Highly Oxygenated Decalins via Michael–Claisen Condensation

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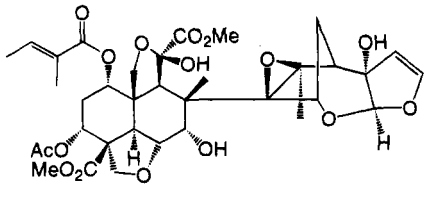
Highly oxygenated decalins were synthesized by Michael–Claisen condensation. The stereochemistry of the intramolecular condensation leading to **13** was found to be cis.

Introduction

The decalin skeleton is an integral structural feature of a wide variety of natural products of biological importance particularly in the agrochemical and medicinal areas.[1] A testament to the importance of this structural type in nature, is perhaps the variety and abundance of annulation/cyclization strategies developed toward its synthesis. In addition to the well-established approaches such as the Robinson annulation (Michael/Aldol), recent reports by Deslongchamps,[2] Liu,[3] and Jas,[4] all utilizing a Diels–Alder approach, and by Shibaski,[5] employing a Heck-type cyclization (Scheme 1, eqs 1–4, respectively), attest to the continuing interest in the synthesis of this class of compounds.

Recently, highly oxygenated decalin natural products have attracted attention because of their biological activities. Azadirachtin (**1**), isolated from the neem tree,[6a] has



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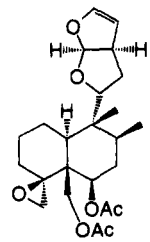

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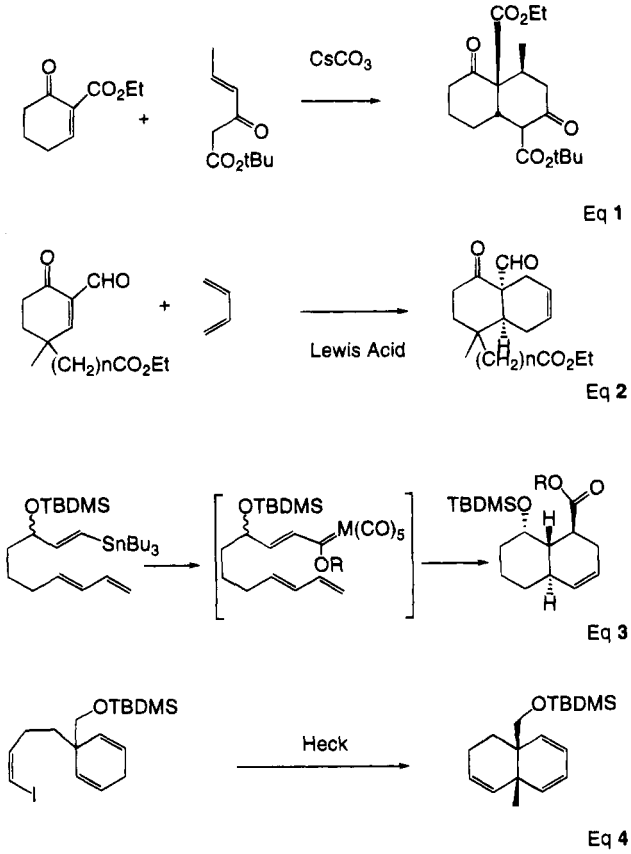
shown considerable potential as a potent insect antifeedant against the desert locust,[6b] the spruce budworm,[6c] and many other insects as well.[6d] Clerodin (**2**), isolated from the Indian bhat tree,[7a] has been reported[7b] to have antifeedant activity. These two compounds have a dense array of oxygen functions on a decalin platform. Of special interest is the shared feature of having an angular hydroxymethyl group and oxygen functions at 1, 4, and 8 positions. Numerous studies have been directed toward the synthesis of both azadirachtin and clerodin. Notable

Scheme 1



success has been achieved by Ley[6] and his co-workers in elucidating the structure–activity relationship of azadirachtin analogues with biological activity.

We have recently reported the use of a tandem Michael–Claisen condensation[8] to assemble a decalin structure (Scheme 2). The approach has been extended to introduce an angular hydroxymethyl substituent by alkoxymethylation[9] of an existing decalin skeleton **3**. We report now the assembly of compound **13** in which oxygen functions are present in positions 1, 4, 8, and 9 by an intramolecular Claisen condensation of the appropriate precursor. Two aspects of this approach attracted our attention. Firstly, the success of this approach would necessarily depend on effecting a Claisen condensation of a keto ester, which to our knowledge is as yet unprecedented in the literature. Secondly, we are interested in the ring junction stereochemistry of such a cyclization. It is known that in the angular alkoxy-

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(1) Hanson, J. R. *Nat. Prod. Rep.* **1992**, *9*, 139–151 and previous reports.

(2) Lavallee, J. F.; Deslongchamps, P. *Tetrahedron Lett.* **1988**, *29*, 6033–6036 and references therein.

(3) Liu, H.-J.; Hen, Y. *Tetrahedron Lett.* **1993**, *34*, 423–426 and references therein.

(4) Muller, G.; Jas, G. *Tetrahedron Lett.* **1992**, *33*, 4417–4420.

(5) Sato, Y.; Watanabe, S.; Shibasaki, M. *Tetrahedron Lett.* **1992**, *33*, 2589–2592.

(6) (a) Ley, S. V.; Denholm, A. A.; Wood, A. *Nat. Prod. Rep.* **1993**, *10*, 110–157. (b) Ley, S. V.; Toogood, P. L. *Chem. Brit.* **1990**, *26*, 31 and references therein. (c)Thomas, A. W.; Strunz, G. M.; Chaisson, M.; Chan, T. H. *Entomol. Exp. App.* **1992**, *62*, 37–46. (d) Warthen, J. D. *Azadirachtica Indica; A source of Insect Feeding Inhibitors and Growth Regulators*; U. S. Dep. Agric. Rev. Man ARM-Ne-4, 1989.

(7) (a) Banerjee, H. N. *J. Indian Chem Soc.* **1937**, *14*, 51. (b) Kato, N.; Takhashi, M.; Shibayama, M.; Munakata, K. *Agric. Biol. Chem.* **1972**, *35*, 2579.

(8) Chan, T. H.; Prasad, C. V. C. *J. Org Chem.* **1987**, *52*, 110–119; **1987**, *52*, 120; **1989**, *54*, 3242.

(9) Chan, T. H.; Schwerdtfeger, A. E. *J. Org. Chem.* **1991**, *56*, 3294–3298.

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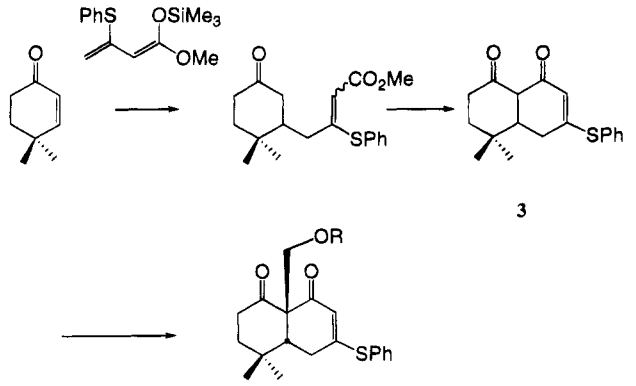
Scheme 2



methylation of the enolate of **3** by reaction with an external electrophile, cis stereochemistry was obtained. In the present approach, the tethered electrophile will have to react with the enolate intramolecularly. Two other groups, those of Ley[10] and, more recently, Lallemand,[11] in their approach to the Clerodane skeleton, have intramolecularly cyclized a keto ester enolate onto an appropriately tethered electrophile. It is interesting to note that opposite stereochemical results were obtained in their reactions.

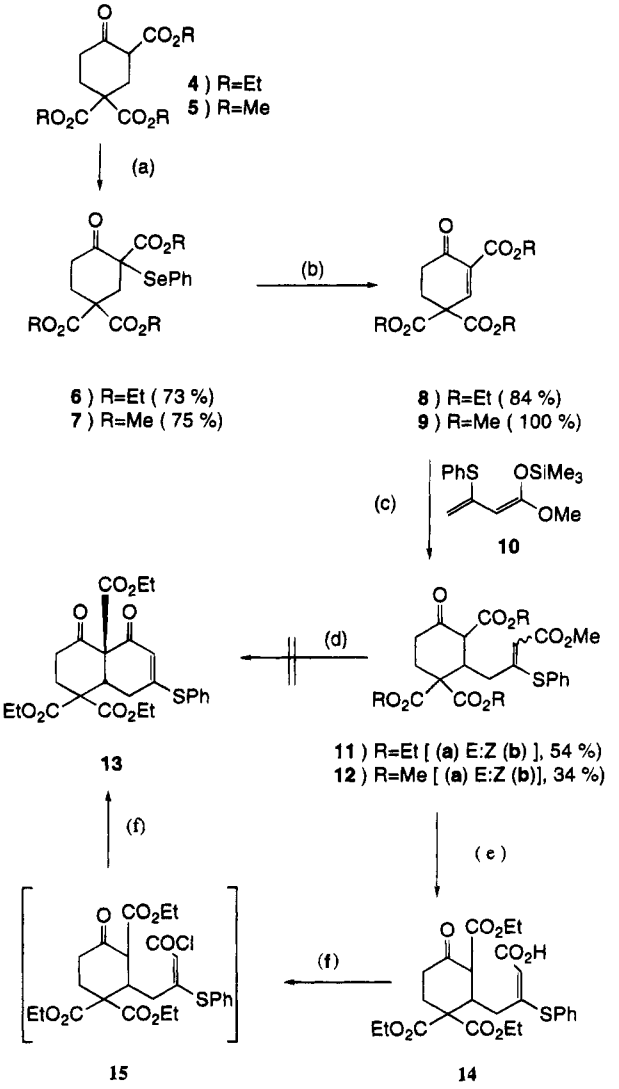
Results and Discussion

Synthesis and Modified Claisen Cyclization of the Michael Adduct 11a. The keto ester **4** was prepared in 70% yield, after distillation, according to a published procedure.[12] Phenylselenation, according to the method of Liotta,[13] followed by oxidation/elimination delivered the enone **8** in 84% yield (Scheme 3). Using slightly modified conditions to those published,[14] the enone was treated with freshly prepared siloxy diene **10**, at −78 °C, in the presence of titanium tetrachloride ($TiCl_4$), to give Michael adduct **11** as an *E*:*Z* mixture in a ratio of 2:1, in 54% yield. Curiously when a crude sample (containing amine salts) of the siloxy diene was used, a better ratio 4:1 of *E*:*Z* was obtained albeit at the expense of yield (34%). The same observation was made in the methyl series (**12**). Perhaps the amine salts moderate the reactivity of the Lewis acid, allowing better selectivity but in poorer yields. The *E*,*Z* isomers are easily distinguished spectroscopically by the chemical shift of the vinylic ester proton which occurs characteristically, at 5.2 ppm in the *E* isomer and at 6 ppm in the *Z*. Furthermore, both isomers are almost 100% enolized in $CDCl_3$, as is evident by a sharp singlet at about 12.4 ppm and the multiplicity (double doublet) and shift of the adjacent C_3 allylic proton ocurring at about 4 ppm. Presumably in these 4,4 disubstituted cyclohexanones the strong developing 1,3 diaxial interaction between the C_2 proton and the 4-substituent coupled with its inherent acidity facilitate enolization.

With the *E* isomer in hand, we proceeded to examine the Claisen condensation. Thus, exposure of **11a** to sublimed KOtBu in THF, under conditions known to cyclize the similar, but more reactive, keto Michael adducts,[15] yielded only recovered starting material. A variety of other bases (KH/THF/−78−0 °C-rt; NaH/THF or DME/−78, 0 °C, rt; PhS^-/THF/reflux; MeONa/THF, −78, 0 °C; K_2CO_3/DMF, 80−90 °C; LDA, 0 °C) under a host of conditions were investigated. In all cases no cyclization was observed. The starting material was recovered or decomposed to an intractable tar. Similarly thiophenoxide induced isomerization of the Z-isomer to the corresponding E-isomer **11a**, under conditions known[14] to effect isomerization/cyclization, failed. The starting isomer was recovered in 45% yield. Clearly, the keto ester enolate is too weak a nucleophile to effect a Claisen condensation in the normal sense, i.e., with an ester as electrophile.

We then considered two options: augmenting either the nucleophilicity of the enolate or the electrophilicity of the electrophile. To test the former approach, the keto carbonyl was masked both as a ketal and an enol ether.

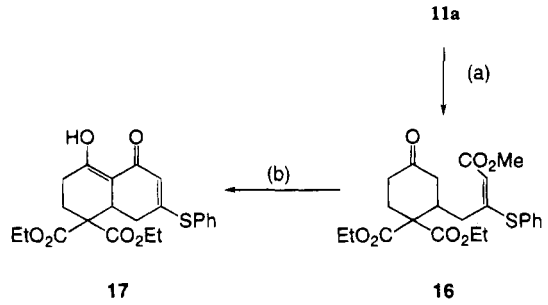
Scheme 3[a]



[a] Key: (a) PhSeCl/pyridine/CH_2Cl_2, 0 °C; (b) H_2O_2, CH_2Cl_2, 0 °C; (c) $TiCl_4$, CH_2Cl_2, 0 °C; (d) base (see text); (e) 2.8 equiv of LiOH/dioxane:water, 3:1/21 °C, 75%; (f) (i) $COCl_2$, DMF, 1.02 equiv, Et_3N, 0 °C, (ii) 1 equiv of Et_3N.

(10) Jackson, W. P.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1516–1517.
(11) Bouchard, H.; Lallemand, J. Y. *Tetrahedron Lett.* **1990**, *31*, 5151–5152.
(12) Schanchez, I. H.; Ortega, A.; Garcia, G.; Larraza, N. I.; Flores, H. J. *Synth. Commun.* **1985**, *15*, 141–149.
(13) Liotta, D.; Barnum, C.; Puleo, R.; Zima, G.; Bayer, C.; Kezar, H. S. *J. Org. Chem.* **1981**, *46*, 2920–2923.
(14) Chan, T. H.; Guertin, K.; Prasad, C. V. C.; Thomas, A. W.; Strunz, G. M.; Salonius, A. *Can J. Chem.* **1990**, *68*, 1170–1177.
(15) Guertin, K. PhD Thesis, McGill University, Montreal, 1992. Schwerdtfeger, A. E. PhD Thesis, McGill University, Montreal, 1991.

Scheme 4[a]



[a] Key: (a) 3 equiv of LiI/DMF/130 °C, 68%; (b) KOtBu, tBuOH, 21 °C.

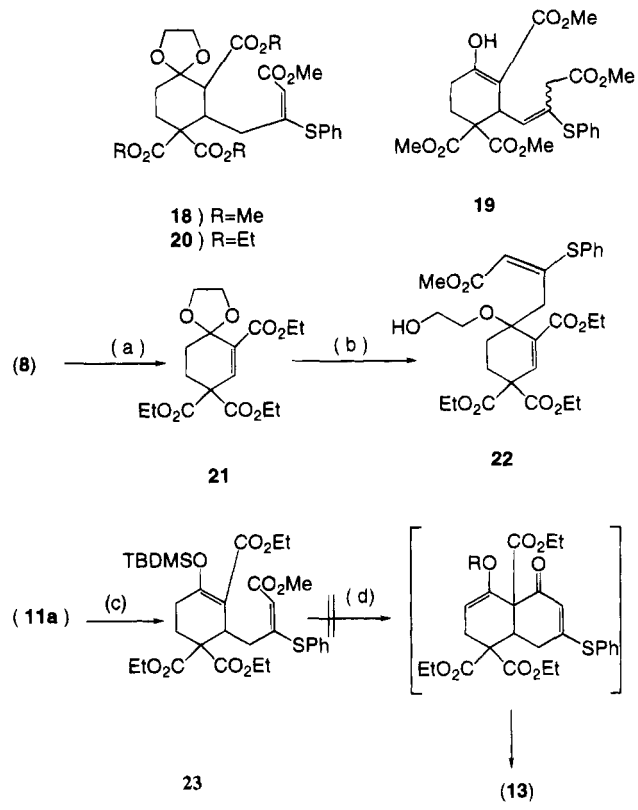
Neither intermediate proved to be a suitable precursor to decalin **13**. The second approach required the selective conversion of the α,β-unsaturated ester **11a** to its corresponding acyl chloride.

Fortunately, we were able to achieve just such selectivity when only the tethered α,β-unsaturated ester of **11a** was hydrolyzed to the acid **14** in 75% yield, following prolonged exposure of **11a**, at ambient temperature, to lithium hydroxide in dioxane:water. A small amount (*ca.* 10%) of overhydrolysis product was observed by TLC. A possible explanation for the observed selectivity might be a combination of two effects operating in the same direction. Firstly, rapid formation of the β-keto ester enolate might serve to protect this ester against hydrolysis. However, such protection of 1,3-dicarbonyl ester compounds in general has not been reported. Secondly, selectivity might be derived from the differential rate of hydrolysis of a methyl versus ethyl ester.[16] Under the Vilsmeyer[17] conditions, acid **14** was smoothly converted to the corresponding acid chloride **15** which without isolation was cleanly cyclized, in the presence of Et_3N, to the crystalline decalin **13** in 72% yield.

The poor nucleophilicity of the keto ester can undoubtedly be attributed to the stabilized nature of this enolate. We were able to confirm this assumption when **11a** was selectively decarboxylated at the 2 position to **16** in a yield of 68%, after heating at 125 °C with lithium iodide in DMF for 2.5 h. Subsequent exposure of this keto compound **16** to sublimed KOtBu in 2-methyl-2-propanol under conditions described before afforded the decalin **17** in 77% yield (Scheme 4). The proton NMR of **17** showed a sharp singlet at 12.7 ppm characteristic of the enol. However, the 8a proton (naphthalene numbering) at 3.04 ppm showed three couplings, one resembling a large trans coupling of 16.5 Hz, presumably to the 4a proton, and two smaller couplings to the C_8 methylene. These couplings taken with the 16.5 Hz doublet at 3.7 ppm assigned to the 4a proton indicated only partial enolization.

Other Attempts To Enhance the Reactivity of 11a toward a Claisen Cyclization. As mentioned earlier the reactivity of the keto ester enolate can be increased by masking the ketone carbonyl either as a ketal or as its enol ether. However, the complete enolization of **11a/12a** in solution (vide-infra) would tend to preclude ketalization of this adduct. Indeed, reaction of **12a** with ethylene glycol, in the presence of camphorsulfonic acid (CSA), under standard conditions, afforded not the ketal **18** but a poor yield of the double-bond migration product **19**. A significant improvement in the yield of **19** was realized (72%) when the adduct **12a** was exposed to 1.1 equiv of trimethylsilyl triflate for 16 h at −20 °C in dichloromethane. In the methyl series, product **19** was easily distinguished from its isomer **12** by proton NMR. A doublet of 10 Hz at 4.83 ppm is observed for the doubly allylic C_1 proton in **19** compared to a double-doublet at 4.02 ppm for the equivalent singly allylic proton in **12**. In principle, the ketal adduct **20** is also available through 1,4-conjugate addition of the siloxy diene **10** to the ketal **21**. However, exposure of **21** to diene **10** in the presence of either $TiCl_4$ or aluminum trichloride, at −78 °C, afforded only the 1,2-addition product **22** in 14% yield along with recovered ketal **21**. The corresponding *Z* isomer was not isolated (Scheme 5).

Scheme 5[a]



[a] Key: (a) $HO(CH_2)_2OH$/CSA/120 °C, 52%; (b) **10**, $AlCl_3/CH_2Cl_2$/0 °C, 14%; (c) 2.2 equiv of TBDMSTfl/Et_3N/CH_2Cl_2/21 °C; (d) base (see text).

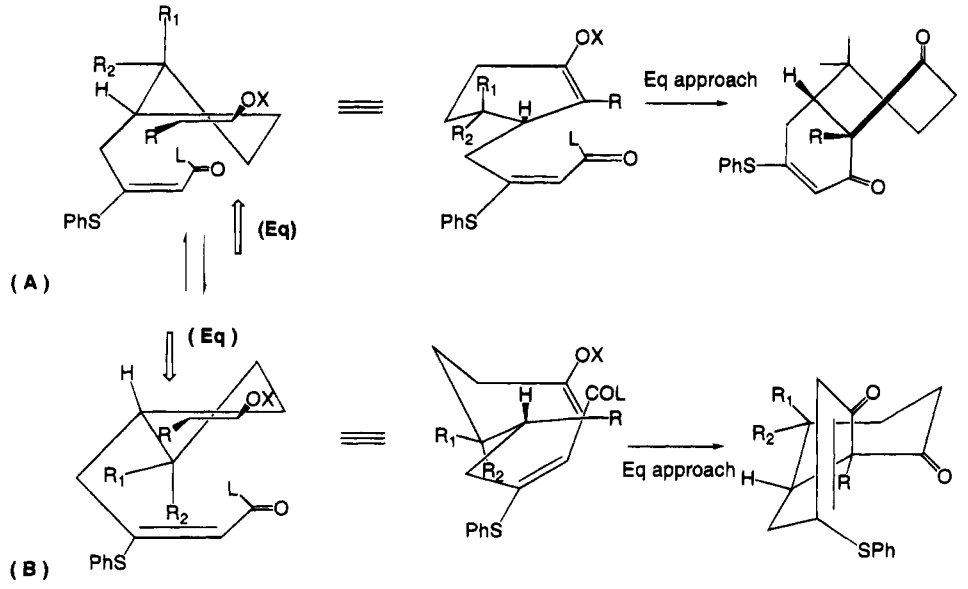
Finally, the TBDMS enol ether **23** in particular was examined as a potential precursor to cyclization. Compound **23** was delivered in 63% yield after chromatography, when **11a** was exposed to TBDMS triflate in the presence of Et_3N. Unfortunately, when enol ether **23** was subjected to base-mediated deprotonation, using a selection of bases, i.e., LDA, LHMDS, LTMP, KOtBu, NaH, at temperatures between −78 °C and ambient, for 2−16 h, the enol ether was recovered intact. Under more forcing conditions, employing 5 equiv of LTMP, partial cleavage of the enol ether was observed to the extent of 31%. In no case was the geometry of the double bond compromised[18] excluding reaction failure due to isomerization to the cis compound.

Stereochemistry. The stereochemistry of the decalone **13** was determined to be cis by X-ray crystal

(16) March, J. *Advanced Organic Chemistry;* McGraw Hill: New York, 1968; Chapter 7, p 220.

(17) (a) Stadler, P. A. *Helv. Chim. Acta* **1978**, *61*, 1675. (b) Fieser, M.; Fieser, L. F. *Reagents for Organic Synthesis;* J. Wiley and Sons: New York, 1981; Vol. 9, p 514.

Scheme 6



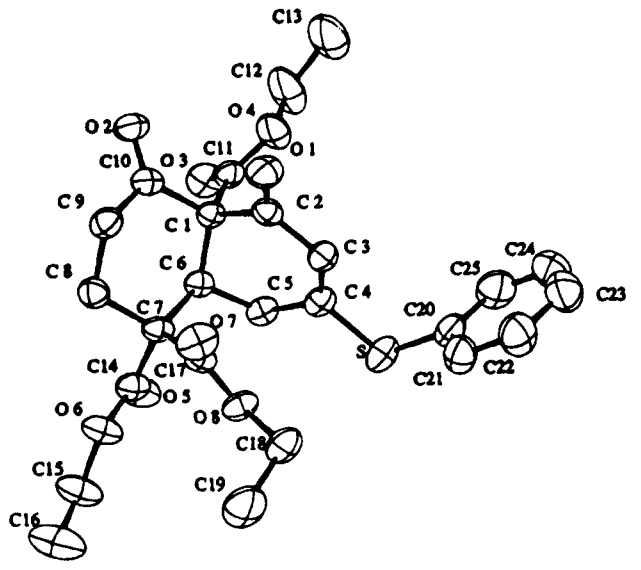


Figure 1. ORTEP drawing of compound **13**.

structure determination (Figure 1). Furthermore, this seemed to be the sole stereoisomer formed since the crude mixture obtained from the cyclization did not show, in its proton NMR, additional vinyl singlets at 5.2–5.4 ppm characteristic[15] of the vinylic C_2 proton expected of the corresponding trans stereoisomer. The preference for cis stereochemistry in the formation of **13** can be rationalized by consideration of the two conformations (A and B, Scheme 6) of the intermediate enolate. Cyclization of this stabilized enolate can occur through either conformer with strong preference for axial[19] approach of the electrophile. Allylic strain considerations,[20] favor conformation A, where the tethered electrophile is placed pseudoaxially. As only one geometrically allowed approach is available to this enolate conformer, cis product geometry is obtained if the reaction is irreversible and kinetically controlled.[21] Two other literature examples,[10] including our own,[8] gave similar stereochemical results. In these examples, a Lewis acid mediated enolate cyclization onto an alkyne and an ene-type cyclization, respectively, are used to effect ring closure to the decalin unit. Both reactions are presumably under kinetic control and essentially irreversible leading to the observed cis products. In contrast, Lallemand[11] obtained only the trans stereoisomer from an aldol cyclization. In this case, opportunity exists for product equilibration *via* a retro-aldol. Similar product equilibration was subsequently reported[22] by this group.

Conclusions

Modified Claisen condensation of a keto ester with an acid chloride as electrophile has been shown to be a viable annulation strategy to the synthesis of a highly oxygenated decalin system by the synthesis of **13** in three steps from the enone **8**. The cis stereochemistry is of interest in that it provides access to the thermodynamically less stable isomer which could well be isomerized to the more stable trans isomer in subsequent transformations. Furthermore, it might provide entry to the *cis*-clerodanes of current interest.[23]

Experimental Section

Distillation temperatures refer to short-path distillations. Melting points are uncorrected. The solvents THF, ether, benzene, and isopropyl ether (IPE) were distilled from sodium/benzophenone ketyl. All other solvents when used dry were distilled under argon from calcium hydride. Chromatography was performed on Merck Kieselgel 60 (mesh 70–230) using distilled solvents. Unless otherwise indicated ^{1}H NMR was recorded in $CDCl_3$ on a 200 or 270 MHz spectrometer. ^{13}C NMR was recorded at 68 MHz in $CDCl_3$. Chemical shifts (δ

(18) A reviewer suggested that this closure was prone to failure as anion formation α to the thioenol ether would lead either to an alternative Claisen product or isomerize the double bond. Given that we recovered the starting material in high yield without inverting the double bond would suggest that this is not the reason for failure.

(19) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Scott, J. W., Eds.; Academic Press: London, U. K., 1983; Chapter 1.

(20) Johnson, F. *Chem Rev.* **1968**, *68*, 375. (b) Johnson, F.; Malhotra, S. K. *J Am. Chem. Soc.* **1965**, *87*, 5492.

(21) One reviewer argues that the product ratio is controlled by the relative energies of the transition states (TS) for axial versus equatorial attack leading to closure via axial approach on conformer B. As this is a stabilized enolate probably involving a late TS (ref 19) under purely stereoelectronic control, this argument is a valid one.

(22) Renard, P. Y.; Lallemand, J. Y. *Synlett.* **1993**, 1.

(23) Hanson, J. R. *Nat. Prod. Rep.* **1993**, *10*, 159–174.

values) are quoted relative to $CHCl_3$ (δ 7.24) for ^1H NMR and $CDCl_3$ (δ 77.0) for ^{13}C NMR. Where necessary, COSY, HETCOR were performed to allow complete peak assignment. Infrared spectra were obtained on an FTIR spectrophotometer.

Triethyl 4-Oxocyclohexane-1,1,3-tricarboxylate (4). The title compound was prepared according to a published procedure[12] in 70% yield. Its bp and ^1H and ^{13}C NMR agreed well with literature values.

Trimethyl 4-Oxocyclohexane-1,1,3-tricarboxylate (5). The title compound was prepared in a similar fashion to that published for the corresponding ethyl derivative **4**, using instead methyl acrylate (18.9 mL, 18.1 g, 0.209 mol) and dimethyl malonate (11.4 mL, 13.2 g, 0.99 mol) in the presence of sodium hydride (60% dispersion, 9.99 g, 0.249 mol) to afford a pale yellow oil (29 g, 100%): bp 132–154 °C; IR (liquid film) 3075, 2850, 1743, 1726, 1661 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 2.16–2.41 (m, 4H), 2.78 (bs, 2H), 3.65 (s, 3H), 3.67 (s, 3H), 3.71 (s, 3H), 12.1 (s, 1H); ^{13}C NMR (270 MHz, $CDCl_3$) 26.0, 26.6, 27.9, 51.6, 52.6, 52.9, 53.0, 95.0, 170.2, 171.2, 172.2 (CO); MS (EI) 272 (M^+, 30), 214 (43), 241 (47), 181 (100); HRMS calcd for $C_{12}H_{16}O_7$ 272.0897, found 272.0896; R_f (hexane:CH_2Cl_2:EtOAc = 10:2:1) = 0.2.

Triethyl 4-Oxo-3-(phenylseleno)cyclohexane-1,1,3-tricarboxylate (6). Phenylselenyl chloride (9.57 g, 0.05 mol) in dry methylene chloride (280 mL), under argon, at 0 °C, was treated with dry pyridine (4.23 mL, 4.14 g, 0.052 mol). The resulting black/red solution was treated after 15 min with a solution of the triester **4** (15.1 g, 0.048 mol) in methylene chloride (50 mL), added dropwise over 30 min. After 1 h at 0 °C, the bright yellow solution was allowed to warm to 10 °C (over 30 min) and then washed with 2 N HCl (2 × 100 mL) and brine. Drying and evaporation of the organic phase afforded a solid which was triturated, first with hexane (2 × 60 mL) and then with hexane:ether (80:3 mL, × 3), and then filtered to give a pale yellow amorphous solid (16.5 g, 73%): mp 96–98 °C; IR (CH_2Cl_2) 1473, 1721, 1314 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.12–1.29 (m, 9H), 1.92–3.05 (m, 6H), 3.9–4.28 (m, 6H), 7.23–7.72 (m, 5H); ^{13}C NMR (270 MHz, $CDCl_3$) 13.75, 13.91, 30.94, 36.52, 40.15, 52.33, 59.21, 61.80, 61.93, 62.12, 125.8, 128.8, 129.68, 138.35, 168.35, 170.33, 170.38, 202.8; MS (EI) 471 (M + 1, 2), 470 (M^+, 2), 469 (M − 1, 9), 313 (33), 268 (32), 234 (37), 167 (100); HRMS calcd for $C_{21}H_{26}O_7Se$ 470.0843, found 470.0854; R_f (hexane:CH_2Cl_2:EtOAc = 10:2:1):0.23.

Trimethyl 4-Oxo-3-(phenylseleno)cyclohexane-1,1,3-tricarboxylate (7). The title compound was prepared in a manner similar to the corresponding ethoxy analogue **6** from the triester **5** (500 mg, 1.83 mmol), pyridine (0.162 mL, 159 mg, 2.01 mmol), and PhSeCl (368 mg, 1.92 mmol) to give a pale yellow solid. Trituration with hexane (3 × 15 mL) afforded an amorphous solid which was crystallized from hot isopropyl ether to give off-white crystals (568 mg, 75%): mp 98–100 °C; IR (CH_2Cl_2) 1733, 1430, 1250 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.9–3.28 (m, 6H), 3.52–3.76 (m, 9H), 7.22–7.62 (m, 5H); ^{13}C NMR (270 MHz, $CDCl_3$) 31.23, 36.57, 40.43, 52.25, 52.93, 53.09, 59.0, 125.6, 128.9, 129.8, 138.55, 168.84, 170.67, 202.4; MS (EI) 428 (M^+, 1), 272 (17), 240 (43), 234 (68), 154 (100); HRMS calcd for $C_{18}H_{20}O_7Se$ 428.0374, found 428.0374; R_f (hexane: CH_2Cl_2:EtOAc = 10:2:1) = 0.14.

Triethyl 4-Oxo-2-cyclohexene-1,1,3-tricarboxylate (8). To a vigorously stirred solution of the selenide **6** (14.4 g, 0.031 mol) in methylene chloride (75 mL), at 0 °C, was added H_2O_2 (30% aqueous solution, 14.4 mL, 4.22 g, 0.124 mol) in water (30 mL). The mixture was stirred for 30 min to a pale yellow color. TLC showed complete reaction. The reaction mixture was diluted with CH_2Cl_2 (80 mL). The organic phase was separated and washed sequentially with water (2 × 200 mL), saturated aqueous $NaHCO_3$ (2 × 100 mL), water (4 × 100 mL, to neutral pH), and brine. Drying and evaporation gave a yellow oil (8.14 g, 84%): IR (liquid film) 1725, 1745 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.3 (t, 6H, J = 7.5 Hz), 1.32 (t, 3H, J = 7.5 Hz), 2.49–2.7 (m, 4H), 4.14–4.4 (m, 6H), 7.64 (s, 1H); ^{13}C NMR (270 MHz, $CDCl_3$) 13.95, 13.99, 14.09, 28.4, 35.03, 55.25, 61.63, 62.78, 133.6, 148.1, 163.88, 167.64, 192.62; MS (CI, NH_3) 311 (M − 1, 18), 313 (M + 1, 100), 330 (M + NH_4, 20); HRMS calcd for $C_{15}H_{20}O_7$ 312.1209, found 312.1206; R_f (hexane:CH_2Cl_2:EtOAc = 4:2:1) = 0.3.

Trimethyl 4-Oxo-2-cyclohexene-1,1,3-tricarboxylate (9). The title compound was prepared in similar manner to the ethoxy analogue, from the corresponding methoxy selenide **7** (1.60 g, 3.74 mmol) and H_2O_2 (30% aqueous solution, 1.27 mL, 382 mg, 0.011 mol). After 40 min at 0 °C, similar workup afforded a colorless oil (990 mg, 100%): IR (liquid film) 1740, 1690, cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 2.54–2.63 (m, 4H), 3.81 (s, 3H), 3.82 (s, 6H), 7.66 (s, 1H); ^{13}C NMR (270 MHz, $CDCl_3$) 28.54, 35.04, 52.56, 53.71, 55.15, 133.24, 148.37, 164.2, 167.98, 192.37; MS (EI) m/z 270 (M^+, 10), 242 (87), 211 (87), 179 (100); HRMS calcd for $C_{12}H_{14}O_7$ 270.0739, found 270.0761; R_f (hexane:CH_2Cl_2:EtOAc = 4:2:1) = 0.24.

Methyl 3-(Phenylthio)-4-(2′,2′,6′-tris(ethoxycarbonyl)-5-oxocyclohexyl)but-2-enoate (11). To a stirred solution of **8** (5.0 g, 0.016 mol) and the freshly made siloxy diene **10** (7.65 g, 0.027 mol) in dry CH_2Cl_2 (50 mL), at −78 °C, under argon, was added over 5 min, via syringe, titanium tetrachloride (1.92 mL, 3.32 g, 0.0175 mol). The resulting black/red solution was stirred for 65 min and then poured into a stirred mixture of cold (0 °C) CH_2Cl_2:saturated aqueous $NaHCO_3$ (1:1, 500 mL). The resulting fine emulsion was filtered through Celite and the organic phase separated and washed sequentially with saturated $NaHCO_3$ (2 × 100 mL), water (100 mL), and brine. The extract was dried and concentrated in vacuo to a brown gum (10.55 g). Flash chromatography of the gum, on silica gel (2 × 500 g) using hexanes:CH_2Cl_2:EtOAc (10:2:1) as eluent, provided the E and Z isomers in a 2:1 ratio (4.99 g, 54%), as brown gums.

E isomer (**11a**): IR (CH_2Cl_2) 3150, 3030, 2945, 1742, 1703, 1649 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 1.17 (t, 3H, J = 7.0 Hz), 1.24 (t, 3H, J = 7.0 Hz), 1.25 (t, 3H, J = 7 Hz), 2.19–2.47 (m, 4H), 2.71 (dd, 1H, J = 9.0, 13.0 Hz), 3.18 (dd, 1H, J = 5.0, 13.0 Hz), 3.56 (s, 3H), 3.99–4.37 (m, 7H), 5.23 (s, 1H), 7.39 (s, 5H), 12.44 (s, 1H); ^{13}C NMR (270 MHz, $CDCl_3$) 13.91, 13.96, 21.71, 25.65, 35.29, 35.65, 50.82, 57.42, 60.49, 61.48, 61.71 100.56, 112.82, 129.69, 130.0, 135.14, 160.71, 165.03, 165.65, 169.65, 170.93; MS (CI, CH_4) 522 (M + 2, 6), 521 (M + 1, 19), 520 (M^+, 11), 489 (17), 475 (14), 313 (100); HRMS calcd for $C_{26}H_{32}O_9S$ 520.1767, found 520.1778; R_f (hexane:CH_2Cl_2:EtOAc = 10:2:1) = 0.21.

Z isomer **11b** containing ca. 7% impurity: IR (CH_2Cl_2) 3130, 1745, 1698, 1654 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 1.12 (t, 3H, J = 7.0 Hz), 1.18 (t, 3H, J = 7.0 Hz), 1.29 (t, 3H, J = 7.0 Hz), 1.85–2.28 (m, 6H), 3.75 (s, 3H), 3.88–4.31 (m, 7H), 6.01 (s, 1H), 7.32–7.45 (m, 5H); ^{13}C NMR (270 MHz, $CDCl_3$) 13.9, 13.98, 21.63, 25.38, 36.97, 38.19, 51.15, 57.18, 60.99, 61.64, 61.82, 100.13, 113.86, 129.09, 129.14, 135.64, 158.74, 166.31, 169.2, 169.59, 170.71, 171.99; MS (EI) 521 (M + 1, 2), 520 (M^+, 8), 443 (8), 313 (100), 267 (37), 195 (37); HRMS calcd for $C_{26}H_{32}O_9S$ 520.1767, found 520.1786; R_f (hexane:CH_2Cl_2:EtOAc = 10:2:1) = 0.18.

Methyl 3-(Phenylthio)-4-(2′,5′,6′-tris(methoxycarbonyl)-5-oxocyclohexyl)but-2-enoate (12). A solution of the keto ester **9** (922 mg, 3.47 mmol) and the trimethylsiloxy diene **10** (1.94 g, 6.94 mmol) in dry CH_2Cl_2 (8 mL), under argon, at −78 °C, was treated dropwise, via syringe, with titanium tetrachloride (0.414 mL, 716 mg, 3.79 mmol) added over 2 min. After 1 h 10 min the dark brown/red mixture was diluted with CH_2Cl_2 (30 mL) and poured into saturated $NaHCO_3$:CH_2Cl_2 (1:2, 60 mL). The resulting yellow emulsion was filtered through Celite and the aqueous phase separated and extracted with CH_2Cl_2 (20 mL). The combined organic extract was washed with sodium bicarbonate (3 × 50 mL), water (50 mL) and brine. Drying and removal of the solvent left a gum which was applied to a column of silica gel (240 g) and flash chromatographed using hexanes:CH_2Cl_2:EtOAc (10:2:1) as eluent to provide the title compound as a mixture of E:Z isomers (545 mg, 34%) in a 4:1 ratio.

E isomer **12a**: IR (CH_2Cl_2) 1734, 1701, 1654, 1582 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 2.31–2.4 (m, 4H), 2.78 (dd, 1H, J = 10.0, 15.0 Hz), 3.11 (dd, 1H, J = 7.5, 15.0 Hz), 3.61 (s, 3H), 3.72 (s, 3H), 3.73 (s, 3H), 3.75 (s, 3H), 4.02 (dd, 1H, J = 7.5, 10.0 Hz), 5.28 (s, 1H), 7.45 (s, 5H), 12.3 (s, 1H); ^{13}C NMR (270 MHz, $CDCl_3$) 24.97, 28.92, 38.86, 38.93, 54.20, 54.55, 56.05,

56.22, 60.51, 103.50, 115.60, 132.85, 133.04, 133.09, 138.54, 164.01, 168.39, 173.41, 174.11, 175.60; MS (EI) 479 (M + 1, 3), 478 (M^+, 11), 447 (12), 271 (100), 239 (8), 195 (3); HRMS calcd for $C_{23}H_{26}O_9S$ 478.1297, found 478.1310; R_f (hexane:CH_2Cl_2:EtOAc = 4:2:1) = 0.42.

Z isomer **12b**: IR (CH_2Cl_2) 1736, 1705 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 1.63–2.24 (m, 6H), 3.4 (s, 3H), 3.62 (s, 3H), 3.72 (s, 3H), 3.75 (s, 3H), 3.65–3.8 (m, 1H), 5.88 (s, 1H), 7.3–7.45 (m, 5H), 12.38 (s, 1H); ^{13}C NMR (270 MHz, $CDCl_3$) 21.63, 25.44, 36.67, 38.53, 51.23, 51.68, 52.93, 52.98, 56.96, 99.66, 114.30, 129.16, 131.12, 135.51, 157.99, 166.16, 169.7, 170.43, 172.25; MS (EI) 479 (M + 1, 3), 478 (M^+, 11), 446 (3), 271 (100), 239 (70), 224 (17), 211 (2); HRMS calcd for $C_{23}H_{26}O_9S$ 478.1297, found 478.1308; R_f (hexane:CH_2Cl_2: tOAc = 4:2:1) = 0.4.

3-(Phenylthio)-4-(2′,2′,6′-tris(ethoxycarbonyl)-5′-oxocyclohexyl)but-2-enoic Acid (14). A solution of the Michael adduct **11a** (100 mg, 0.192 mmol) in dioxane:water (3:1, 1.2 mL) was treated under argon at 21 °C with lithium hydroxide hydrate (22 mg, 0.53 mmol). The solution was stirred for 64 h to complete reaction. The resulting yellow solution was diluted with ethyl acetate (15 mL) and extracted with saturated $NaHCO_3$ (2 × 4 mL). The organic phase was washed with a mixture of water:brine (1:1, 5 mL), dried, and evaporated to a yellow oil (77 mg). The oil was purified by flash chromatography on silica gel (10 g) (eluent:toluene:EtOAc:HOAc = 120:10:1) to provide the acid **14** (71 mg, 75%) as an off-white solid: mp 128–130 °C; IR (CH_2Cl_2) 2690–2980, 1739, 1718, 1650 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 1.17 (t, 3H, J = 7.3 Hz), 1.21 (t, 3H, J = 7.3 Hz), 1.25 (t, 3H, J = 7.3 Hz), 2.23–2.41 (m, 4.27H), 2.58 (dd, 1H, J = 9.9, 13.2 Hz), 3.24 (dd, 1H, J = 5.3, 13.2 Hz), 4.02–4.31 (m, 7H), 5.2 (s, 1H), 7.41 (bs, 5H), 12.44 (bs, 0.73H); ^{13}C NMR (270 MHz, $CDCl_3$) 13.93, 13.98, 14.08, 21.71, 25.62, 35.19, 36.02, 57.39, 60.57, 61.57, 61.71, 100.48, 111.53, 129.4, 129.84, 130.01, 135.3, 164.45, 168.79, 169.78, 170.85, 172.08; MS (CI, CH_4) 507 (M + 1, 3), 506 (M, 3), 505 (4), 489 (13), 416 (100), 312 (32); HMRS calcd for $C_{25}H_{30}O_9S$ 506.1611, found 506.1611; R_f (toluene:ethyl acetate:acetic acid = 120:10:1) = 0.14.

Methyl 3-(Phenylthio)-4-(2′,2′-bis(ethoxycarbonyl)-5′-oxocyclohexyl)but-2-enoate (16). To a solution of the trans Michael adduct **11a** (30 mg, 0.058 mmol) in dry DMF (0.6 mL) was added lithium iodide (23 mg, 0.17 mmol). The mixture was heated to a bath temperature of 125–130 °C over 2.5 h to complete reaction. The solution was cooled to ambient temperature, diluted with CH_2Cl_2 (10 mL), and washed sequentially with 2 N HCl (2 × 5 mL), water (5 mL), and brine. The organic extract was dried and evaporated to a yellow gum (21 mg). The gum was applied to a column of silica gel (2 g) and eluted under medium pressure with (hexanes:CH_2Cl_2:EtOAc = 6:2:1) to furnish the title compound (18 mg, 68%) as a gum: IR (CH_2Cl_2) 1721, 1178 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 1.29 (t, 3H, J = 7.2 Hz), 1.32 (t, 3H, J = 7.2 Hz), 2.23–2.65 (m, 7H), 2.92–3.12 (m, 1H), 3.56 (s, 3H), 3.9 (dd, 1H, J = 11.7, 13.4 Hz), 4.29 (q, 2H, J = 7.2 Hz), 4.31 (q, 3H, J = 7.2 Hz), 5.23 (s, 1H), 7.4–7.52 (m, 5H); ^{13}C NMR (270 MHz, $CDCl_3$) 14.53, 30.28, 33.75, 38, 41.26, 41.76, 51.54, 57.9, 62.18, 62.4, 113.47, 129.43, 130.36, 130.45, 136.05, 161.71, 165.45, 169.99, 171.08; MS (CI, CH_4) 450 (M + 2, 4), 449 (M + 1, 13), 448 (M^+, 14), 417 (100); HRMS calcd for $C_{23}H_{28}O_7S$ 448.1557, found 448.1563; R_f (hexane:CH_2Cl_2:EtOAc = 6:2:1) = 0.2.

Diethyl 4,5-Dioxo-7-(phenylthio)-1,2,3,4,4a,5,8,8a-octahydronaphthalene-1,1-dicarboxylate (17). To a solution of the decarboxylated Michael adduct **16** (10 mg, 0.022 mmol) in dry 2-methyl-2-propanol (0.2 mL), at 21 °C, under argon, was added solid KOtBu (sublimed, 3 mg, 0.028 mmol). The brown/yellow reaction was monitored by TLC. Complete consumption of starting material was observed after 1 h 45 min. The resulting yellow solution was diluted with CH_2Cl_2 (10 mL) and washed with 2 N HCl (2 × 5 mL), water (5 mL), and brine. Drying and evaporation of the organic phase gave a yellow gum (9 mg) which was purified by flash chromatography on silica gel (2 g) (eluent:hexanes:CH_2Cl_2:EtOAc = 10:2:1) to furnish the decalone **17** as a yellow oil (7 mg, 77%): IR (film): 3500–3400, 1730, 1620 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 1.25 (t, 3H, J = 7.2 Hz), 1.26 (t, 3H, J = 7.2 Hz), 2.02–2.54 (m, 5H), 3.04 (ddd, 1H, J = 2.0, 14.0, 16.5 Hz), 3.37 (dd, 1H, J = 6.0, 14.0 Hz), 3.7 (d, 0.5H, J = 16.5 Hz), 4.16–4.21 (m, 6H), 5.46 (s, 1H), 7.39–7.49 (m, 5H), 12.69 (s, 0.5 × 1H); ^{13}C NMR (270 MHz, $CDCl_3$) 14.08, 27.16, 27.91, 31.83, 37.71, 55.67, 61.4, 61.85, 103.1, 118.66, 128.04, 129.9, 130.21, 135.42, 162.87, 169.18, 170.74, 175.34, 186.76; MS (EI) 417 (M + 1, 8), 416 (M, 3), 414 (31), 244 (100), 229 (45); HMRS calcd for $C_{22}H_{24}O_6S$ 416.1294, found 416.1289; R_f (hexanes:CH_2Cl_2:EtOAc = 10:2:1) = 0.24.

Methyl 3-(Phenylthio)-4-(2′,2′,6′-tris(methoxycarbonyl)-5′-oxocyclohexyl)but-3-enoate (19). To a stirred solution of the Michael adduct **12a** (20 mg, 0.043 mmol), in dry CH_2Cl_2 (0.5 mL), under argon, at −78 °C, was rapidly added trimethylsilyl trifilate (distilled, 9 μL, 10.3 mg, 0.047 mmol). The solution was left standing at −20 °C for 16 h and then diluted with aqueous saturated $NaHCO_3$ (1 mL) followed by CH_2Cl_2 (5 mL). The aqueous phase was separated and extracted with CH_2Cl_2 (5 mL). The combined organic phase was washed with water (5 mL) and brine, dried, and evaporated to a glassy residue (16.3 mg). The material was flash chromatographed on silica gel (2 g) using (hexanes:CH_2Cl_2:EtOAc = 10:2:1) as eluent. The major fraction was concentrated to a solid which, after trituration with eluent, afforded the title compound (14.4 mg, 72%) as an off-white amorphous solid: mp 141–142 °C; IR (CH_2Cl_2) 3132, 1739, 1653 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 2.16–2.49 (m, 4H), 3.12 (s, 2H), 3.60 (s, 3H), 3.62 (s, 3H), 3.65 (s, 3H), 3.66 (s, 3H), 4.83 (d, 1H, J = 10.0 Hz), 5.66 (d, 1H, J = 10.0 Hz), 7.18–7.33 (m, 5H); ^{13}C NMR (270 MHz, $CDCl_3$) 27.89, 31.18, 42.51, 47.14, 57.11, 58.22, 62.18, 104.14, 131.8, 134.09, 134.21, 134.63, 135.38, 139.26, 141.37, 174.71, 175.06, 175.58, 175.85, 177.55; MS (CI, CH_4) 478 (M^+, 1), 477 (6), 446 (1) 368 (18), 336 (33), 84 (100); HRMS calcd for $C_{23}H_{26}O_9S$ 478.1298, found 478.1299; R_f (hexane:CH_2Cl_2:EtOAc = 4:2:1) = 0.4.

2,4,4-Tris(ethoxycarbonyl)cyclohex-2-en-1-one, Ethylene Ketal (21). A solution of the enone **8** (2.0 g, 6.42 mmol) and ethylene glycol (1.08 mL, 1.2 g, 0.019 mol) was treated with a catalytic amount of *p*-toluenesulfonic acid (20 mg, 10%, w/w) and the solution heated to reflux over a Dean-Stark trap for 21 h. The solution was then concentrated to a yellow oil (1.9 g) which after flash column chromatography (eluent: hexanes:CH_2Cl_2:EtOAc = 4:2:1) provided the title compound as a viscous oil. The oil crystallized on standing to needle crystals (1.18 g, 52%): mp 63–65 °C; IR (CH_2Cl_2) 2790, 1727 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.22–1.34 (m, 9H), 1.81–2.36 (m, 4H), 3.98 (m, 4H), 4.11–4.3 (m, 4H), 7.13 (s, 1H); ^{13}C MNR (270 MHz, $CDCl_3$) 13.89, 13.9, 13.92, 26.6, 32.5, 55.5, 60.08, 62.1, 65.8, 104.8, 134.01, 139.2, 164.7, 168.8; MS (CI, CH_4) 357 (M + 1, 100), 356 (M^+, 1), 311 (18), 184 (15); HRMS calcd for $C_{17}H_{24}O_8S$ 356.1472, found 356.1471; R_f (hexane:CH_2Cl_2:EtOAc = 4:2:1) = 0.15.

Methyl 3-(Phenylthio)-4-(1′-((hydroxyethyl)oxy)-2′,4′,4′-tris(ethoxycarbonyl)cyclohex-2-enyl)but-2-enoate (22). A mixture of the ethylene ketal **21** (840 mg, 2.36 mmol) and dry aluminum trichloride (418 mg, 3.14 mmol) in dry CH_2Cl_2 (6 mL), at 0 °C, under argon, was treated dropwise, after 1 min of stirring, with a solution of the siloxy diene **10** (1.06 g, 3.76 mmol) in dry CH_2Cl_2 (6 mL), over 5 min. The initial yellow solution gradually turned red. After 6 h at 0 °C, the resulting deep-red solution was allowed to warm to 21 °C over 30 min and then diluted with CH_2Cl_2:saturated aqueous $NaHCO_3$ (1:2, 30 mL). The resulting yellow emulsion was filtered through Celite and the aqueous phase separated and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extract was washed sequentially with saturated $NaHCO_3$ (10 mL), water (10 mL), and brine and then dried. The solvent was removed in vacuo to leave an oil (1.56 g) which was purified by silica gel (200 g) chromatography (eluent:hexanes:CH_2Cl_2:EtOAc = 4:2:1) to give the starting ketal **21** (300 mg) and the title compound (124 mg, 14%) as a clear gum. Compound **22**: IR (film) 3500–3400, 2900, 1730, 1639, 1600 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.26 (t, 3H, J = 7.0 Hz), 1.29 (t, 3H, J = 7.0 Hz), 1.32 (t, 3H, J = 7.0 Hz), 1.94–2.36 (m, 4H), 3.28–3.72 (m, 4H), 3.58 (s, 3H), 3.73 (d, 1H, J = 14.0 Hz), 3.96 (d, 1H, J = 14.0 Hz), 4.17–4.30 (m, 6H), 5.22 (s, 1H), 7.19 (s, 1H), 7.39–7.52 (m, 5H); ^{13}C NMR (270 MHz, $CDCl_3$) 13.95, 13.99, 14.12, 25.77, 26.68, 39.24, 50.94, 55.46, 61.12, 62.11, 62.18, 61.88, 64.16,

76.38, 113.8, 129.8, 130.14, 135.63, 136.16, 139.15, 159.74, 165.74, 165.74, 169.03; MS (CI, CH_4) 533 (3), 505 (11), 504 (28), 503 (100), 471 (27), 357 (21); HRMS calcd for $C_{28}H_{36}O_{10}S$ 564.2029, found 564.2015; R_f (hexane:CH_2Cl_2:EtOAc = 1:1:1) = 0.2.

Methyl 3-(Phenylthio)-4-(2′,2′,6′-tris(ethoxycarbonyl)-5′-(*tert*-butyldimethylsilyl)oxy)cyclohex-5′-enyl)but-2-enoate (23). A solution of the Michael adduct **11a** (145 mg, 0.278 mmol) in dry CH_2Cl_2 (1.5 mL) at 21 °C was treated with dry triethylamine (8.5 μL, 0.612 mmol) followed by *tert*-butyldimethylsilyl trifilate (0.140 mL, 0.162 mmol). After 24 h, reaction was complete. The solution was diluted with CH_2Cl_2 (10 mL), washed with water (2 × 8 mL) and brine and dried. Concentration of the organic phase gave an oil (202 mg) which was flash chromatographed on silica gel (eluent:hexanes:CH_2Cl_2:EtOAc = 10:2:1) to provide the enol ether as a colorless gum (111 mg, 63%): IR (film) 2850–2980, 1739, 1718, 1603, 1280, 1229 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 0.14 (s, 3H), 0.15 (s, 3H), 0.92 (s, 9H) 1.21 (t, 3H, J = 8.0 Hz), 1.24 (t, 3H, J = 8.0 Hz), 1.31 (t, 3H, J = 8.0 Hz), 2.1–2.48 (m, 4H), 2.88 (dd, 1H, J = 6.0, 14.0 Hz), 3.22 (dd, 1H, J = 12.0, 14.0 Hz), 3.98 (dd, 1H, J = 6.0, 12.0 Hz), 4.07–4.3 (m, 6H), 5.12 (s, 1H), 7.38–7.6 (m, 5H); ^{13}C NMR (270 MHz, $CDCl_3$) −3.71, −3.60, 13.98, 14.2, 18.26, 22.62, 25.70, 28.70, 35.34, 30.08, 50.69, 57.22, 61.45, 61.54, 111.07, 112.21, 129.61, 129.71, 135.63, 157.21, 161.48, 165.04, 167, 169.65, 170.04; MS (CI, CH_4): 634 (M, 4), 602 (6), 588 (100), 576 (42); HRMS calcd for $C_{32}H_{46}O_9SSi$ 634.2632, found 634.2622; R_f (hexane:CH_2Cl_2:EtOAc = 10:2:1) = 0.3.

***cis*-Triethyl 4,5-Dioxo-7-(phenylthio)-1,2,3,4a,8,8a-hexahydronaphthalene-1,1,4a-tricarboxylate (13).** A solution of the Michael adduct **14** (10 mg, 0.0198 mmol) and triethylamine (3.0 μL, 0.020 mmol) in dry CH_2Cl_2 (1 mL), under argon, at 0 °C, was treated with DMF (1μL) followed by oxalyl chloride (2.3 μL, 3.3 mg, 0.026 mmol) when vigorous effervescence was observed. The reaction was followed by TLC by quenching aliquots with methanol. After 1 h, the starting substrate was completely consumed. The reaction was then treated with another portion of triethylamine (6 μL, 0.043 mmol). The initial pale yellow solution turned deep orange, and a precipitate (presumably Et_3NHCl) emerged. After 20 min at 0 °C, the reaction was diluted with CH_2Cl_2 (8 mL) and washed sequentially with 2 N HCl (3 mL), water (3 mL), saturated $NaHCO_3$ (3 mL), and brine. Drying and evaporation of the organic phase gave a yellow solid (9 mg) which was purified by flash chromatography on silica gel (eluent:toluene:EtOAc:acetic acid = 120:10:1) to give the title compound (7 mg, 72%) as a pale yellow amorphous powder. A crystalline sample was obtained by dissolution of the powder in hot isopropyl ether:ethyl acetate (9:1, 1 mL) to give after 24 h at 21 °C colorless rhombic crystals (2.8 mg, 40% recovery):[24] mp 158–159 °C; IR (CH_2Cl_2) 2346, 2305, 1687 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 1.26 (t, 6H, J = 7.2 Hz), 1.32 (t, 3H, J = 7.3 Hz), 1.98–2.12 (m, 1H), 2.5–2.6 (m, 2H), 2.85 (dd, 2H, J = 4.0, 1.6 Hz), 3.12–3.26 (m, 1H), 3.97 (t, 1H, J = 4.0 Hz), 4.01–4.2 (m, 2H), 4.17 to 4.33 (m, 4H), 5.49 (s, 1H), 7.38 to 7.45 (m, 5H); ^{13}C NMR (270 MHz, $CDCl_3$) 13.88, 13.93, 13.98, 30.47, 31.22, 36.63, 43.85, 54.1, 62.19, 62.24, 62.47, 70.25, 119.2, 127.21, 130.08, 130.53, 135.32, 165.77, 167.14, 169.55 , 170.19, 186.76; MS (CI, NH_3) 490 (M + 2, 28), 489 (M + 1, 100), 488 (M, 3), 414 (20); HRMS calcd for $C_{25}H_{28}O_8S$ 488.1505, found 488.1505; R_f (hexanes:CH_2Cl_2:EtOAc = 4:2:1) = 0.4.

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of **13**, **14** (^1H only), **23**, **22**, **21**, **19**, **17**, **16**, **12a/b**, **11a/b**, **9**, **7**, **6**, and **5** (30 pages). This material is contained in libraries on microfiche and immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(24) The author has deposited atomic coordinates for **13** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.