, 44.40, 173.61, 174.67. Compound **6a** crystallized to a white solid: mp 43−44 °C; ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.6 Hz), 1.26 (24H, bs), 1.40 (3H, d, J = 7.1 Hz), 1.65 (1H, cm), 1.86 (1H, cm), 2.71 (1H, dt, J = 5.5, 7.5 Hz), 2.84 (1H, p, J = 7.5 Hz); ^{13}C NMR (CD_2Cl_2) δ 14.27, 15.63, 23.06, 27.01, 29.65, 29.67, 29.74, 29.88, 29.97, 30.02 (2C's), 30.05, 30.07, 30.25, 32.30, 41.51, 48.28, 173.22, 174.08. Compound **5b** was a colorless oil: ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t), 1.25−1.51 (20H, cm), 1.41 (3H, d, J = 7.3 Hz), 1.67 (2H, cm), 2.07−2.15 (4H, cm), 3.07 (1H, dt, J = 6.8 Hz), 3.23 (1H, dq, J = 9.1 Hz); ^{13}C NMR (CD_2Cl_2) δ 11.31, 14.25, 18.91, 18.99, 23.00, 26.47, 27.40, 28.75, 29.17, 29.19, 29.35, 29.46, 29.54, 29.57, 32.20, 39.26, 44.51, 80.08, 80.56, 173.51, 174.56. Compound **6b** was a colorless oil: ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t), 1.26−1.54 (20H, cm), 1.40 (3H, d, J = 7.1 Hz), 1.68 (1H, bcm), 1.87 (1H, bcm), 2.07−2.15 (4H, bcm), 2.70 (1H, dt, J = 5.6, 7.5 Hz), 2.84 (1H, dq, J = 7.5 Hz); ^{13}C NMR (CD_2Cl_2) δ 14.43, 15.67, 19.08, 19.16, 23.18, 27.09, 28.94, 29.32, 29.36, 29.51, 29.64, 29.72, 29.76, 30.30, 32.37, 41.47, 48.18, 80.05, 80.52, 173.16, 174.00.

Succinate to Maleate Oxidation (8a and 8b). Excellent yields of maleic anhydrides were obtained only under rigorously anhydrous conditions. Mixed anhydrides **5a**, **6a** or **5b**, **6b** (15 mmol) were dissolved in 50 mL of dry benzene at 0 °C under argon in a flame dried two-neck round-bottom flask equipped with a septum and condenser. Via syringe, triethylamine (45 mmol) was added and the mixture stirred for 15 min, followed by addition of TMSOTf (45 mmol), and the solution heated under reflux for 2 h. The formation of 2,5-bis((trimethylsilyl)oxy)furans **7a** and **7b** was monitored by ^{1}H NMR. The solution of **7a** or **7b** was cooled to 0 °C, and a solution of pure tetra-*n*-butylammonnium bromide (1 mol % relative to starting anhydride) in 50 mL of CH_2Cl_2 was added via syringe. To furan **7a**, *pure* bromine (15 mmol) was added slowly by syringe and the reaction mixture then stirred for 15 min at 0 °C. To furan **7b** was added NBS (15 mmol, 30 mL of 0.5 M stock solution containing NBS in THF under 5A molecular sieves) and the reaction mixture stirred for 15 min at 0 °C. The crude products were concentrated to thick dark oils and chromatographed on a silica gel column eluting with pentane/CH_2Cl_2 (3:1) to afford **6a** (6%) and Chaetomellic anhydride A (**8a**) (91%) as a colorless oil which crystallized at 0 °C to a white waxy solid (one component by GC analysis): ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.7 Hz), 1.26 (22H, bs), 1.56 (2H, p, J = 7.3 Hz), 2.05 (3H, t, J = 0.7 Hz), 2.44 (2H, t, J = 7.3

Hz); ^{13}C NMR (CD_2Cl_2) δ 9.60, 14.28, 23.09, 24.69, 27.92, 29.62, 29.78, 29.79, 29.87, 30.00, 30.05, 30.08 (2C's), 30.11, 32.34, 140.93, 145.02, 166.27, 166.68. ^{1}H and ^{13}C data are in agreement with liturature values.[2a] Anal. Calcd for $C_{19}H_{32}O_3$: C, 73.98; H,10.45. Found: C,73.64; H,10.57.

Similarly, column chromatography afforded **6b** (9%) and **8b** (88%) as a colorless oil: ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.8 Hz), 1.25−1.46 (18H, bcm), 1.57 (2H, bp), 2.05 (3H, s), 2.12 (4H, cm), 2.45 (2H, t, J = 7.8 Hz); ^{13}C NMR (CD_2Cl_2) δ 9.51, 14.27, 18.94, 19.01, 23.04, 24.58, 27.77, 28.70, 29.23, 29.26, 29.33, 29.52, 29.59, 29.64, 32.24, 79.97, 80.48, 140.91, 144.75, 166.13, 166.50.

Reduction of 8b to Chaetomellic Anhydride B (9). A mixture of 0.15 g (10% w/w) of Lindlar catalyst ($Pd/CaCO_3/PbO$) in 8 mL of cyclohexane was prepared under argon. To this was added 1.5 g of alkyne **8b** and the flask evacuated and subjected to H_2 gas (1 atm, rt) until no further uptake was observed (~36−40 h). The solution was then filtered through Celite and concentrated to give a quantitative yield of the *cis*-alkene **9** (Chaetomellic anhydride B) as a colorless oil, observed to be one component by GC analysis: ^{1}H NMR (CD_2Cl_2) δ 0.88 (3H, t, J = 6.6 Hz), 1.26−1.38 (18H, cm), 1.56 (2H, p), 2.02 (4H, cm), 2.05 (3H, s), 2.44 (2H, t, J = 7.9 Hz), 5.35 (2H, cm); ^{13}C NMR (CD_2Cl_2) δ 9.52, 14.27, 23.06, 24.63, 27.42, 27.55, 27.85, 29.20, 29.66, 29.70, 29.73, 29.92 (2C's), 30.15, 32.31, 129.80, 130.36, 140.85, 144.85, 166.14, 166.53. ^{1}H and ^{13}C data are in agreement with literature values.[2a, f] Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.60; H, 9.95.

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Supporting Information Available: ^{13}C NMR spectra of compounds **1a**,**b**, **2a**,**b**, **5a**,**b**, **6a**,**b**, **8b**, and **10** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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