Synthesis of 1-Oxadecalones via the Lewis Acid Catalyzed Dihydropyrone Diels−Alder Reaction

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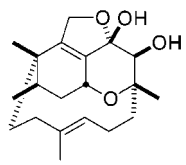
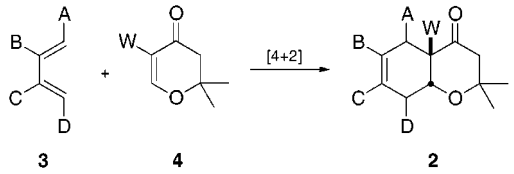
The 1-oxadecalin unit serves as the structural core for a diverse variety of natural products, including the PAF antagonist phomactin A (**1**, Figure 1).[1] Our interest in this area led us to consider an expedient method for the preparation of the 1-oxadecalone framework (e.g., **2**) as part of a synthetic effort geared toward this natural product.[2] Toward this end, we recently reported the facile preparation of highly functionalized 1-oxadecalone derivatives via the Diels−Alder reaction of 5-substituted 2,3-dihydro-4*H*-pyran-4-ones (**4**).[3] Though this work demonstrated for the first time that dihydropyrones could be used effectively as dienophiles in this application, in practice, the thermal reaction is limited to the use of dienes that contain two or more electron-donating groups due to the relatively low reactivity of the dihydropyrone dienophile. We now report an extension of the dihydropyrone Diels−Alder reaction via the use of Lewis acid catalysis.[4] In this way, the scope of this method can be expanded to include the synthesis of 1-oxadecalone derivatives that were previously inaccessible under thermal conditions.

Results and Discussion

We first examined the Diels−Alder reaction of the *tert*-butyldimethylsilyloxy derivative of Danishefsky's diene **5** with the 5-carbethoxy dihydropyrone derivative **4a** (Scheme 1). A variety of Lewis acids ($TiCl_4$, $AlCl_3$, $EtAlCl_2$, Et_2AlCl, and $BF_3{\cdot}OEt_2$) were screened as catalysts in this application, albeit without success. Indeed, under a variety of reaction conditions decomposition of the diene predominated even in the presence of substoichiometric amounts of Lewis acid and at low reaction temperatures.[5] However, when 1 equiv of $ZnCl_2$ was utilized as the catalyst, Diels−Alder reaction occurred cleanly to give the desired cycloadduct **6**[6,7] that was



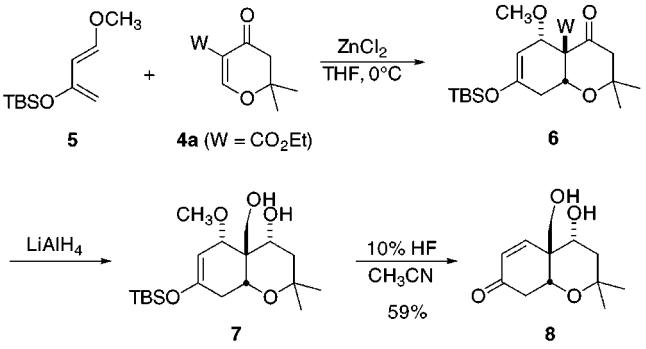
phomactin A (**1**)



3 **4** **2**

Figure 1.

Scheme 1



5 **4a** (W = CO_2Et) **6** **7** **8**

reduced directly with $LiAlH_4$.[8] Subsequent hydrolysis provided the 1-oxadecalone **8** in 59% overall yield.

As shown in Table 1, a variety of 1-oxadecalone derivatives are accessible via the Lewis acid-catalyzed Diels−Alder reaction of dihydropyrones **4**. In general, yields for the two-step cycloaddition/hydrolysis sequence exceed those observed when the corresponding Diels−Alder reaction is carried out under thermal conditions. For example, reaction of the doubly activated diene **13** with dihydropyrone **4a** at 110 °C (entry 2) provides, upon hydrolysis, oxadecalone **20a** in 48% overall yield. However, when the Lewis acid-catalyzed reaction is used in place of the thermal cycloaddition, yields for the sequence increase to 66% overall. Though in this same sequence, yields show no apparent improvement when the C5 nitrile **4b** is utilized (entry 3), in this case a substantial amount (21%) of the β-silyloxyketone (e.g., **11**, R = CH_3, R′ = OTBS, W = CN) is also recovered. A modest enhancement in overall yield is noted for the reaction of the activated diene **12** with dihydropyrone **4a** (entry 1).

Our previous studies demonstrated that monooxygenated dienes do not readily participate in the dihydropyrone Diels−Alder reaction under thermal conditions.[9] Indeed, dienes **14**−**18** do not undergo cycloaddition reactions with dihydropyrone **4a**, even at elevated reac-

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(1) Sugano, M.; Sato, A.; Iijima, Y.; Oshima, T.; Furuya, K.; Kuwano, H.; Hata, T.; Hanzawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 5463.

(2) For a synthetic approach to the tricyclic furanochroman core of phomactin A, see: Foote, K. M.; Hayes, C. J.; Pattenden, G. *Tetrahedron Lett.* **1996**, *37*, 275.

(3) Chen, D.; Wang, J.; Totah, N. I. *J. Org. Chem.* **1999**, *64*, 1776.

(4) The use of Lewis acid catalysis to enhance the reactivity of pyrone derivatives as dienophiles remains largely unexplored. For Lewis acid-catalyzed Diels−Alder reactions of benzopyrones, see: (a) Cremins, P. J.; Saengchantara, S. T.; Wallace, T. W. *Tetrahedron* **1987**, *43*, 2293. (b) Ohkata, K.; Kubo, T.; Miyamoto, K.; Ono, M.; Yamamoto, J.; Akiba, K. *Heterocycles* **1994**, *38*, 1483. (c) Hsung, R. P. *J. Org. Chem.* **1997**, *62*, 7904.

(5) In these applications the dihydropyrone dienophile is recovered intact. No other products were isolated from the reaction mixture.

(6) Compound **6** is formed as a ca. 8:1 mixture of diastereomers. The stereochemistry of the major product (shown) was determined by NOE studies on the diol **7** and its minor diastereomer.

(7) That this process is catalyzed by Lewis acid rather than a protic acid source is supported by the observation that, in the presence of $ZnCl_2$, the Diels−Alder reaction is facile even when the reaction is carried out in the presence of 0.2 equiv of di-*tert*-butylpyridine. Furthermore, trace amounts of protic acid (*p*-TsOH) do not catalyze the cycloaddition reaction in the absence of $ZnCl_2$.

(8) In this case, direct hydrolysis of the enol ether is complicated by the facile degradation of the product 1-oxadecalone. See ref 3.

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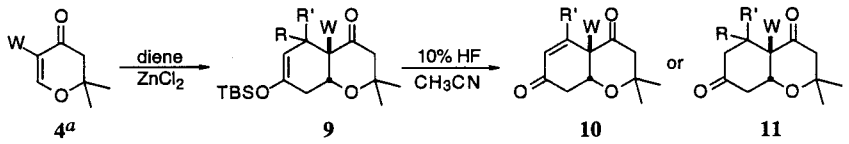
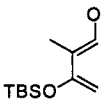
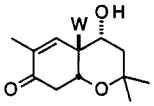
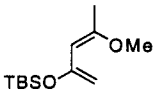
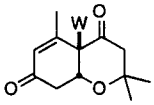
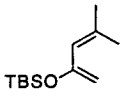
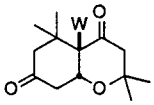
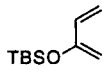
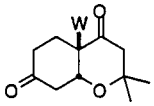
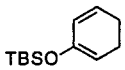
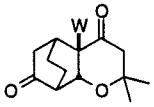
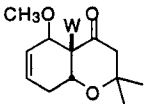
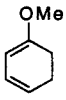
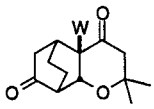
Table 1. Synthesis of 1-Oxadecalones



4[a] 9 10 11

entry	diene	reaction conditions	product	yield[b]
1	 **12**	**4a**, 0°C, THF, 2h; $NaBH_4$; 10% HF, CH_3CN	 **19a** W = CO_2Et	59% (56%)
2	 **13**	**4a**, 0°C, THF, 45 min; 10% HF, CH_3CN	 **20a** W = CO_2Et	66% (48%)
3	**13**	**4b**, 0°C, THF, 45 min; 10% HF, CH_3CN	**20b** W = CN	40%[c] (40%)
4	 **14**	**4a**, 25°C, THF, 2h; 10% HF, CH_3CN	 **21a** W = CO_2Et	76% (0%)
5	**14**	**4b**, 25°C, THF, 14h; 10% HF, CH_3CN	**21b** W = CN	51% (38%)
6	 **15**	**4a**, 25°C, THF, 20h; 10% HF, CH_3CN	 **22a** W = CO_2Et	73% (0%)
7	 **16**	**4a**, 25°C, THF, 2h; 10% HF, CH_3CN	 **23a** W = CO_2Et	62%[d] (0%)
8	 **17**	**4a**, 25°C, THF, 16h	 **24a** W = CO_2Et	0% (0%)
9	 **18**	**4a**, 25°C, THF, 2h; 10% HF, CH_3CN	 **23a** W = CO_2Et	55%[d] (0%)

[a] **4a** W = CO_2Et; **4b** W = CN; [b] Isolated yields based on starting dihydropyrone. Yields in parentheses reflect those obtained under thermal conditions; [c] Along with 21% of the corresponding β–silyloxy ketone; [d] Isolated as a *ca.* 1.4:1 mixture of diastereomers.

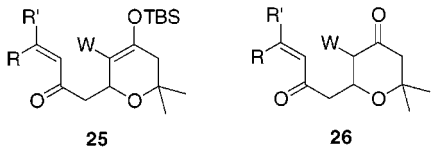
tion temperatures and under sealed tube conditions. However, in the presence of $ZnCl_2$, good to excellent overall yields of 1-oxadecalone derivatives can be obtained using dienes that contain a single oxygen substituent. It is interesting to note that while even hindered dienes such as **14** that are oxygenated at the 2-position undergo facile Diels–Alder reaction with dihydropyrone **4a** in the presence of Lewis acid (entries 4, 6, and 7), the corresponding 1-alkoxy derivatives are unreactive. Indeed, 1-methoxy-1,3-butadiene **17** does not undergo cycloaddition reactions with dihydropyrone **4a** in the presence of $ZnCl_2$ (entry 8),[10] while the use of 1-methoxy-1,3-cyclohexadiene **18** (entry 9) gives exclusively the oxadecalone **23a** via isomerization of the contaminant 1-methoxy-1,4-cyclohexadiene[11] to the diene **16** under the conditions of the reaction.

Though the use of Lewis acid extends both the utility and efficiency of the dihydropyrone Diels–Alder reaction, isolation of the 1-oxadecalone products is sometimes complicated by degradation of the initially formed cycloadduct. Upon prolonged exposure to $ZnCl_2$, significant amounts (10–25%) of the ring opened products **25** and **26** can be isolated from the reaction mixture (Figure 2), particularly when highly activated or hindered dienes are

(9) The corresponding pyrone derivatives do react with dienes of this type, although generally in low yields or under forcing conditions. (a) Groundwater, P. W.; Hibbs, D. E.; Hursthouse, M. B.; Nyerges, M. *Heterocycles* **1996**, *43*, 745. (b) Hsung, R. P. *Heterocycles* **1998**, *48*, 421. See also ref 4c.

(10) Nor does the reaction proceed in the presence of stronger Lewis acids such as Et_2AlCl, $EtAlCl_2$, or $AlCl_3$.

(11) 1-Methoxy-1,3-cyclohexadiene is purchased from Aldrich Chemical Co., Inc. and contains approximately 35% of 1-methoxy-1,4-cyclohexadiene.



25 **26**

Figure 2.

utilized. Compounds of this type are thought to arise via fragmentation of the initially formed Diels−Alder adduct **9**. Though the possibility of a stepwise reaction mechanism cannot be discounted,[12] in this case, direct cycloaddition to give the Diels−Alder adduct is supported by the observation that the amount of ring-opened products increases with increasing reaction time as determined by ^{1}H NMR of the crude reaction mixture. In general, this fragmentation can be suppressed by minimizing the reaction time and lowering the reaction temperature.[13]

The work described herein represents an extension of the dihydropyrone Diels−Alder reaction to include the preparation of 1-oxadecalone derivatives that were previously inaccessible by direct cycloaddition. Through the use of Lewis acid, dienes that contain a single oxygenated function at C2 can now be utilized in this application. This ability should allow for added flexibility in the synthesis of more complex substrates. In addition, overall yields of the oxadecalone products are generally higher, relative to those obtained using thermal cycloaddition protocols, when Lewis acid catalysis is utilized in the Diels−Alder reactions of dihydropyrone dienophiles with highly activated dienes. Further studies aimed at the application of this methodology to the synthesis of complex molecules are currently underway. These results will be reported in due course.

Experimental Section

General Methods. All air-sensitive reactions were performed in base washed, flame dried glassware under an argon atmosphere. Ether and tetrahydrofuran were dried over sodium/benzophenone ketyl and were distilled just prior to use. $ZnCl_2$ was flame dried just prior to use. All other reagents were reagent grade and purified where necessary. NMR coupling constants are reported in hertz. Mass spectra were obtained on a VG ZAB-HF high-resolution instrument by the University of Iowa Mass Spectrometry Laboratory. Elemental analyses were performed by Atlantic Microlab, Inc. (Norcross, GA).

General Procedure A: Reaction of Dihydropyrones 4a and 4b with Doubly Activated Dienes. A solution of $ZnCl_2$ (0.2 mmol) in THF (0.2 mL) was added to a mixture of the pyrone (0.2 mmol) and diene (0.8 mmol) in THF (0.2 mL) at 0 °C. The mixture was stirred at 0 °C for 2 h, after which time it was diluted with ether, washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was dissolved in CH_3CN (2 mL) and treated with 10% HF in CH_3CN (0.3 mL). The reaction was then allowed to stir for 2 h at room temperature, after which time it was diluted with ether, washed with saturated $NaHCO_3$ (aq) and brine, dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by flash chromatography (SiO_2; hexanes/EtOAc, 4:1).

Oxadecalone 8. Diels−Alder reaction of dihydropyrone **4a** and diene **5** was carried out as outlined in general procedure A with the following modification: Prior to hydrolysis, the crude cycloadduct was dissolved in ether (2 mL) and the resulting solution cooled to −78 °C. $LiAlH_4$ (1.5 mmol) was added and the reaction mixture allowed to warm gradually to room temperature over 3 h. After 16 h, it was diluted with wet ether (7 mL), treated sequentially with 3 M NaOH (0.08 mL) and H_2O (0.24 mL), and then stirred for 10 min. The resulting suspension was filtered through Celite and concentrated in vacuo. The crude material thus obtained was treated with 10% HF in CH_3CN as described above. The crude residue was purified by flash chromatography (SiO_2; $CHCl_3$/MeOH, 50:1−20:1) to provide the enone (59%) as a white solid (mp 126−127 °C). ^{1}H NMR ($CDCl_3$, 360 MHz): δ 7.01 (1H, dd, J = 10.4, 2.5), 6.22 (1H, d, J = 10.4), 4.33 (1H, m), 4.12 (1H, dd, J = 5.7, 3.0), 3.97 (1H, dd, J = 10.6, 5.5), 3.79 (1H, dd, J = 10.6, 3.4), 2.90 (1H, d, J = 3.0), 2.77 (1H, dd, J = 17.5, 3.2), 2.58 (1H, m), 2.50 (1H, ddd, J = 17.5, 3.0, 1.0), 1.72 (1H, dd, J = 12.7, 4.6), 1.49 (1H, t, J = 12.7), 1.24 (3H, s), 1.17 (3H, s). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 197.71, 146.47, 131.53, 72.69, 69.51, 68.25, 66.94, 46.62, 41.90, 40.90, 31.31, 22.63. IR (film): 3414, 1670 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{18}O_5$ ([M + Na]$^+$) 249.1103, found 249.1100. Anal. Calcd for $C_{12}H_{18}O_5$: C, 63.70; H, 8.02. Found: C, 63.36; H, 8.05.

Oxadecalone 19a. Diels−Alder reaction of dihydropyrone **4a** and diene **12** was carried out as outlined in general procedure A with the following modification: Prior to hydrolysis, the crude cycloadduct was passed through a plug of silica gel (hexanes/EtOAc, 13:1 containing 1% Et_3N) to remove lower R_f materials and concentrated. The partially purified product was then dissolved in MeOH and cooled to 0 °C. $NaBH_4$ (0.29 mmol) was added and the resulting solution stirred for 1 h at 0 °C. The reaction was quenched by addition of water, extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated. The crude material thus obtained was treated with 10% HF in CH_3CN as described above. The reside was purified by flash chromatography (SiO_2; hexanes/EtOAc, 3:1) to provide the 1-oxadecalone (59%) as a light yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.61 (1H, t, J = 1.2), 4.42 (1H, dt, J = 12.3, 3.8), 4.30 (1H, dd, J = 5.2, 2.3), 4.20 (2H, q, J = 7.1), 2.63 (1H, dd, J = 17.0, 2.2), 2.51 (1H, dd, J = 17.0, 2.7), 2.50 (1H, d, J = 3.4; OH), 1.86 (3H, d, J = 1.2), 1.67 (1H, dd, J = 12.7, 4.6), 1.42 (1H, t, J = 12.7), 1.25 (3H, t, J = 7.1), 1.22 (3H, s), 1.12 (3H, s). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 197.06, 172.42, 137.70, 135.93, 72.85, 70.30, 69.15, 62.02, 54.14, 41.90, 40.05, 31.14, 22.53, 16.14, 14.12. IR (film): 3457, 1724, 1683 cm^{-1}. HRMS (EI): calcd for $C_{15}H_{22}O_5$ ([M + H]$^+$: 282.1467, found 282.1482.

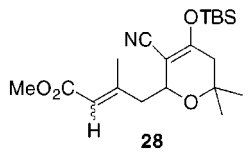
Oxadecalone 20a. Diels−Alder reaction of dihydropyrone **4a** and diene **13** with subsequent hydrolysis was carried out as outlined in general procedure A except that the Diels−Alder reaction was conducted at 0 °C for 45 min. Upon hydrolysis and purification, the 1-oxadecalone was obtained in 66% yield as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.14 (1H, br s), 4.92 (1H, t J = 3.0), 4.29 (2H, m), 2.68 (1H, dd J = 17.1, 2.9), 2.46 (1H, dd J = 17.1, 3.0), 2.37 (2H, s), 1.97 (3H, d J = 1.4), 1.29 (9H, m). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 203.31, 194.82, 167.54, 149.99, 129.60, 75.80, 72.62, 66.21, 62.23, 50.90, 40.58, 30.46, 23.44, 22.00, 13.99. IR (film): 1737, 1717, 1687 cm^{-1}. HRMS (EI): calcd for $C_{15}H_{20}O_5$ ([M]$^+$) 280.1312, found 280.1311.

Oxadecalone 20b. Diels−Alder reaction of dihydropyrone **4b** and diene **13** with subsequent hydrolysis was carried out as outlined in general procedure A except that the Diels−Alder reaction was conducted at 0 °C for 45 min. Upon hydrolysis and purification, the 1-oxadecalone was obtained in 40% yield as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.18 (1H, d, J = 1.5), 4.63 (1H, t, J = 3.0), 2.86 (1H, dd, J = 16.8, 2.9), 2.78 (1H, dd, J = 16.8, 3.1), 2.42 (2H, m), 1.90 (3H, d, J = 1.5), 1.31 (3H, s), 1.24 (3H, s). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 197.54, 192.99, 144.62, 130.57, 114.20, 76.76, 72.43, 55.97, 49.72, 40.58, 30.30, 22.90, 20.27. IR (film): 2243, 1726, 1689 cm^{-1}. HRMS (EI): calcd for $C_{13}H_{15}O_3N$ ([M + Na]$^+$) 256.0950, found 256.0939.

General Procedure B: Reaction of Dihydropyrones 4a and 4b with Monooxygenated Dienes. A solution of $ZnCl_2$ (0.2 mmol) in THF (0.2 mL) was added to a mixture of pyrone

(12) Lee, Y.-G.; Ishimaru, K.; Iwasaki, H.; Ohkata, K.; Akiba, K. *J. Org. Chem.* **1991**, *56*, 6, 2058.

(13) A related ring-opened system is obtained in the reaction of 1-(*tert*-butyldimethylsilyloxy)-1-methoxy-3-methyl-1,3-butadiene **27** with dihydropyrone **4a** in the presence of Et_2AlCl. Though we originally reported the product of this reaction to be the corresponding cycloadduct (ref 3), reevaluation of available spectral data has led us to conclude that this compound is instead the ring opened product **28**.



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(0.2 mmol) and diene (0.8 mmol) at room temperature. The mixture was stirred for 2 h, after which time it was diluted with ether, washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was dissolved in CH_3CN (2 mL) and treated with 10% HF in CH_3CN (0.3 mL). The reaction was then allowed to stir for 2 h at room temperature, after which time it was diluted with ether, washed with saturated $NaHCO_3$ (aq) and brine, dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by flash chromatography (SiO_2; hexanes/EtOAc, 4:1).

Oxadecalone 21a. Diels−Alder reaction of dihydropyrone **4a** and diene **14** with subsequent hydrolysis was carried out as outlined in general procedure B. Upon purification, the 1-oxadecalone was obtained in 76% yield as a white solid (mp 75−76 °C). ^{1}H NMR ($CDCl_3$, 360 MHz): δ 4.79 (1H, dd, J = 6.2, 2.0), 4.24 (2H, q, J = 7.1), 3.17 (1H, d, J = 13.7), 3.00 (1H, ddd, J = 15.2, 6.3, 0.8), 2.76 (1H, d, J = 15.0), 2.53 (1H, dt, J = 15.2, 2.1), 2.37 (1H, d, J = 15.0), 2.00 (1H, dd, J = 13.7, 2.4), 1.30 (6H, s), 1.29 (3H, t, J = 7.1), 1.20 (3H, s), 1.14 (3h, s). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 208.00, 204.39, 169.61, 74.63, 74.36, 64.88, 61.76, 53.20, 50.66, 44.40, 41.24, 29.18, 28.21, 26.99, 26.88, 14.07. IR (film): 1733, 1717 cm^{-1}. HRMS FAB): calcd for $C_{16}H_{24}O_5$ ([M + Na]$^+$) 319.1521, found 319.1523. Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 65.00; H, 8.26.

Oxadecalone 21b. Diels−Alder reaction of dihydropyrone **4b** and diene **14** with subsequent hydrolysis was carried out as outlined in general procedure B except that the diene and dienophile were stirred for 20 h at room temperature. Upon purification, the 1-oxadecalone was obtained in 51% yield as a white solid (mp 130−132 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.71 (1H, dd, J = 5.8, 1.8), 2.95 (1H, ddd, J = 15.6, 5.8, 0.7), 2.79 (1H, d, J = 13.9), 2.65 (1H, dt, J = 15.6, 2.2), 2.60 (1H, d, J = 16.6), 2.49 (1H, d, J = 16.6), 2.23 (1H, dd, J = 13.9, 2.2), 1.32 (3H, s), 1.29 (3H, s), 1.24 (3H, s), 1.22 (3H, s). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 204.51, 199.00, 117.30, 74.62, 73.57, 58.11, 53.55, 51.08, 43.56, 41.57, 30.48, 28.77, 26.39, 24.96. IR (film): 2244, 1722, 1712 cm^{-1} HRMS (EI): calcd for $C_{14}H_{19}O_3N$ ([M]$^+$) 249.1365, found 249.1340.

Oxadecalone 22a. Diels−Alder reaction of dihydropyrone **4b** and diene **15** with subsequent hydrolysis was carried out as outlined in general procedure B except that the diene and dienophile were stirred for 20 h at room temperature. Upon purification, the 1-oxadecalone was obtained in 73% yield as a colorless oil. ^{1}H NMR ($CDCl_3$, 360 MHz): δ 4.85 (1H, m), 4.32 (2H, q, J = 7.2), 2.61 (1H, d, J = 14.7), 2.59−2.38 (6H, m), 2.35 (1H, d, J = 14.5), 1.34 (3H, s), 1.32 (3H, t, J = 7.2), 1.28 (3H, s). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 207.12, 205.31, 169.30, 75.66, 72.71, 61.82, 61.39, 48.36, 44.04, 37.89, 30.60, 26.69, 24.74, 14.11. IR (film): 1727 cm^{-1}. Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.53; H, 7.64.

Oxadecalone 23a. Diels−Alder reaction of dihydropyrone **4a** and diene **16** with subsequent hydrolysis was carried out as outlined in general procedure B. Upon purification, the 1-oxadecalone was obtained in 62% yield to provide the 1-oxadecalone as a 1.4:1 mixture of diastereomers that could be separated. Major diastereomer: white solid (mp 88−89 °C). ^{1}H NMR ($CDCl_3$, 360 MHz): δ 5.17 (1H, d, J = 4.7), 4.19 (2H, m), 2.98 (1H, m), 2.68 (1H, m), 2.62 (1H, d, J = 13.9), 2.40 (1H, d, J = 13.9), 2.29 (1H, dd, J = 19.1, 2.4), 2.19 (1H, m), 2.08 (1H, dt, J = 19.1, 3.1), 1.90 (1H, m), 1.61 (1H, m), 1.47 (1H, m), 1.45 (3H, s), 1.29 (3H, s), 1.24 (3H, t, J = 7.0). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 212.01, 201.05, 169.06, 76.23, 70.66, 63.76, 62.41, 49.61, 48.37, 40.91, 31.83, 30.89, 27.10, 20.16, 15.29, 13.97. IR (film): 1733, 1721 cm^{-1}. HRMS (FAB): calcd for $C_{16}H_{22}O_5$ ([M + Na]$^+$) 317.1365, found 317.1362. Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.22; H, 7.49. Minor diastereomer: ^{1}H NMR ($CDCl_3$, 360 MHz): δ 5.34 (1H, dd, J = 4.7, 1.4), 4.25 (2H, m), 3.01 (1H, m), 2.69 (1H, d, J = 13.0), 2.64 (1H, m), 2.46 (1H, dt, J = 19.1, 2.3), 2.36 (1H, d, J = 13.0), 2.12 (1H, dd, J = 19.1, 3.8), 1.82 (2H, m), 1.54 (2H, m), 1.44 (3H, s), 1.28 (3H, t, J = 7.1), 1.18 (3H, s). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 212.11, 201.36, 169.58, 76.81, 74.16, 64.46, 62.37, 49.37, 48.28, 41.13, 32.46, 30.27, 27.04, 21.98, 18.58, 14.05. IR (film): 1734, 1718 cm^{-1}. HRMS (FAB): calcd for $C_{16}H_{22}O_5$ ([M + Na]$^+$) 317.1365, found 317.1364.

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Supporting Information Available: Copies of ^{1}H and ^{13}C spectra for compounds **8** and **19**−**23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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