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Synthesis of the Pentacylic Core of (+)-Salvileucalin B

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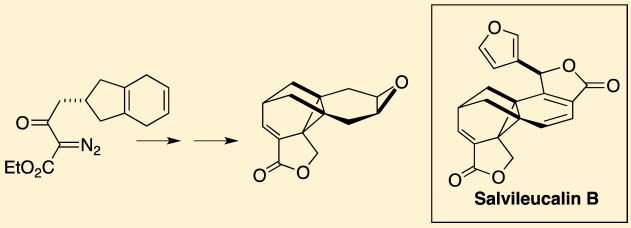
Supporting Information

ABSTRACT: A concise preparation of the prochiral pentacyclic core of (+)-salvileucalin B is presented. The key feature in the synthesis is the Cu-catalyzed intramolecular cyclopropanation of a symmetrical indane-derived α-diazo β-keto ester. This symmetry is carried through the remainder of the synthesis. This practical approach could allow the ready preparation of derivatives for further chemical and biological studies of this class of natural products.



INTRODUCTION

Salvileucalins A and B (**1**) were isolated from the aerial parts of *Salvia leucantha* Cav. by Takeya and co-workers[1] in 2008. Salvileucalins C and D were also isolated from *Salvia leucantha* Cav. by Takeya and co-workers[2] in 2011 (Figure 1). The

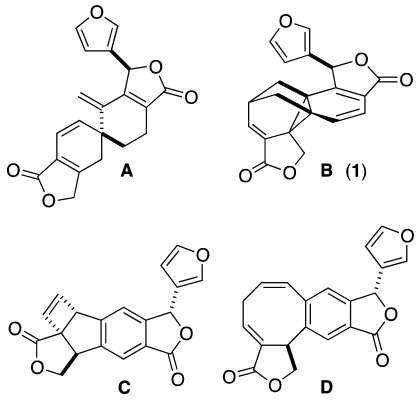


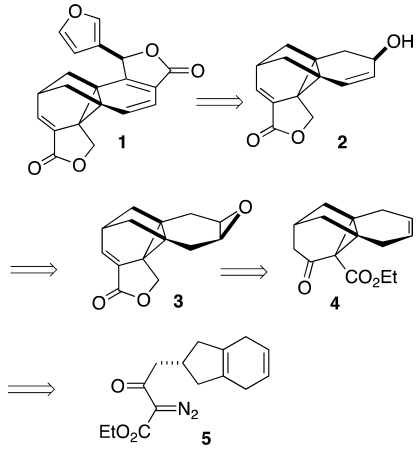
Figure 1. Salvileucalins A–D.

bislactone **1** presented an interesting puzzle for total synthesis. The unusually stable norcaradiene[3] core includes seven rings. The molecule also contains three heterocycles, two lactones, and one furan. It also features a hexasubstituted cyclopropane, a significantly challenging structure. Of interest, **1** showed promising cytotoxicity against A549 (human lung adenocarcinoma) and HT-29 (human colon adenocarcinoma). To date, only one total synthesis of this architecturally complex rearranged neoclerodane diterpene[4] by Reisman and co-workers[5] has been reported. In addition, a modular synthesis of the structural domains by Chen and co-workers[6] and a synthesis of the norcaradiene core by Banwell and co-workers[7] have been described.

RESULTS AND DISCUSSION

When we began our work, no efforts toward the synthesis of **1** had yet been reported. A retrosynthetic analysis (Scheme 1)

Scheme 1. Retrosynthetic Analysis of (+)-Salvileucalin B



revealed an element of symmetry in the core structure. We envisioned using this to our advantage. A copper-mediated cyclopropanation of compound **5** could lead to the *meso*-norcaradiene core **4**. Further manipulation would deliver the lactone, completing the southern portion of **1**. Rearrangement of the epoxide **3** could lead to the allylic alcohol **2**, either in its racemic form or as a single enantiomer. Banwell[7] recognized this same advantage, effecting intramolecular cyclopropanation of a symmetrical arene. Reisman[5] also effected intramolecular cyclopropanation of an arene, but further along in the synthesis.

Accessing the cyclopropane **4** required the construction of the diazo ketone **5** (Scheme 2). Our starting material was the 2-indanylacetic acid **7**. This commercially available acid was expensive, so we prepared it on a 20 g scale from 1-indanone following the Hay[8] protocol. The acid **6** was reduced with Pd/C under 300 psi H_2 for 24 h to give the acid **7**. Birch reduction with lithium metal and NH_3 gave the diene **8** that was shelf-stable. The crude derived acid chloride was treated with the

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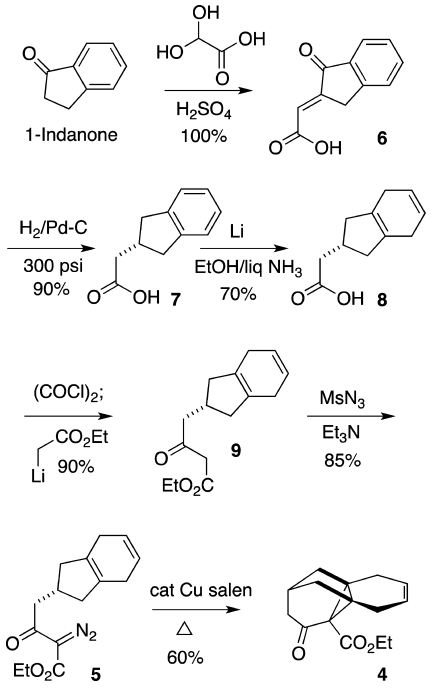
Scheme 2. Route to the Neoclerodane Core

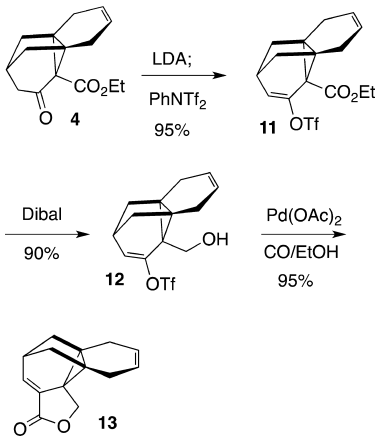


enolate of ethyl acetate[9] to give the β-keto ester **9**. Diazo transfer using mesyl azide[10] set the stage for the cyclization.

Treatment of the diazo ester **9** with catalytic copper gave the cyclopropane **4**. With this method, gram quantities of **4** were easily prepared with minimal need for purification. A brief screen of copper catalysts was performed. We found that a soluble Cu(II) catalyst[11] gave a slightly better yield of the cyclopropane than did Cu bronze powder.

With a scalable route to the neoclerodane core in hand, we turned our attention to installing the southern lactone (Scheme 3). This was readily accomplished by first forming the vinyl

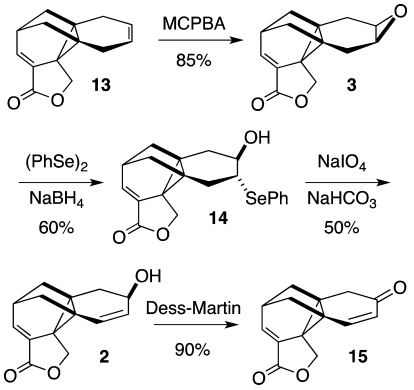
Scheme 3. Formation of the Southern Lactone



triflate of the β-keto ester **4** by treatment with LDA followed by exposure to the McMurry–Hendrickson reagent.[12] The ester **11** was then reduced to the primary alcohol **12**. Exposure to CO in the presence of Pd then delivered the lactone **13**, previously reported[7] by Banwell.

We next addressed the northern functionality of salvileucalin B **1** (Scheme 4). The *meso*-epoxide **3**, the structure of which

Scheme 4. Route to Racemic Enone



was secured by X-ray crystallography, was prepared by exposure of **13** to *m*CPBA. Treatment of the epoxide **3** with diphenyl diselenide and sodium borohydride gave the phenylselenyl alcohol **14**. Oxidation of **14** with sodium periodate led to the selenoxide, which upon heating underwent elimination to give the allylic alcohol **2**. Dess-Martin periodinane oxidation delivered the required enone **15**.

CONCLUSION

The work presented here provides an alternative approach to the prochiral pentacylic core of (+)-salvileucalin B **1**. The route to the alkene **13** from the commercial acid **7** is eight steps with 26% overall yield. The highlights of this route include the short practical preparation of the neoclerodane core **4**. The enone **15** could potentially be converted into a variety of derivatives for biological screening.

EXPERIMENTAL SECTION

General Experimental: ^{1}H NMR and ^{13}C NMR spectra were recorded as solutions in deuteriochloroform ($CDCl_3$) at 400 and 100 MHz, respectively. ^{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. R_f values indicated refer to thin layer chromatography (TLC) on 2.5 × 10 cm, 250 μm analytical plates coated with silica gel GF, unless otherwise noted, and developed in the solvent system indicated. All glassware was oven-dried and rinsed with dry solvent before use. THF and diethyl ether were distilled from sodium metal/benzophenone ketyl under dry nitrogen. MTBE is methyl *tert*-butyl ether, and PE is 30–60 petroleum ether. All reactions were conducted under N_2 and stirred magnetically. HRMS data were obtained by a EI method of ionization on a sector instrument.

2-(2,3,4,7-Tetrahydro-1*H*-inden-2-yl)acetic acid (8): In a 500 mL three-neck round-bottom flask, 2-indanone acetic acid (3.5 g, 19.88 mmol) and anhydrous EtOH (100 mL) were combined. The reaction was cooled to −78 °C by a dry ice acetone bath. Anhydrous ammonia (100 mL) was condensed into the flask via a coldfinger condenser. Pieces of lithium metal were added portionwise until a blue color persisted. The reaction was allowed to stir at rt overnight. Ice water was added, and the mixture was acidified with concentrated aqueous HCl. The mixture was extracted with Et_2O, and the organic extract was dried (Na_2SO_4) and concentrated. The resulting oil was diluted with 50 mL of PE and placed in the freezer overnight. The resulting off white crystals were filtered and washed with cold PE to afford **8** (2.45 g, 70% yield): mp = 68–72 °C; TLC R_f (Et_2O) = 0.46; ^{1}H NMR δ 1.98 (m, 2 H), 2.47 (d, J = 7.6 Hz, 2 H), 2.56 (m, 2 H), 2.64 (s, 4 H), 2.70 (m, 1 H), 5.76 (s, 2 H); ^{13}C NMR δ (u) 179.7, 130.6, 41.8, 40.9, 27.4; (d) 124.6, 32.0; IR (film, cm^{-1}) 3438, 2841, 1698, 1439; HRMS calcd for $C_{11}H_{14}O_2$ 178.0989, observed 178.1001.

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Ethyl 3-Oxo-4-(2,3,4,7-tetrahydro-1*H*-inden-2-yl)butanoate (9): In a 100 mL round-bottom flask **8** (1.89 g, 10.62 mmol), CH_2Cl_2 (30 mL), and 10 drops of DMF were combined at 0 °C. Oxalyl chloride (4.00 g, 31.85 mmol) was added dropwise over 10 min to maintain control of foaming. Once the foaming ended, the reaction mixture was concentrated and then diluted with THF (30 mL). In a separate 250 mL round-bottom flask, diisopropylamine (6.69 g, 66.9 mmol) and THF (60 mL) were combined at −78 °C. *n*BuLi (2.0 M in hexanes, 30.0 mL, 60.0 mmol) was added dropwise over 5 min. The solution was allowed to warm to −30 °C. The solution was then cooled to −78 °C. EtOAc (4.40 g, 50.0 mmol) was added all at once. The solution was held for 15 min, then the acid chloride solution was added dropwise over 5 min. The mixture was allowed to stir for 2 h at −78 °C. The reaction was quenched with 100 mL of 1 M aqueous HCl. The mixture was extracted with Et_2O. The organic extract was dried (Na_2SO_4) and concentrated. The residual oil was chromatographed to obtain **9** (2.36 g, 90% yield) as a clear oil: TLC R_f (30% MTBE/PE) = 0.43; ^{1}H NMR δ 1.29 (t, J = 11.6 Hz, 3 H), 1.92 (d, J = 14.8 Hz, 2 H), 2.52 (m, 2 H), 2.55 (s, 4 H), 2.57 (d, J = 6.8 Hz, 2 H), 3.45 (d, J = 11.6 Hz, 2 H), 4.22 (q, J = 11.6 Hz, 2 H), 5.75 (s, 2 H); ^{13}C NMR δ (u) 202.9, 167.2, 130.8, 61.9, 50.5, 42.1, 39.0, 27.3; (d) 124.9, 31.1, 14.0; IR (film, cm^{-1}) 3439, 2880, 1740, 1643, 1403; HRMS calcd for $C_{15}H_{20}O_3$ 248.1408, observed 248.1415.

Ethyl 2-Diazo-3-oxo-4-(2,3,4,7-tetrahydro-1*H*-inden-2-yl)-butanoate (5): In a 250 mL round-bottom flask, β-keto ester **9** (2.0 g, 8.06 mmol), CH_2Cl_2 (40 mL), and triethylamine (1.63 g, 16.12 mmol) were combined at 0 °C. Mesyl azide (1.46 g, 12.09 mmol) was added all at once. The reaction was stirred for 4 h in the dark. The reaction was quenched with 1 M aqueous HCl and extracted with CH_2Cl_2. The organic extract was dried (Na_2SO_4) and concentrated. The residual oil was chromatographed to obtain **5** (1.89 g, 85% yield) as clear oil: TLC R_f (30% MTBE:PE) = 0.75; ^{1}H NMR δ 1.35 (t, J = 7.2 Hz, 3 H), 1.98 (d, J = 5.5 Hz, 2 H), 2.56 (m, 2 H), 2.63 (s, 4 H), 2.78 (m, 1 H), 2.99 (d, J = 7.3 Hz, 2 H), 4.31 (q, J = 7.2 Hz, 2 H), 5.76 (s, 2 H); ^{13}C NMR δ (u) 192.7, 130.7, 61.4, 47.2, 41.9, 27.4; (d) 124.6, 31.7, 14.4; IR (film, cm^{-1}) 2837, 2511, 1851, 1753, 1441; HRMS calcd for $C_{15}H_{19}O_3N_2$ 275.1391, observed 275.1392.

Ethyl 10-Oxotetracyclo[6.3.1.0^{1,6}.0^{6,11}]dodec-3-ene-11-carboxylate (4): In a 100 mL round-bottom, flask diazo ester **5** (1.09 g, 3.98 mmol), toluene (40 mL), and copper(II) salicylideneimine (0.166 g, 0.40 mmol) were combined. The reaction was stirred at reflux for 1 h. The mixture was chromatographed directly to obtain **4** (0.587 g, 60% yield) as off white crystals: mp = 105−108 °C; TLC R_f (60% MTBE/PE) = 0.41; ^{1}H NMR δ 1.26 (t, J = 7.2 Hz, 3 H), 1.96 (s, 4 H), 2.16 (d, J = 3.2 Hz, 2 H), 2.34 (d, J = 15.6 Hz, 3 H), 2.89 (m, 2 H), 4.15 (q, J = 7.2 Hz, 2 H), 5.49 (s, 2 H); ^{13}C NMR δ (u) 204.0, 167.3, 130.7, 61.0, 43.7, 38.7, 36.0, 26.5; (d) 123.8, 27.3, 14.0; IR (film, cm^{-1}) 3421 (br), 2931, 2091, 1728, 1644; HRMS calcd for $C_{15}H_{18}O_3$ 246.1251, observed 246.1252.

{10-(Trifluoromethylsulfonyloxy)tetracyclo[6.3.1.0^{1,6}.0^{6,11}]-dodeca-3,9-dien-11-yl}methanol (12): In a 25 mL round-bottom flask, diisopropylamine (0.250 g, 2.03 mmol) and THF (4 mL) were cooled to −78 °C, then *n*BuLi (2.5 M in hexanes, 0.8 mL, 2.03 mmol) was added dropwise over 5 min. The solution was allowed to warm to −35 °C, then recooled to −78 °C, and β-keto ester **4** (0.201 g 0.81 mmol) in THF (4 mL) was added dropwise over 5 min. The solution was stirred for 30 min; *N*-phenylbis(trifluoromethanesulfonimide) (0.348 g 0.975 mmol) was added, and the solution was stirred overnight. The reaction was quenched with water and extracted with Et_2O. The organic extract was dried (Na_2SO_4) and concentrated to yield **11** (0.292 g, crude 95% yield) as a clear oil: TLC R_f (40% MTBE/PE) = 0.69; ^{1}H NMR δ 1.27 (t, J = 7.2 Hz, 3 H), 1.55 (d, J = 11.9 Hz, 2 H), 1.60 (m, 2 H), 2.50 (d, J = 16.0 Hz, 2 H), 2.68 (m, 1 H), 2.80 (m, 2 H), 4.13 (q, J = 7.3 Hz, 2 H), 5.57 (s, 2 H), 5.96 (d, J = 8.3 Hz, 1 H); ^{13}C NMR δ (u) 166.0, 143.2, 129.8, 127.4, 120.0, 61.4, 35.0, 28.4, 24.4; (d) 124.5, 115.2, 29.4, 13.8; IR (film, cm^{-1}) 3436 (br), 2925, 1732, 1651, 1421; HRMS calcd for $C_{16}H_{18}O_5F_3S$ 379.0822, observed 379.0821.

In a 250 mL round-bottom flask, the crude ester **11** (0.30 g, 0.770 mmol) and CH_2Cl_2 (4 mL) were cooled to −30 °C via a dry ice bath, then Dibal-H (1.2 M in toluene, 1.75 mL, 2.1 mmol) was added dropwise over 5 min. The solution was held at −30 °C for 30 min. The reaction was quenched slowly with saturated aqueous sodium fluoride and stirred until solids formed. The solution was filtered, and the filter cake was washed with EtOAc. The filtrate was concentrated then taken up in PE and cooled to −78 °C. The crystals formed were filtered to yield **12** (0.242 g 90% yield from **4**) as white crystals: mp = 60−63 °C; TLC R_f (30% MTBE/PE) = 0.63; ^{1}H NMR δ 1.37 (d, J = 11.9 Hz, 2 H), 1.57 (m, 4 H), 2.50 (s, 4 H), 2.60 (m, 1 H), 3.95 (d, J = 5.5 Hz, 2 H), 5.78 (s, 2 H), 5.94 (d, J = 8.1 Hz, 1 H); ^{13}C NMR δ (u) 146.7, 57.7, 36.6, 34.0, 26.4, 23.3; (d) 125.6, 116.1, 30.2; IR (film, cm^{-1}) 3336 (br), 2915, 1446, 1651, 1421; HRMS [M − H_2O] calcd for $C_{14}H_{13}O_3F_3S$ 318.0533, observed 318.0522.

4-Oxapentacyclo[6.6.1.0^{1,10}.0^{2,6}.0^{2,10}]pentadeca-6,12-dien-5-one (13): In a 25 mL round-bottom flask, the alcohol **12** (3.4 g, 10.17 mmol) was added to DMF (8 mL), EtOH (3 mL), and triethylamine (3 mL). The solution was sparged with CO via a balloon for 10 min. Under the CO balloon, $Pd(OAc)_2$ (0.068 g, 0.305 mmol) and triphenylphosphine (0.160 g, 0.610 mmol) were added. The solution was stirred for 2 h at rt. The reaction was quenched with 1 M aqueous HCl and extracted with Et_2O. The organic extract was dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield **13** (2.06 g, 95% yield) as a white powder: mp = 140−143 °C; TLC R_f (60% MTBE/PE) = 0.66 ; ^{1}H NMR δ 0.98 (d, J = 11.9 Hz, 2 H), 1.69 (dd, J = 11.9, 4.8 Hz, 2 H), 2.3−2.6 (m, 4H) 2.90 (dt, J = 6.8, 4.8 Hz, 1 H), 4.11 (s, 2 H), 5.74 (s, 2 H), 6.96 (d, J = 7.1 Hz, 1 H); ^{13}C NMR δ (u) 169.8, 126.4, 67.2, 32.9, 31.6, 25.3, 23.6; (d) 133.8, 124.6, 32.7; IR (film, cm^{-1}) 3479, 2918, 2840, 1751, 1643; HRMS calcd for $C_{14}H_{14}O_2$ 214.0989, observed 214.0998.

4,13-Dioxahexacyclo[7.6.1.0^{1,7}.0^{3,5}.0^{7,15}.0^{11,15}]hexadec-10-en-12-one (3): In a 25 mL round-bottom flask, lactone **13** (0.025 g, 0.114 mmol), *m*CPBA (0.025 g 0.114 mmol), and CH_2Cl_2 (1 mL) were combined at 0 °C. The reaction was stirred overnight at 0 °C. The residue was chromatographed directly to yield **3** (0.012 g, 41% yield, 80% yield based on starting material not recovered) as white crystals: mp = 180−185 °C; TLC R_f (60% MTBE/PE) = 0.33; ^{1}H NMR δ 0.92 (d, J = 12.0 Hz, 2 H), 1.66 (d, J = 16.7 Hz, 2 H), 1.95 (d, J = 16.7 Hz, 2 H), 2.46 (d, J = 16.7 Hz, 2 H), 2.85 (dt, J = 6.9, 4.8 Hz, 1 H), 3.15 (s, 2 H), 4.23 (s, 2 H), 6.96 (d, J = 7.1 Hz, 1 H); ^{13}C NMR δ (u) 169.2, 125.7, 65.8, 33.1, 21.6, 20.2; (d) 134.3, 50.4, 33.1; IR (film, cm^{-1}) 3488.9, 2919.9, 2850.0, 1788.0, 1666.4; HRMS calcd for $C_{14}H_{14}O_3$ 230.0938, observed 230.0952.

4-Hydroxy-12-oxapentacyclo[6.6.1.0^{1,6}.0^{6,14}.0^{10,14}]pentadeca-2,9-dien-11-one (2): In a 100 mL round-bottom flask, diphenyl diselenide (2.17 g, 6.96 mmol) and EtOH (40 mL) were combined. Sodium borohydride (0.514 g, 13.90 mmol) was added. The solution was held at rt until the foaming stopped, and a clear solution was obtained. In a separate 250 mL round-bottom flask, the epoxide **3** (0.326 g, 1.39 mmol) and EtOH (40 mL) were combined. The two solutions were combined all at once. The solution was heated to reflux for 2 h. The solution was quenched with 1 M aqueous HCl and extracted with Et_2O. The organic extract was dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield **14** (0.323 g, 60% yield) as white crystals: mp = 160−165 °C; TLC R_f (80% MTBE/PE) = 0.54; ^{1}H NMR δ 0.87 (d, J = 11.9 Hz, 1 H), 1.00 (d, J = 11.9 Hz, 1 H), 1.63 (m, 3 H), 1.80 (dd, J = 14.2, 10.1 Hz, 1 H), 1.94 (dd, J = 14.2, 10.1 Hz, 1 H), 2.44 (dd, J = 13.9, 5.1 Hz, 1 H), 2.60 (dd, J = 15.4, 5.3 Hz, 1 H), 2.90 (m, 3 H), 3.28 (s, 1 H), 3.78 (d, J = 9.6 Hz, 1 H), 4.15 (d, J = 9.6 Hz, 1 H), 6.92 (d, J = 7.1 Hz, 1 H), 7.38 (m, 3 H), 7.60 (d, J = 8.1 Hz, 2 H); ^{13}C NMR δ (u) 169.1, 125.6, 124.6, 65.9, 34.2, 33.1, 30.6, 28.2, 27.2, 26.2; (d) 136.8, 134.3, 129.4, 129.2, 68.3, 49.6, 33.7.

In a 50 mL round-bottom flask, selenide **14** (0.323 g, 0.836 mmol), sodium periodate (2.50 g, 13.60 mmol), saturated aqueous sodium bicarbonate (15 mL), and THF (10 mL) were combined. The solution was stirred at rt for 1 h. The solution was diluted with brine and extracted with EtOAc. The organic extract was dried (Na_2SO_4) and then heated to reflux for 20 min until a yellow color developed. The solution was concentrated and chromatographed to yield **2** (0.096 g, 30% yield from **3**) as a white powder: mp = 163−165 °C; TLC R_f

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(80% MTBE/PE) = 0.30; ^{1}H NMR δ 1.00 (d, J = 11.9 Hz, 1 H), 1.10 (d, J = 11.9 Hz, 1 H), 1.59 (dd, J = 12.0, 4.7 Hz, 1 H), 1.73 (dd, J = 13.8, 9.5 Hz, 1 H), 1.83 (m, 1 H), 1.95 (s, 1 H), 2.48 (dd, J = 13.5, 8.0 Hz, 1 H), 3.04 (dt, J = 6.8, 4.8 Hz, 1 H), 3.93 (t, J = 8.5 Hz, 1 H), 4.11 (d, J = 9.6 Hz, 1 H), 4.32 (d, J = 9.6 Hz, 1 H), 5.84 (dd, J = 10.1, 1.8 Hz, 1 H), 6.01 (dd, J = 10.1, 1.8 Hz, 1 H), 7.05 (d, J = 7.1 Hz, 1 H); ^{13}C NMR δ (u) 169.3, 125.5, 67.3, 31.1, 29.8, 29.5; (d) 135.3, 131.4, 125.5, 65.0, 34.6; IR (film, cm^{-1}) 3338 (br s), 2861, 1770, 1169, 1019; HRMS calcd for $C_{14}H_{14}O_3$ 230.0938, observed 230.0958.

12-Oxapentacyclo[6.6.1.0^{1,6}.0^{6,14}.0^{10,14}]pentadeca-4,9-diene-3,11-dione (15). In a 25 mL round-bottom flask, the allylic alcohol **3** (0.153 g, 0.660 mmol) and CH_2Cl_2 (6 mL) were combined. Dess-Martin periodinane (15% in CH_2Cl_2, 2.25 mL, 0.79 mmol) was added all at once. The solution was held at rt for 20 min, then chromatographed directly to yield **15** (0.135 g, 90% yield) as a white powder: mp = 148−150 °C; TLC R_f (80% MTBE/PE developed twice) = 0.40; ^{1}H NMR δ 1.15 (m, 2 H), 1.75 (dd, J = 12.0, 4.7 Hz, 1 H), 2.02 (dd, J = 12.1, 4.8 Hz, 1 H), 2.80 (m, 1 H), 3.11 (m, 1 H), 4.21 (d, J = 4.3 Hz, 2 H), 6.12 (d, J = 10.1 Hz, 1 H), 7.05 (d, J = 12.0 Hz, 1 H), 7.15 (d, J = 8.0 Hz, 1 H); ^{13}C NMR δ (u) 194.6, 168.5, 125.4, 65.7, 39.9, 34.8, 33.5, 29.3, 29.1, 27.6; (d) 146.7, 135.5, 128.4, 33.9; IR (film, cm^{-1}); 3341 (br s), 2951, 1775, 1171, 1022; HRMS calcd for $C_{14}H_{12}O_3$ 228.0782, observed 228.0797.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Aoyagi, Y.; Yamazaki, A.; Nakatsugawa, C.; Fukaya, H.; Takeya, K.; Kawauchi, S.; Izumi, H. *Org. Lett.* **2008**, *10*, 4429.

(2) Aoyagi, Y.; Yamazaki, A.; Kato, R.; Tobe, F.; Fukaya, H.; Nishikawa, T.; Nakahashi, A.; Miura, N.; Monde, K.; Takeya, K. *Tetrahedron Lett.* **2011**, *52*, 1851.

(3) Buchner, E.; Curtius, T. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 2377.

(4) Esquivel, B.; Dominguez, R. M.; Hernandez-Ortega, S.; Toscano, R. A.; Rodriguez-Hahn, L. *Tetrahedron* **1994**, *50*, 11593.

(5) Levin, S.; Nani, R. R.; Reisman, S. E. *J. Am. Chem. Soc.* **2011**, *133*, 774.

(6) Tseng, C.; Ding, H.; Li, A.; Guan, Y.; Chen, D. Y. *Org. Lett.* **2011**, *13*, 4410.

(7) Heinrich, N.; Banwell, M. G.; Willis, A. C.; Cade, A. I.; Capon, R. J.; Huang, X.-C. *Aust. J. Chem.* **2012**, *65*, 1679.

(8) Hay, M. P.; Hicks, K. O.; Pchalek, K.; Lee, H. H.; Blaser, A.; Pruijn, F. B.; Anderson, R. F.; Shinde, S. S.; Wilson, W. R.; Denny, W. A. *J. Med. Chem.* **2008**, *51*, 6853.

(9) Taber, D. F.; Deker, P. B.; Fales, H. M.; Jones, T. H.; Lloyd, H. A. *J. Org. Chem.* **1988**, *53*, 2968.

(10) Taber, D. F.; Ruckle, R. E., Jr.; Hennessey, M. J. *J. Org. Chem.* **1986**, *51*, 4077.

(11) For the preparation of the Cu(II) complex from salicylaldehyde and *t*-butylamine, see: (a) Charles, R. G. *J. Org. Chem.* **1957**, *22*, 677. For its use as a cyclopropanation catalyst, see: (b) Corey, E. J.; Myers, A. G. *Tetrahedron Lett.* **1984**, *25*, 3559.

(12) Hendrickson, J. B.; Bergeron, R. *Tetrahedron Lett.* **1973**, *46*, 4607.