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Synthetic Studies on Furanosteroids: Construction of the Viridin Core Structure *via* Diels–Alder/*retro*-Diels–Alder and Vinylogous Mukaiyama Aldol-Type Reaction

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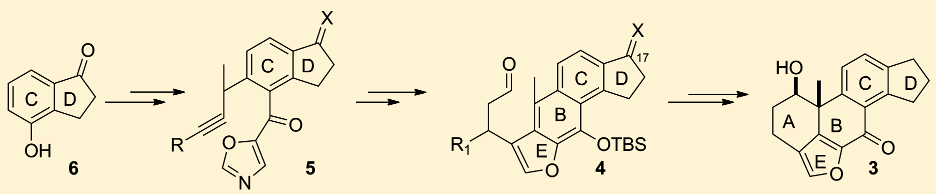
Supporting Information



ABSTRACT: The synthesis of the viridin class of furanosteroids core skeleton from the readily available 2,3-dihydro-4-hydroxyinden-1-one (**6**) is described. Our strategy was broken down into three parts: (1) Synthesis of functionalized alkyne oxazoles of type **5**; (2) intramolecular Diels–Alder/*retro*-Diels–Alder reaction of **5** followed by tautomerization and elaboration of R to give silylated furanonaphthols **4** bearing an aldehyde side chain; and (3) annulation of ring A by intramolecular vinylogous Mukaiyama aldol-type cyclization. Two major challenges were faced in the last step: (i) furanonaphthol derivatives bearing a *β*-hydroxyaldehyde functionality (R_1 = OH) suffered from dehydration to the *E*-enal, which is geometrically incapable of cyclization, and (ii) the functionality at C17 had a strong influence on the conversion of **4** to **3**, as exemplified by the failure of the free ketone (X = O) or its derivatives (X = H, OH; X = H, OAc) to cyclize. In the end, success was realized with the analogous C17-norketone (X = H, H).

INTRODUCTION

The furanosteroids are a special class of natural products that feature a furan ring fused to the steroid nucleus at C-4 and C-6, thus making the pentacyclic core highly strained (Figure 1). In 1945, viridin (**1a**), the parent member of this group, was isolated from the fungus *Gliocladium virens*.[1] The structure of **1a** was determined 24 years later through chemical degradation, spectroscopic, and X-ray studies.[2] To date several other members of the viridin family have been isolated from various fungal species and characterized.[3−6] These fungal metabolites have attracted attention for many years because of their potent anti-inflammatory and antibiotic properties.[4,7] However, it is their selective inhibition of certain intracellular pathways that has attracted the most attention.[8] For example, wortmannin (**2a**) is a potent and irreversible inhibitor of phosphatidylinositol-3-kinase (PI3−K) at nanomolar concentrations (IC_{50} = 4.2 nM), and more recently it has been shown to inhibit Polo-like kinase 1 and 3 at IC_{50} = 24−49 nM.[9] It also inhibits other PI3-related kinases at higher concentrations.[10,11]

Mechanistically, PI3-kinase is proposed to interact with **2a** through covalent bonding of Lys-802, found in the ATP-binding site, to the C20-position of wortmannin, leading to opening of the furan ring and formation of an enamine that is stable at physiological pH.[12,13] The opening of the furan ring, rendered highly electrophilic by virtue of being flanked by the C3- and C7- carbonyls, relieves ring strain. This mechanism has been supported by an X-ray structure[14] showing wortmannin bound to the PI3-kinase, and further validated by *in vitro* studies in which amines and thiols rapidly open the furan ring.[15,16] Other congeners have a similar mechanism of action due to the identical furan ring system. However, the development of furanosteroids into pharmaceutical drugs has been slow due to toxicity, instability, and selectivity issues.[16−18] These challenges were recently featured in Chemical and Engineering News[19] under the title: "PI3K at the Clinical Crossroads." There are ongoing intense efforts to derivatize these molecules by medicinal and biological chemists, aimed at finding more potent, less toxic, and more stable analogues.[12,13,15,20−22] There is therefore a need to develop more efficient synthetic routes to these targets to meet the above demands.

Although the furanosteroids are relatively small in size, the synthetic assembly of the strained pentacyclic structure has been particularly challenging. In the case of wortmannin, Shibasaki has accomplished two racemic and one formal enantioselective syntheses.[23−25] Only one total synthesis of viridin in racemic form has been achieved, by the Sorensen group.[26] There are also several incomplete syntheses targeting either the core or some select rings.[27−29] Five years ago,[30,31] and more recently,[32] our group completed the synthesis of the A,B,C,E-ring core of viridin and wortmannin. The skeleton contained many of the key structural features found in **1** and **2**, but lacked the D ring and also the C2- and C3- functional

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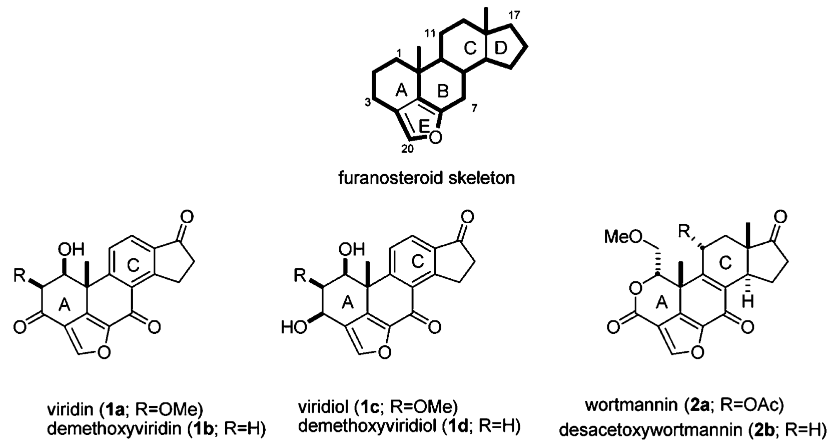
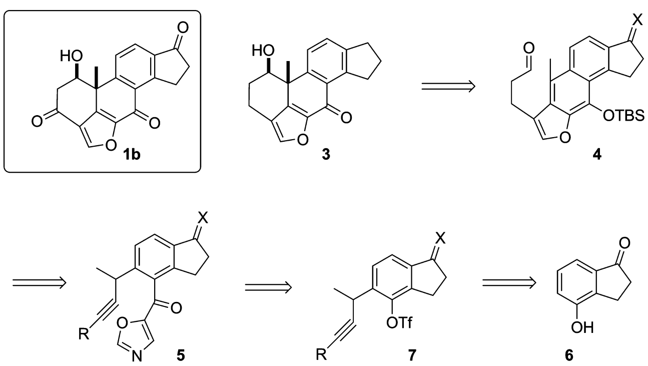


Figure 1. Furanosteroid class of PI3-kinase inhibitors.

groups. We therefore planned a synthetic scheme that incorporates ring D early in the synthesis, with the hope of functionalizing ring A at the very end of the synthetic sequence.

In the retrosynthetic analysis delineated in Scheme 1, the skeleton **3** is considered to be a precursor to demethoxyviridin (**1b**) and other congeners. It was expected that on treatment with an appropriate Lewis acid catalyst furanoaldehyde intermediate **4** would undergo a diastereoselective vinylogous Mukaiyama aldol-type reaction to afford **3**. A key consideration in our retrosynthetic approach was that **4** could be assembled by intramolecular Diels–Alder/*retro*-Diels–Alder reaction of alkyne oxazole precursors of general structure **5**. It was further envisioned that a palladium-catalyzed C–C bond formation between an oxazole derivative and alkyne triflate **7**, itself derived from *ortho*-functionalization of the known starting material **6**, would give alkyne oxazole **5**.

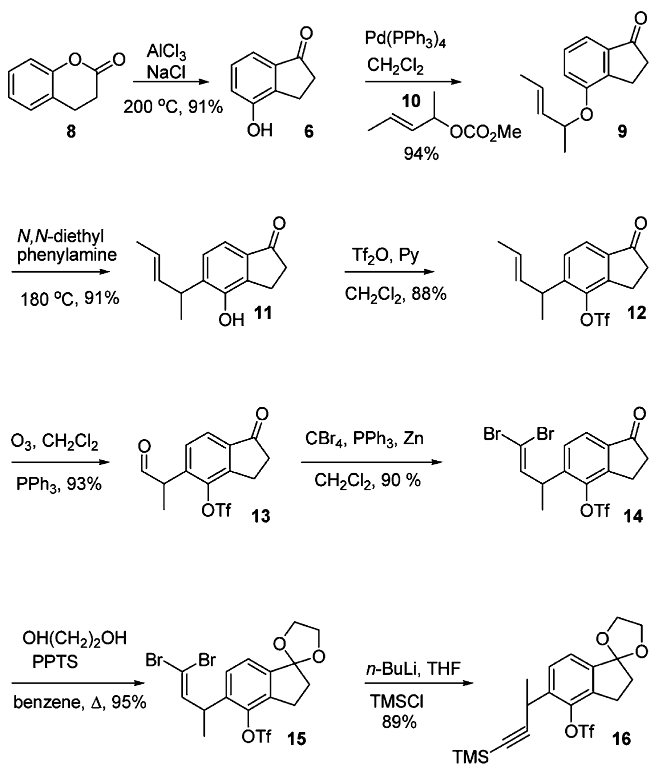
Scheme 1. Synthetic Analysis of Viridin Skeleton 3



RESULTS AND DISCUSSION

The implementation of this strategy began with the multigram synthesis of hydroxyindanone **6** from the inexpensive dihydrocumarin **8** through a literature procedure.[33] In preparation for a Claisen rearrangement, allylic ether precursor **9** was synthesized in a yield of 94% *via* Tsuji–Trost allylation[34] of **6** with the known allylic carbonate **10**.[35] Gratifyingly, thermal Claisen rearrangement in *N*,*N*-diethylaniline furnished only the *ortho*-allyl phenol **11** in a yield of 91%.[36] Triflation of the phenol under conditions which suppress the enol triflation of the ketone furnished the triflate **12** in a yield of 88%.[37] Ozonolysis of the double bond followed by reductive workup with PPh_3 provided the most practical access to the aldehyde **13**, in a yield of 93%. Aldehyde **13** was then reacted with carbon tetrabromide and triphenylphosphine in the presence of zinc dust to give the dibromo olefin **14** in a yield of 90%.[38] Ketalization of the ketone with ethylene glycol gave the dioxolane **15** in a yield of 95%. Lithiation of the dibromo olefin followed by *in situ* capture of the resulting lithium acetylide with chlorotrimethylsilane furnished the alkyne triflate **16** in a yield of 89% (Scheme 2).

Scheme 2. Synthesis of Alkyne Triflate 16



With the attachment of the alkyne side chain nearly complete, attention was turned to the oxazole side chain. Several C–C bond forming reactions were explored, but in the end Stille cross-coupling proved to be the most promising in terms of reproducibility and scalability. Vinyl arene **17** was thus formed in a yield of 91% by simply heating the triflate **16** and commercially available tributyl(vinyl)stannane to 90 °C in

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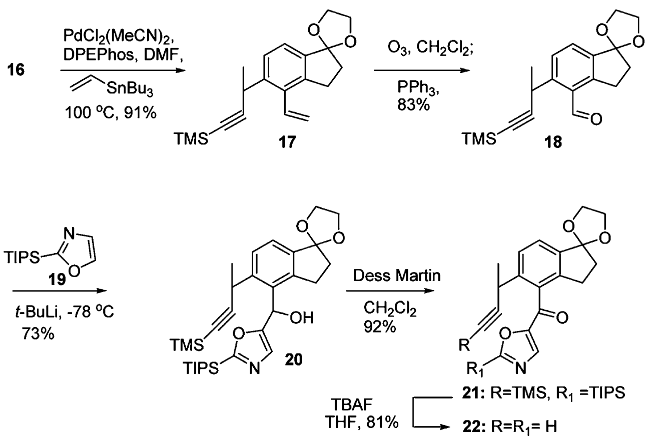
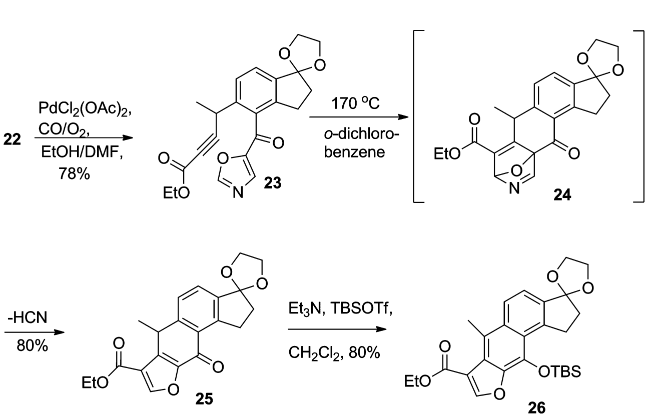
DMF in the presence of $PdCl_2(MeCN)_2$ and DPEPhos (Scheme 3). Although substrate **16** was sterically hindered, no special additives were required.[39−41] In fact, their inclusion decreased the rate of this reaction. However, we did observe a strong dependency on the rate of the Stille reaction on remote functionality in the molecule. For example, this reaction failed when the dioxolane ring was replaced with an OTBS or OPMB group, or when the TMS group was replaced with CO_2Me. Furthermore, an initial attempt to cleave the double bond in **17** using $OsO_4/NaIO_4$[42] gave only modest yields and was not amenable to scale up. Instead, a scalable synthesis of the aldehyde **18** was achieved in a yield of 83% by careful ozonolysis under conditions in which Red 23 (0.1% Sudan III solution) was added as an internal indicator, allowing for selective cleavage of the olefin in the presence of the alkyne.[43] Lithiation of the known TIPS oxazole **19**[44] with *tert*-BuLi, followed by electrophilic capture of the resulting lithium oxazole with the aldeyhde **18**, then led to the expected secondary alcohol **20** as an inconsequential mixture of diastereomers (73%).[45] The alcohol was then oxidized to the corresponding ketone **21** employing the Dess−Martin periodinane procedure, followed by TBAF induced desilylation of both the TMS and TIPS protecting groups to give the terminal alkyne **22**.

Scheme 3. Synthesis of Alkyne-Oxazole 22



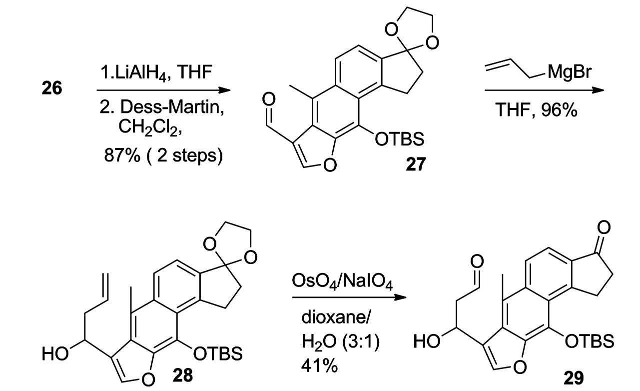
Next, palladium-catalyzed ethoxycarbonylation[31] converted the terminal alkyne **22** to the ynoate **23** in a yield of 78% and set the stage for a bis-heteroannulation reaction (Scheme 4). Thus, upon heating **23** in *o*-dichlorobenzene, thermal activation was achieved at 170 °C and the much anticipated Diels−Alder reaction, followed by *retro*-Diels−Alder reaction of the transient adduct **24**, furnished dienone **25**. Tautomerization of **25** with Et_3N in the presence of TBSOTf then gave the phenolic TBS derivative **26** in a yield of 80%.

Scheme 4. Diels−Alder/*retro*-Diels−Alder Reaction



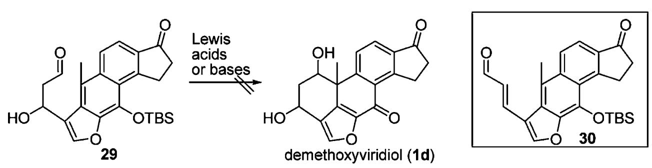
The synthesis of the aldehyde side chain was initiated by $LiAlH_4$ reduction of ester **26** to the corresponding alcohol, followed by Dess−Martin oxidation of the crude alcohol to the aldehyde **27** in an overall yield of 87%. With **27** in hand, the ultimate goal was to perform its enantioselective allylation to a homoallylic alcohol.[46] However, for the purpose of obtaining material for testing, the final ring closing reaction, racemic homoallylic alcohol **28**, was prepared in 96% yield by treatment of **27** with allylmagnesium bromide. We had planned to protect the alcohol functionality in **28** either as its PMB or Bn ether for the purpose of chelation control, prior to oxidative cleavage of the double bond. Unfortunately, though, all attempts to install these protecting groups under basic, acidic, or neutral conditions led to degradation of the starting material to unidentified polar products. We thus continued with the unprotected alcohol **28**. In this case, $OsO_4/NaIO_4$ mediated oxidative cleavage of the olefin was selective and gave the β-hydroxyaldehyde **29**, in which ketal deprotection to the ketone occurred during silica gel purification (yield 41%, Scheme 5).

Scheme 5. Synthesis of β-Hydroxyaldehyde 29

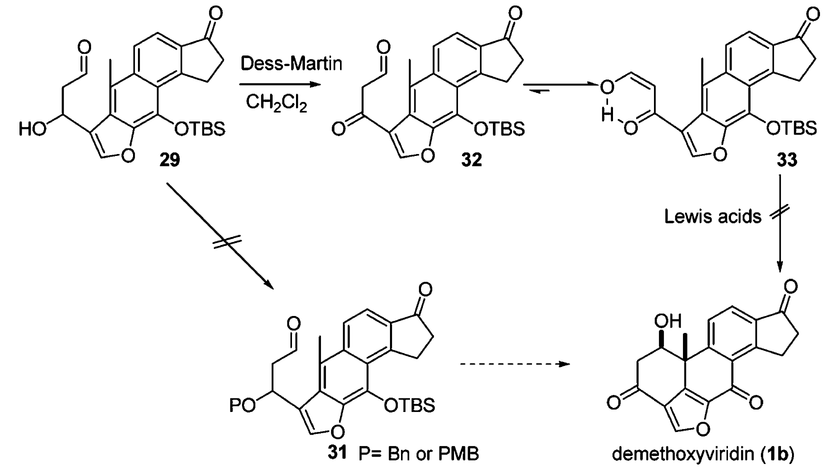


The synthesis of β-hydroxyaldehyde **29** set the stage for the final ring closing reaction. Successful cyclization of this aldehyde was expected to provide demethoxyviridiol (**1d**, Scheme 6). The free hydroxyl, in principle, could chelate Lewis acids as reported by Reetz,[47] resulting in a diastereoselective aldol reaction. With the report by Reetz as a precedent, **29** was submitted to various Mukaiyama aldol reaction conditions. However, **29** turned out to be relatively stable to $TiCl_4$ and other Lewis acids ($BF_3.OEt_2$, TMSOTf, and lanthanide triflates[48−50]) at temperatures between −78 and −30 °C. Quenching the reaction at low temperatures essentially gave back the starting material. In a separate experiment, when a reaction conducted at −78 °C was allowed to warm to room

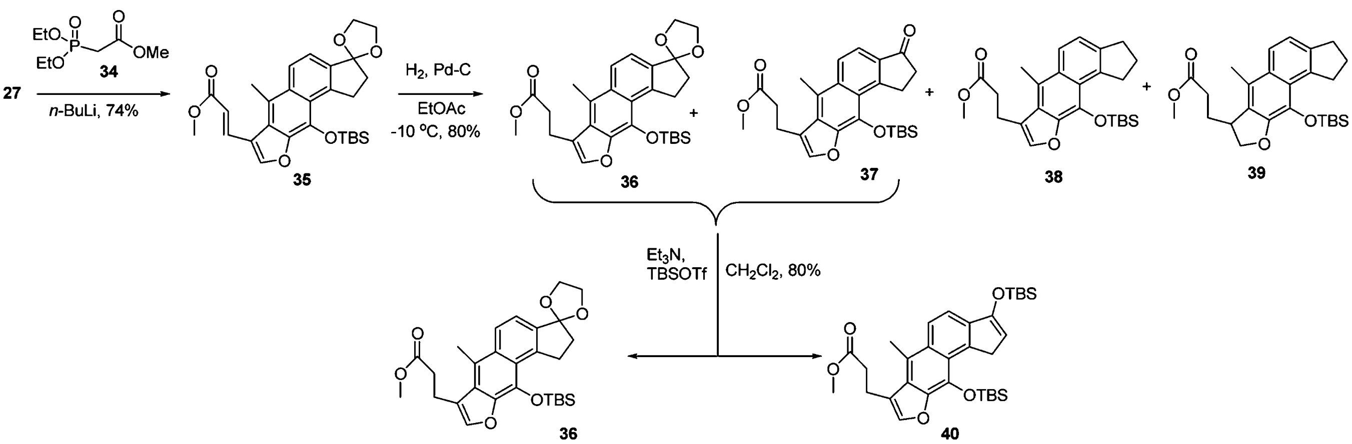
Scheme 6. Unsuccessful Attempt at Cyclization



Scheme 7. Attempts at Avoiding Dehydration of 29



Scheme 8. Synthesis and Hydrogenation of 35



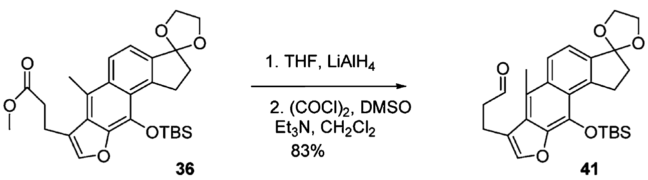
temperature, TLC analysis showed dehydration to the thermodynamically stable *E*-enal **30** (see insert in Scheme 6), which occurred slowly at approx. −30 °C and rapidly at higher temperatures. No desilylation was observed. Also, treatment of **29** with TBAF or HF·Py complex gave intractable mixtures.

Two conclusions were drawn at this point: (i) substrate **29** is inert to Lewis acids and bases at low temperatures, and (ii) higher temperatures favor dehydration, wherein the resultant *E*-α,β-unsaturated aldehyde **30** is incapable of cyclization.[51] We then unsuccessfully attempted to protect the alcohol functionality in **29** either as its Bn or PMB derivative as in **31** (Scheme 7). We also sought to stem the competitive elimination of the hydroxyl group by oxidizing it to the ketone **32** prior to treatment with $TiCl_4$. However, in this case equilibration favored the strongly hydrogen bonded *Z*-keto−enol tautomer **33**, which was also configurationally incapable of cyclization. Examples from the literature show that for such dicarbonyl systems, the keto−enol form is favored over the keto-aldehyde tautomer.[52,53] Nevertheless we still treated the product from the Dess−Martin oxidation with $TiCl_4$, with the hope that any **32** in equilibrium with **33** would undergo cyclization. However, no cyclization product was observed from those attempts. Cyclization of **32** could have potentially given demethoxyviridin (**1b**) directly.

Since it was apparent that the desired cyclization reaction of **29** was being forestalled by competitive elimination of the hydroxyl group, our attempts at cyclization of a β-hydroxyaldehyde were put on hold. Instead, the synthesis of an analogous aldehyde lacking the β-hydroxyl group was pursued. Two strategies for achieving this goal were developed. In the first method (Scheme 8), Horner−Wadsworth−Emmons reaction of the aldehyde **27** with methyl diethyl phosphonoacetate (**34**) extended the chain to the *E*-α,β-unsaturated ester **35** in a yield of 74%.[54] Next, catalytic hydrogenation of the α,β-unsaturated ester **35** with 5% Pd/C left the furan ring intact and gave the saturated ester **36** in a yield of 79% for reactions run on a small scale. However, in larger scale reactions (>50 mg), hydrogenation gave significant amounts of side products **37**−**39** in addition to **36**. This difficulty was circumvented by careful adjustment of the reaction conditions (H_2, freshly distilled EtOAc, −10 °C, and portion wise addition of "fresh"[55] 5% Pd/C over 1 h), which provided a 3:1 mixture of **36** and **37** in a yield of (69%), with formation of only small amounts (10%) of **38** and a trace of **39**. Hydrogenation under ionic conditions ($PdCl_2$, $Et_3SiH/BF_3\cdot OEt_2$)[56] gave similar results. The loss of the ketal protecting group in **35** was not without precedent. Palladium on carbon is known to be acidic enough to induce the cleavage of labile groups, and in our case, older batches of this catalyst led to instant deketalization and subsequent hydrogenolytic cleavage of the free ketone.[57,58] Fortunately, the mixture could be separated by column chromatography, with **38** and **39** eluting together from the first fractions, followed by an inseparable mixture of **36** and **37**. Further purification by successive recrystallization from hexanes separated **38** from **39**, while the ketone **37** was separated from **36** by enol-silylation (Et_3N/TBSOTf) to **40** (Scheme 8).

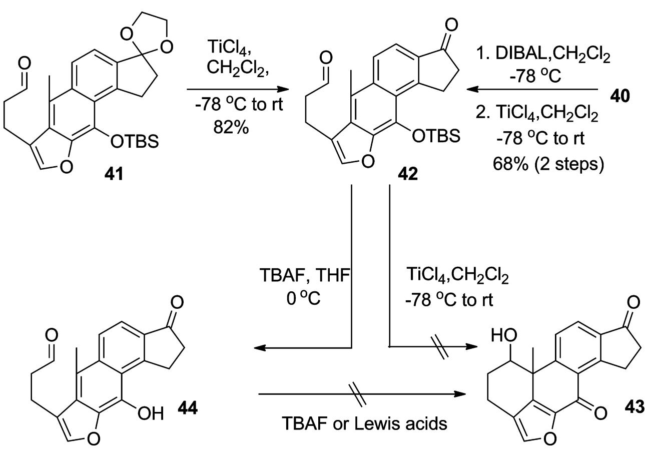
The ketal **36** and enol silyl ether **40** were prone to hydrolysis and, following ^{1}H NMR characterization, were immediately used in the next step. The originally intended monoreduction of the ester moiety of **36** to the aldehyde **41** in one step using DIBAL failed (*vide infra*). However, $LiAlH_4$ reduction of **36** to the corresponding alcohol, followed by Swern oxidation furnished the aldehyde **41** in a yield of 83% (Scheme 9).

Scheme 9. Synthesis of Aldehyde 41



With the aldehyde **41** in hand, we turned our attention to its cyclization. The expectation was that Lewis acids would in addition to initiating the ring closure, hydrolyze the dioxolane ring to the ketone. However, when **41** was reacted with typical Lewis acids ($TiCl_4$, $BF_3{\cdot}OEt_2$) at room temperature, only deketalization occurred to furnish the ketone **42** in a yield of 82% (Scheme 10). The ester **40** was also converted to the aldehyde **42** in a similar fashion. Following purification, **42** was also submitted to various ring closing reaction conditions. However, only starting material was recovered from these reactions.

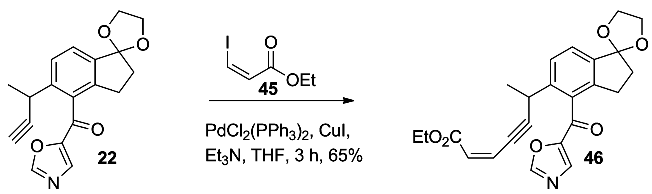
Scheme 10. Attempted Cyclization of 42



The observed lack of reactivity of **42** toward cyclization was surprising, in view of the fact that an analogous aldehyde only lacking ring D, employed in model studies, underwent smooth cyclization when reacted with two equivalents of $TiCl_4$ at room temperature.[31] The possibility that the bulky TBS was more stable toward Lewis acids in this case prompted us to synthesize the analogous phenolic TES derivative, but that too was inert to the reaction conditions. Exposure of **42** to TBAF at 0 °C released the TBS to afford the unstable phenol **44** that also failed to cyclize (Scheme 10). When allowed to warm to room temperature in the presence of TBAF, **44** eventually degraded into an intractable mixture. Treatment of **44** with Lewis acids also gave a complex mixture. The fact that desilylation was achieved in TBAF without subsequent cyclization indicated that electronic rather than steric factors were probably at play.

In order to explore this possibility, we developed a second route to synthesizing **42** in a more efficient way (Scheme 11).

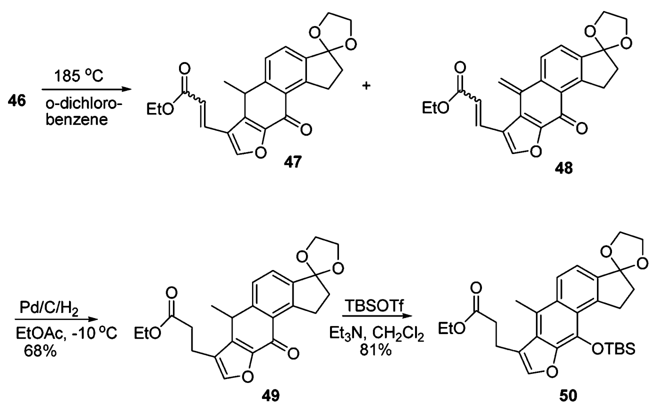
Scheme 11. Synthesis of the Enyne 46 *via* Sonogashira Reaction



In this second method, $PdCl_2(PPh_3)_2$/CuI catalyzed Sonogashira cross-coupling of the terminal alkyne **22** with the known (*Z*)-ethyl 3-iodoacrylate (**45**) furnished the *Z*-enyne **46** in a yield of 65%.[59]

Diels–Alder/*retro*-Diels–Alder reaction of **46** then gave a mixture of dienone **47** and the quinone methide oxidation product **48** (*E,Z* mixtures, Scheme 12). Thermolysis of **46** was

Scheme 12. Diels-Alder Reaction of Enyne 46



a relatively slow reaction, requiring heating to 185 °C for 8 h. Partial isomerization of the double bond occurs during this transformation, as evidenced by the large ^{1}H NMR coupling constant observed for **47**-*E* (J = 12.8 Hz), consistent with a *trans* vicinal relationship. Separation of **47** from **48** was not necessary, and the entire mixture was instead hydrogenated under mild conditions (5% Pd/C, H_2, EtOAc, −10 °C) to the saturated ester dienone **49** in a yield of 65% from **46**. The dienone **49** was very unstable and prone to aromatization with subsequent oxidation to the corresponding *p*-quinol. Therefore, it was only characterized by ^{1}H NMR and then converted to the more stable TBS-phenol derivative **50** in a yield of 81%. In addition to reducing the number of steps required to arrive at **50**, another advantage of this approach was that the dioxolane ring is not lost during hydrogenation. This observation was not surprising, since studies in our laboratory had by this time shown that the ketal protecting group is relatively stable in intermediates in which the B ring has not been aromatized, as in **49**. In intermediates of type **36** (Scheme 9), hydrolysis of the ketal group is favored because of resonance stabilization of the intermediate cation by the lone pair of electrons of the phenol TBS ether.

Upon treatment of **50** with DIBAL-H at −78 °C, the ester moiety was partially reduced to the corresponding aldehyde

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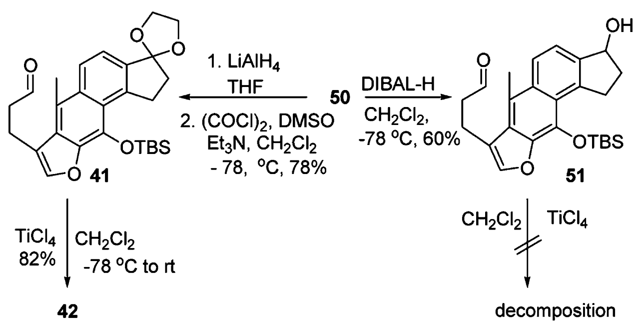
(Scheme 13). However, coordination between DIBAL-H and the oxygen atom of the dioxolane ring also led to its cleavage

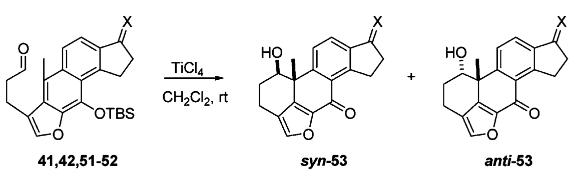
Scheme 13. Synthesis and Attempted Cyclization of 51



with subsequent reduction of the free ketone to the unstable alcohol **51**, in a yield of 60%. In contrast, exposure of **50** to $LiAlH_4$, which lacks a free coordination site, permitted chemoselective reduction of the ester to the alcohol without causing deketalization. Swern oxidation of the alcohol then furnished the aldehyde **41** in a yield of 78%.

Upon the basis of TLC analysis, both alcohol **51** and its acetate derivative **51a** appeared to cyclize upon treatment with $TiCl_4$, but the anticipated products underwent rapid decomposition. This observation led us to suspect that the C17 ketone might be inductively deactivating the furanonaphthol ring toward the Mukaiyama aldol reaction. To test this hypothesis, the C17 norketone **52** was synthesized by DIBAL reduction of its ester precursor **38**, earlier obtained as a side product by the route outlined in Scheme 8. We were pleased to observe the cyclization of **52** at room temperature under $TiCl_4$ catalysis, to give *syn*-**53** (=3) and *anti*-**53** in combined yield of 72% (Table 1). The *syn* relationship between the OH and Me groups was confirmed by X-ray analysis.[60]

Table 1. Cyclization Studies of 42 and its Derivatives



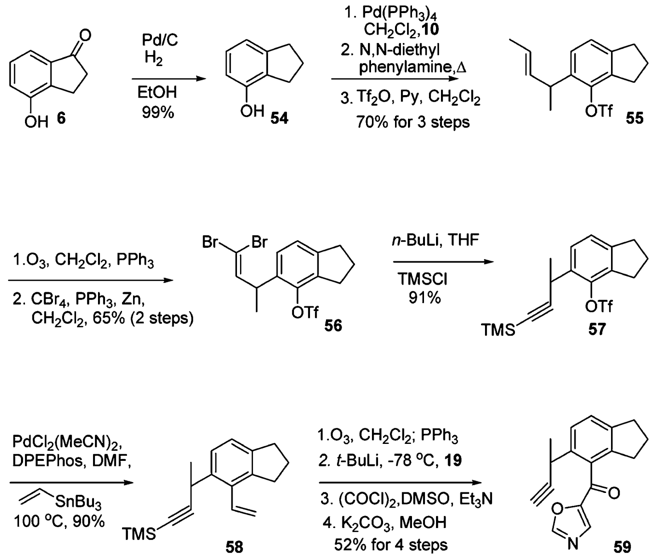
41: X= $O(CH_2)_2O$, **42**: X=O, **51**: X= H, OH, **51a**: X= H, OAc, **52**: X= H, H

entry	X	conditions	result
1	41	$TiCl_4$, −78 °C or rt	No reaction[a]
2	42	$TiCl_4$, −78 °C	No reaction
3	51	$TiCl_4$, −78 °C or rt	Decomposition
4	51a	$TiCl_4$, −78 °C or rt	Decomposition
5	52	$TiCl_4$, rt	72% of 53

[a]Only hydrolysis of the ketal protecting group is observed.

The C17 norketone **52** was then synthesized in more efficient fashion beginning with the known 2,3-dihydro-1H-inden-4-ol (**54**, Scheme 14).[61] All steps leading from **54** to **52** were analogous to those employed in the conversion of **6** to **42** (cf. Schemes 2−13). However, alternative reagents whose utility had been precluded by the presence of the labile ketal

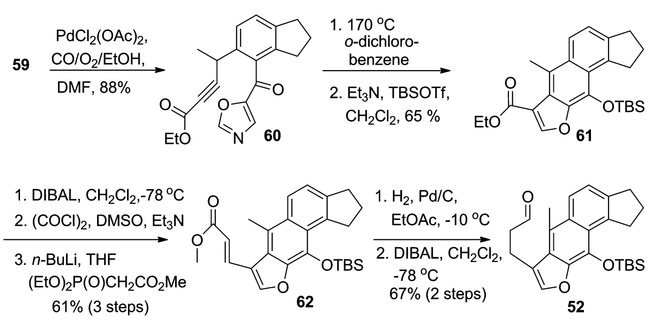
Scheme 14. Synthesis of the Common Alkyne 59



group were employed because of lower cost and ease of operation.[62] Thus, after palladium on carbon mediated hydrogenolytic cleavage of the ketone moiety of **6** in near quantitative yield, the resultant dihydroindenol **54** was subjected to Tsuji−Trost allylation, Claisen rearrangement, and triflation to give **55** in an overall yield of 70% from **54**. Next, dibromo olefin **56** was obtained in an overall yield of 65% upon ozonolysis of **55** followed by Corey−Fuchs alkenylation. Lithiation of **56**, followed by trapping of the lithium acetylide with chlorotrimethylsilane, then furnished 91% of the TMS alkyne **57**, that was employed in a robust Stille cross-coupling with tributyl(vinyl)tin to furnish the vinyl arene **58** in 90% yield. After chemoselective ozonolytic cleavage of the olefin, the resultant aldehyde was trapped with lithiated oxazole **19** to afford an alcohol that was oxidized to the corresponding ketone under Swern conditions. Removal of both silyl protecting groups with K_2CO_3 in MeOH (which was much cleaner and higher yielding than TBAF) then produced the terminal alkyne **59**, a common intermediate for both routes.

Once the terminal alkyne **59** was in hand, palladium catalyzed carboethoxylation gave the ynoate **60** in a yield of 88% (Scheme 15). Subjecting **60** to the Diels−Alder/*retro*-Diels−Alder/tautomerization sequence furnished the phenol TBS derivative **61** in a combined yield of 65% for two steps. The ester moiety of **61** was then converted in two steps to the corresponding aldehyde that was subsequently extended to the *α*,*β*-unsaturated ester **62** using standard Horner−Wadsworth−

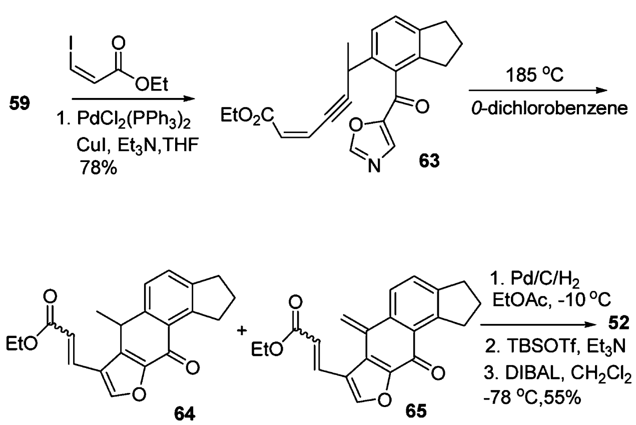
Scheme 15. Synthesis of Aldehyde 52 *via* Carboethoxylation



Emmons reaction conditions. Finally, catalytic hydrogenation of the double bond in **62** with H_2/Pd−C, followed by DIBAL reduction of the ester, gave the aldehyde **52** in a yield of 67%.

Finally, we also developed an improved route to the target aldehyde **52** employing a Sonogashira reaction (Scheme 16).

Scheme 16. Synthesis of 52 *via* Sonogashira Reaction



Thus, the terminal alkyne **59** underwent clean cross-coupling with the *Z*-iodoacrylate **45**, affording enyne **63** in a yield of 78%. Thermolyis of **63** at 185 °C then induced the Diels−Alder/*retro*-Diels−Alder reaction to yield a mixture of **64** and **65**. As before, this mixture was hydrogenated over palladium on carbon and then converted to the target aldehyde **52** by a two-step sequence involving silylation with TBSOTf followed by DIBAL reduction (55% yield).

With two secure synthetic routes to the furanoaldehyde **52** established, we set out to optimize the conditions for the ring closing reaction forming ring A. Cyclization at low temperature was desirable because it would lay a foundation for the cyclization of aldehydes bearing the sensitive *β*-hydroxy functionality. Although several attempts were made, **52** did not undergo cyclization at low temperatures with $TiCl_4$. Starting material was recovered at −78 °C and at 0 °C only slow decomposition occurred. It was eventually determined that stirring a rigorously degassed CH_2Cl_2 solution of aldehyde **52** with 4 equivalents of $TiCl_4$ at room temperature were the best conditions for this transformation. The reaction proceeded largely under kinetic control, affording 72% of *syn*-**53** and *anti*-**53** with the desired *syn*-**53** dominating in a ratio of 5:1, due to a more a favorable Burgi−Dunitz trajectory angle (Scheme 17, best seen with models). Colorless needle crystals of *syn*-**53** were obtained after recrystallization from methylene chloride. A side-by-side comparison of the ^{1}H NMR spectra of **53** to that of a closely related alcohol previously synthesized in our group,[31] and to demethoxyviridin itself, showed a strong correlation between diagnostic protons. In particular the chemical shifts observed for H_1 (4.12 ppm) and H_{11} (8.14 ppm) in the ^{1}H NMR spectra of *syn*-**53** is nearly identical to those observed in the spectra of advanced viridin intermediates.[31] In addition to the X-ray analysis,[60] NOE studies confirmed the *syn* relationship between the OH and the methyl group.

CONCLUSIONS

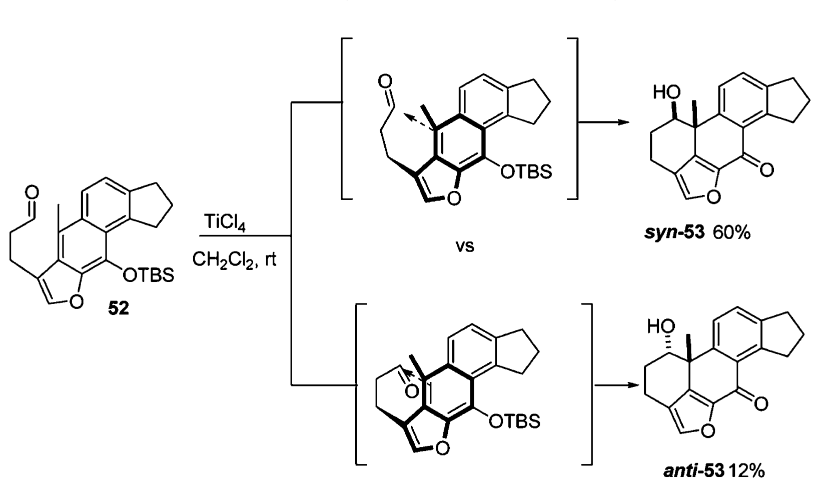
We have synthesized the aldehyde **42** and its C17-norketone analogue **52** through two separate routes. The shorter of the two routes involved 16 steps and is preferred. The C17 ketone had a strong electronic effect on the cyclization reaction leading to ring A, as exemplified by the fact that only **52** underwent cyclization to **53** under mild conditions. Other substrates in Table 1 did not afford the cyclized product. Functionalization of rings A and D *via* benzylic oxidation of C3 and C17 is currently under investigation. We are also screening for conditions that would allow for cyclization of *β*-hydroxyaldehydes of type **29** and subsequent enantioselective synthesis of viridin.

EXPERIMENTAL SECTION

The general experimental methods are provided in the Supporting Information.

4-((*E*)-Pent-3-en-yloxy)-2,3-dihydroinden-1-one (9). To a solution of hydroxyindanone **6** (11 g, 74.24 mmol) and allyl carbonate **10** (11.77 g, 81.67 mmol) in CH_2Cl_2 (150 mL) was added $Pd(PPh_3)_4$ (857.89 mg, 0.74 mmol). The mixture was then refluxed for 3 h, cooled to room temperature and the solvent removed under reduced pressure. Purification by column chromatography (SiO_2, 30:1 hexanes/EtOAc) gave 15.1 g (94%) of the desired product as a yellow solid. Mp: 42.0−44.0 °C. R_f = 0.75 (3:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (1H, d, J = 7.0 Hz), 7.29 (1H, d, J = 7.0 Hz), 7.05 (1H, d, J = 8.0), 5.77−5.70 (1H, m), 5.58−5.52 (1H, m), 5.50−4.80 (1H, m), 3.06−3.02 (2H, m), 2.69−2.65 (2H, m), 1.69 (3H, d, J = 6.3 Hz), 1.45 (3H, d, J = 6.3 Hz). ^{13}C

Scheme 17. Kinetic Control *via* the Most Favorable Burgi−Dunitz Trajectory Angle



NMR (75 MHz, $CDCl_3$) δ 207.5, 155.8, 145.1, 138.8, 132.0, 128.7, 127.8, 118.2, 115.4, 75.0, 36.4, 22.9, 21.9, 17.9. FT-IR ($CDCl_3$ cm^{-1}) 3243.9, 2928.6, 1680.8, 1427.8, 1283.6. HRMS (EI) calcd for $C_{14}H_{16}O_2$ 216.1150, found 216.1147.

2,3-Dihydro-4-hydroxy-5-((E)-pent-3-en-2-yl)inden-1-one (11). A solution of **9** (10 g, 46.24 mmol) in Et_2NPh (50 mL) was heated at 180 °C for 6 h. The dark brown mixture was then cooled to room temperature, diluted with 50 mL of ice water and then stirred at room temperature for several minutes. The two layers were separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with dil. HCl, rinsed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 20:1 to 5:1 hexanes/EtOAc) gave 9.1 g (91%) of **11** as a brown solid. Recrystallization from EtOAc gave white round crystals; Mp: 112−114 °C. R_f = 0.35 (2:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (1H, d, J = 7.5 Hz), 7.18 (1H, d, J = 8.0 Hz), 5.78−5.98 (2H, m), 5.69 (1H, s), 3.05 (2H, t, J = 6.0 Hz), 2.71 (2H, t, J = 5.7 Hz), 1.74 (3H, d, J = 7.2 Hz), 1.41 (3H, d, J = 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7, 142.7, 134.4, 128.0, 126.1, 116.1, 37.8, 37.7, 36.7, 22.4, 19.5, 18.1. FT-IR ($CDCl_3$ cm^{-1}) 3481, 2974, 2922, 1712, 1602.2, 1482, 1440, 1202, 969, 770. HRMS (EI) calcd for $C_{14}H_{16}O_2$ 216.1150, found 216.1147.

2,3-Dihydro-1-oxo-5-((*E*)-pent-3-en-2-yl)-1*H*-inden-4-yl Trifluoromethanesulfonate (12). To a solution of **11** (9 g, 41.61 mmol) in CH_2Cl_2 (50 mL) at 0 °C was added pyridine (6.70 mL, 83.22 mmol) followed by Tf_2O (8.4 mL, 49.93 mmol) dropwise over 20 min and the mixture was then stirred for an additional 10 min. The resulting purple reaction was diluted with Et_2O and then quenched with dil. HCl. The aqueous layer was extracted twice with CH_2Cl_2, the combined organic extracts washed with $NaHCO_3$, rinsed with brine, dried over $MgSO_4$ and then concentrated under reduced pressure. Purification by column chromatography (SiO_2, 20:1 hexanes/EtOAc) gave 12.76 g (88%) of the triflate **12** as a yellow oil. R_f = 0.82 (3:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (1H, d, J = 7.8 Hz), 7.25 (1H, d, J = 8.1 Hz), 5.59−5.5.7 (2H, m), 3.86−3.81 (1H, m), 3.08−3.03 (2H, m), 2.34−2.30 (2H, m), 1.69−1.68 (2H, m), 1.35 (2H, d, J = 7.2 Hz), ^{13}C NMR (75 MHz,$CDCl_3$) δ 204.7, 147.8, 147.2, 143.6, 138.5, 133.3, 129.3, 126.1, 124.2, 120.9, 116.7, 36.3, 35.6, 23.6, 21.2, 18.1. FT-IR ($CDCl_3$, cm^{-1}) 3274, 2953, 1686, 1695, 1435, 1286, 1200, 1066, 970. HRMS (EI) calcd for $C_{15}H_{15}O_4F_3S$ 348.0643, found 348.0636.

2,3-Dihydro-1-oxo-5-(1-formylethyl)-1H-inden-4-yl Trifluoromethanesulfonate (13). To stirred solution of the olefin **12** (4.24 g, 12.17 mmol) in CH_2Cl_2 (120 mL) was bubbled ozone at −78 °C until a pale blue solution resulted and persisted (approximately 20 min). Excess ozone was removed by a nitrogen stream, triphenylphosphine (7.98 g, 30.43 mmol) was added, and the mixture warmed to rt and stirred overnight. Silica gel was added to the mixture and the solvent removed under reduced pressure. Dry pack silica gel column chromatography (10:1 to 3:1 hexanes/EtOAc) gave 3.78 g (93%) of the aldehyde **13** as an off white solid. R_f = 0.55 (3:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.72 (1H, s), 7.83 (1H, d, J = 8.1 Hz), 7.31 (1H, d, J = 8.1 Hz), 4.18 (1H, q, J = 7.2 Hz), 3.30 (2H, t, J = 6.3 Hz), 2.83 (2H, t, J = 6.5 Hz), 1.36 (3H, d, J = 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.3, 198.4, 148.0, 138.9, 129.9, 124.5, 120.8, 116.6, 46.5, 36.2, 23.6, 15.1. FT-IR ($CDCl_3$, cm^{-1}) 1725, 1615, 1411, 1215, 1051, 815, 630. HRMS (EI) calcd for $C_{13}H_{11}O_5F_3S$ 336.0279, found 336.0275.

5-(4,4-Dibromobut-3-en-2-yl)-2,3−1-oxo-1*H*-inden-4-yl Trifluoromethanesulfonate (14). To a solution of the aldehyde **13** (3.77 g, 11.21 mmol) in CH_2Cl_2 (100 mL) at 0 °C was added, carbon tetrabromide (7.44 g, 22.42 mmol), triphenylphosphine (5.88 g, 22.42 mmol), and zinc dust (1.47 g, 22.42 mmol). The mixture was warmed to room temperature and stirred for 30 min. The mixture was then filtered through a thin film of silica gel, the cake washed twice with CH_2Cl_2, silica gel (30 g) was added to the filtrate and the solvent was removed under reduced pressure. The residue was purified by dry pack column chromatography (SiO_2, 20:1 hexanes/EtOAc) to give 4.98 g (90%) of the dibromoolefin **14** as a yellow solid. Recrystallization from hexanes gave pale yellow needle crystals. Mp: 74−76 °C. R_f = 0.70 (5:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (1H, d, J = 7.8 Hz), 7.42 (1H, d, J = 8.1 Hz), 6.59 (1H, d, J = 8.7 Hz), 4.20 (1H, q, J = 7.2 Hz), 3.34−3.18 (2H, m), 2.78−2.71 (2H, m), 1.44 (3H, d, J = 8.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.4, 148.1, 144.1, 140.3, 128.8, 124.5, 120.9, 116.7, 91.9, 37.5, 36.3, 23.7, 21.3. FT-IR ($CDCl_3$, cm^{-1}) 1723, 1408, 1216, 1133, 817. HRMS (EI) calcd for $C_{14}H_{11}Br_2F_3O_4S$ 489.8697, found 489.8692.

5-(4,4-Dibromobut-3-en-2-yl)-2′,3′-dihydrospiro(1,3-dioxolane-1-oxo-1*H*-inden-4-yl) Trifluoromethanesulfonate (15). A solution of **14** (3.5 g, 7.11 mmol), ethylene glycol (1.17 mL, 21.33 mmol) and pyridinium *p*-tosylate (893.3 mg, 3.56 mmol) in benzene (50 mL) was placed in 100 mL round-bottom flask. A Dean−Stark trap equipped with a condenser was fitted and the reaction mixture refluxed for 24 h. The reaction mixture was cooled and then washed vigorously with saturated $NaHCO_3$, rinsed with brine, dried over $MgSO_4$ and concentrated under reduced pressure to give 4.8 g of brown crude material. Trituration from hexanes gave 3.62 g (95%) of the pure desired ketal as a pale yellow oil. R_f = 0.75 (5:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (1H, d, J = 7.8 Hz), 7.27 (1H, d, J = 8.1 Hz), 6.57 (1H, d, J = 8.7 Hz), 4.21−4.10 (5H, m), 3.11−3.06 (2H, m), 2.36−2.30 (2H, m), 1.40 (3H, d, J = 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 142.4, 141.2, 138.2, 137.5, 128.2, 123.8, 120.9, 116.7, 90.8, 65.6, 37.2, 37.1, 26.6, 21.0. FT-IR ($CDCl_3$, cm^{-1}) 2966, 2883, 1408, 1320, 1138, 1014, 908, 820. HRMS (EI) calcd for $C_{16}H_{15}Br_2F_3O_5S$ 533.8959, found 533.8959.

5′-[4-(Trimethylsilyl)but-3-yn-2-yl]-2′,3′-dihydrospiro-[1,3-dioxolane-2,1′-indene]-4′-yl Trifluoromethanesulfonate (16). To a solution of compound **15** (2 g, 3.73 mmol) in THF (60 mL) at −78 °C was added *n*-BuLi (2.50 M solution in hexanes, 3.28 mL, 8.21 mmol) dropwise over 30 min under a nitrogen atmosphere. After 30 min, TMSCl (1.05 mL, 8.21 mmol) was added and the mixture stirred for an additional 30 min and then quenched with H_2O. The resulting white suspension was warmed to room temperature, extracted with ethyl acetate, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 10:1 hexanes/EtOAc) gave 1.48 g (88%) of **16** as a clear oil. R_f = 0.55 (5:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (1H, d, J = 7.8 Hz), 7.38 (1H, d, J = 9.3 Hz), 4.22−4.06 (5H, m), 3.06 (2H, t, J = 7.5 Hz), 2.34 (2H, t, J = 7.2 Hz), 1.45 (3H, d, J = 6.9 Hz), 0.16 (9H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.8, 142.1, 137.9, 137.0, 129.4, 123.8, 116.7, 108.0, 86.8, 65.6, 37.3, 27.2, 26.5, 23.8, 0.2. FT-IR ($CDCl_3$,

cm^{-1}) 2960, 2174, 1408, 1216, 1144, 1017, 911, 845. HRMS (EI) calcd for $C_{19}H_{23}F_3O_5SSi$ 448.0988, found 448.0994.

5-(4-(Trimethylsilyl)but-3-yn-2-yl-2′,3′-dihydrospiro-[1,3-dioxolane-2,1′-inden]-4′-yl)-4-vinylinden-1-one (17). A solution of the triflate **16** (2.5 g, 5.57 mmol), $PdCl_2(MeCN)_2$ (72.38 mg, 0.279 mmol) and DPEPhos (299.98 mg, 0.557 mmol) in DMF (50 mL) was sparged with nitrogen for 10 min. Tributyl(vinyl)tin (1.95 mL, 6.68 mmol) was added and the mixture heated at 100 °C for 54 h, cooled to room temperature, diluted with 50 mL of water, extracted with ethyl acetate, washed with brine and finally dried over $MgSO_4$. Purification by column chromatography (SiO_2, 30:1 to 10:1 hexanes/EtOAc) gave 1.68 g (91%) of **17** as a pale yellow oil. R_f = 0.45 (5:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (1H, d, J = 7.8 Hz), 7.27 (1H, d, J = 9.6 Hz), 6.79 (1H, dd, J = 11.7, 17.7 Hz), 5.54 (1H, d, J = 11.7 Hz), 5.39 (1H, d, J = 17.7 Hz), 4.22−4.03 (5H, m), 2.96−2.91 (2H, m), 2.27 (2H, t, J = 6.9 Hz), 1.40 (3H, d, J = 7.2 Hz), 0.15 (9H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 142.1, 140.9, 133.1, 126.6, 122.3, 120.5, 110.3, 85.8, 65.5, 65.4, 37.4, 29.7, 29.0, 27.1, 23.9, 17.8, 13.8, 0.4. FT-IR ($CDCl_3$ cm^{-1}) 2960, 2174, 1409, 1317, 1216, 1144, 1017, 911, 844. HRMS (EI) calcd for $C_{20}H_{26}O_2Si$ 326.1702, found 326.1711.

5′-[4-(Trimethylsilyl)but-3-yn-2-yl]-2′,3′-dihydrospiro-[1,3-dioxolane-2,1′-indene]-4′-carbaldehyde (18). The vinyl arene **17** (1.7 g, 5.21 mmol) in CH_2Cl_2 (100 mL) was cooled to −78 °C and then exposed to a stream of ozone. Red 23 (0.1% solution of Sudan III in MeOH, 2 mL) was used as an internal indicator. Triphenylphosphine (3.4 g, 13.03 mmol) was added when the pink color had faded. The resulting mixture was allowed to warm to rt and stirred for an additional 6 h. The solvent was removed under reduced pressure and the residue purified by column chromatography (SiO_2, hexanes/EtOAc 100:1 to 50:1 to 20:1) to give 1.5 g (87%) of the aldehyde **18** as a white solid. Mp: 93−95 °C. R_f = 0.50 (3:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.57 (1H, s), 7.71 (1H, d, J = 8.1 Hz), 7.56 (1H, d, J = 8.1 Hz), 4.74, (1H, q, J = 6.9 Hz), 4.22−4.11 (2H, m), 4.11−4.07 (2H, m), 3.29 (2H, t, J = 6.9 Hz), 2.34 (2H, t, J = 7.2 Hz), 1.50 (3H, d, J = 6.9 Hz), 0.16 (9H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.5, 147.6, 142.4, 127.0, 128.8, 128.6, 128.3, 116.3, 109.4, 87.1, 65.5, 37.2, 29.2, 28.4, 25.1, −0.3. FT-IR ($CDCl_3$ cm^{-1}) 2928, 2238, 1690, 843. HRMS (EI) calcd for $C_{19}H_{24}O_3Si$ 328.1495, found 328.1492.

5′-[4-(Trimethylsilyl)but-3-yn-2-yl]-2′,3′-dihydrospiro-[1,3-dioxolane-2,1′-indene]-4′-yl({2-[tris(propan-2-yl)-silyl]-1,3-oxazol-5-yl})methanol (20). *tert*-BuLi (1.6 M in pentane, 5.32 mL, 8.52 mmol) was added to TIPS oxazole **19** (1.92 g, 8.52 mmol) at −78 °C in THF (50 mL). In a separate flask, the aldehyde **18** (1.4 g, 4.26 mmol) was dissolved in THF (50 mL) and cooled to −78 °C. After 10 min, the anion of the TIPS oxazole was added *via* cannula to the aldehyde. The mixture was stirred for an additional 20 min, quenched with saturated aqueous $NaHCO_3$, diluted with water, extracted with EtOAc and washed with brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 5:1 hexanes/EtOAc) gave 1.72 g (73%) of **20** as a white waxy solid. Major diastereomer: R_f = 0.25 (3:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (1H, d, J = 8.1 Hz), 7.36, (1H, d, J = 8.1 Hz), 6.91 (1H, s), 6.37 (1H, brs), 4.21−4.04 (5H, m), 3.06−2.96 (1H, m), 2.82−2.74 (1H, m), 2.27−2.18 (2H, m), 1.43 (3H, d, J = 7.2 Hz), 1.39−1.23 (3H, m), 1.08 (18H, d, J = 7.2 Hz), 0.12 (9H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 143.6, 143.1, 141.4, 133.0, 128.3, 128.0, 124.3, 123.7, 116.9, 110.5, 85.7, 65.9, 65.3, 37.1, 29.9, 27.9, 24.9, 18.5, 11.1, 0.3. FT-IR ($CDCl_3$, cm^{-1}) 3425, 2947, 2868, 2167, 1465, 1319, 1250, 1040, 914, 843, 734. HRMS (ESI) calcd for $C_{31}H_{48}NO_4Si_2$ $[M + H]^+$ 554.3122, found 554.3126.

4-((Triisopropyl)oxazol-5-yl)(hydroxy)methyl)-trimethylsilyl)but-3-yn-2-yl-2′,3′-dihydrospiro[1,3-diox-olane-2,1′-inden]-4′-yl)-4-methanone (21). The alcohol **20** (700 mg, 1.26 mmol) in CH_2Cl_2 (50 mL) was treated with Dess−Martin periodinane (806 mg, 1.90 mmol) at 0 °C and stirred for 4 h. The mixture was quenched with 20 mL of $NaHCO_3$−Na_2SO_3 (1:1) and then extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave 640 mg (92%) of **21** as a pale yellow waxy solid. R_f = 0.60 (3:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.6 (1H, d, J = 7.8 Hz), 7.49 (1H, s), 7.48 (1H, d, J = 7.8 Hz), 4.21−4.18 (2H, m), 4.11−4.06 (2H, m), 3.78 (1H, q, J = 6.9 Hz), 2.76−2.67 (2H, m), 2.24 (2H, t, J = 6.9 Hz), 1.53−1.39 (3H, m), 1.42 (3H, d, J = 6.9 Hz), 1.13 (18H, d, J = 7.5 Hz), 0.13 (9H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.0, 151.9, 142.7, 141.4, 136.9, 134.2, 127.3, 125.5, 116.6, 109.1, 86.5, 65.6, 65.5, 37.3, 30.2, 27.4, 25.1, 18.5, 11.1, 0.3. FT-IR ($CDCl_3$, cm^{-1}) δ 2947, 2869, 1665, 1548, 1249, 1114, 879, 842. HRMS (ESI) calcd for $C_{31}H_{45}NO_4Si_2$ $[M + H]^+$ 552.2965, found 552.2966.

(5-(But-3-yn-2-yl)-2,3-dihydrospiro[1,3-dioxolane-2,1′-inden]-4′-yl)(oxazol-5-yl)methanone (22). The starting material **21** (520 mg, 0.94 mmol) in THF (40 mL) was treated with TBAF (1 M in THF, 0.47 mL, 0.47 mmol; use of more than 0.5 equivalents of TBAF leads to extensive decomposition) at 0 °C and stirred for 30 min. The mixture was then quenched with water. The two layers were separated and the aqueous layer extracted with Et_2O, the combined organic extracts washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 3:1 hexanes/EtOAc) gave 245 mg (81%) of **22** as a yellow waxy oil. R_f = 0.25 (1:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (1H, s), 7.60 (1H, d, J = 8.1 Hz), 7.59 (1H, s), 7.49 (1H, d, J = 7.2 Hz), 4.20−4.05 (4H, m), 3.75 (1H, q, J = 6.9 Hz), 2.83−2.68 (2H, m), 2.26 (2H, t, J = 6.9 Hz), 2.16 (1H, s), 1.44 (3H, t, J = 7.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.4, 154.6, 142.5, 141.9, 141.5, 136.4, 127.3, 125.9, 116.5, 86.6, 70.6, 65.6, 37.3, 29.1, 27.5, 24.7, 24.1, 18.5, 11.2. FT-IR ($CDCl_3$, cm^{-1}) 2359, 1665, 1560, 1317, 1127, 1041, 638. HRMS (ESI) calcd for $C_{19}H_{18}NO_4$ $[M + H]^+$ 324.1236, found 324.1230.

Ethyl 4-{4′-[(1,3-Oxazol-5-yl)carbonyl]-2′,3′-dihydrospiro[1,3-dioxolane-2,1′-indene]-5′-yl}pent-2-ynoate (23). The terminal alkyne **22** (240 mg, 0.74 mmol) in DMF (30 mL) was treated with $Pd(OAc)_2(PPh_3)_2$ (55.6 mg, 0.074 mmol) at rt. The flask was evacuated and backfilled with CO/O_2 (1:1) in a balloon. 2.17 mL of EtOH (approx 50 mmol) was added *via* syringe and the mixture stirred at rt for 65 h and then quenched with sat. aq. NH_4Cl. The cloudy suspension was filtered through short pad of Celite. The two layers were separated and the aqueous layer extracted with EtOAc. The combined organic extracts were washed twice with water and then rinsed with brine. After drying over $MgSO_4$ the extracts were concentrated under reduced pressure. Purification by column chromatography (SiO_2, 3:1 hexanes/EtOAc) gave 228 mg (78%) of **23** as a yellow sticky oil. R_f = 0.20 (1:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (1H, s), 7.62 (1H, s), 7.56 (1H, d, J = 8.1 Hz), 7.51 (1H, d, J = 8.1 Hz), 4.22−4.06 (6H, m), 3.91 (1H, q, J = 6.9 Hz), 2.77−2.67 (2H, m), 2.26 (2H, t, J = 7.2 Hz), 1.50 (3H, d, J = 6.9 Hz), 1.27 (3H, t, J = 7.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.1, 154.7, 153.7, 150.1, 142.4, 141.7, 140.6, 136.5, 133.5, 127.4, 126.2, 116.3, 89.9, 74.9, 65.6, 62.2, 37.3, 29.2, 27.6, 23.7, 14.2. FT-IR ($CDCl_3$, cm^{-1}) 2980, 2237, 1710, 1666, 1561, 1469, 1253, 1127, 1037. HRMS (ESI) calcd for $C_{22}H_{22}NO_6$ [M + H]$^+$ 396.1447, found 396.1442.

Ethyl-4,9-drospiro[1,3-dioxolane-2,1′-inden]-4′-yl-4-methyl-9-oxonaphtho[2,3-b]furan-3-carboxylate (25). A solution of the alkyne oxazole **23** (200 mg, 0.51 mmol) in 10 mL of dry 1,2-dichlorobenzene was stirred for 4 h at 170 °C under a nitrogen atmosphere. After cooling to rt, the solution was passed through a short plug of silica gel using hexanes to elute 1,2-dichlorobenzene. The product was then eluted from the silica gel with hexanes/ethyl acetate (5:1) to give 148 mg (80%) of the dienone **25** as a pale yellow oil. R_f = 0.35 (1:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (1H, s), 7.59 (1H, d, J = 8.0 Hz), 7.48 (1H, d, J = 8.0 Hz), 4.56 (1H, q, J = 7.0 Hz), 4.42 (2H, q, J = 7.2 Hz), 4.21−4.08 (4H, m), 3.65−3.42 (2H, m), 2.35 (2H, t, J = 7.5 Hz), 1.62 (3H, d, J = 7.0 Hz), 1.41 (3H, t, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 162.4, 152.5, 149.7, 146.7, 142.1, 138.8, 128.5, 127.5, 118.8, 116.6, 65.5, 65.4, 61.2, 37.2, 34.6, 30.5, 25.5, 14.5. FT-IR ($CDCl_3$, cm^{-1}) 2977, 1722, 1668, 1302, 1125, 1035. HRMS (ESI) calcd for $C_{21}H_{21}O_6$ [M + H]$^+$ 369.1338, found 369.1335.

Ethyl 16′-[(tert-butyldimethylsilyl)oxy]-10′- methyl-14′-oxaspiro[1,3-dioxolane-2,5′- tetracyclo-[7.7.0.0^{2,6}.0^{11,15}]hexadecane]- 1′,6′,8′,10′,12′,15′-hexaene-12′-carboxylate (26). To a solution of **25** (130 mg, 0.35 mmol) in THF (20 mL) at ice bath temperature was added Et_3N (146 μL, 1.05 mmol) followed by TBSOTf (160 μL, 0.7 mmol). The mixture was gradually warmed to rt and stirred for an additional 30 min and then quenched with sat. aq. $NaHCO_3$. The two layers were separated and aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 20:1 hexanes/EtOAc) gave 135 mg (80%) of **26** as a yellow oil. R_f = 0.75 (3:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$). δ 8.31 (1H, s), 8.11 (1H, d, J = 9.0 Hz), 7.14 (1H, d, J = 9.0 Hz), 4.40 (2H, q, J = 6.9 Hz), 4.26−4.24 (2H, m), 4.16−4.11 (2H, m), 3.67 (2H, t, J = 6.6 Hz), 3.10 (3H, s), 2.40 (2H, t, J = 6.6 Hz), 1.42 (3H, t, J = 7.2 Hz), 0.97 (9H, s), 0.35 (6H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 153.6, 144.2, 139.9, 137.9, 135.2, 133.1, 124.9, 123.2, 121.4, 119.6, 117.8, 116.2, 65.6, 61.1, 37.2, 31.7, 26.5, 25.9, 19.4, 16.8, 14.6, −2.3. FT-IR ($CDCl_3$, cm^{-1}) 2930, 1728, 1465, 1373, 1253, 1142, 832. HRMS (ESI) calcd for $C_{27}H_{35}O_6Si$ [M + H]$^+$ 483.2203, found 483.2203.

16′-[(tert-Butyldimethylsilyl)oxy]-10′-methyl-14′-oxaspiro[1,3-dioxolane-2,5′-tetracyclo[7.7.0.0^{2,6}.0^{11,15}]-hexadecane]- 1′,6′,8′,10′,12′,15′-hexaene-12′-carbaldehyde (27). $LiAlH_4$ (4 M in Et_2O, 32.5 μL, 0.13 mmol) was added dropwise to a solution of the ester **26** (130 mg, 0.27 mmol) in 10 mL of anhydrous THF at 0 °C. After addition was complete, the reaction mixture was stirred for 30 min, and then slowly quenched with 2.5 mL of MeOH and 5 mL of Rochelle's salt. The gelatinous mixture was diluted with Et_2O and then stirred at room temperature for 20 min followed by filtration through a Celite pad and the cake washed with Et_2O. The filtrate was washed with brine, dried over anhydrous $MgSO_4$, and the solvent evaporated under reduced pressure to afford 120 mg of the crude alcohol that was used without further purification. The crude alcohol (120 mg, 0.27 mmol) in 30 mL of CH_2Cl_2 was treated with Dess−Martin periodinane (127 mg, 0.3 mmol) at 0 °C and stirred for 2 h. The mixture was then quenched with 10 mL of $NaHCO_3$−Na_2SO_3 (1:1), diluted with more CH_2Cl_2 and stirred vigorously at room temperature for 10 min. The two layers were separated and the aqueous layer extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave 103 mg (87%) of the aldehyde **27** as a pale yellow solid. R_f = 0.55 (3:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.17 (1H, s), 8.32 (1H, s), 8.15 (1H, d, J = 9.0 Hz), 7.44 (1H, d, J = 9.0 Hz), 4.26−4.24 (2H, m), 4.16−4.11 (2H, m), 3.76 (2H, t, J = 7.5 Hz), 3.20 (3H, s), 2,27 (2H, t, J = 6.9 Hz), 0.99 (9H, s), 0.30 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.9, 159.8, 144.8, 140.0, 138.4, 133.4, 126.2, 125.0, 123.7, 122.2, 120.0, 117.7, 65.6, 37.1, 31.7, 26.5, 19.4, 18.0, −2.5. FT-IR ($CDCl_3$ cm^{-1}) 1691, 1158, 832. HRMS (ESI) calcd for $C_{25}H_{31}O_5Si$ [M + H]$^+$ 439.1941, found 439.1932.

1-{16′-[(tert-butyldimethylsilyl)oxy]-10′-methyl-14′-oxaspiro[1,3-dioxolane-2,5′-tetracyclo[7.7.0.0^{2,6}.0^{11,15}]-hexadecane]- 1′,6′,8′,10′,12′,15′-hexaen-12′-yl}but-3-en-1-ol (28). A solution of the aldehyde **27** (50 mg, 0 11 mmol) in 5 mL of THF at ice bath temperature was treated with allylmagnesium bromide (1.0 M in Et_2O, 0.57 mL, 0.57 mmol). The mixture was warmed to room temperature and stirred for 2 h, quenched with $NaHCO_3$ and extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 3:1 hexanes/EtAOc) gave 51 mg (96%) of the product **28** as a pale yellow oil. R_f = 0.50 (3:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (1H, d, J = 9 Hz), 7.68 (1H, s), 7.40 (1H, d, J = 9 Hz), 5.97−5.94 (1H, m), 5.30−5.22 (3H, m), 4.28−4.23 (2H, m), 4.17−4.13 (2H, m), 3.67, (2H, t, J = 7 Hz), 2.91 (3H, s), 2.86−2.83 (1H, m), 2.66−2.62 (1H, m), 2.38 (2H, dt, J = 7.5 Hz, J = 6 Hz), 2.12 (1H, s), 1.06 (9H, s), 0.96 (9H, s), 0.35 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 140.0, 137.2, 134.5, 132.6, 127.2, 124.6, 124.3, 119.1, 66.7, 65.5, 42.3, 37.1, 31.8, 26.6, 19.4, 16.2, −2.4. FT-IR ($CDCl_3$, cm^{-1}) 3446, 2929, 1623, 1462, 1372, 1315, 1130, 1039, 833, 733. HRMS (EI) calcd for $C_{28}H_{36}O_5Si$ 480.2332, found 480.2341.

3-{16-[(tert-Butyldimethylsilyl)oxy]-10-methyl-5- oxo-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,12,15-hexaen-12-yl}-3-hydroxypropanal (29). To a solution of the olefin **28** (25 mg, 0.05 mmol) in dioxane-water (4 mL; 3:1) was added OsO_4 (4% weight in H_2O, 35 μL, 0.005 mmol), and $NaIO_4$ (43 mg, 0.2 mmol). The mixture was stirred at rt for 1 h and then diluted with CH_2Cl_2 (2 mL) and H_2O (1 mL). The two layers were separated and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$ and then concentrated *in vacuo* to give a brown oil. Purification by preparative thin layer chromatography (1:1 hexanes/EtOAc) gave 9 mg (41%) of **29** as a pale yellow oil. R_f = 0.35 (2:1 hexanes/EtOAc) ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.99 (1H, s), 8.05 (1H, d, J = 8.5 Hz), 7.78 (1H, s), 7.67 (1H, d, J = 9.0 Hz), 5.82 (1H, d, J = 8 Hz), 3.82−3.80 (2H, t, J = 6.5 Hz), 3.18−3.16 (1H, m), 3.06−2.91 (1H, m), 2.92 (3H, s), 2.77−2.75 (2H, m), 0.98 (9H, s), 0.42 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.4, 157.1, 144.8, 133.7, 129.1, 124.8, 119.5, 117.8, 63.9, 62.5, 51.1, 36.4, 29.7, 26.5, 16.2, 14.0, −2.2. FT-IR ($CDCl_3$, cm^{-1}) 3419, 2930, 1731, 1620, 1374, 1254, 1171, 830. HRMS (ESI) calcd for $C_{25}H_{31}O_5Si$ $[M + H]^+$ 439.1941, found 439.1933.

(2*E*)-3-{16-[(tert-Butyldimethylsilyl)oxy]-10-methyl-5-oxo-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,12,15-hexaen-12-yl}prop-2-enal (30). A solution of the aldehyde **29** (5.0 mg, 0.01 mmol) in 2 mL of dry degassed CH_2Cl_2 at rt under atmosphere of N_2 was slowly added $TiCl_4$ (1.0 M in CH_2Cl_2, 20 μL, 0.020 mmol) The resulting dark purple reaction was stirred for 45 min and then quenched *via* the dropwise addition of $NaHCO_3$. The solution was diluted with CH_2Cl_2 and then washed with H_2O. The aqueous portion was extracted three times with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by preparative thin layer chromatography (3:1 hexanes/EtOAc) gave 1.5 mg (35%) of the enal **30** as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (1H, d, J = 7.5 Hz), 8.09 (1H, d, J = 9.0 Hz), 8.05 (1H, s), 7.98 (1H, d, J = 16.0 Hz), 7.73 (1H, d, J = 8.5 Hz), 7.68 (1H, d, J = 9.0 Hz), 6.66 (1H, dd, J = 16.0, 7.5 Hz), 3.85−3.83 (2H, m), 2.97 (3H, s), 2.80−2.78 (2H, m), 1.00 (9H, s), 0.44 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.5, 145.8, 144.2, 142.7, 140.8, 138.4, 131.1, 129.9, 124.5, 124.0, 122.8, 122.7, 121.9, 119.7, 119.343.8, 36.0, 33.2, 29.9, 26.6, 25.4, 19.4, 19.0, 16.1, −2.5. FT-IR ($CDCl_3$, cm^{-1}) 2359, 1682, 1669, 1360, 1120, 833. HRMS (EI) calcd for $C_{25}H_{28}O_4Si$ 420.1757, found 420.1761.

Methyl (2*E*)-3-{16′-[(tert- butyldimethylsilyl)oxy]-10′-methyl-14′-oxaspiro[1,3-dioxolane-2,5′-tetracyclo-[7.7.0.0^{2,6}.0^{11,15}]hexadecane]-1′,6′,8′,10′,12′,15′-hexaen-12′-yl}prop-2-enoate (35). To a stirred solution of *n*-BuLi (1.6 M in hexanes, 1.05 mL, 1.71 mmol) in THF (15 mL) was added the phosphonate reagent **34** (418.5 μL, 2.28 mmol) at ice bath temperature. The mixture was then warmed to room temperature. After 15 min, a solution of the aldehyde **27** (250 mg, 0.57 mmol) in THF (15 mL) was added at 0 °C. The resulting mixture was stirred at 0 °C for 1 h, quenched with $NaHCO_3$, and extracted with EtOAc. The organic extracts were dried over $MgSO_4$, concentrated under reduced pressure and purified by column chromatography (SiO_2, hexanes/EtOAc; 10:1) to give 209 mg (74%) of **35** as a yellow solid. M.p: 192−194 °C. R_f =0.75 (5:1 hexanes:EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (1H, d, J = 15.6 Hz), 8.02 (1H, d, J = 8.7 Hz), 7.86 (1H, s), 7.41 (1H, d, J = 9.0 Hz), 6.32 (1H, d, J = 15.9 Hz), 4.29−4.11 (4H, m), 3.85 (3H, s), 3.67 (1H, t, J = 6.9 Hz), 2.89 (3H, s), 2.38 (2H, t, J = 6.9 Hz), 2,27 (2H, t, J = 7.2 Hz), 0.97 (9H, s), 0.36 (6H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 144.8, 143.8, 140.1, 137.6, 136.3, 135.3, 132.5, 126.4, 125.8, 124.3, 123.1, 119.8, 119.5, 117.8, 65.6, 52.0, 37.1, 31.8, 30.5, 26.5, 19.4, 16.1, −2.3. FT-IR ($CDCl_3$ cm^{-1}) 2952, 1719, 1633, 1370, 1312, 1169, 1038, 832. HRMS (EI) calcd for $C_{28}H_{34}O_6Si$ 494.2125, found 494.2131.

Methyl 3-{16′-[(tert-Butyldimethylsilyl)oxy]-10′-methyl-14′-oxaspiro[1,3-dioxolane-2,5′-tetracyclo-[7.7.0.0^{2,6}.0^{11,15}]hexadecane]-1′,6′,8′,10′,12′,15′-hexaen-12′-yl}propanoate (36), Methyl 3-{16-[(tert-Butyldimethylsilyl)oxy]-10-methyl-14-oxatetracyclo-[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,12,15-hexaen-12-yl}-propanoate (37), Methyl 3-{16-[(tert-Butyldimethylsilyl)-oxy]-10-methyl-14-oxatetracyclo[7.7.0.0.^{2,6}.0^{11,15}]-hexadeca-1,6,8,10,12,15-hexaen-12-yl}propanoate (38) and Methyl 3-{16-[(tert-Butyldimethylsilyl)oxy]-10-methyl-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,15-pentaen-12-yl}propanoate (39). To a solution of the unsaturated ester **35** (120 mg, 0.242 mmol) in 6 mL of ethyl acetate at −10 °C was added 5% Pd on carbon (50.68 mg, 0.024 mmol) portionwise over 1 h. The reaction mixture was stirred for 1.5 h under a balloon of H_2 at −10 °C and then filtered through a Celite pad. The filtrate was concentrated *in vacuo* to give a yellow residue. Purification by column chromatography (SiO_2, 10:1 hexanes/EtAOc) gave 80 mg (69%) 3:1 mixture of **36** and **37** a yellow solid. R_f = 0.50 (5:1 hexanes/EtOAc) and 12 mg mixture of the C17-norketone **38** and dihydrofuran **39** as a yellow solid. Recrystallization of the mixture of **38** and **39** from hexanes gave 8 mg (8%) of **38** as pale yellow needle crystals. Mp: 140−142 °C, and 2 mg (1%) of dihydrodrofuran **39** as yellow oil. Compound **38**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (1H, d, J = 9.0 Hz), 7.39 (1H, s), 7.34 (1H, d, J = 8.7 Hz), 3.71 (3H, s), 3.65 (2H, t, J = 7.5 Hz), 3.26 (2H, t, J = 8.1 Hz), 3.02 (2H, t, J = 7.5 Hz), 2.89 (3H, s), 2.76 (2H, t, J = 7.5 Hz), 2.17 (2H, q, J = 7.5 Hz), 0.96 (H, s), 0.34 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 142.6, 140.0, 138.2, 130.5, 126.9, 123.5, 122.3, 121.8, 119.9, 118.8, 52.0, 36.0, 34.4, 33.2, 26.6, 25.4, 21.9, 19.4, 15.2, −2.5. FT-IR ($CDCl_3$, cm^{-1}) HRMS (ESI) calcd for $C_{26}H_{35}O_4Si$ $[M + H]^+$ 439.2305, found 439.2300.

Compound **39**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (1H, d, J = 8.4 Hz), 7.24 (1H, d, J = 8.4 Hz), 6.98 (1H, s), 4.42−4.35 (2H, m), 3.65 (3H, s), 3.55 (2H, t, J = 7.5 Hz), 2.99 (2H, t, J = 8.7 Hz), 2.54 (3H, s), 2.39−2.27 (2H, m), 2.09 (2H, t, J = 7.5 Hz), 1.92−1.89 (2H, m), 0.96 (9H, s), 0.28 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 145.3, 141.4, 137.9, 130.7, 129.8, 127.2, 125.8, 122.9, 122.6, 120.9, 75.3, 51.8, 41.2, 35.8, 33.1, 31.2, 30.5, 29.9, 26.3, 19.5, 15.8, −2.6. FT-IR ($CDCl_3$, cm^{-1}) 2953, 1739, 1256, 837. HRMS (ESI) calcd for $C_{26}H_{37}O_4Si$ $[M + H]^+$ 441.2461, found 441.2455.

3-{16′-[(tert-Butyldimethylsilyl)oxy]-10′-methyl-14′-oxaspiro[1,3-dioxolane-2,5′-tetracyclo[7.7.0.0^{2,6}.0^{11,15}]-hexadecane]-1′,6′,8′,10′,12′,15′-hexaen-12′-yl}propanal (41). To a solution of a 3:1 mixture of the ketal **36** and ketone **37** (80 mg) in CH_2Cl_2 (5 mL) at ice bath was added Et_3N (31.2 μL, 0.132 mmol) followed by TBSOTf (20 μL, 0 09 mmol). The mixture was stirred at ice bath temperature for 30 min and then quenched with sat. aq. $NaHCO_3$. The two layers were separated and the aqueous layer extracted twice with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a brown oil. Purification by column chromatography (SiO_2, 20:1 hexanes/EtOAc) gave 48 mg of the ketal **36** as a yellow solid. Mp = 174−177 °C, and gave 20 mg of silyl enol ether **40** as a yellow oil. Compound **36**: R_f = 0.25 (5:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (1H, d, J = 9 Hz), 7.43 (1H, s), 7.39 (1H, d, J = 9.0 Hz), 4.28−4.25 (2H, m), 4.15−4.12 (2H, m), 3.71 (3H, s), 3.67 (2H, t, J = 6.5 Hz), 3.27 (2H, t, J = 8.0 Hz), 2.88 (3H, s), 2.77 (2H, t, J = 8.4 Hz), 2.38 (2H, 6.5 Hz), 0.96 ((H, s), 0.34 (6H, s). HRMS (EI) calcd for $C_{28}H_{36}O_6Si$: 496.2279, found 496.2281. Compound **40**: R_f = 0.65 (5:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (1H, d, J = 9.0 Hz), 7.57 (1H, d, J = 8.5 Hz), 5.56 (1H, t, J = 4.5 Hz), 3.95 (2H, d, J = 1.5 Hz), 3.78 (3H, s), 3.28 (2H, t, J = 8.0 Hz), 2.92−2.91 (2H, m), 2.92 (3H, s), 2.78−2.76 (2H, t, J = 7.0 Hz), 1.07 (9H, s), 0.97 (9H, s), 0.43 (6H, s), 0.29 (6H, s). HRMS (EI) calcd for $C_{32}H_{46}O_5Si_2$ 566.2884, found 566.2878. A solution of the ester **36** (24 mg, 0.048 mmol) in 6 mL of dry THF was cooled to 0 °C. $LiAlH_4$ (4 M in Et_2O, 6

μL, 0.024 mmol) was added dropwise. The mixture was stirred for 30 min and then slowly quenched with 0.5 mL of MeOH followed by 1 mL of Rochelle's salt. The mixture was diluted with Et_2O, warmed to room temperature and stirred vigorously for 30 min. The precipitate was filtered through a Celite pad and the filtrate was washed with brine, dried over anhydrous $MgSO_4$, and the solvent evaporated *in vacuo* to afford the corresponding alcohol (22 mg). This alcohol was used in the next step without further purification. Oxalyl chloride (9 μL, 0.11 mmol) in 0.5 mL of CH_2Cl_2 was cooled to −78 °C. DMSO (12 μL, 0.21 mmol) in 0.5 mL of CH_2Cl_2 was added *via* syringe and the mixture stirred for 5 min. The crude alcohol above (22 mg, 0.048 mmol) in 0.5 mL of CH_2Cl_2 was added *via* syringe followed by Et_3N (34 μL, 0.24 mmol). The mixture was allowed to warm to room temperature and then quenched with water. The two layers were separated and aqueous layer extracted with CH_2Cl_2. The combined organic extracts were washed with water twice, rinsed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave 18.6 mg (83%) of **41** as a pale yellow oil. R_f =0.65 (2:1 hexanes/EtOAc) ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.90 (1H, s), 8.00 (1H, d, J = 8.5 Hz), 7.41 (1H, s), 7.40 (1H, d, J = 9.5 Hz), 4.28−4.25 (2H, m), 4.15−4.12 (2H, m), 3.67 (2H, t, J = 7 Hz), 3.27 (2H, t, J = 7 Hz), 2.95−2.91 (2H, m), 2.88 (3H, s), 2.38 (2H, t, J = 6.5 Hz), 0.96 (9H, s), 0.35 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.3, 143.1, 140.1, 137.1, 132.0, 128.0, 124.1, 119.9, 119.0, 110.0, 65.5, 43.7, 37.1, 31.8, 29.9, 26.5, 19.4, 18.9, 15.3, −2.2. FT-IR ($CDCl_3$, cm^{-1}) 2928, 2359, 1716, 1372, 832. HRMS (ESI) calcd for $C_{27}H_{35}O_5Si$ [M + H]$^+$ 467.2254, found 467.2259.

3-{16-[(tert-Butyldimethylsilyl)oxy]-10-methyl-5-oxo-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,12,15-hexaen-12-yl}propanal (42). To a solution of the aldehyde **41** (10.0 mg, 0.02 mmol) in 4 mL of dry CH_2Cl_2 at rt under N_2 was slowly added $TiCl_4$ (1.0 M in CH_2Cl_2, 40 μL, 0.04 mmol). The resulting dark purple reaction was stirred for 45 min and then quenched with $NaHCO_3$, extracted with CH_2Cl_2, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by preparative thin layer chromatography (SiO_2, 3:1 hexanes/EtOAc) gave 7.6 mg (82%) of the ketone **42** as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.91 (1H, s), 8.04 (1H, d, J = 5.5 Hz), 7.67 (1H, d, J = 5.7 Hz), 7.5 (1H, s), 3.84−3.82 (2H, m), 3.30 (2H, t, J = 4.5 Hz), 2.95 (2H, d, J = 4.5 Hz), 2.92 (3H, s), 2.78−2.76 (2H, m), 0.97 (9H, s), 0.42 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.4, 200.9, 157.2, 144.2, 136.7, 136.0, 133.7, 133.4, 130.4, 125.8, 124.6, 122.5, 120.3, 119.6, 117.6, 43.7, 36.5, 30.6, 29.8, 26.5, 22.9, 21.5, 18.8, 15.3, −2.2. FT-IR ($CDCl_3$, cm^{-1}) HRMS (ESI) calcd for $C_{25}H_{30}O_4Si$ [M + H]$^+$ 423.1992, found 423.1986.

Bis(ethyl (2Z)-6-{4′-[(1,3-oxazol-5-yl)carbonyl]-2′,3′-dihydrospiro[1,3-dioxolane-2,1′-indene]-5′-yl}hept-2-en-4-ynoate) (46). A mixture of the terminal alkyne **22** (200 mg, 0.62 mmol) and iodoacrylate **45** (168 mg, 0.74 mmol) in THF (20 mL) was treated with $PdCl_2(PPh_3)_2$ (21 mg, 0.03 mmol) and CuI (5.7 mg, 0.03 mmol) under N_2. Et_3N (432 μL, 3.1 mmol) was added *via* syringe and the mixture stirred at rt for 3 h then quenched with sat. aq. NH_4Cl. The two layers were separated and the aqueous layer extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 2:1 hexanes/EtOAc) gave 170 mg (65%) of **46** as a sticky yellow oil. R_f = 0.25 (1:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (1H, s), 7.70 (1H, d, J = 8.0 Hz), 7.63 (1H, s), 7.51 (1H, d, J = 8.0 Hz), 6.06−6.01 (2H, m), 4.22−4.16 (4H, m), 4.12−4.09 (2H, m), 3.98 (1H, q, J = 7.5 Hz), 2.83 (1H, m), 2.73−2.67 (1H, m), 2.27 (2H, t, J = 7.0 Hz), 1.51 (3H, d, J = 7.0 Hz), 1.28 (3H, t, J = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.4, 164.8, 142.4, 141.9, 141.5, 133.4, 128.8, 127.7, 126.0, 123.0, 116.5, 104.7, 79.7, 65.6, 65.5, 60.6, 37.3, 30.6, 27.5, 24.7, 14.5, 14.4. FT-IR ($CDCl_3$, cm^{-1}) 2979, 1720, 1666, 1184, 1042. HRMS (ESI) calcd for $C_{24}H_{24}NO_6$ [M + H]$^+$ 422.1604, found 422.1608.

Ethyl 3-{16′-[(tert-Butyldimethylsilyl)oxy]-10′-methyl-14′-oxaspiro[1,3-dioxolane-2,5′-tetracyclo-[7.7.0.0^{2,6}.0^{11,15}]hexadecane]-1′,6′,8′,10′,12′,15′-hexaen-12′-yl}propanoate (50). A solution of the enyne oxazole **46** (100 mg, 0.24 mmol) in 10 mL of dry 1,2-dichlorobenzene was stirred for 8 h in a 30 mL round-bottom flask at 180 °C under a nitrogen atmosphere. After cooling to rt, the solution was passed through a plug of silica gel using hexanes to elute the 1,2-dichlorobenzene. The product was then eluted from the silica gel with hexanes/EtOAc (4:1) to give 70 mg of **47** and **48** as a yellow solid, R_f = 0.45 (1:1 hexanes/EtOAc). To a solution of the mixture of **47** and **48** (70 mg) in EtOAc (10 mL) at −10 °C was added approximately 10% of 5% Palladium on carbon. The flask was evacuated and then backfilled by attaching a balloon full of H_2. The mixture was vigorously stirred for 1 h at −10 °C and then filtered through a Celite pad. The product and starting material have very close R_f, but the stronger fluorescence of the product makes it easy to monitor the reaction. The filtrate was concentrated *in vacuo* to give 65 mg (68%) of the dienone saturated ester **49** as a pale yellow oil. R_f = 0.40 (1:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (1H, d, J = 7.8 Hz), 7.52 (1H, s), 7.46 (1H, d, J = 7.8 Hz), 4.26−4.09 (5H, m), 3.58 (2H, q, J = 6.6 Hz), 2.91 (2H, t, J = 7.2 Hz), 2.68 (2H, t, J = 7.5 Hz), 2.34 (2H, t, J = 6.9 Hz), 1.55 (3H, d, J = 9 Hz), 1.26 (3H, t, J = 7.8 Hz). A solution of dienone **49** (65 mg, 0.17 mmol) in CH_2Cl_2 (10 mL) at ice bath temperature was treated with Et_3N (71 μL, 0.51 mmol) followed by TBSOTf (58 μL, 0.34 mmol). The mixture was stirred at ice bath temperature for 30 min and then quenched with sat. aq. $NaHCO_3$. The two layers were separated and the aqueous layer extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 10:1 hexanes/EtOAc) gave 70 mg (81%) of the desired product (**50**) as a yellow oil. R_f = 0.75 (3:1 hexanes/EtOAc) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.0 (1H, d, J = 8.5 Hz), 7.43 (1H, s), 7.39 (1H, d, J = 9.0 Hz), 4.28−4.25 (2H, m), 4.56 (2H, q, J = 7.5 Hz), 4.42−4.22 (2H, m), 4.21−4.08 (4H, m), 3.67 (2H, t, J = 7.0 Hz), 3.26 (2H, t, J = 7.0 Hz), 2.88 (3H, s), 2.76 (2H, t, J = 7.5 Hz), 2.38 (2H, t, J = 6.5 Hz), 1.26 (3H, t, J = 7.0 Hz), 0.95 (9H, s), 0.35 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 143.0, 140.0, 137.1, 132.0, 128.1, 124.1, 122.7, 120.1, 119.1, 118.0, 65.5, 60.9, 37.1, 34.6, 31.8, 26.6, 21.9, 19.4, 15.2, 14.5, −2.4. FT-IR ($CDCl_3$ cm^{-1}) 2929, 1735, 1163, 833. HRMS (ESI) calcd for $C_{29}H_{39}O_6Si$ [M + H]$^+$ 511.2516, found 511.2523.

3-{16-[(tert-Butyldimethylsilyl)oxy]-5-hydroxy-10-methyl-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,12,15-hexaen-12-yl}propanal (51). A solution of the ester **50** (6.5 mg, 0.013 mmol) in 2.5 mL of dry CH_2Cl_2 was cooled to −78 °C. DIBAL-H (1 M in toluene, 14 μL, 0.014 mmol) was added dropwise. After the addition was complete, the reaction mixture was stirred for 30 min, and then slowly quenched with 0.5 mL of MeOH followed by 1 mL of Rochelle's salt and the mixture warmed and stirred at room temperature for 30 min. The precipitate was filtered through a Celite pad and filtrate washed with brine, dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure to afford 3.3 mg (60%) of the aldehyde **51** as a yellow oil. R_f = 0.25 (3:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.90 (1H, s), 8.00 (1H, d, J = 9.0 Hz), 7.50 (1H, d, J = 8.7 Hz), 7.40 (1H, s), 5.37 (1H, t, J = 5.7 Hz), 3.80 (2H, t, J = 8.4 Hz), 3.27 (2H, t, J = 7.2 Hz), 2.92 (2H, t, J = 6.6 Hz), 2.88 (3H, s), 2.63–2.54 (2H, m), 2.06–1.97 (2H, m), 0.95 (9H, s), 0.34 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.4, 142.6, 142.4, 138.4, 134.5, 131.7, 123.1, 119.2, 63.9, 43.8, 43.5, 37.4, 33.3, 29.9, 26.5, 22.9, 19.0, 15.2, 14.4, −2.1. FT-IR ($CDCl_3$, cm^{-1}) 3420, 2927, 1725, 1624, 1461, 1388, 1258, 834. HRMS (ESI) calcd for $C_{25}H_{33}O_4Si$ [M + H]$^+$ 425.2148, found 425.2155.

3-{16-[(tert-butyldimethylsilyl)oxy]-10-methyl-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,12,15-hexaen-12-yl}propanal (52). A solution of the ester **38** (200 mg, 0.5 mmol) in 50 mL of dry CH_2Cl_2 was cooled to −78 °C. DIBAL-H (1 M in toluene, 600 μL, 0.6 mmol) was added dropwise. The reaction mixture was stirred for 30 min, and then slowly quenched with 5 mL of MeOH followed by 10 mL of Rochelle's salt and warmed and stirred at room temperature for 30 min. The precipitate was filtered through a Celite pad and the filtrate washed with brine, dried over anhydrous $MgSO_4$, and the solvent was evaporated *in vacuo* to afford 170 mg (81%) of the aldehyde **52** as white solid. Recrystallization from hexanes gave colorless needle crystals. Mp: 175–176 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.89 (1H, s), 7.90 (1H, d, J = 8.7 Hz), 7.36 (1H, d, J = 9 Hz), 3.66 (2H, t, J = 7.2 Hz), 3.26 (2H, t, J = 7.2 Hz), 3.03 (2H, t, J = 7.5 Hz), 2.93 (2H, t, J = 7.8 Hz), 2.88 (3H, s), 2.16 (2H, t, J = 8.2 Hz), 0.97 (9H, s), 0.35 (6H, s), ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.4, 142.6, 140.1, 138.2, 130.5, 122.7, 121.9, 119.8, 118.7, 43.7, 36.1, 33.3, 26.7, 26.6, 25.6, 19.0, 15.2, −2.4. FT-IR ($CDCl_3$, cm^{-1}) 2926, 1721, 1361, 1254, 1110, 845, 788. HRMS (ESI) calcd for $C_{25}H_{33}O_3Si$ [M + H]$^+$ 409.2199, found 409.2208.

18-Hydroxy-1-methyl-13-oxapentacyclo-[10.6.1.0^{2,10}.0^{5,9}.0^{15,19}]nonadeca-2,4,9,12(19),14-pentaen-11-one (53) (=3). A solution of the aldehyde **52** (100 mg, 0.24 mmol) in 25 mL of dry CH_2Cl_2 at room temperature was added $TiCl_4$ (1 M in CH_2Cl_2, 960 μL, 0.96 mmol) dropwise. The reaction mixture was stirred for 30 min, and then slowly quenched with 1 mL of H_2O. The two layers were separated and aqueous layer extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 2:1 hexanes/EtOAc) gave 43 mg (60%) of *syn*-**53** as a yellow solid and 12 mg (12%) of *anti*-**53** as a purple oil. Recrystallization of *syn*-**53** from CH_2Cl_2 gave colorless needle crystals. Mp: 208–210 °C. *Syn*-**53**: R_f = 0.35 (2:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (1H, d, J = 8 Hz), 7.40 (1H, s), 7.39 (1H, d, J = 9.5 Hz), 4.12 (1H, dd, J = 11.5 Hz, 5.5 Hz), 3.64–3.52 (2H, m), 3.50–3.45 (2H, m), 2.95–2.89 (4H, m), 2.80–2.73 (2H, m), 2.28 (2H, dd, J = 14, 3 Hz), 2.19–2.05 (3H, m), 2.00 (1H, d, J = 5.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.0, 148.5, 147.7, 146.2, 144.9, 144.1, 142.8, 129.8, 127.9, 126.5, 120.6, 73.1, 41.4, 35.2, 32.1, 29.8, 26.3, 25.4, 17.3. FT-IR ($CDCl_3$, cm^{-1}) 3417, 2952, 1659, 1429, 1027, 731. HRMS (ESI) calcd for $C_{19}H_{19}O_3$ [M + H]$^+$ 295.1334, found 295.1333. *Anti*-**53**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (1H, d, J = 8.1 Hz), 7.50 (1H, d, J = 8.0 Hz), 7.40 (1H, s), 4.70 (1H, t, J = 2.8 Hz), 3.67–3.38 (2H, m), 3.02–2.81 (4H, m), 2.12 (2H, t, J = 8.5 Hz), 1.45 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.0, 148.2, 147.0, 146.4, 145.6, 143.5, 129.0, 128.1, 125.1, 122.6, 80.6, 71.4, 44.1, 35.1 34.6, 32.7, 32.3, 32.1, 25.4, 25.1, 16.5, 13.9. FT-IR ($CDCl_3$, cm^{-1}) 3421, 2953, 1660, 1030, 732.

2,3-Dihydro-1-oxo-5-((*E*)-pent-3-en-2-yl)-1*H*-inden-4-yl Trifluoromethanesulfonate (55). To a solution of 2,3-dihydro-1H-inden-4-ol (**54**)[61] (6 g, 44.72 mmol) and allyl carbonate **10** (7.74 g, 53.66 mmol) in CH_2Cl_2 (150 mL) was added $Pd(PPh_3)_4$ (516.5 mg, 0.45 mmol). The mixture was then refluxed for 3 h, cooled to room temperature and the solvent removed under reduced pressure. Purification by column chromatography (SiO_2, 100:1 hexanes/EtOAc) gave 8.68 g (96%) of 4-[(3*E*)-pent-3-en-2-yloxy]-2,3-dihydro-1H-indene as a colorless oil. R_f = 0.75 (10:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (1H, t, J = 7.2 Hz), 6.83 (1H, d, J = 7.2 Hz), 6.69 (1H, d, J = 8.1 Hz), 5.74–5.65 (1H, m), 5.59–5.51 (1H, m), 4.79–4.71 (1H, m), 2.93–2.85 (4H, m), 2.05 (2H, q, J = 7.5 Hz), 1.68 (2H, d, J = 6.3 Hz), 1.40 (2H, d, J = 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 146.5, 133.2, 133.0, 127.5, 127.0, 117.1, 111.5, 74.7, 33.6. 30.0, 25.3, 22.0, 18.0. FT-IR ($CDCl_3$, cm^{-1}) 2953, 1587, 1474, 1259, 1051, 964, 764. HRMS (EI) calcd for $C_{14}H_{18}O$ 202.1358, found 202.1367. The solution of 4-[(3*E*)-pent-3-en-2-yloxy]-2,3-dihydro-1H-indene (8 g, 39.55 mmol) obtained above in Et_2NPh (50 mL) was heated at 180 °C for 15 h. The dark brown mixture was then cooled to room temperature, diluted with 50 mL of ice water, and then stirred at room temperature for several minutes. The two layers were separated and the aqueous layer extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 30:1 to 10:1 hexanes/EtOAc) gave 7.36 g (92%) of 2,3-dihydro-5-((*E*)-pent-3-en-2-yl)-1H-inden-4-ol as a pale yellow oil. R_f =0.35 (5:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94 (1H, d, J = 7.8 Hz), 6.79 (1H, d, J = 7.5 Hz), 5.74–5.67 (2H, m), 5.16 (1H, s), 3.61–3.57 (1H, m), 2.90 (2H, t, J = 8.1 Hz), 2.84 (2H, t, J = 7.2 Hz), 2.09 (2H, t, J = 7.8 Hz), 1.74 (3H, d, J = 7.2 Hz), 1.38 (3H, d, J = 7.2 Hz). ^{13}C NMR (125 Hz, $CDCl_3$) δ 150.5, 144.8, 135.9, 135.4, 130.6, 128.3, 126.4, 125.5, 124.5, 116.9, 37.3, 33.2, 29.1, 25.5, 19.9, 18.2. FT-IR ($CDCl_3$, cm^{-1}) 3418, 2960, 1446, 1196, 998, 809. HRMS (EI) calcd for $C_{14}H_{18}O$ 202.1349, found 202.1358. To a solution of 2,3-dihydro-5-((*E*)-pent-3-en-2-yl)-1H-inden-4-ol (7 g, 34.6 mmol) in CH_2Cl_2 (50 mL) at 0 °C was added pyridine (5.57 mL, 69.2 mmol) followed by dropwise addition of Tf_2O (6.99 mL, 41.52 mmol). The reaction was then stirred for an additional 10 min. The resulting dark green residue was diluted with Et_2O and then quenched with dil. HCl. The aqueous layer was extracted with CH_2Cl_2, the combined organic extracts washed with $NaHCO_3$, rinsed with brine, dried over $MgSO_4$ and then concentrated under reduced pressure. Purification by column chromatography (SiO_2, 80:1 hexanes/EtOAc) gave 11.33 g (98%) of the triflate **55** as a colorless oil. R_f = 0.8 (10:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (1H, d, J = 6.5 Hz), 7.13 (1H, d, J = 7.5 Hz), 5.60–5.48 (2H, m), 3.84–3.81 (1H, m), 3.06 (2H, t, J = 7.5 Hz), 2.95 (2H, t, J = 7.5 Hz), 2.16–10 (2H, m), 1.68 (3H, d, J = 7.2 Hz), 1.35 (3H, d, J = 7.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.0, 143.3, 137.2, 134.7, 127.5, 124.9, 120.1, 117.6, 34.9, 33.3, 31.2, 25.7, 22.9, 18.1. FT-IR ($CDCl_3$, cm^{-1}) 2966, 1407, 1212, 1144, 970, 852, 825, 643. HRMS (EI) calcd for$C_{15}H_{17}O_3F_3S$ 334.0851, found 334.0843.

5-(4,4-Dibromobut-3-en-2-yl)-2,3-dihydro-1H-inden-4-yl Trifluoromethanesulfonate (56). To a solution of the triflate **55** (10 g, 29.91 mmol) in CH_2Cl_2 (200 mL) was bubbled ozone at −78 °C until a blue solution resulted and persisted (approximately 30 min). Excess ozone was removed by a nitrogen stream, triphenylphosphine (19.61 g, 74.77 mmol) was added, the mixture warmed to rt and stirred overnight. Silica gel was added to the mixture and the solvent removed under reduced pressure. Dry pack silica gel column chromatography purification (100% hexanes to 100:1 hexanes/EtOAc) gave 7.71 g (80%) of the corresponding aldehyde as colorless oil. R_f = 0.50 (10:1 hexanes/EtOAc) ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.67 (1H, s), 7.24 (1H, d, J = 7.5 Hz), 6.96 (1H, d, J = 7.5 Hz), 4.03 (1H, q, J = 7.2 Hz), 3.08 (2H, t, J = 7.2 Hz), 2.98 (2H, t, J = 7.5 Hz), 2.17 (2H, t, J = 7.8 Hz),1.36 (3H, d, J = 6.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.7, 148.2, 138.3, 129.2, 128.3, 125.3, 120.0, 117.5, 46.1, 33.4, 31.1, 25.6, 15.2. FT-IR ($CDCl_3$, cm^{-1}) 2961, 1730, 1407, 1214, 1143, 970, 849, 642. HRMS (EI) calcd for $C_{13}H_{13}O_4F_3S$ 322.0487, found 322.0486. To a solution of the aldehyde obtained above (7 g, 21.72 mmol) in CH_2Cl_2 (150 mL) at 0 °C was added, carbon tetrabromide (14.41 g, 43.44 mmol), triphenylphosphine (11.39 g, 43.44 mmol), and zinc dust (2.84 g, 43.44 mmol). The mixture was warmed to room temperature and stirred until TLC analysis showed all the starting material consumed (about 30 min). The mixture was filtered through a thin film of silica gel, and the cake washed twice with CH_2Cl_2. The solvent was removed under reduced pressure and the residue taken up in hexanes where upon most of the triphenylphosphine oxide precipitated at the bottom of the flask. The solvent was decanted and concentrated under reduced pressure to give an orange residue. The residue was purified by silica gel column chromatography (SiO_2, 100:1 hexanes/EtOAc) to give 9.24 g (89%) of the dibromoolefin **56** as a yellow oil. R_f = 0.70 (5:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (1H, d, J = 7.8 Hz), 7.12 (1H, d, J = 7.8 Hz), 6.56 (1H, d, J = 9.0 Hz), 4.10 (1H, q, J = 6.9 Hz), 3.07 (2H, t, J = 8.1 Hz), 2.95(2H, t, J = 7.5 Hz), 2.19−2.06 (2H, m), 1.39 (3H, d, J = 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 141.7, 137.9, 134.4, 127.0, 125.1, 121.0, 116.7, 90.2, 36.9, 33.3, 31.2, 25.6, 21.4. FT-IR ($CDCl_3$, cm^{-1}). 1723, 1408, 1216, 1133, 817. HRMS (EI) calcd for $C_{14}H_{13}O_3F_3S$ Br_2 475.8905, found 475.8895.

2,3-Dihydro-5-(4-(trimethylsilyl)but-3-yn-2-yl)-1H-inden-4-yl trifluoromethanesulfonate (57). To a solution of the dibromoolefin **56** (9 g, 18.82 mmol) in THF (200 mL) at −78 °C was added *n*-BuLi (1.6 M solution in hexanes, 25.88 mL, 41.40 mmol) dropwise under a nitrogen atmosphere. After 30 min, TMSCl (5.25 mL, 41.40 mmol) was added and the mixture stirred for an additional 30 min and then quenched with dil. HCl. The resulting white suspension was warmed to room temperature, extracted with ethyl acetate, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 100:1 to 50:1 hexanes/EtOAc) gave 6.69 g (91%) of the TMS alkyne **57** as a clear oil. R_f = 0.55 (10:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (1H, d, J = 7.8 Hz), 7.23 (1H, d, 7.8 Hz), 4.09 (1H, q, J = 7.2 Hz), 3.04 (2H, t, J = 7.5 Hz), 2.96 (2H, t, J = 7.5 Hz), 2.13 (2H, q, J = 7.5 Hz), 1.45 (3H, d, J = 6.9 Hz), 0.16 (9H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.2, 142.5, 137.4, 134.0, 128.1, 125.0, 120.1, 117.6, 108 6. 86.4, 33.3, 31.4, 27.1, 25.7, 24.1, 0.3. FT-IR ($CDCl_3$, cm^{-1}) 2961, 2174, 1408, 1214, 1143, 972, 846, 643. HRMS (EI) calcd for $C_{17}H_{21}F_3O_3SSi$ 390.0933, found 390.0930.

(3-(2,3-Dihydro-4-vinyl-1H-inden-5-yl)but-1-ynyl)-trimethylsilane (58). A solution of the triflate **57** (3 g, 7.68 mmol), $PdCl_2(MeCN)_2$ (98.58 mg, 0.38 mmol), and DPEPhos (409.98 mg, 0.76 mmol) in DMF (50 mL) was sparged with nitrogen for 10 min. Tributyl(vinyl)tin (2.92 mL, 9.98 mmol) was added and the mixture heated at 110 °C for 66 h, cooled to room temperature, diluted with 50 mL of water, extracted with ethyl acetate, washed with brine and finally dried over $MgSO_4$. Purification by column chromatography (100% hexanes to 100:1 to 30:1 hexanes/EtOAc) gave 1.86 g (85%) of **58** as a pale yellow oil. R_f = 0.55 (5:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (1H, d, J = 7.5 Hz), 7.16 (1H, d, J = 7.5 Hz), 6.83 (1H, dd, J = 11.0, 17.5 Hz), 5.53 (1H, d, J = 11.0 Hz), 5.37 (1H, d, J = 17.5 Hz), 4.06 (1H, q, J = 7.0 Hz), 2.94−2.90 (4H, m), 2.08−2.02 (2H, m), 1.42 (3H, d, J = 8.0 Hz), 0.18 (9H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.2, 142.8, 138.8, 134.0, 133.1, 125.5, 123.7, 119.8, 110.8, 85.5, 33.5, 33.2, 29.6, 25.8, 24.2, 0.4. FT-IR ($CDCl_3$, cm^{-1}) 2956, 2168, 1464, 1317, 1249, 842. HRMS (EI) calcd for $C_{18}H_{24}Si$ 268.1647, found 268.1638.

(5-(but-3-yn-2-yl)-2,3-dihydro-1H-inden-4-yl)(oxazol-5-yl)methanone (59). A solution of the vinyl arene **58** (1.7 g, 6.33 mmol) in CH_2Cl_2 (100 mL) containing a drop of Red 23 (0.1% solution of Sudan III in MeOH) was cooled to −78 °C and then exposed to a stream of ozone. Triphenylphosphine (4.15 g, 15.83 mmol) was added when the pink color had faded. The resulting mixture was allowed to warm to rt and stirred overnight. The solvent was evaporated *in vacuo* and the residue purified by column chromatography (SiO_2, 200:1 to 100:1 to 50:1 hexanes/EtOAc) to give 1.23 g (72%) of the corresponding aldehyde as a clear oil. R_f = 0.50 (3:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.54 (1H, s), 7.56 (1H, d, J = 7.8 Hz), 7.42 (1H, d, J = 7.8 Hz), 4.75 (1H, q, J = 6.9 Hz), 3.25 (2H, t, J = 7.8 Hz), 2.90 (2H, t, J = 7.5 Hz), 2.13 (2H, t, J = 7.8 Hz), 1.49 (3H, d, J = 6.9 Hz), 0.17 (9H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.5, 148.7, 144.8, 143.5, 130.1, 128.6, 127.2, 110.0, 86.6, 32.3, 32.1, 29.0, 25.5, 25.2, 0.3. FT-IR ($CDCl_3$, cm^{-1}) 2958, 2168, 1690, 1249, 843. HRMS (EI) calcd for $C_{17}H_{22}Si$ O 270.1440, found 270.1437. *tert*-BuLi (1.7 M in pentane, 2.86 mL, 4.48 mmol) was added to TIPS oxazole **19** (1 g, 4.48 mmol) at −78 °C in THF (40 mL). In a separate flask, the aldehyde above (1.2 g, 4.44 mmol) was dissolved in THF (40 mL) and cooled to −78 °C. After 5 min, the anion of the TIPS oxazole **19** was added *via* cannula to the aldehyde. The mixture was stirred for an additional 20 min, quenched with saturated aqueous $NaHCO_3$, diluted with water and extracted with EtOAc. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give 1.6 g of the alcohol pure enough to be used in the next reaction. Oxalyl chloride (610.4 μL, 7.11 mmol) in 30 mL of CH_2Cl_2 was cooled to −78 °C. DMSO (1.01 mL, 14.21 mmol) in 5 mL of CH_2Cl_2 was added *via* syringe and the mixture stirred for 5 min. The crude alcohol above (1.6 g, 3.23 mmol) in 30 mL of CH_2Cl_2 was added *via* syringe followed by Et_3N (9.9 mL, 71.10 mmol). The mixture was allowed to warm to room temperature and quenched with 1 N HCl. The two layers were separated and the aqueous layer extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 5:1 hexanes/EtOAc) gave 1.4 g (90%) of the corresponding 4 (2,3-dihydro-5-(4-(trimethylsilyl)but-3-yn-2-yl)-1H-inden-4-yl)(2-(triisopropylsilyl)oxazol-5-yl)methanone as a pale yellow waxy oil. R_f = 0.40 (5:1 hexanes/EtOAc) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.6 (1H, s), 7.49 (2H, d, J = 8 Hz), 7.33 (1H, d, J = 8 Hz), 3.77 (1H, q, J = 7.0 Hz), 2.90 (2H, t, J = 7.0 Hz), 2.67−2.64 (2H, m), 2.03 (2H, t, J = 7.0 Hz), 1.49−1.43 (3H, m), 1.39 (3H, d, J = 6.9 Hz), 1.13 (18H, d, J = 7.5 Hz), 0.13 (9H, s) ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.7, 152.1, 143.6, 141.5, 138.9, 136.5, 133.8, 126.6, 126.0, 109.7, 86.1, 32.5, 31.9, 30.0, 25.8,25.3 11.2, 11.1, 0.3. FT-IR ($CDCl_3$, cm^{-1}). 2957, 1668, 1250. HRMS (ESI) calcd for $C_{29}H_{44}NO_2Si_2$ [M + H]$^+$ 494.2911, found 494.2906. The solution of 4 (2,3-dihydro-5-(4-(trimethylsilyl)but-3-yn-2-yl)-1H-inden-4-yl)(2-(triisopropylsilyl)oxazol-5-yl)methanone (1.4 g, 2.83 mmol) in MeOH (40 mL) was treated with K_2CO_3 (1.56 g, 11.32 mmol) at ice bath temperature. The mixture was warmed up to room temperature and stirred for 4 h. The mixture was then quenched with water, the two layers separated and the aqueous layer extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 5:1 to 2:1 hexanes/EtOAc) gave 608 mg (80%) of **59** as a pale yellow waxy oil. R_f = 0.25 (2:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (1H, s), 7.56 (1H, s), 7.47 (1H, d, J = 7.8 Hz), 7.36 (1H, d, J = 7.8 Hz), 3.72 (1H, q, J = 7.2 Hz), 2.91 (2H, t, J = 7.5 Hz), 2.80−2.60 (2H, m), 2.14 (1H, s), 2.04 (2H, t, J = 7.5 Hz), 1.44 (3H, d, J = 7.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.2, 154.6, 150.4, 144.0, 141.8, 141.9, 138.6, 136.0, 133.0, 127.5, 126.4, 126.1, 87.1, 70.4, 32.8, 31.9, 28.7, 25.8, 24.9. FT-IR ($CDCl_3$, cm^{-1}) 3289, 2934, 1666, 1560, 1469, 1335, 1125, 848. HRMS (ESI) calcd for $C_{17}H_{16}NO_2$ [M + H]$^+$ 266.1181, found 266.1183.

Ethyl 4-{4-[(1,3-Oxazol-5-yl)carbonyl]-2,3-dihydro-1H-inden-5-yl}pent-2-ynoate (60). The terminal alkyne **59** (600 mg, 2.26 mmol) in DMF (40 mL) was treated with $Pd(OAc)_2(PPh_3)_2$ (84.65 mg, 0.011 mmol) at rt. The flask was evacuated and backfilled with CO/O_2 (1:1) in a balloon. EtOH (6.6 mL, 50 mmol) was added *via* syringe and the mixture stirred at rt for 64 h. After quenching with sat. aq. NH_4Cl, the two layers were separated and the aqueous layer extracted with EtOAc. The combined organic extracts were washed twice with water and then rinsed with brine. After drying over $MgSO_4$ the extracts were concentrated under reduced pressure. Purification by column chromatography (SiO_2, 3:1 hexanes/EtOAc) gave 671 mg (88%) of the ester **60** as a pale yellow sticky oil. R_f = 0.20 (1:1 hexanes/EtOAc) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (1H, s), 7.59 (1H, s), 7.42 (1H, d, J = 7.8 Hz), 7.37 (1H, d, J = 7.8 Hz), 4.17 (2H, q, J = 7.8 Hz), 3.87 (1H, q, J = 7.2 Hz), 2.92 (2H, t, J = 7.2 Hz), 2.69 (2H, q, J = 7.5 Hz), 2.07 (2H, t, J = 7.5 Hz), 1.50 (3H, d, J = 7.2 Hz), 1.27 (3H, t, J = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.2, 155.6, 150.1, 142.0, 139, 138.2, 132.5, 125.8, 125.2, 90.3, 74.2, 62.2, 32.5, 32.1, 28.5, 24.2, 23.9,14.2. FT-IR ($CDCl_3$, cm^{-1}) 2980, 2237, 1710, 1666, 1561, 1469, 1253, 1127, 1037. HRMS (ESI) calcd for $C_{20}H_{20}NO_4$ [M + H]$^+$ 338.1392 found, 338.1399.

Ethyl 16-[(tert-Butyldimethylsilyl)oxy]-10-methyl-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,12,15-hexaene-12-carboxylate (61). A solution of the alkyne oxazole **60** (600 mg, 1.78 mmol) in 20 mL of dry 1,2-dichlorobenzene was stirred for 6 h at 170 °C under a nitrogen atmosphere. After cooling to rt, the mixture was passed through a plug of silica gel using hexanes to elute 1,2-dichlorobenzene. The product was then eluted from the silica gel with 30% EtOAc/hexanes to give 392 mg (71%) of ethyl 10-methyl-16-oxo-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,11(15),12-pentaene-12-carboxylate as a yellow solid. Mp: 128−130 °C. R_f = 0.35 (1:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (1H, s), 7.45 (1H, d, J = 7.8 Hz), 7.35 (1H, d, J = 7.8. Hz), 4.53 (1H, q, J = 7.2 Hz), 4.42 (2H, q, J = 7.2 Hz), 3.65−3.44 (2H, m), 2.93 (2H, t, J = 7.5 Hz), 2.13 (2H, t, J = 7.5 Hz), 1.62 (3H, d, J = 7.2 Hz), 1.41 (3H, t, J = 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2, 162.4, 152.3, 148.7, 146.9, 145.8, 144.6, 138.6, 128.6, 128.1, 127.3, 118.8, 116.6, 61.1, 34.6, 34.2, 32.0, 25.7, 25.3, 14.5. FT-IR ($CDCl_3$, cm^{-1}) 2977, 1722, 1668, 1302, 1125, 1035. HRMS (ESI) calcd for $C_{19}H_{19}O_4$ [M + H]$^+$ 311.1283, found 311.1285. To a solution of the dienone (350 mg, 1.13 mmol) in CH_2Cl_2 (30 mL) at ice bath temperature was added Et_3N (478 μL, 3.39 mmol) followed by TBSOTf (519 μL, 2.26 mmol). The mixture was stirred for 30 min and then quenched with sat. aq. $NaHCO_3$. The two layers were separated and the aqueous layer extracted twice with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography (20:1 hexanes/EtOAc) gave 441 mg (92%) of the TBS phenol derivative as a yellow solid. Mp: 146−148 °C. R_f = 0.75 (5:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (1H, s), 8.0 (1H, d, J = 8.7 Hz), 7.39 (1H, d, J = 8.7 Hz), 4.42 (2H, q, J = 7.2 Hz), 3.65 (2H, t, J = 7.5 Hz), 3.09 (3H, s), 3.03 (2H, t, J = 7.5 Hz), 2.16 (2H, t, J = 7.5 Hz), 1.42 (3H, t, J = 7.2 Hz), 0.98 (9H, s), 0.33 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.7, 153.6, 144.2, 139.9, 137.9, 135.2, 133.1, 124.9, 123.2, 121.4, 119.6, 117.8, 116.2, 65.6, 61.1, 37.2, 31.7, 26.5, 25.9, 19.4, 16.8, 14.6, −2.3. FT-IR ($CDCl_3$, cm^{-1}) 2930, 1728, 1465, 1373, 1253, 1142, 832. HRMS (ESI) calcd for $C_{25}H_{33}O_4Si$ [M + H]$^+$ 425.2148, found 425.2147.

Methyl (2E)-3-{16-[(tert-Butyldimethylsilyl)oxy]-10-methyl-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,12,15-hexaen-12-yl}prop-2-enoate (62). DIBAL (1 M in toluene, 1.13 mL, 1.13 mmol) was added dropwise to a solution of the ester **61** (400 mg, 0.94 mol) in 10 mL of anhydrous CH_2Cl_2 at −78 °C. After the addition was complete, the reaction mixture was stirred for 30 min, and then slowly quenched with 2.5 mL of MeOH and 5 mL of Rochelle's salt. The gelatinous mixture was stirred at room temperature for 30 min. The precipitate was filtered through a Celite pad and the cake washed with EtOAc. The filtrate was washed with brine, dried over $MgSO_4$, and the solvent evaporated *in vacuo* to afford 359 mg of the alcohol which was used without further purification. Oxalyl chloride (177.5 μL, 2.07 mmol) in 20 mL of CH_2Cl_2 was cooled to −78 °C. DMSO (323 μL, 4.14 mmol) in 3 mL of CH_2Cl_2 was added *via* syringe and the mixture stirred for 5 min The crude alcohol (359 mg, 0.94 mmol) in 20 mL of CH_2Cl_2 was added and the mixture stirred for 15 min. Et_3N (1.3 mL, 9.4 mmol) was added and the mixture was allowed to warm to room temperature and quenched with dil. HCl. The two layers were separated and the aqueous layer extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (10:1 hexanes/EtOAc) gave 322 mg (90%) of the furanoaldehyde as a pale yellow solid. Mp: 156−158 °C. R_f = 0.75 (3:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.13 (1H, s), 8.29 (1H, s), 8.10 (1H, d, J = 9.0 Hz), 7.42 (1H, d, J = 8.7 Hz), 3.65 (2H, t, J = 7.2 Hz), 3.15 (3H, s), 3.04 (2H, t, J = 7.5

Hz), 2,17 (2H, t, J = 7.5 Hz), 0.98 (9H, s), 0.34 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.9, 159.8, 144.8, 140.0, 138.4, 133.4, 126.2, 125.0, 123.7, 122.2, 120.0, 117.7, 65.6, 37.1, 31.7, 26.5, 19.4, 18.0, −2.5. FT-IR ($CDCl_3$, cm^{-1}) 2928, 1690, 1153, 1390, 1370, 1252, 1160, 833. HRMS (ESI) calcd for $C_{23}H_{29}O_3Si$ [M + H]$^+$ 381.1886, found 381.1880. To a stirred solution of *n*-BuLi (1.6 M in hexanes, 1.48 mL, 2.37 mmol) in THF (15 mL) was added the phosphonate reagent **34** (664 mg, 3.16 mmol) at ice bath temperature; the mixture was then warmed to room temperature. After 15 min, a solution of the aldehyde above (300 mg, 0.79 mmol) in THF (15 mL) was added at 0 °C. The resulting mixture was stirred at 0 °C for 1 h, quenched with $NaHCO_3$ (5 mL) and extracted with EtOAc. The organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 10:1 hexanes/EtOAc) gave 238 mg (69%) of the unsaturated ester **62** as a yellow solid. Mp: 168−170 °C. R_f = 0.5 (10:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (1H, d, J = 15.6 Hz), 7.92 (1H, d, J = 9.0 Hz), 7.84 (1H, s), 7.38 (1H, d, J = 8.7 Hz), 6.32 (1H, d, J = 15.9 Hz), 3.84 (3H, s), 3.65 (2H, t, J = 7.2 Hz), 3.03 (2H, t, J = 7.8 Hz), 2.89 (3H, s), 2,27 (2H, t, J = 7.5 Hz), 0.98 (9H, s), 0.34 (6H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 144.6, 140.6, 138.3, 136.6, 130.9, 122.9, 122.3, 119.5, 52.0, 36.0, 33.2, 26.5, 25.4, 19.4, 16.0, −2.5. FT-IR ($CDCl_3$ cm^{-1}) 2951, 1719, 1169, 832. HRMS (ESI) calcd for $C_{26}H_{33}O_4Si$ [M + H]$^+$ 437.2148, found 437.2150.

Methyl 3-{16-[tert-Butyldimethylsilyl)oxy]-10-methyl-14-oxatetracyclo methyl-14-oxatetracyclo-[7.7.0.0.^{2,6}.0^{11,15}]hexadeca-1,6,8,10,12,15-hexaen-12-yl}-propanoate (38) and Methyl 3-{16-[tert-Butyldimethylsilyl)oxy]-10-methyl-14-oxatetracyclo [7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,10,15-pentaen-12-yl}-propanoate (39). To a solution of unsaturated ester **62** (200 mg, 0.46 mmol) in 10 mL of ethyl acetate at −10 °C was added 5% Pd on carbon (96 mg, 0.046 mmol) portion wise over 1 h. The reaction mixture was stirred for 1.5 h under a balloon of H_2 at −10 °C and then filtered through a Celite pad. The filtrate was concentrated *in vacuo* to give a yellow residue. Purification by column chromatography (SiO_2, 10:1 hexanes/EtAOc) gave 160 mg mixture of **38** and **39**. Recrystallization from hexanes gave 139 mg (69%) of the furan saturated ester **38** as pale yellow needle crystals and 20 mg (10%) of dihydrofuran **39** as a yellow oil.

Ethyl (2Z)-6-{4-[(1,3-Oxazol-5-yl)carbonyl]-2,3-dihydro-1H-inden-5-yl}hept-2-en-4-ynoate (63). A mixture of the terminal alkyne **59** (100 mg, 0.38 mmol) and iodoacrylate **45** (103 mg, 0.46 mmol) in THF (10 mL) were treated with $PdCl_2(PPh_3)_2$ (14 mg, 0.02 mmol) and CuI (3.8 mg, 0.02 mmol) under N_2 atmosphere; 2.17 mL of Et_3N (265 μL, 1.9 mmol) was added *via* syringe and the mixture stirred at rt for 3 days then quenched with sat. aq. NH_4Cl. The two layers were separated and the aqueous layer extracted with EtOAc. The combined organic extracts were dried over $MgSO_4$, washed with brine, and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 3:1 hexanes/EtOAc) gave 108 mg (78%) of **63** as a brown sticky oil. R_f = 0.25 (2:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (1H, s), 7.59 (1H, s), 7.56 (1H, d, J = 7.5 Hz), 7.38 (1H, d, J = 8.0 Hz), 6.07−6.00 (2H, m), 4.21 (2H, q, J = 7.0 Hz), 3.96 (1H, q, J = 7.5 Hz), 2.92 (2H, t, J = 7.5 Hz), 2.77−2.73 (1H, m), 2.69−2.63 (1H, m), 2.09−2.03 (2H, m), 1.52 (3H, d, J = 7.0 Hz), 1,27 (3H, t, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.2, 164.9, 154.5, 144.1, 141.8, 138.6, 136.1, 133.0, 128.5, 127.2, 126.6, 123.2, 105.3, 79.5, 60.6, 32.5, 31.9, 30.4, 25.8, 24.7, 14.5. FT-IR ($CDCl_3$, cm^{-1}) 2979, 1720, 1666, 1184, 1042. HRMS (ESI) calcd for $C_{22}H_{21}NO_4$ [M + H]$^+$ 364.1549 found 364.1555.

3-{16-[(tert-butyldimethylsilyl)oxy]-10-methyl-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca- 1,6,8,10,12,15-hexaen-12-yl}propanal (52). A solution of the enyne oxazole **63** (100 mg, 0.28 mmol) in 10 mL of dry 1,2-dichlorobenzene was stirred for 10 h in a 30 mL round-bottom flask at 180 °C under a nitrogen atmosphere. After cooling to room temperature, the mixture was passed through a plug of silica gel using 100% hexanes to elute 1,2-dichlorobenzene. The product was then eluted from the silica gel with 5:1 (hexanes/EtOAc) to give 65 mg of **64** and **65** as a yellow solid. R_f = 0.45 (1:1 hexanes/EtOAc). To a solution of the mixture of **64** and **65** (65 mg) in EtOAc (5 mL) at −10 °C was added approximately 40 mg (10%) of 5% Pd/C. The flask was evacuated and then backfilled by attaching a balloon full of H_2. The mixture was vigorously stirred for 1 h at −10 °C and then filtered through a Celite pad. The filtrate was concentrated *in vacuo* to give 60 mg of the corresponding ethyl 3-{10-methyl-16-oxo-14-oxatetracyclo[7.7.0.0^{2,6}.0^{11,15}]hexadeca-1,6,8,11(15)-12-pentaen-12-yl}propanoate, as pale yellow oil. R_f = 0.40 (1:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (1H, s), 7.46 (1H, d, J = 7.8 Hz), 7.30 (1H, d, J = 7.8 Hz), 4.18 (2H, q, J = 6.8 Hz), 3.58 (2H, q, J = 6.8 Hz), 2.92 (2H, t, J = 7.2 Hz), 2.68 (2H, t, J = 7.5 Hz), 2.34 (2H, t, J = 6.9 Hz), 1.54 (3H, d, J = 9 Hz), 1.26 (3H, t, J = 7.8 Hz). A solution of the dienone above (60 mg, 0.18 mmol) in CH_2Cl_2 (5 mL) at ice bath temperature was treated with Et_3N (75 μL, 0.54 mmol) followed by TBSOTf (83 μL, 0.36 mmol). The mixture was stirred at ice bath temperature for 30 min and then quenched with sat. aq. $NaHCO_3$.The two layers were separated and the aqueous layer extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, 10:1 hexanes/EtOAc) gave 71 mg (86%) of the desired product as a yellow oil. R_f = 0.75 (4:1 hexanes/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (1H, d, J = 8.7 Hz), 7.39 (1H, s), 7.34 (1H, d, J = 8.7 Hz), 4.18 (2H, q, J = 7.5 Hz), 3.65 (2H, t, J = 7.2 Hz), 3.25 (2H, t, J = 8.4 Hz), 3.02 (2H, t, J = 7.5 Hz), 2.89 (3H, s), 2.76 (2H, t, J = 7.2 Hz), 2.15 (2H, q, J = 7.2 Hz), 1.26 (3H, t, J = 7.0 Hz), 0.95 (9H, s), 0.35 (6H, s). A solution of the ester above (70 mg, 0.15 mmol) in 8 mL of dry CH_2Cl_2 was cooled to −78 °C. DIBAL-H (1 M in toluene, 165 μL, 0.165 mmol) was added dropwise. The reaction mixture was stirred for 30 min and then slowly quenched with 1 mL of MeOH followed by 2 mL of Rochelle's salt and warmed and stirred at room temperature for 30 min. The precipitate was filtered through a Celite pad and the filtrate was washed with brine, dried over anhydrous $MgSO_4$, and the solvent evaporated *in vacuo* to afford 48 mg (79%) of the aldehyde **52**.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra for new compounds and a CIF file for *syn*-**53** (=3). 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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