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The Synthesis of Deoxyfusapyrone. 1. An Approach to the Pyrone Moiety

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An effective synthesis of the C1−C10 component of deoxyfusapyrone has been achieved that will allow for the synthesis of both the (*R*) and (*S*) form of the C-8 chiral center starting from optically pure (+)- and (−)-3,3-dimethyl-2-hydroxy-gammalactone (pantolactone).

Introduction

Deoxyfusapyrone (**1**), a secondary metabolite isolated from rice cultures of *Fusarium semitectum*, has demonstrated pronounced anti-fungal activity against plant pathogenic and/or mycotoxigenic filamentous fungi.[1] Compound **1** is a candidate for biotechnology applications and has potential as a natural and safe herbicide to suppress parasite seed germination.[2]

Structurally, **1** can be divided into three components: a 4-deoxy glucose moiety, a pyrone component, and a long-chain polyene fragment. Synthetically, there are a number of challenges to consider when planning a route for the preparation of **1**. In particular, stereoselective bond formation between the sp^2 carbon of the pyrone (C3) to the anomeric carbon of the sugar, the bis allylic chiral center at C13, and the neopentyl/allylic chiral center at C8 make the preparation of each subsection difficult. Owing to the complexity of the structure, three of the seven stereocenters of **1** remain undetermined, which adds further intrigue to its synthesis. Thus, any proposed synthetic route would have to be general enough to facilitate the preparation of all possible diastereomers of **1** to confirm the relative and absolute stereochemistry of the compound.

The route that we have proposed for the preparation of **1** is modular and allows for the parallel synthesis of all eight diastereomers that arise from unassigned stereocenters 8, 13, and 17 (i.e., the deoxy glucose stereochemistry has been assigned unambiguously).[1] The disconnections outlined in Figure 1 require the synthesis of **2**, **3**, and **4** as the principal building blocks. The alkyne in **3** will be hydrometalated in situ and connected to **4** by cross-coupling. Metalation of the resultant pyrone followed by addition to epoxy glycal **2** will provide **1**.

Central to this approach is the stereoselective synthesis of both enantiomers of **3**, which is the focus of this paper. 4-Hydroxy-6-methyl-2-pyrone (**6**) is available inexpensively, thus we were drawn strongly toward trying to work at alkylating the methyl position via extended enolate chemistry. However, this did not prove fruitful in preliminary studies, especially when trying to alkylate stereoselectively. We also considered an enantioselective addition of an acetylene unit to an aldehyde (**7**) but were concerned about the gem dimethyl next to the aldehyde affecting both reactivity and selectivity at the carbonyl site. With these issues in mind, it occurred to us that starting off with C8 optically pure and already bearing the alcohol would prove to be a productive approach to make both enantiomers and to eliminate late-stage enantioselective transformations. Conveniently, the entire carbon framework of pantolactone (**5**), which is available in both (*R*) and (*S*) forms, can be manipulated into carbons 6−9 of **3** to provide both enantiomers of **3**. This approach is the opposite of those that begin with the pyrone intact as the ring has to be constructed at the end and this chemistry is discussed herein.

Results and Discussion

Pantolactone was reductively opened efficiently to triol **8**,[3] which was then selectively protected under thermodynamic conditions with acid and *p*-methoxybenzaldehyde dimethyl acetal.[4] After oxidation,[5] the Corey−Fuchs procedure provided acetylene **11** (Scheme 1).[6] At this stage we attempted selective deprotection of the primary alcohol to produce the PMB-protected secondary alcohol using DIBAL-H.[7] Despite repeated attempts, we could not get this reaction to proceed selectively, always obtaining a mixture of the free primary and secondary alcohol in a ratio of approximately 1.2:1, respectively. Ultimately, the free primary alcohol **15** was obtained by a short series of selective protection/deprotection steps (Scheme 2).[8] We are continuing our efforts in the mean-

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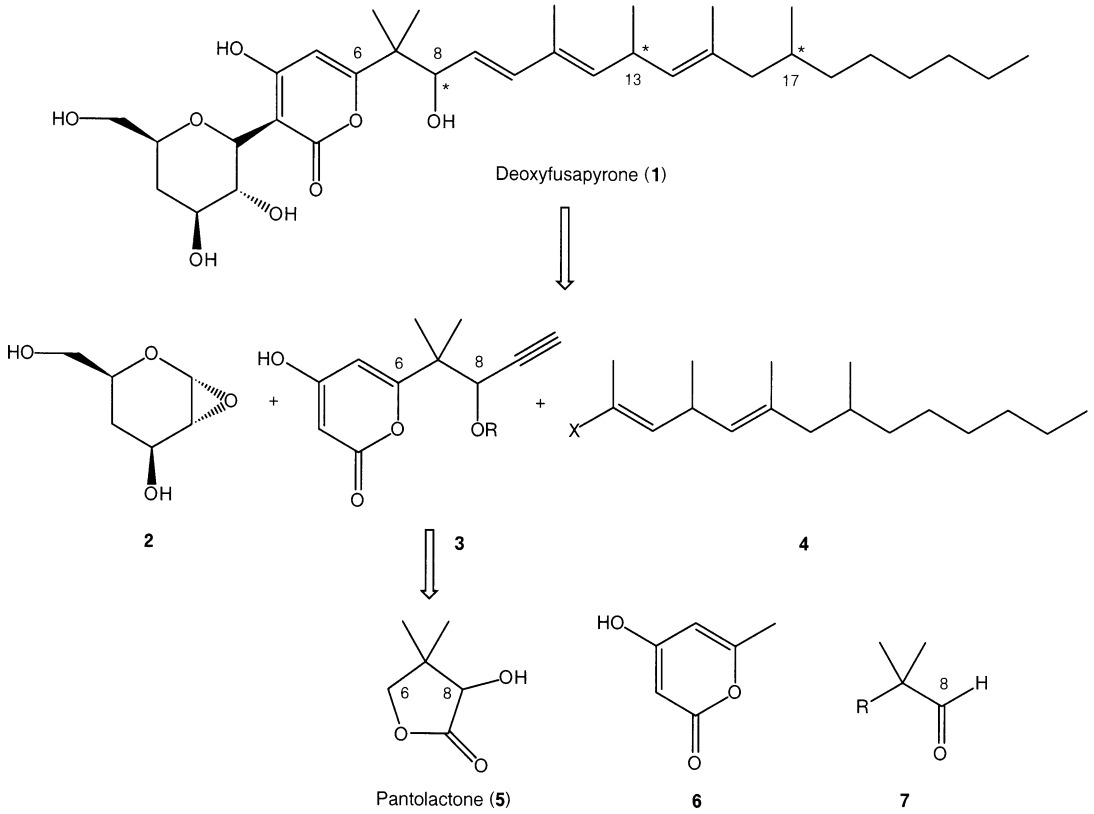
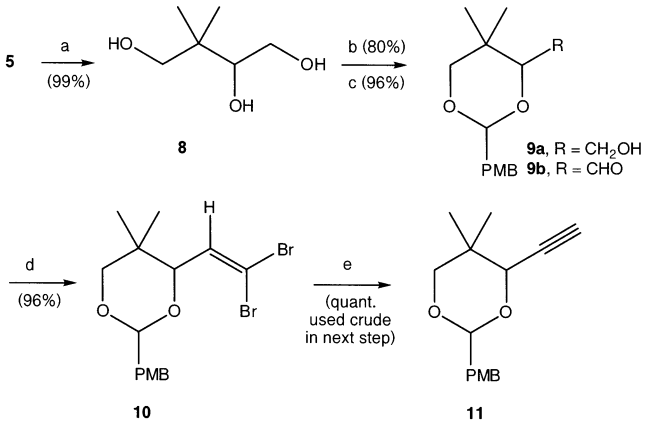


FIGURE 1. Retrosynthetic analysis of deoxyfusapyrone.

SCHEME 1[a]

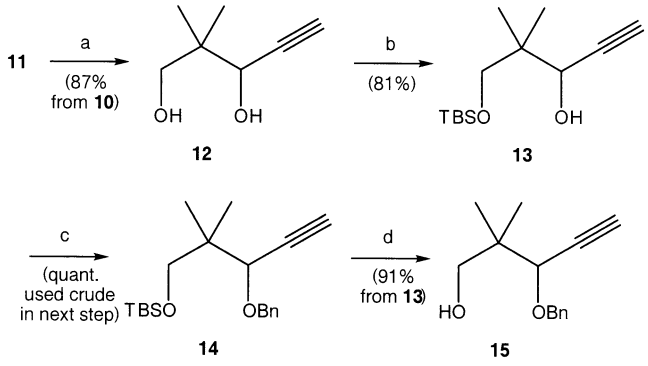


[a] Reagents and conditions: (a) LAH, THF, 0 °C; (b) PMPCH(OMe)$_2$, camphor sulfonic acid, CH_2Cl_2, rt; (c) DMSO, $(COCl)_2$, TEA, CH_2Cl_2, −78 °C to rt; (d) CBr_4, PPh_3, CH_2Cl_2, rt; (e) n-BuLi, THF, −78 °C to rt, then NH_4Cl (aq).

time to selectively open the dioxane ring using other procedures.[9]

Oxidation followed by aldol condensation[10] provided **17** as a mixture of diastereomers (Scheme 3). Formation of

SCHEME 2[a]



[a] Reagents and conditions: (a) 80% HOAc, rt, 2 h;(b) TBDMSCl, TEA, 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2, rt; (c) NaH, THF, then BnBr, rt; (d) TBAF, THF, rt.

β-keto ester **18** was followed by saponification to provide **19** and condensation with 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid) to yield the critical tetracarbonyl penultimate compound **20**.[4]

Thermal rearrangement of **20** in refluxing toluene for a short period of time selectively yielded carboxylic acid **21**[11] quantitatively, which upon re-submission to these reaction conditions decarboxylated providing the desired protected alcohol **22** in excellent yield (Scheme 4).[4] Conveniently, the two steps can be compressed into one by simply heating for a prolonged period of time. Deprotection of **22** would yield **3**, although the alcohol would be kept protected until after the bond connections to **2** and **4** have been established to complete the synthesis of the various diastereoisomers of **1**.

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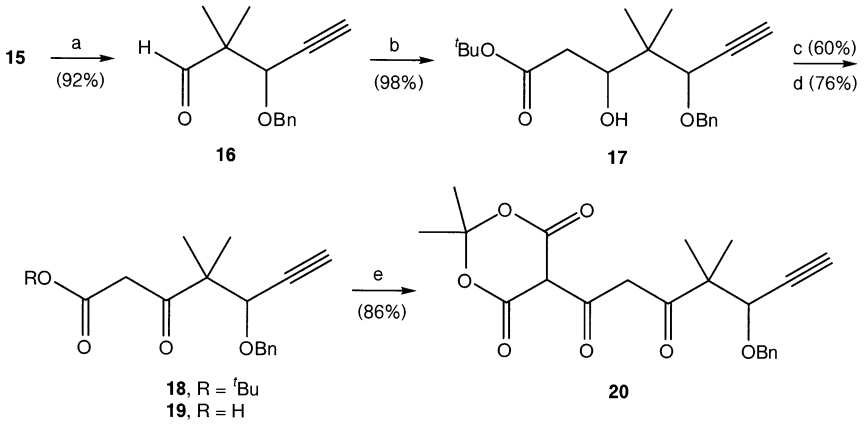
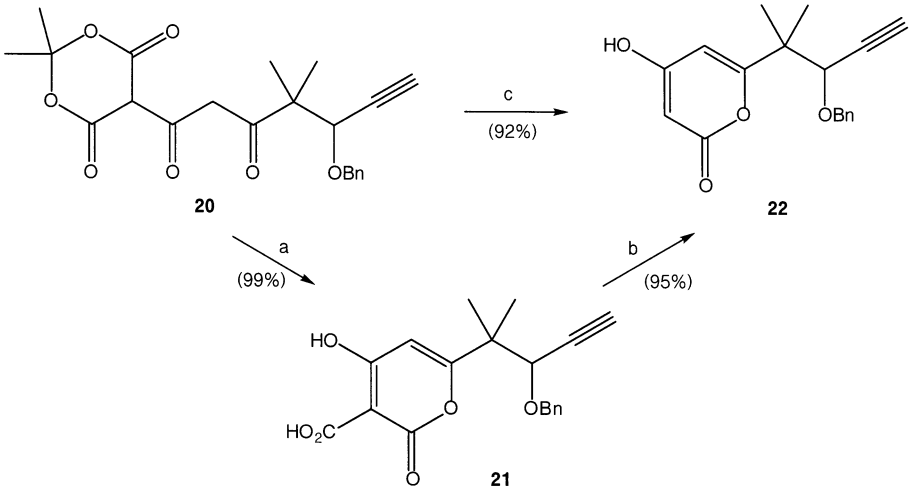
SCHEME 3[a]



[a] Reagents and conditions: (a) DMSO, $(COCl)_2$, TEA, CH_2Cl_2, −78 °C to rt; (b) $LiCH_2COO^tBu$, THF, −78 °C to rt, then NH_4Cl (aq); (c) PCC, NaOAc, CH_2Cl_2, rt; (d) TFA, CH_2Cl_2, 0 °C; (e) Meldrum's acid, TEA, DMAP, DCC, CH_2Cl_2, rt.

SCHEME 4[a]



[a] Reagents and conditions: (a) reflux, toluene, 1.5 h; (b) reflux, toluene, 30 h; (c) reflux, toluene, 72 h.

Mechanistic Considerations. This last result has shed new evidence on the mechanism of similar cyclization/decarboxylation reactions reported in the literature. Tetracarbonyl compounds resembling **23** (see Figure 2) were reported to undergo decarboxylation first leading to dioxinones **24**[4] which are known to be in equilibrium between the corresponding ketene (**25**) and acetone.[12] Cyclization of the enol onto the ketene moiety would then provide the pyrone (**26**) directly. Indeed, when compounds resembling **24** were prepared by an alternate means, heating them provided the pyrone, which in this case proceeds via the corresponding ketene with little doubt.[12] The results from the present study suggest that **20** (or **23**) is thermally stable toward decarboxylation and it undergoes concurrent rearrangement and liberation of acetone with no decarboxylation (via a structure like **27**). However, on prolonged heating, decarboxylation does take place providing **22** (or **26**). This finding has provided a new and very efficient synthesis of 3-carboxypyrones and we are presently working to determine the scope of this synthetic sequence.

In summary, a concise and efficient synthetic route has been devised to prepare pyrone **22**, which has a chiral alcohol-bearing center on it adjacent to the gem dimethyl group. This route will allow the synthesis of both the (*R*) and (*S*) isomers of **22** beginning with both isomers of optically pure pantolactone. The careful isolation of the 3-carboxypyrone **28** has cast doubt on the currently accepted mechanism for the decarboxylative cyclizations of tetracarbonyl compounds resembling **23** while providing an effective entry into the synthesis of 3-carboxypyrones.

Experimental Section

General Procedures. All reactions were carried out under dry argon unless otherwise indicated. Solvents were distilled prior to use: Et_2O was distilled from sodium benzophenone; CH_2Cl_2 was distilled from CaH_2. Melting points are uncorrected. Proton and carbon NMR spectra were recorded at 400 and 100 MHz, respectively. NMR chemical shifts are listed relative to $CHCl_3$ (δ 7.24) for ^1H NMR and (δ 77.00) for ^{13}C NMR. All carbon NMR spectra were obtained using the

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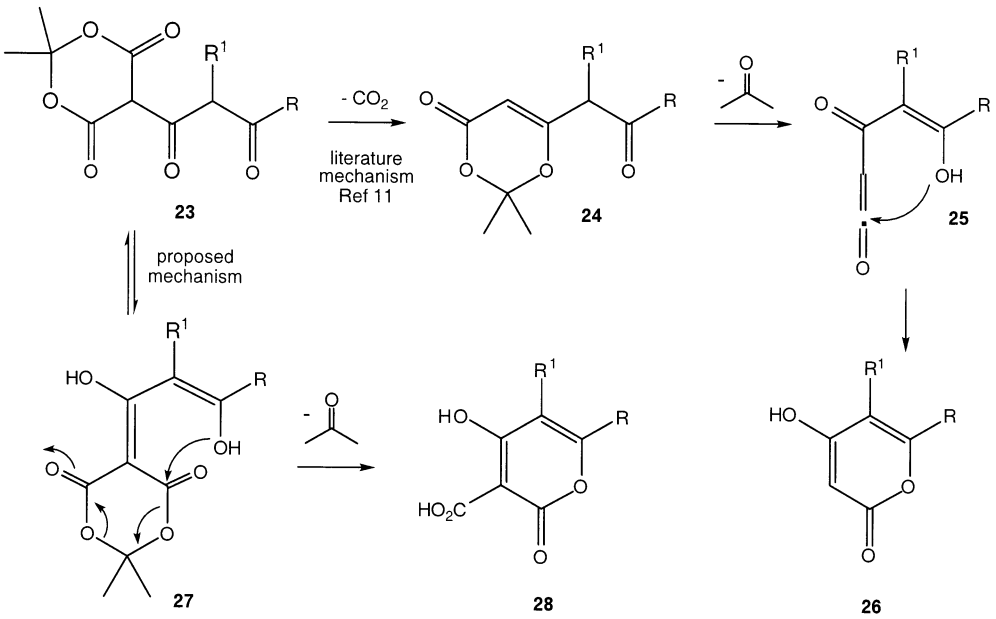

FIGURE 2. Mechanism of the cyclization/decarboxylation sequence.

attached proton test (APT) pulse sequence where carbons attached to an odd number of protons are down (−) and all other signals are up (+).

3,3-Dimethylbutane-1,2,4-triol (8), [2-(4-Methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl]methanol (9a), and 2-(4-Methoxyphenyl)-5,5-dimethyl-1,3-dioxane-4-carbaldehyde (9b). These compounds were prepared following the procedure outlined by Lokot and co-workers.[4] Spectral data generated for these compounds compared well with those reported.

4-(2,2-Dibromovinyl)-2-(4-methoxyphenyl)-5,5-dimethyl-[1,3]dioxane (10). To a stirred brown suspension of Ph_3P (71.34 g, 272 mmol) and CBr_4 (45.1 g, 136 mmol) in CH_2Cl_2 (150 mL) was added a solution of aldehyde **9b** (17.0 g, 68 mmol) in CH_2Cl_2 (50 mL) at 0 °C. The mixture was stirred for 2 h at rt, diluted with ether, and filtered. The brown solid was washed with ether. Hexane was added to the filtrate resulting in additional precipitation. The product was filtered off, the volume of the mother liquor was reduced, and the flask was placed in the refrigerator for 16 h resulting in additional precipitation. This process was repeated twice more providing 27.5 g of **10** in total (96%) as white needles. Mp 77−78 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 7.46 (d, J = 8.1 Hz, 2H), 6.93 (d, J = 8.1 Hz, 2H), 6.53 (d, J = 8.5 Hz, 1H), 5.52 (s, 1H), 4.35 (d, J = 8.6 Hz, 1H), 3.83 (s, 3H), 3.80 (d, J = 11.6 Hz, 1H), 3.71 (d, J = 11.6 Hz, 1H), 1.25 (s, 3H), 0.89 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 160.2 (+), 134.9 (−), 130.6 (+), 127.6 (−), 113.8 (−), 101.9 (−), 93.5 (+), 85.0 (−), 78.5 (+), 55.3 (−), 34.1 (+), 21.4 (−), 19.4 (−). Anal. Calcd for $C_{15}H_{18}Br_2O_3$: C, 44.36; H, 4.47. Found: C, 44.67; H, 4.58.

4-Ethynyl-2-(4-methoxyphenyl)-5,5-dimethyl[1,3]-dioxane (11). To a stirred solution of **10** (15.28 g, 37.64 mmol) in THF (120 mL) was added *n*-BuLi (82.8 mmol, 2.2 equiv, 1.5 M solution in hexanes) at −78 °C. The mixture was allowed to reach rt over a period of 2 h where it was stirred for 0.5 h. A saturated NH_4Cl solution was added and the mixture was extracted into ether (2×). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed in vacuo to give the crude **11** as a light yellow solid that underwent ketal hydrolysis without further purification.

2,2-Dimethylpent-4-yne-1,3-diol (12). Crude alkyne **11** (9.28 g, 37.64 mmol) was dissolved in 80% acetic acid and stirred for 2 h at rt. The acetic acid was removed in vacuo and the product was purified by flash chromatography (4:1 hexane/ethyl acetate) providing 4.19 g of **12** (87% from **10**) as a white solid. Mp 54−56 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 4.31 (s, 1H), 3.76 (d, J = 10.8 Hz, 1H), 3.51 (d, J = 10.8 Hz, 1H), 2.81 (br s, 2H), 2.51 (d, J = 1.8 Hz, 1H), 1.06 (s, 3H), 1.02 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 83.1 (+), 74.2 (+), 70.4 (+), 70.1 (−), 39.2 (+), 21.5 (−), 19.7 (−); IR (neat) 3307, 2114 cm^{-1}.

5-(*tert*-Butyldimethylsilanyloxy)-4,4-dimethylpent-1-yn-3-ol (13). To a solution of diol **12** (2.05 g, 16 mmol), TBDMSCl (2.65 g, 17.6 mmol), and DMAP (0.08 g, 0.64 mmol) in CH_2Cl_2 (30 mL) was added triethylamine (2.5 mL, 1.78 g, 17.6 mmol) at rt. After being stirred for 16 h, the mixture was washed successively with water, saturated NH_4Cl, and brine. The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was removed in vacuo. Purification by flash chromatography (hexane:ethyl acetate, 15:1) provided 3.15 g of **13** (81%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 4.20 (d, J = 5.8 Hz, 1H), 3.76 (d, J = 9.7 Hz, 1H), 3.75 (s, 1H), 3.39 (d, J = 9.8 Hz, 1H), 2.42 (s, 1H), 1.02 (s, 3H), 0.93 (s, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 83.5 (+), 73.4 (+), 71.0 (+), 70.4 (−), 39.0 (+), 25.8 (−), 21.6 (−), 20.2 (−), 18.1 (+), −5.7 (−); IR (neat) 3464, 3312, 2114 cm^{-1}.

(3-Benzyloxy-2,2-dimethylpent-4-yne)-1-*tert*-butyldimethylsilane (14). To a suspension of NaH (0.20 g, 5.0 mmol, 60% suspension in mineral oil) in THF (5 mL) was added a solution of **13** (1.10 g, 4.52 mmol) in THF (8 mL) at 0 °C. After the solution was stirred for 0.5 h, benzyl bromide (0.70 mL, 1.01 g, 5.89 mmol) and DMF (3 mL) were added and the mixture was stirred for 16 h at rt. Saturated NH_4Cl solution (30 mL) was added and the mixture was extracted with ether (3×). The combined organic solutions were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Following solvent removal in vacuo, the crude material was directly desilylated.

3-Benzyloxy-2,2-dimethylpent-4-yn-1-ol (15). To a solution of crude **14** in THF (10 mL) was added TBAF (1.0 M in THF, 6.8 mL) at rt. After the mixture was stirred for 16 h, saturated NH_4Cl was added and the solution was extracted with ether (2×). The combined ether extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed in vacuo and the product was purified by flash chromatography (hexane:ethyl acetate, 8:1) to provide 901 mg of **15** (91% from **13**) as a clear, colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.39−7.32 (m, 5H), 4.89 (d, J = 11.8 Hz, 1H), 4.52 (d, J = 11.8 Hz, 1H), 4.01 (d, J = 1.4 Hz, 1H), 3.66 (dd, J = 10.9 Hz, 6.0 Hz, 1H), 3.44 (dd, J = 10.9 Hz, 6.0 Hz, 1H), 2.55 (d, J = 1.4 Hz, 1H), 2.45 (t, J = 6.0 Hz, 1H), 1.06 (s, 3H), 1.05

(s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.5 (+), 128.5 (−), 128.0 (−), 127.9 (−), 80.7 (+), 76.0 (−), 75.6 (+), 71.1 (+), 70.0 (+), 39.6 (+), 21.8 (−), 20.1 (−); IR (neat) 3424, 3297, 2110 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{18}O_2$ [M]$^+$ 218.1307, found 218.1297.

3-Benzyloxy-2,2-dimethylpent-4-ynal (16). To a stirred solution of oxalyl chloride (0.20 mL, 0.290 g, 2.29 mmol) in CH_2Cl_2 (15 mL) at −78 °C was added DMSO (0.36 mL, 0.390 g, 5.0 mmol) dropwise. The mixture was stirred for 0.5 h after which **15** (0.453 g, 2.08 mmol) in CH_2Cl_2 (15 mL) was added via cannula. After the solution was stirred for 40 min, triethylamine (0.87 mL, 0.632 g, 6.24 mmol) was added and the mixture was allowed to warm to rt over 2 h. Water (30 mL) was added and the phases were separated. The organic layer was washed with brine (2×), dried over anhydrous $MgSO_4$, and filtered. The solvent was removed in vacuo and the crude product was purified by flash chromatography (hexane:ethyl acetate, 5:1) to provide 415 mg of **16** (92%) as a clear oil. ^{1}H NMR ($CDCl_3$) δ 9.63 (s, 1H), 7.40−7.32 (m, 5H), 4.87 (d, J = 11.9 Hz, 1H), 4.53 (d, J = 11.9 Hz, 1H), 4.22 (s, 1H), 2.60 (s, 1H), 1.27 (s, 3H), 1.15 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 203.9 (−), 137.3 (+), 128.4 (−), 128.0 (−), 127.9 (−), 79.3 (+), 76.5 (+), 72.8 (−), 71.0 (+), 50.0 (+), 19.3 (−), 17.3 (−); IR (neat) 3287, 2873, 2720, 2113, 1729 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{16}O_2$ [M]$^+$ 215.1072, found 215.1097.

***tert*-Butyl 5-Benzyloxy-3-hydroxy-4,4-dimethylhept-6-ynoate (17).** To a solution of diisopropylamine (0.54 mL, 0.39 g, 3.85 mmol) in THF (5 mL) was added *n*-BuLi (1.5 M in hexane, 2.6 mL, 3.85 mmol) dropwise at −78 °C. After 10 min, *tert*-butyl acetate was added and the mixture was stirred for 40 min after which a solution of **16** (0.756 g, 3.50 mmol) in THF (5 mL) was added via cannula. The mixture was allowed to warm to rt slowly at which time a solution of saturated NH_4-Cl was added. The mixture was extracted with ether and the combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Following filtration, the solvent was removed in vacuo and the crude material was purified by flash chromatography (hexane:ethyl acetate, 10:1) to give 1.14 g of **17** (98%) as a colorless oil. This material was used directly in the next step with no further purification. ^{1}H NMR ($CDCl_3$) δ 7.38−7.31 (m), 4.87 (d), 4.51 (d), 4.52−4.13 (m), 3.36 (d), 3.18 (d), 2.53 (s), 2.39−2.29 (m), 1.49 (s), 1.09 (s), 1.02 (s), 0.99 (s), 0.98 (s); HRMS (EI) calcd for $C_{20}H_{28}O_4$ [M + H]$^+$ 333.2066, found 333.2069.

***tert*-Butyl 5-Benzyloxy-4,4-dimethyl-3-oxohept-6-ynoate (18).** A mixture of **17** (0.446 g, 1.343 mmol), sodium acetate (0.1 g), and PCC (1.74 g, 8.06 mmol, 6 equiv) in CH_2Cl_2 (20 mL) was stirred for 16 h at rt and then diluted with ether (20 mL). The solution was decanted out of the flask and passed through a short column of Florisil. The column was flushed with ether and the eluent pooled. Following solvent removal in vacuo, the product was purified by flash chromatography (hexane:ethyl acetate, 15:1) to afford 264 mg of **18** (60%) as a colorless oil. The reaction was very clean and unreacted β-hydroxyester **17** (0.135 g, 30% recovered) was readily recovered. ^{1}H NMR ($CDCl_3$) δ 12.51 (s, 1H), 7.34 (br s, 5H), 4.81 (d, J = 11.6 Hz, 1H), 4.48 (d, J = 11.2 Hz, 1H), 3.48 (s, 2H), 2.55 (s, 1H), 1.48 (s, 9H), 1.35 (s, 3H), 1.22 (s, 3H).

5-Benzyloxy-4,4-dimethyl-3-oxohept-6-ynoic Acid (19). Trifluoroacetic acid (1.5 mL) was added to a stirred solution of **18** (0.450 g, 1.364 mmol) in CH_2Cl_2 (3 mL) at 0 °C. After the mixture was stirred for 2.5 h, a solution of saturated sodium bicarbonate was added dropwise until the bubbling subsided. A saturated NH_4Cl solution (10 mL) was added to keep the mixture mildly acidic and the mixture was extracted with ether (3×). The combined organic layers were washed with brine (2×), dried over anhydrous $MgSO_4$, and filtered. Following solvent removal in vacuo, the crude product (285 mg, 76%) was collected and used in the next step with no further purification. ^{1}H NMR ($CDCl_3$) δ 12.12 (s, 1H), 7.39−7.33 (m, 5H), 4.83 (d, J = 11.6 Hz, 1H), 4.51 (d, J = 11.6 Hz, 1H), 4.38 (s, 1H), 3.63 (d, J = 3.2 Hz, 2H), 2.60 (s, 1H), 1.38 (s, 3H), 1.25 (s, 3H).

5-(1,3-Dioxo-4,4-dimethyl-5-benzyloxy-6-yne)-2,2-dimethyl[1,3]dioxane-4,6-dione (20). To a solution of Meldrum's acid (157 mg, 1.092 mmol), DMAP (38 mg, 0.312 mmol), and DCC (225 mg, 1.092 mmol) in CH_2Cl_2 (1 mL) was added a solution of **19** (285 mg, 1.04 mmol) in CH_2Cl_2 (4 mL). The mixture was stirred for 16 h at rt, diluted with ether (10 mL), and filtered. The white solid was washed with ether and the combined organic solution was washed successively with 5% HCl, water, and brine and then dried over anhydrous $MgSO_4$. Following filtration, the solvent was removed in vacuo providing essentially pure **20** (359 mg, 86% yield). The product was re-crystallized from ether/pentane (298 mg, 71% yield) as a yellow solid. ^{1}H NMR ($CDCl_3$) δ 15.0 (br s, 1H), 7.37−7.31 (m, 5H), 4.83 (d, J = 11.6 Hz, 1H), 4.50 (d, J = 11.4 Hz, 1H), 4.44 (d, J = 16.2 Hz, 1H), 4.29 (s, 1H), 4.19 (d, J = 16.4 Hz, 1H), 2.58 (d, J = 1.3 Hz, 1H), 1.76 (s, 6H), 1.42 (s, 3H), 1.30 (s, 3H); ^{13}C NMR ($CDCl_3$) APT, δ 205.6 (+), 190.3 (+), 170.0 (+), 160.6 (+), 137.1 (+), 128.4 (−), 128.2 (−), 127.9 (−), 105.4 (+), 93.7 (+), 79.6 (+), 76.3 (+), 74.5 (−), 71.3 (+), 52.3 (+), 47.3 (+), 26.9 (−), 22.0 (−), 19.3 (−); IR (neat) 3286, 2113, 1739, 1717 cm^{-1}.

6-(2-Benzyloxy-1,1-dimethylbut-3-ynyl)-4-hydroxy-2-oxo-2*H*-pyran-3-carboxylic Acid (21). A solution of **20** (78 mg, 0.195 mmol) in dry toluene (4 mL) was heated under reflux for 1.5 h and then cooled to rt. The solvent was removed in vacuo to provide essentially pure product that was purified by re-crystallization from ether/pentane to provide 66 mg of **21** (99%) as a white powder. Mp 90−92 °C dec; ^{1}H NMR ($CDCl_3$) δ 13.92 (s, 1H), 12.58 (br s, 1H), 7.33−7.21 (m, 5H), 6.30 (s, 1H), 4.81 (d, J = 12.0 Hz, 1H), 4.46 (d, J = 12.1 Hz, 1H), 4.35 (d, J = 1.3 Hz, 1H), 2.58 (d, J = 1.6 Hz, 1H), 1.45 (s, 3H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.0 (+), 174.1 (+), 171.2 (+), 165.8 (+), 136.8 (+), 128.5 (−), 128.1 (−), 128.0 (−), 101.5 (−), 90.7 (+), 79.1 (+), 76.6 (+), 72.9 (−), 71.1 (+), 45.1 (+), 22.8 (−), 20.0 (−); IR (neat) 3288, 3200−2400 (br), 2114, 1713, 1669 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{18}O_6$ [M]$^+$ 342.108, found 342.108.

6-(2-Benzyloxy-1,1-dimethylbut-3-ynyl)-4-hydroxypyran-2-one (22). A solution of **20** (69 mg, 0.173 mmol) in dry toluene (5 mL) was heated under reflux for 72 h and then cooled to rt. The solvent was removed in vacuo to provide essentially pure product that was purified by re-crystallization from ether/pentane to provide 47 mg of **22** (92%).

Pyrone **22** was also obtained from compound **21** by decarboxylation. A solution of **21** (25 mg, 0.073 mmol) in dry toluene (3 mL) was heated under reflux for 24 h and then cooled to rt. The solvent was removed to provide essentially pure product that was purified by re-crystallization from ether/pentane to provide 21 mg of **22** (95%) as light yellow prisms. Mp 123−125 °C ($CHCl_3$/hexanes); ^{1}H NMR ($CDCl_3$) δ 11.08 (br s, 1H), 7.32−7.21 (m, 5H), 6.16 (s, 1H), 5.63 (s, 1H), 4.80 (d, J = 11.9 Hz, 1H), 4.47 (d, J = 11.8 Hz, 1H), 4.36 (d, J = 0.5 Hz, 1H), 2.52 (s, 1H), 1.40 (s, 3H), 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 172.4 (+), 169.9 (+), 167.6 (+), 137.2 (+), 128.4 (−), 127.9 (−), 127.8 (−), 101.3 (−), 90.1 (−), 79.7 (+), 76.1 (+), 73.4 (−), 71.2 (+), 44.2 (+), 22.7 (−), 20.3 (−); IR (neat) 3293, 3032, 2113, 1690. Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.15; H, 6.37.

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Supporting Information Available: ^{1}H NMR spectra for **10**, **12**, **13**, **15**−**22** and ^{13}C NMR spectra for **10**, **12**, **13**, **15**, **16**, **20**−**22**. This material is available free of charge via the Internet at http://pubs.acs.org.

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