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Lactone-Directed Intramolecular Diels−Alder Cyclization: Synthesis of *trans*-Dihydroconfertifolin

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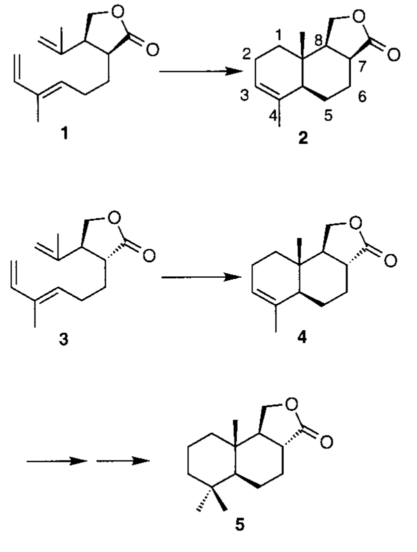
Trienes **1** and **3** were obtained in five steps from ethyl 4-acetoxy-3-oxobutanoate and 6-iodo-3-methyl-1,3-hexadiene. Intramolecular Diels−Alder cyclization of **1** and **3** gave tricyclic lactones **2** and **4** as the major products, respectively. The key intermediate **4** was converted in two steps to *trans*-dihydroconfertifolin (**5**).

Introduction

trans-Dihydroconfertifolin (**5**), a terpenoid lactone isolated from the New Zealand marine sponge *Dysidea* sp., displayed antimicrobial activity.[1,2] Lactone **5** is a simple representative of a ubiquitous theme among polycyclic terpenoids, the trans-fused angularly substituted 7,8-dialkyldecalin. The polycyclic terpenoids that fall in this class can be further subdivided on the basis of the stereochemical relationships at C-7 and C-8—natural products in each of the four diastereomeric series are known. We have found that the unactivated intramolecular Diels−Alder reaction allows easy access to two of the four diastereomeric series. Cyclization of **1** leads to the crystalline lactone **2**, and cyclization of **3** leads to the crystalline lactone **4**. The lactone **4** was converted in two steps to *trans*-dihydroconfertifolin (**5**).



Unactivated Intramolecular Diels−Alder (UIDA) Reaction. The unactivated intramolecular Diels−Alder reaction, which could be dated back to its introduction by Wilson in 1978,[3] has been widely used in the synthesis of polycyclic natural products.[4] However, it is still a challenge to control the stereochemical course of the UIDA reaction. Recently, we found[5] that it was possible to direct the UIDA reaction to give predominantly *either* the cis *or* the trans angularly substituted 6/5 product by modifying the substituents on the cyclizations precursors **6** and **8** (Scheme 1). In the current work, we have extended this investigation to the 6/6 series, focusing on the trans-fused lactone **4** and the cis-fused lactone **2**.

Preparation of Trienes 1 and 3. The lactones **1** and **3** were prepared as outlined in Scheme 2. The keto ester **10**[6] was alkylated with the iododiene **11**[7] (*E*/*Z* = 3:1 mixture) to give **12**. The reduction of ketone **12** with $NaBH_4$ was followed by hydrolysis, which resulted in lactonization to produce **13**. This was not isolated but was directly dehydrated via the corresponding mesylate to provide unsaturated lactone **14** (*E*/*Z* = 7:3) in 50% overall yield from **12**.

Conjugate addition of 2-propenylmagnesium bromide in the presence of catalytic Cu(I) gave a 1:1 mixture of diastereomers **1** (*E*/*Z* = 5:1) and **3** (*E*/*Z* = 2:1), which could be separated chromatographically. The relative configuration of the two stereogenic centers in **1** and **3** was established by comparison of one of their methylene signals (**1**: δ 4.22; **3**: δ 3.94; the other methylene signals

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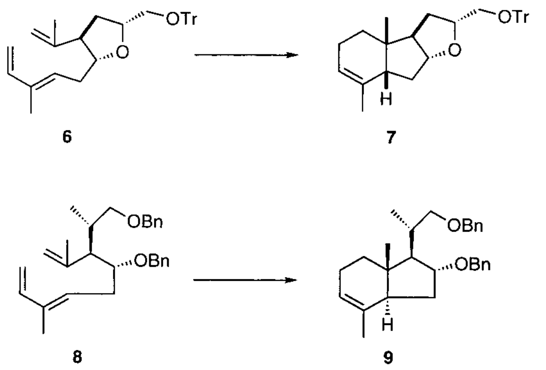
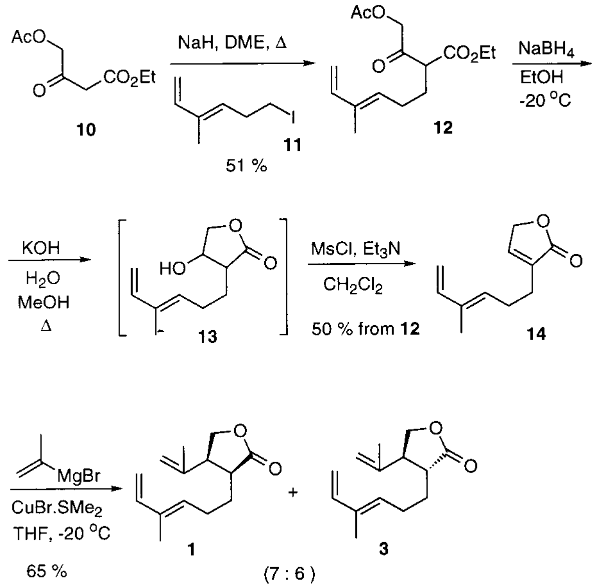
Scheme 1



Scheme 2

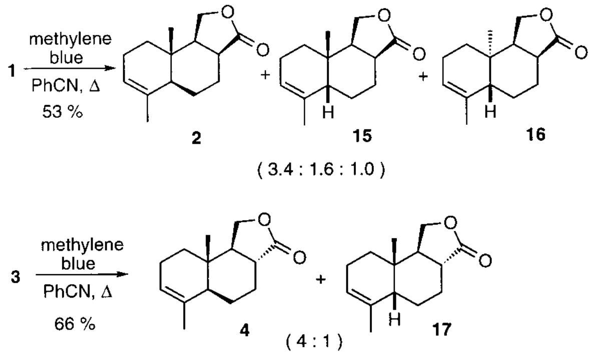


of **1** and **3** overlapped at δ 4.33−4.32) α to the lactone oxygen to those reported for α-methyl-β-(2-propenyl)-γ-lactone (trans: δ 3.90; cis: δ 4.24).[8] This approach can be modified to lead to either **1** or **3** as the dominant product. An improved ratio of **1** over **3** (7:3) could be obtained by kinetic protonation of the enolates from **1** and **3** with *dl*-camphorsulfonic acid.[8] Conversely, the *trans*-lactone **3** could be obtained by epimerization of the *cis*-lactone **1** with Et_3N/MeOH.

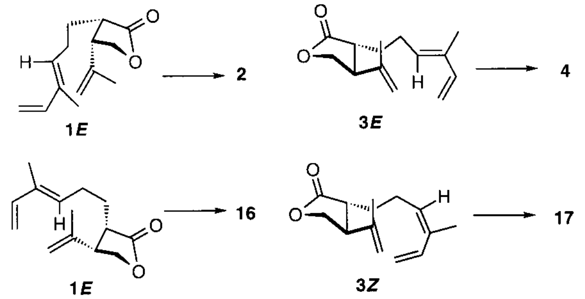
UIDA Reaction of 1 and 3. Heating a mixture of **1** (*E*/*Z* = 5:1) and methylene blue in benzonitrile under reflux (Scheme 3) gave a mixture of **2**, **15,** and **16** in a 3.4:1.6:1.0 ratio, in 53% combined yield. The major product **2** was separated chromatographically and crystallized. Its structure was unequivocally confirmed by X-ray crystallography, which showed that the lactone moiety was on the same face as the angular methyl group of the trans-fused decahydronaphthalene.

The same conditions were applied to the UIDA reaction of **3** (*E*/*Z* = 2:1) (Scheme 3) to afford **4** and **17** in a 4:1 ratio in 66% yield. Pure **4** was obtained from the mixture by chromatography followed by crystallization. The relative configurations of **4** and **17** were assigned on the basis of their ^{1}H NMR spectra, with the chemical shift of the

Scheme 3



Scheme 4



angular methyl group further upfield in the trans-fused diastereomer (δ 0.88 vs δ 1.04).[3a,b]

The minor products **15** and **16** were obtained as an inseparable mixture. Comparison of the chemical shifts of the alkene signals (**2**, δ 5.37; **4**, δ 5.34; **15**, δ 5.27; **16**, δ 5.36; **17**, δ 5.50) suggested that **16** could possess a trans-fused 6/6 ring. We therefore hypothesized that the structure of **15** was the cis-fused 6/6 ring with lactone ring on the same side as the angular methyl group (**15**, δ 0.86, vs **2**, δ 0.74), and not opposite from it (**16**, δ 0.97).

Reasoning that the UIDA reaction would proceed through a chairlike transition state, the conformers **1a** and **3a** would lead to the formation of the major products **2** and **4** (Scheme 4), respectively. Due to the high proportion of *Z*-isomer in **3** (*E*/*Z* = 2:1), the possibility of the formation of cis isomer **17** from *Z*-triene **3b** could not be excluded.[9]

Synthesis of *trans*-Dihydroconfertifolin. The *gem*-dimethyl of **5** was established following the procedure of Abad.[10] Exposure of the *trans*-lactone **4** to the standard Simmons−Smith reaction conditions afforded cyclopropane **18** (Scheme 5). The structure of **18** was firmly determined by 2D-COSY and NOESY spectra analysis. The cyclopropane **18** was regioselectively cleaved by stirring under H_2 (6 atm)/PtO_2 in HOAc.

Conclusions

The unactivated intramolecular Diels−Alder (UIDA) cyclization of the trienes **1** and **3** provided the crystalline lactones **2** and **4** as the major products, respectively. We expect that **2** and **4** will be valuable intermediates for target-directed synthesis. The first total synthesis of

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(9) For a previous example of the formation of a cis-fused 6/6 bicyclic product from a *Z*-diene, see: Pyne, S. G.; Hensel, M. J.; Byrn, S. R.; McKenzie, A. T.; Fuchs, P. L. *J. Am. Chem. Soc.* **1980**, *102*, 5960.

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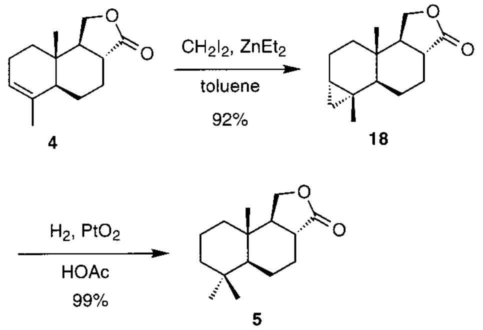
Scheme 5



trans-dihydroconfertifolin **5** was achieved in excellent yield from lactone **4**.

Experimental Section

General Methods. ^{1}H NMR and^{13}C NMR spectra were obtained as solutions in deuteriochloroform ($CDCl_3$) at 400 and 100 MHz, respectively, with tetramethylsilane = 0.00 as an internal standard. ^{13}C multiplicities were determined with the aid of a JVERT pulse sequence, differentiating the signals for methyl and methine carbons as "d" from methylene and quaternary carbons as "u". The infrared (IR) spectra were determined as neat oils. Mass spectra (MS) were obtained by chemical ionization. Substances for which C, H analyses are not reported were purified as specified and gave spectroscopic data consistent with being >95% the assigned structure. R_f values indicated refer to thin-layer chromatography (TLC) on 2.5 × 10 cm, 250 μm analytical plates coated with silica gel GF and developed in the solvent system indicated. Column chromatography was carried out with Merck 35−60 μm silica gel, following the procedure described by Taber.[11] Solvents are referred as volume/volume mixtures. All glassware was flame dried under a dry nitrogen stream immediately before use. Tetrahydrofuran (THF) and 1,2-dimethoxyethane (DME) were distilled from sodium metal/benzophenone ketyl under dry nitrogen. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride under dry nitrogen. Benzonitrile was distilled at atmospheric pressure. MTBE is methyl *tert*-butyl ether. All reaction mixtures were stirred magnetically under a nitrogen atmosphere, unless otherwise noted.

Keto Ester 12. NaH (60% dispersion, 2.43 g, 60.8 mmol) was washed twice with petroleum ether and suspended in DME (50 mL) at 0 °C. A solution of **10** (10.23 g, 54.41 mmol) in DME (10 mL) was added at 0 °C, and the mixture was stirred at room temperature for 45 min. A solution of **11** (9.19 g, 41.4 mmol) in DME (10 mL) was added. The mixture was heated to reflux for 17.5 h, cooled to room temperature and partitioned between MTBE and 3 M aqueous HCl. The combined organic extract was dried ($MgSO_4$) and concentrated. Chromatography of the crude product gave 5.96 g (51%) of **12** as a yellow oil: TLC R_f (20% MTBE/petroleum ether) = 0.54; ^{1}H NMR δ 6.70 (dd, J = 17.3, 10.9 Hz, 0.25 H), 6.35 (dd, J = 17.4, 10.6 Hz, 0.75 H), 5.41 (t, J = 7.4 Hz, 0.75 H), 5.31 (t, J = 7.8 Hz, 0.25 H), 5.23 (d, J = 17.3 Hz, 0.25 H), 5.11 (d, J = 17.4 Hz, 0.75 H), 5.11 (d, J = 10.9 Hz, 0.25 H), 4.97 (d, J = 10.7 Hz, 0.75 H), 4.85−4.70 (m, 2 H), 4.20 (q, J = 7.1 Hz, 2 H), 3.51 (t, J = 7.2 Hz, 1 H), 2.24−2.13 (m, 2 H), 2.16 (s, 3 H), 2.04−1.95 (m, 2 H), 1.82 (s, 0.75 H), 1.72 (s, 2.25 H), 1.28 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (common signals to *E* and *Z* isomers) δ d 13.8, 11.4, u 198.7, 169.7, 168.6, 67.3, 61.5; (*E* isomer) δ d 140.9, 130.5, 54.6, 20.1, u 135.4, 111.2, 27.2, 25.5; (*Z* isomer) δ 133.0, 128.6, 54.4, 19.6, u 133.8, 114.1, 27.5, 24.6; IR 1747, 1725 cm^{-1}; MS (CI) m/z 300 (M + NH_4^+, 13), 124 (100); HRMS calcd for $C_{15}H_{26}NO_5$ (M + NH_4^+) 300.1811, obsd 300.1825.

Unsaturated Lactone 14. A solution of **12** (4.61 g, 16.3 mmol) in EtOH (10 mL) was added to a suspension of $NaBH_4$ (1.85 g, 48.9 mmol) in EtOH (40 mL) at −20 °C. The mixture was stirred at −20 °C for 15 min. Excess $NaBH_4$ was destroyed by cautious addition of 3 M aqueous HCl. The mixture was partitioned between MTBE and 3 M aqueous HCl. The combined organic extract was dried ($MgSO_4$) and concetrated to give a brown oil, which was taken up in MeOH (30 mL).

A solution of KOH (3.90 g, 69.6 mmol) in water (6 mL) was added, and the mixture was heated to reflux for 50 min and then cooled to room temperature. The mixture was partitioned between MTBE and 3 M aqueous HCl. The combined organic extract (total 200 mL) was then stirred with 3 M aqueous HCl (100 mL) at room temperature for 45 min to ensure complete lactonization.

The mixture was partitioned between MTBE and 3 M aqueous HCl, and the combined organic extract was dried ($MgSO_4$) and concentrated. The residual brown oil (a mixture of major **13** and minor **14**) was taken up in CH_2Cl_2 (40 mL) and triethylamine (4.95 g, 49.0 mmol), and the mixture was cooled to 0 °C. MsCl (3.75 g, 32.7 mmol) was added, and the mixture was stirred at 0 °C for 30 min and then at room temperature for 20 min. The mixture was concentrated, and the residue was partitioned between MTBE and, sequentially, 3 M aqueous KOH and 3 M aqueous HCl. The combined organic extract was dried ($MgSO_4$) and concentrated. Chromatography of the crude product gave 1.46 g (50%) of **14** as a yellow oil: TLC R_f (30% MTBE/petroleum ether) = 0.38; ^{1}H NMR δ 7.12 (m, 1 H), 6.73 (dd, J = 17.2, 10.8 Hz, 0.3 H), 6.35 (dd, J = 17.4, 10.7 Hz, 0.7 H), 5.45 (t, J = 7.0 Hz, 0.7 H), 5.35 (t, J = 7.2 Hz, 0.3 H), 5.22 (d, J = 17.1 Hz, 0.3 H), 5.11 (d, J = 17.3 Hz, 0.7 H), 5.11 (d, J = 10.9 Hz, 0.3 H), 4.96 (d, J = 10.7 Hz, 0.7 H), 4.77 (m, 2 H), 2.48−2.32 (m, 4 H), 1.82 (s, 0.9 H), 1.74 (s, 2.1 H); ^{13}C NMR (common signals to *E* and *Z* isomers) δ u 70.1; (*E* isomer) δ d 144.6, 141.0, 130.7, 11.7, u 174.2, 135.3, 133.6, 111.3, 25.9, 25.1; (*Z* isomer) δ d 144.6, 133.2, 128.7, 19.7, u 174.3, 133.7, 133.5, 114.2, 25.4, 25.0; IR 1754 cm^{-1}; MS (CI) m/z 179 (MH$^+$, 100); HRMS calcd for $C_{11}H_{15}O_2$ (MH$^+$) 179.1072, obsd 179.1070.

Trienes 1 and 3. A small portion of a solution of 2-bromopropene (2.91 g, 24.1 mmol) in THF (20 mL) was added to magnesium (683 mg, 28.1 mmol) in THF (5 mL). The mixture was gently heated to initiate the reaction. Once the mixture became grayish to brown color with an exothermic reaction, the remaining THF solution of 2-bromopropene was added dropwise over 15−20 min to maintain gentle reflux. The mixture was then heated to reflux for 1 h and cooled to room temperature. Titration indicated the concentration of 2-propenylmagnesium bromide to be 0.73 M. This Grignard reagent (20 mL, 14.6 mmol) was added to a suspension of $CuBr{\cdot}SMe_2$ (190 mg, 0.92 mmol) in THF (10 mL) at −40 °C over 10 min. The mixture was warmed to −20 °C over 10 min. A solution of **14** (826 mg, 4.64 mmol) in THF (10 mL) was added dropwise over 25 min at −20 °C. The mixture was warmed slowly to −10 °C over 25 min and then was partitioned between saturated aqueous NH_4Cl and MTBE. The combined organic extract was dried ($MgSO_4$) and concentrated. Chromatography of the crude product gave 362 mg (35%) of **1** and 302 mg (30%) of **3** as yellow oils. **1**: TLC R_f (10% MTBE/petroleum ether) = 0.24; ^{1}H NMR δ 6.76 (dd, J = 17.3, 10.8 Hz, 0.17 H), 6.36 (dd, J = 17.4, 10.7 Hz, 0.83 H), 5.45 (t, J = 7.4 Hz, 0.83 H), 5.35 (t, J = 7.8 Hz, 0.17 H), 5.23 (d, J = 17.0 Hz, 0.17 H), 5.11 (d, J = 17.4 Hz, 0.83 H), 5.11 (d, J = 11.0 Hz, 0.17 H), 4.96 (d, J = 10.7 Hz, 0.83 H), 4.93 (t, J = 1.5 Hz, 1 H), 4.83 (s, 1 H), 4.33 (dd, J = 9.4, 6.1 Hz, 0.83 H), 4.32 (dd, J = 9.3, 6.1 Hz, 0.17 H), 4.22 (dd, J = 9.3, 2.8 Hz, 0.83 H), 4.217 (dd, J = 9.3, 3.0 Hz, 0.17 H), 3.19 (ddd, J = 8.3, 5.8, 2.6 Hz, 1 H), 2.57 (dt, J = 8.1, 6.2 Hz, 1 H), 2.35−2.26 (m, 2 H), 1.85−1.78 (m, 1 H), 1.75 (s, 3 H), 1.69 (s, 3 H), 1.49−1.39 (m, 1 H); ^{13}C NMR (common signals to *E* and *Z* isomers) δ d 11.6, u 115.0, 70.0; (*E* isomer) δ d 141.1, 131.2, 46.1, 41.5, 20.0, u 178.38, 141.56, 135.1, 111.0, 26.0, 25.2; (*Z* isomer) δ d 133.2, 129.3, 46.1, 41.3, 19.7, u 178.44, 141.64, 133.5, 113.9, 25.5, 25.1; IR 1770 cm^{-1}; MS (CI) m/z 221(MH$^+$, 100), 126 (35); HRMS calcd for $C_{14}H_{21}O_2$ (MH$^+$) 221.1542, obsd 221.1545.

3: TLC R_f (10% MTBE/petroleum ether) = 0.35; ^{1}H NMR δ 6.75 (dd, J = 17.3, 10.9 Hz, 0.33 H), 6.35 (dd, J = 17.4, 10.6

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(11) Taber, D. F. *J. Org. Chem.* **1982**, *47*, 1351.

Hz, 0.67 H), 5.44 (t, $J = 7.1$ Hz, 0.67 H), 5.34 (t, $J = 7.8$ Hz, 0.33 H), 5.21 (d, $J = 17.1$ Hz, 0.33 H), 5.10 (d, $J = 17.3$ Hz, 0.67 H), 5.10 (d, $J = 10.9$ Hz, 0.33 H), 4.96−4.92 (m, 2.67 H), 4.33 (dd, $J = 9.0$, 8.1 Hz, 0.67 H), 4.32 (dd, $J = 9.1$, 8.2 Hz, 0.33 H), 3.945 (dd, $J = 9.5$, 9.1 Hz, 0.67 H), 3.939 (dd, $J = 9.7$, 9.0 Hz, 0.33 H), 2.99−2.89 (m, 1 H), 2.54−2.47 (m, 1 H), 2.38−2.30 (m, 2 H), 1.91−1.73 (m, 7 H), 1.70−1.59 (m, 1 H); ^{13}C NMR (common signals to *E* and *Z* isomers) δ d 49.1, 11.5, u 140.9, 114.1, 69.2; (*E* isomer) δ d 141.0, 131.2, 41.8, 19.1, u 178.3, 135.1, 110.9, 28.9, 25.0; (*Z* isomer) δ d 133.2, 129.3, 41.7, 19.6, u 178.4, 133.4, 113.8, 29.2, 24.1; IR 1777 cm^{-1}; MS (CI) *m*/*z* 221(MH$^+$, 100), 126 (50); HRMS calcd for $C_{14}H_{21}O_2$ (MH$^+$) 221.1542, obsd 221.1536.

Kinetic protonation of the lithium enolates from **1** and **3** with *dl*-camphor sulfonic acid (CSA) was also studied. This gave a higher portion of the *cis*-lactone (1:3 = 7:3 ratio). Thus, *n*-butyllithium (2.2 M, 8.0 mL, 17.6 mmol) was added to a solution of diisopropylamine (1.89 g, 18.7 mmol) in THF (20 mL) at −78 °C, and the mixture was stirred at this temperature for 10 min. A solution of a mixture of **3** and **1** (5:2 ratio) (1.97 g, 8.95 mmol) in THF (10 mL) was added, and the mixture was stirred at −78 °C for 15 min. The mixture was then transferred into a solution of *dl*-CSA (5.95 g, 25.6 mmol) in THF (50 mL). The mixture was stirred at −78 °C for 10 min and was then partitioned between MTBE and dilute aqueous KOH. The combined organic extract was dried ($MgSO_4$) and concentrated. The ^{1}H NMR spectrum of the crude mixture showed the ratio of **1** and **3** to be 7:3.

Heating a mixture of **1** (48 mg, 0.22 mmol) and Et_3N (12 mg, 0.12 mmol) in MeOH (3 mL) to reflux for 4.5 h, followed by concentration in vacuo, gave a 3:2 mixture of **1** and **3**.

Tricyclic Lactones 2, 15, and 16. A mixture of **1** (*E*/*Z* = 5:1, 155 mg, 0.705 mmol) and methylene blue (3 mg, 8 mmol) in benzonitrile (10 mL) was heated to reflux for 16 h under nitrogen and then cooled to room temperature. Most of the benzonitrile was removed by distillation in vacuo. The residual oil was chromatographed to give 46 mg (30%) of 2 as a white solid (mp 136−138 °C) and 35 mg (23%) of an inseparable mixture of **15** and **16** as a light yellow oil. The X-ray sample of **2** was obtained by recrystallization from $CHCl_3$−petroleum ether. **2**: TLC R_f (20% MTBE/petroleum ether) = 0.27; ^{1}H NMR δ 5.37 (m, 1 H), 4.29 (d, $J = 9.6$ Hz, 1 H), 4.19 (dd, $J = 9.7$, 5.7 Hz, 1 H), 2.63 (br t, $J = 8.2$ Hz, 1 H), 2.35 (dd, $J = 13.3$, 5.2 Hz, 1 H), 2.17 (dd, $J = 7.9$, 5.7 Hz, 1 H), 2.10−1.90 (m, 2 H), 1.85−1.63 (m, 3 H), 1.62−1.55 (m, 1 H), 1.62 (s, 3 H), 1.28−1.15 (m, 2 H), 0.74 (s, 3 H); ^{13}C NMR δ d 121.3, 46.3, 45.0, 36.9, 21.4, 12.2, u 179.3, 133.7, 67.7, 35.2, 33.3, 21.9, 21.8, 19.6; IR 1770 cm^{-1}; MS (CI) *m*/*z* 221(MH$^+$, 100), 205 (35); HRMS calcd for $C_{14}H_{21}O_2$ (MH$^+$) 221.1542, obsd 221.1537.

15 and 16: TLC R_f (20% MTBE/petroleum ether) = 0.39; ^{1}H NMR (common signals to **15** and **16**) _ 4.35−4.20 (m, 2 H), 2.70−2.32 (m, 2 H), 2.19−1.75 (m, 5 H), 1.55−1.05 (m, 4 H); (**15**) δ 5.27 (m, 1 H), 1.69 (s, 3 H), 0.86 (s, 3 H); (**16**) δ 5.36 (m, 1 H), 1.64 (s, 3 H), 0.97 (s, 3 H); ^{13}C NMR (all signals to both **15** and **16**) δ d 121.3, 119.3, 47.0, 46.8, 43.2, 40.9, 38.0, 37.5, 22.6, 21.2, 21.1, 19.6, u 179.7, 179.6, 135.1, 133.9, 68.2, 67.9, 33.0, 32.6, 31.8, 29.3, 27.0, 25.2, 23.5, 22.31, 22.25, 21.6; IR 1770 cm^{-1}; MS (CI) *m*/*z* 221(MH$^+$, 100), 205 (33); HRMS calcd for $C_{14}H_{21}O_2$ (MH$^+$) 221.1542, obsd 221.1540.

Tricyclic Lactones 4 and 17. A mixture of **3** (*E*/*Z* = 2:1, 91 mg, 0.41 mmol) and methylene blue (1.4 mg, 3.7 mmol) in benzonitrile (6 mL) was heated to reflux for 19 h under nitrogen and then cooled to room temperature. Most of the benzonitrile was removed by distillation in vacuo. The residual oil was chromatographed to give 60 mg (66%) of a mixture of **4** and **17** (4:1 ratio) as a light yellow oil: TLC R_f (20% MTBE/petroleum ether) = 0.38. Crystallization from petroleum ether gave pure **4** as a white solid: mp 81−83 °C; ^{1}H NMR δ 5.34 (m, 1 H), 4.29 (dd, $J = 8.3$, 6.4 Hz, 1 H), 3.96 (dd, $J = 11.5$, 8.3 Hz, 1 H), 2.45−2.35 (m, 1 H), 2.28−2.20 (m, 1 H), 2.15−1.89 (m, 5 H), 1.64 (s, 3 H), 1.52−1.20 (m, 4 H), 0.88 (s, 3 H); ^{13}C NMR δ d 120.8, 53.1, 47.7, 39.2, 21.5, 11.4, u 177.8, 133.7, 68.3, 34.8, 33.7, 25.3, 23.6, 22.3; IR 1778 cm^{-1}; MS (CI) *m*/*z* 220 (M$^+$, 86), 205 (100); HRMS calcd for $C_{14}H_{20}O_2$ (M$^+$) 220.1463, obsd 220.1463.

17: ^{1}H NMR (signals separated from those of **4**) δ 5.50 (m, 1 H), 4.26 (dd, $J = 8.3$, 6.7 Hz, 1 H), 3.95 (dd, $J = 11.5$, 8.2 Hz, 1 H), 1.04 (s, 3 H); ^{13}C NMR δ d 123.2, 45.2, 42.6, 39.0, 21.8, 11.4, u 178.0, 138.1, 68.5, 34.5, 33.9, 23.4, 22.0, 21.6.

Cyclopropane 18. To a mixture of lactone **4** (33 mg, 0.15 mmol) and $ZnEt_2$ (1.2 mL, 1.0 M in hexane, 1.2 mmol) in toluene (3 mL) was added CH_2I_2 (642 mg, 2.4 mmol) at room temperature. The mixture was stirred for 6 h at room temperature and was then partitioned between MTBE and 5% aqueous HCl. The combined organic extract was dried (Na_2SO_4) and concentrated. Chromatography of the crude product gave cyclopropane **18** (32 mg, 0.14 mmol, 92%) as a white solid (mp 136−138 °C). **18**: TLC R_f (20% MTBE/petroleum ether) = 0.38; ^{1}H NMR δ 4.23 (dd, $J = 8.3$, 6.7 Hz, 1 H), 3.88 (dd, $J = 11.6$, 8.3 Hz, 1 H), 2.30 (ddd, $J = 15.4$, 11.9, 2.3 Hz, 1H), 2.19−2.24 (m, 1H), 1.92−1.98 (m, 2H), 1.69−1.78 (m, 2H), 1.42 (ddd, $J = 16.0$, 13.0, 3.5 Hz, 1H), 1.24−1.33 (m, 2H), 1.03 (dd, $J = 12.8$, 3.7 Hz, 1H), 0.97 (s, 3H), 0.92 (s, 3H), 0.85−0.93 (m, 1H), 0.61−0.65 (m, 1H), 0.50 (dd, $J = 9.4$, 4.2 Hz, 1H), 0.04 (dd, $J = 5.8$, 4.3 Hz, 1H); ^{13}C NMR δ d 53.0, 50.7, 39.3, 23.8, 18.6, 11.6, u 178.3, 68.6, 34.4, 34.0, 25.8, 25.5, 22.4, 18.6, 15.4; IR 1768 cm^{-1}; MS (ESI) *m*/*z* 250 (M + NH_4, 50), 235 (M + 1, 100); HRMS calcd for $C_{15}H_{26}NO_2$ (M + NH_4) 252.1964, obsd 252.1965.

***trans*-Dihydroconfertifolin (5).** A mixture of cyclopropane **18** (13 mg, 0.056 mmol) and PtO_2 (7 mg, 0.03 mmol) in HOAc (1.2 mL) was stirred at 50 °C under H_2 (6 atm) for 24 h. The mixture was partitioned between MTBE and saturated aqueous solution of $NaHCO_3$. The combined organic extract was dried (Na_2SO_4) and concentrated. The residue was chromatographed to provide *trans*-dihydroconfertifolin **5** (13 mg, 0.055 mmol, 99%) as a white solid (mp 116−118 °C). **5**: TLC R_f (20% MTBE/petroleum ether) = 0.38; ^{1}H NMR δ 4.21 (dd, $J = 8.4$, 6.8 Hz, 1 H), 3.95 (dd, $J = 11.5$, 8.4 Hz, 1 H), 2.19−2.32 (m, 2H), 1.79−1.92 (m, 2H), 1.58−1.66 (m, 1H), 1.44−1.49 (m, 3H), 1.17−1.33 (m, 4H), 0.95 (s, 3H), 0.91−0.95 (m, 1H), 0.88 (s, 3H), 0.85 (s, 3H); ^{13}C NMR δ d 56.0, 55.2, 39.3, 33.8, 21.6, 14.3, u 178.3, 68.1, 42.4, 38.9, 36.2, 33.1, 26.0, 21.6, 18.6; IR 1769 cm^{-1}; MS (CI) *m*/*z* 237 (M + 1, 98), 236 (M, 41), 221 (100), 123 (82); HRMS calcd for $C_{15}H_{25}O_2$ (M + H), 237.1855, obsd 237.1854.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for all new compounds; 2D-COSY and NOESY spectra of cyclopropane **18**; tables of crystal data, atomic coordinates, bond lengths and angles, anistropic thermal parameters for **2**; ORTEP diagram of **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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