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Molecular complexity from aromatics. Cycloaddition of cyclohexa-2,4-dienones, sigmatropic 1,2-acyl shift and ring-closing metathesis: a new, efficient, and stereoselective synthesis of (±)-hirsutic acid C and medium ring carbocycles

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Abstract—A new, stereoselective formal synthesis of hirsutic acid and medium ring carbocyclic systems from salicyl alcohol is described. Cycloaddition between electron deficient partners such as cyclohexa-2,4-dienone and methylmethacrylate, triplet sensitized 1,2-acyl shift and ring-closing metathesis are the key features of our approach.

1. Introduction

Cycloaddition reactions, especially the Diels–Alder reaction, are one of the most general and powerful tools for the creation of various types of molecular structures in a regio- and stereoselective fashion.[1,2] The generation of structural, functional, and stereochemical complexities from simple precursors in an efficient manner is some of the important aspects of the development of new methodology.[3] Multicomponent reactions,[4] and reactions in tandem[5,6] are some of the ways to achieve efficiency and molecular complexity. Recently, reactive and short-lived species such as *o*-iminioquinones,[7] quinols, and cyclohexadienone ketals[8] and their congeners derived from aromatic compounds have received increasingly greater attention for the development of an efficient methodology. Recently, we also developed a new method for rapid generation of molecular complexity from simple aromatic precursors that involved cycloaddition of cyclohexa-2,4-dienones with various types of π-systems.[9]

Polyquinane natural products have stimulated a sustained interest because of their wide occurrence in nature, their intricate molecular structures and their biological properties.[10–12] Moreover, new complex cyclopentanoidal natural products are continuously being isolated from various sources.[13] For example, connatusin A **1** (Fig. 1) and its congeners were isolated from *Lentinus connatus*.[13b] Recently, Steglich and co-workers[13d] have isolated a number of triquinane natural products belonging to the hirsutane and cucumane groups such as **2**–**4** from mycelial cultures of *Macrocystidia cucumis*, which were found to exhibit cytotoxic and antibacterial activities. Hirsutic acid **5a** is the oldest member of this family that was isolated from *Stereum hirsutum* and *Stereum complicatum* along with a closely related compound complicatic acid **5b** that exhibited interesting biological properties.[14] Unlike other members of this family such as coriolin and hirsutene, only a few syntheses of hirsutic acid have been reported.[12,15] Recently, an elegant synthesis of (+)-hirsutic acid and (−)-complicatic acid was reported by Banwell and co-workers.[16] It appears that the presence of an angular methyl group at C-3 and a quaternary center bearing methyl and carboxyl groups (C-11) in **5a** poses considerable problems in its synthesis, in addition to the generation of the triquinane framework. Most of the earlier routes

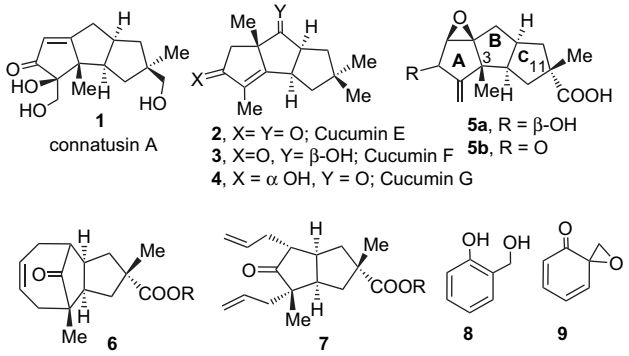

Figure 1.

Keywords: Cyclohexa-2,4-dienone; Diels–Alder reaction; Oxa-di-π-methane rearrangement; Hirsutic acid.
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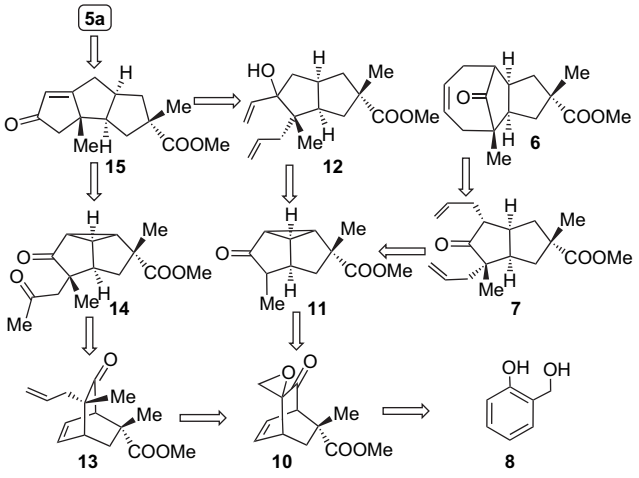
generate the *cis–anti–cis* triquinane framework after a multi-step sequence. Moreover, except in a couple of cases, the angular methyl group at C-3 and the quaternary carbon at C-11 having the methyl and carboxyl groups were introduced at later stages of the route, often via a multi-step sequence.

We wish to report herein[17] a short and stereoselective formal synthesis of hirsutic acid C **5a** from salicyl alcohol **8** that involves cycloaddition of spiroepoxycyclohexadienone **9**, a sigmatropic 1,2-acyl shift (or oxa-di-π-methane rearrangement) and ring-closing metathesis. We also report an efficient and stereoselective entry into the bicyclic compound **7** and its ring-closing metathesis to carbocyclic systems of type **6** containing an eight-membered ring system, which has generated a significant interest recently.[18]

The cornerstone of our strategy is the identification of the structural, functional, and stereochemical features of hirsutic acid and the key tricyclic intermediate **15**, which has already been converted to **5a**,[15a,c,f] with those of the keto-epoxide **10** (Scheme 1). It was contemplated that the ketoepoxide may be easily transformed into the diquinane **11** via reduction of the oxirane ring into a methyl group followed by a photochemical oxa-di-π-methane rearrangement. The diquinane **11** would then be manipulated to the intermediate **12** that upon ring-closing metathesis and oxidative transposition of the resulting tricyclic compound would readily give the intermediate **15**. Alternatively, it was also considered that the keto-epoxide **10** may be elaborated into bicyclo[2.2.2]octenone **13**, which upon photochemical 1,2-acyl shift and subsequent Wacker type oxidation would give the tricyclic compound **14**. The reductive cleavage of the cyclopropane ring and aldol condensation would give the intermediate **15**. The keto-ester **10** itself was considered to be obtained from salicyl alcohol **8** via oxidation to spiroepoxycyclohexadienone **9** followed by interception with methylmethacrylate.



Scheme 1.

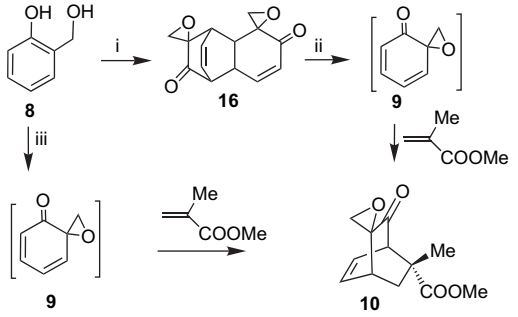
Further, it was considered that the intermediate **11** may be converted into the diquinane **7** via reductive cleavage of the cyclopropane ring and stereoselective alkylation, which upon ring-closing metathesis would furnish the carbocyclic system **6** (Scheme 1).

There are several noteworthy features of our strategy. For example, 11 carbons of the triquinane intermediate **15** and hirsutic acid are derived from salicyl alcohol and methylmethacrylate and assembled to form the bicyclic precursor **10**. Remarkably, two five-membered rings (rings B and C) and three stereogenic centers of **5** are present in the precursor **10** in latent form. Moreover, the oxirane ring in **10** provides an opportunity for its manipulation into the angular methyl group and stereoselective introduction of a three carbon chain so as to create the stereocenter at C-3 and the third cyclopentane ring (ring A) of the intermediate **15** and hirsutic acid.

2. Results and discussion

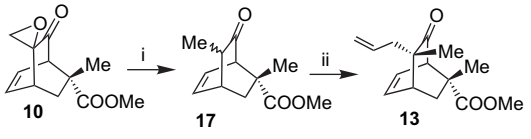
Toward objectives described above, oxidation of salicyl alcohol to spiroepoxycyclohexadienone **9** and its interception with methylmethacrylate was attempted. However, it mostly gave the dimer **16** and the adduct **10** was obtained in a very poor yield (~3%). Hence, we considered generating the cyclohexadienone **9** via retro Diels–Alder reaction of the dimer **16** and intercepting it with methylmethacrylate.

Therefore, salicyl alcohol was oxidized with aq sodium metaperiodate[19] to give the epoxydimer **16**. Pyrolysis of **16** in the presence of methylmethacrylate gave the desired *endo* adduct **10** as a major product (70%) along with a minor amount of stereoisomeric products (Scheme 2). The structure of the adduct was clearly deduced from its spectroscopic features and by comparison with a sample prepared by a previously described route.[17]



Scheme 2. Reagents and conditions: (i) aq $NaIO_4$, 90%; (ii) diphenyl ether, xylene, methylmethacrylate, 160 °C, 70%; and (iii) aq $NaIO_4$, CH_3CN, 0 °C–rt, 3%.

Treatment of the adduct **10** with zinc in refluxing dry dioxane containing ammonium chloride following a procedure developed in our laboratory, furnished the ketone **17** (*syn–anti* mixture) in major amounts as a result of deoxygenation of the oxirane ring (Scheme 3). Alkylation of **17** with allyl bromide in the presence of sodium hydride in refluxing THF gave the allylated product **13** in 65% yield as a major product.



Scheme 3. Reagents and conditions: (i) Zn, NH_4Cl, dry dioxane, Δ, 68% and (ii) NaH–THF, allyl bromide, Δ, 65%.

The *syn*-stereochemical orientation of the allyl chain in **13** was clearly indicated from the chemical shift of the methyl

group α to the ketone, which appeared at δ 1.08 in accordance with earlier observations on similar systems. Such types of π-facial stereoselectivity during alkylation of bicyclo[2.2.2]-octenones have been observed earlier by us as well as others.[20] The stereochemistry of the alkylated product **13** was also confirmed by further chemical transformations (vide infra). After having prepared the bicyclic compound **13**, we considered to examine its triplet sensitized photochemical reaction and further transformation to the intermediate **15**.

In general, rigid β,γ-enones undergo two unique reactions that are characteristic of excited states. The triplet sensitized irradiation leads to a 1,2-acyl shift (or oxa-di-π-methane rearrangement) and singlet excitation induces a 1,3-acyl shift.[21,22] However, the photoreactivity depends on the structure of the chromophoric system and functional groups in a subtle fashion.[21b,c] Keeping in mind the structural and functional complexity of our chromophoric system, a solution of **13** in acetone (solvent as well as sensitizer) was irradiated with a mercury vapor lamp (APP, 125 W) for 3.5 h. Chromatography of the photolysate yielded the photoproduct **18** in low yield (30%) along with some recovered starting material. At this juncture, we thought that the low efficiency of 1,2-acyl shift (or oxa-di-π-methane rearrangement) in the above photoreaction could be due to competitive absorption of light by the olefinic group present in the allylic chain.

Therefore, we considered to convert **13** into the dione ester **19** and examine its photoreaction with a view to explore the efficiency of the photoreaction. Thus, the dione ester **19** was prepared by Wacker oxidation[23] of **13** and irradiated in acetone to give the precursor **14** in a slightly better yield (42%) (Scheme 4), as a solid. The diquinane **14** was also prepared by oxidation of **18**. Although, the structure of the diquinane **14** was revealed from its spectral data, its stereostructure was also determined through an X-ray crystal structure (Fig. 2) since this constitutes an important intermediate. Thus, the structures and stereochemistries of the preceding intermediates were also established.

Toward the synthesis of hirsutic acid, the cyclopropane ring in diquinane **14** was reductively cleaved by treatment with tributyl tin hydride-AIBN[24] in refluxing benzene to give **20** in good yield (60%). Aldol condensation in **20** readily gave the linearly fused tricyclopentanoid **15** (Scheme 4), which has already been elaborated to hirsutic acid. The structure of the triquinane intermediate **15** was deduced from its spectral data, which is in good agreement with those reported in the literature.[15a,c]

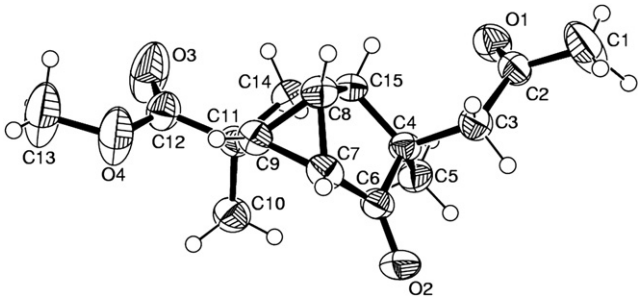
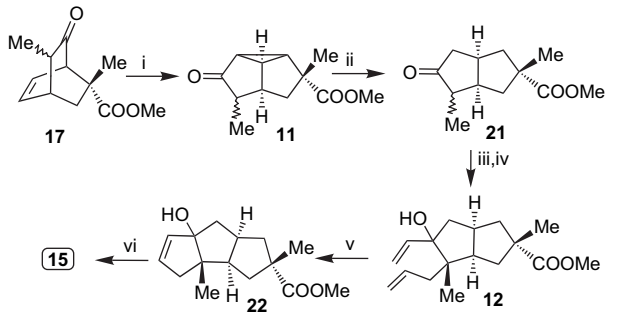
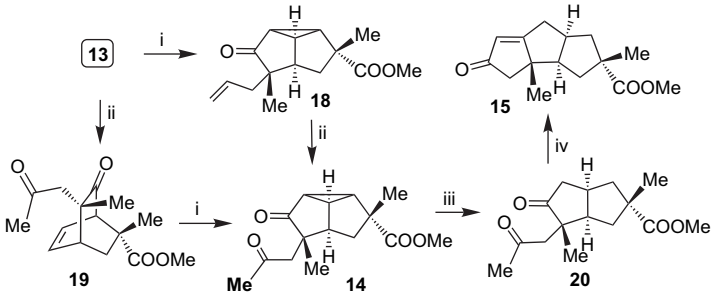


Figure 2. X-ray crystal structure of the compound **14**.

In order to avoid the problems due to low yields in the oxa-di-π-methane rearrangement in the bridged bicyclic compounds **13** and **19**, we thought to design an alternate route to the intermediate **15** by employing the oxa-di-π-methane rearrangement in bicyclooctenone **17** and ring-closing metathesis reaction, which has proved to be a method of choice for ring construction.[11b,25,26] It was considered that **17** would undergo the photoreaction with better efficiency since it contains only a β,γ-enone chromophore. Further, the resulting photoproduct is well suited for manipulation to the intermediate **12** containing olefinic chains by virtue of its folded geometry. Thus, a solution of **17** in acetone was irradiated for 1.25 h. Removal of solvent and chromatography gave the photoproduct **11** in very good yield (61%). Reductive cleavage of the cyclopropane ring in **11** gave the diquinane **21**. Stereoselective alkylation of **21** with allyl bromide followed by addition of vinyl Grignard reagent readily furnished the intermediate **12** in excellent yield. Ring-closing metathesis with Grubbs' second generation catalyst followed by oxidation with PCC gave the intermediate **15** (Scheme 5).

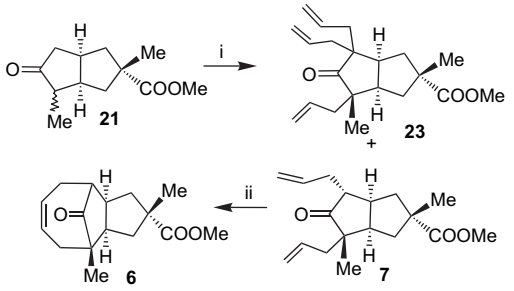


Scheme 5. Reagents and conditions: (i) *hν*, acetone, 1.25 h, 61%; (ii) $(Bu)_3SnH$, AIBN, benzene, Δ, 14 h, 63%; (iii) NaH, DME, allyl bromide, rt, 63%; (iv) vinylMgBr, $CeCl_3$, THF, −78 °C to reflux, 63%; (v) second generation Grubbs' catalyst, CH_2Cl_2, 30 min, 70% and (vi) PCC, CH_2Cl_2, 1.5 h, 87%.



Scheme 4. Reagents and conditions: (i) *hν*, acetone (3.5 h for **18**, 30%; 1.5 h for **14**, 42%); (ii) $PdCl_2$, CuCl, O_2, aq DMF (24 h for **18**–**14**, 68%; 12 h for **13**–**19**, 75%); (iii) $(Bu)_3SnH$, AIBN, benzene, Δ, 60%; (iv) KO^{t}Bu–^{t}BuOH, 15 min, 70%.

The diquinane **21** appeared to be a potential precursor for the synthesis of compounds containing an eight-membered ring especially since it provides an opportunity to introduce alkenyl chains on the both sides of carbonyl group. In order to explore this possibility, the keto-ester **21** was treated with allyl bromide in the presence of sodium hydride in refluxing THF, which gave the desired diallylated compound **7** as well as **23**. The compound **7** underwent a smooth ring-closing metathesis to give the tricyclic compound **6** (Scheme 6).



Scheme 6. Reagents and conditions: (i) NaH, THF, reflux, 1.5 h, **23** (43%), **7** (29%) and (ii) second generation Grubbs' catalyst, CH_2Cl_2, 45 min, 66%.

3. Conclusion

In summary, we have described a short and an efficient formal synthesis of hirsutic acid from salicyl alcohol and methylmethacrylate (eight steps) involving cycloaddition between electron deficient partners, photochemical 1,2-acyl shift and ring-closing metathesis as key features. A stereoselective route to the tricyclic system containing an eight-membered ring by ring-closing metathesis in an appropriately appended diquinane is also described. In addition to the brevity, stereoselectivity, and rapid generation of molecular complexity, the simplicities of the reagents and conditions are noteworthy features of our methodology.

4. Experimental section

4.1. General remarks

IR spectra were recorded on Nicolet Impact 400 FT-IR Instrument. UV spectra were recorded using Schimadzu U 260 instrument. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded on Varian VXR 300 instrument. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on Varian 400 MHz instrument. Most of the samples were dilute solutions in $CDCl_3$ with $Si(CH_3)_4$ as an internal standard. In some cases to conserve $CDCl_3$, CCl_4 were used. Mass spectra were recorded on HP GCD 1800A GC-MS spectrometer. High-resolution mass spectra were recorded in Q-T of micro (YA-105) Mass Spectrometer. Microanalyses were done on a CEST 1106 instrument. Melting points were determined on a Veego apparatus of Buchi type.

All the organic extracts were dried over anhydrous sodium sulfate. Reactions were monitored with thin-layer chromatography and spots were visualized with iodine vapor. Column chromatography was performed using SRL/Thomas Baker silica gel (60–120 and 100–200 mesh). The elution was done with petroleum ether (60–80 °C) and ethyl acetate mixture. The fractions eluted from column were concentrated at reduced pressure on a Buchi-RE 111 rotary evaporator. The solvent used for all reactions was purified/dried by using standard procedures.

4.1.1. 2-Methyl-2-*endo* carbomethoxy-5-spiroepoxy bicyclo[2.2.2]oct-7-ene-6-one (10). A mixture of the dimer **16** (1.22 g, 5 mmol) in xylene–diphenyl ether (30 mL, 2:1) and methylmethacrylate (7 mL, excess) was heated at ~160 °C for 12 h. Xylene was distilled off and the residue was charged on a column of silica gel. Elution with petroleum ether removed the diphenyl ether and other impurities. Further elution with petroleum ether–ethyl acetate (95:5) gave the epoxy ketone **10** (1.2 g, 70%) as a colorless solid, mp: 66–67 °C. IR ν_{max} (film): 1734 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.53 (superimposed dd, J_1=J_2=7.0 Hz, 1H, γH of β,γ-enone moiety), 6.27 (superimposed dd, J_1=J_2=7 Hz, 1H, βH of β,γ-enone moiety), 3.7 (s, 3H, –COOCH_3), 3.55 (dd, J=6 Hz, J_2=1.4 Hz, 1H), 3.19 (part of AB system, J_{AB}=6 Hz, 1H, –CH_2O–), 2.86 (part of AB system, J_{AB}=6 Hz, 1H, –CH_2O–), 2.60–2.48 (overlapped m, 2H), 1.90 (d with structure, J=12.3 Hz, 1H, methylene H), and 1.35 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.4 (CO), 175.8 (*C*OOCH$_3$), 135.2, 129.3 (olefinic carbons), 57.5, 56.2, 53.2, 52.5, 46.8, 38.0, 33.8, and 25.8. HRMS (ESI) (*m*/*z*): Found 223.0967 (M$^+$+H); Calcd for $C_{12}H_{14}O_4$: 223.0970 (M$^+$+H).

4.1.2. Oxidation of salicyl alcohol to spiroepoxycyclohexadienone and interception with methylmethacrylate: 2-methyl-2-*endo* carbomethoxy-5-spiroepoxy bicyclo-[2.2.2]oct-7-ene-6-one (10). To a solution of salicyl alcohol **8** (3.0 g, 24.2 mmol) and methylmethacrylate (6 mL, excess) in acetonitrile (60 mL) at 0 °C was added a saturated solution of sodium metaperiodate (18 g, 84 mmol, 25 mL) dropwise over a period of 2 h. After stirring the reaction mixture for an additional hour, more methylmethacrylate (3 mL) was added. The reaction mixture was further stirred overnight at room temperature. The organic layer was separated and the aqueous layer extracted with ethyl acetate (4×25 mL). The extract was combined with the organic layer and washed with brine and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel. Elution with petroleum ether–ethyl acetate (98:2) gave the unreacted methylmethacrylate. Further elution with petroleum ether–ethyl acetate (96:4) gave the compound **10** (0.161 g, 3%) as a colorless solid, mp 66–68 °C, which was found identical to the compound prepared previously.

4.1.3. 2,5-Dimethyl-2-*endo* carbomethoxy bicyclo[2.2.2]-oct-7-ene-6-one (17). To a suspension of activated zinc (26 g, excess) and ammonium chloride (2.6 g, excess) in dry dioxane (77 mL) was added a solution of the compound **10** (3.25 g, 14.62 mmol) in dry dioxane (20 mL). The reaction mixture was refluxed for 12 h, after which it was brought to room temperature, and filtered on a Celite pad to remove zinc and washed with ethyl acetate. The filtrate was concentrated in vacuo, so as to remove most of the solvent and the residue was diluted with water (20 mL) and extracted with ethyl acetate (3×30 mL). The combined organic layer was washed with brine (25 mL) and dried.

The solvent was removed under vacuum and the residue was chromatographed on silica gel. Elution with petroleum ether–ethyl acetate (97:3) gave the compound **17** (2.07 g, 68%) as a *syn–anti* mixture. IR ν_{max} (neat): 1727 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$+CCl_4) δ: 6.50 (superimposed dd, J_1=J_2=7.2 Hz, 1H, γH of β,γ-enone moiety), 6.1 (superimposed dd, J_1=J_2=7.2 Hz, 1H, βH of β,γ-enone moiety), 3.61 (s, 3H, –COOCH_3), 3.24 (d, J=6 Hz, 1H, methine), 2.69 (br s, 1H), 2.32 (d, J=13.8 Hz, 1H), 2.01 (m, 1H), 1.62 (d, J=15 Hz, 1H), 1.18 (s, 3H, methyl H), and 1.06 (d, J=7.5 Hz, 3H, methyl H). ^{13}C NMR (75 MHz, $CDCl_3$+CCl_4) δ: 213.1 (CO), 175.9 (*C*OOCH$_3$), 138.5, 128.6 (olefinic carbons), 56.5, 52.2, 47.6, 42.7, 37.8, 30.7, 25.8, and 13.6. HRMS (EI) (*m*/*z*): Found 231.0986 (M^++Na); Calcd for $C_{12}H_{16}O_3$: 231.0992 (M^++Na).

4.1.4. 5-Allyl 2,5-dimethyl-2-*endo* carbomethoxy bicyclo[2.2.2]oct-7-ene-6-one (13). Sodium hydride (0.8 g of 60% w/w suspension in oil, excess) was placed in a dry two-necked flask and washed with dry petroleum ether and tetrahydrofuran (10 mL) was added to it. A solution of ketone **17** (0.35 g, 1.68 mmol) in tetrahydrofuran (10 mL) was added slowly to the reaction mixture and the reaction mixture was refluxed for 1 h. It was brought to room temperature and allyl bromide (3 mL, excess) was added and the reaction mixture was further refluxed for 6 h. The reaction mixture was cooled and quenched with ice-cold water. The aqueous layer was separated and extracted with ethyl acetate (3×15 mL). The combined extracts were washed with brine (25 mL) and dried. The solvent was removed under vacuum and the residue was chromatographed on silica gel. Elution with petroleum ether–ethyl acetate (95:5) gave the compound **13** (0.270 g, 65%) as a colorless liquid. IR ν_{max} (film): 1736 and 1722 cm^{-1}. UV (MeOH) λ_{max}: 300 (w) nm. ^1H NMR (400 MHz, $CDCl_3$) δ: 6.47 (superimposed dd, J_1=J_2=7.0 Hz, 1H, γH of β,γ-enone moiety), 6.14 (superimposed dd, J_1=J_2=7.0 Hz, 1H, βH of β,γ-enone moiety), 5.75 (m, 1H, olefinic H of allyl group), 5.00–5.08 (m, 2H, olefinic H of allyl group), 3.67 (s, 3H, –COOCH_3), 3.35 (d, J=5.2 Hz, 1H), 2.65 (br s, 1H), 2.35 (dd, J_1=14.2 Hz, J_2=3.5 Hz, 1H,), 2.08–1.88 (m, 2H), 1.75 (d, J=14.2 Hz, 1H), 1.29 (s, 3H, methyl H), and 1.12 (s, 3H, methyl H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 215.4 (CO), 176.6 (*C*OOCH$_3$), 137.4, 133.3, 127.5, 118.3 (four olefinic carbons), 57.4, 52.4, 47.8, 46.9, 44.0, 40.8, 31.9, 25.7, and 19.9. HRMS (EI) (*m*/*z*): Found 249.1494 (M^++H); Calcd for $C_{15}H_{20}O_3$: 248.1491 (M^+).

4.1.5. 2-Allyl-2,7-dimethyl-7-carbomethoxytricyclo[3.3.0.0^{4,6}]oct-3-one (18). A solution of the ketone **13** (0.1 g, 0.4 mmol) in degassed acetone (110 mL, solvent as well as sensitizer) was irradiated with mercury vapor lamp (125 W, Applied Photophysics) in a Pyrex immersion well for 3.5 h, under nitrogen. Acetone was evaporated under vacuum and the residue was chromatographed. Elution with petroleum ether–ethyl acetate (96:4) first gave some unreacted starting material (0.053 g). Further elution with petroleum ether–ethyl acetate (92:8) furnished the product **18** (0.030 g, 30%) as a colorless liquid. IR ν_{max} (neat): 1724 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$+CCl_4) δ: 5.72–5.66 (m, 1H, olefinic H), 5.11–5.02 (m, 2H, olefinic H), 3.71 (s, 3H, –COOCH_3), 2.78–2.76 (m, 1H), 2.64–2.62 (m, 1H), 2.52–2.43 (m, 2H), 2.16 (d, J=7.2 Hz, 2H), 1.91 (m, 1H), 1.69 (d, J=13.8 Hz, 1H), 1.24 (s, 3H, methyl H), and 0.93 (s, 3H, methyl H). ^{13}C NMR (75 MHz, $CDCl_3$+CCl_4) δ: 216.8 (CO), 177.2 (*C*OOCH$_3$), 133.1, 118.8 (olefinic carbons), 56.6, 52.2, 51.6, 48.5, 45.5, 43.0, 41.7, 36.3, 34.6, 22.9, and 17.0. HRMS (EI) (*m*/*z*): Found 248.1421 (M^+); Calcd for $C_{15}H_{20}O_3$: 248.1412 (M^+).

4.1.6. 2-Acetonyl-2,7-dimethyl-7-carbomethoxytricyclo[3.3.0.0^{4,6}]oct-3-one (14). $PdCl_2$ (0.158 g), cuprous chloride (0.442 g), and water (0.5 mL) were taken in DMF (6 mL) and oxygen was bubbled into the reaction mixture for 20 min. A solution of the compound **18** (0.550 g, 0.4 mmol) in DMF (14 mL) was then added to the reaction mixture and the contents were stirred at room temperature in an oxygen atmosphere. After 24 h, the reaction mixture was quenched with 10% HCl and it was extracted with ether (3×20 mL). The combined organic layers were washed with brine (20 mL) and dried over anhydrous sodium sulfate. Removal of solvent followed by column chromatography (petroleum ether–ethyl acetate 80:20) of the residue furnished the diketo ester **14** (0.4 g, 68%) as a colorless solid, which was recrystallized from petroleum ether–ethyl acetate mixture, mp: 104–106 °C. IR ν_{max} (film): 1726 and 1703 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.72 (s, 3H, –COOCH_3), 3.12 (m, 1H), 2.80 (m, 1H), 2.60–2.46 (m, 4H), 2.13 (s, 3H, methyl H), 1.97 (m, 1H), 1.75 (d, J=14.3 Hz, 1H), 1.24 (s, 3H, methyl H), and 1.09 (s, 3H, methyl H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 217.4 (CO), 206.0 (CO), 177.4 (*C*OOCH$_3$), 56.1, 52.3, 51.6, 51.2, 47.2, 43.0, 42.2, 36.4, 34.5, 32.0, 23.0, and 16.7. Mass (*m*/*z*): 264 (M^+).

Crystal data: $C_{15}H_{20}O_4$, M 264.13, space group, monoclinic, $P21/c$, a=5.997(8), b=11.3480(9), c=21.2510(16) Å, λ=0.70903 Å, α=90.000(6), β=97.327(8), γ=90.000(8)°, U 1434.4(2) $Å^3$, Z=4, D_c=1.224 mg/m^3, T=293(2) K, F(000)=568, size=0.4×0.15×0.10 mm. Reflections/collected/unique 1996/1996 [R(int)=0.0000], final R indices [I>2sigma(I)]=R_1=0.0508, wR_2=0.1111], R indices (all data) R_1=0.0784, wR_2=0.1272. CCDC No. 226012, see http://www.ccdc.cam.ac.uk/conts/retrieving.html (e mail: deposit@ccdc.cam.ac.uk).

4.1.7. 5-Acetonyl-2,5-dimethyl-2-*endo* carbomethoxy bicyclo[2.2.2]oct-7-ene-6-one (19). $PdCl_2$ (0.196 g), cuprous chloride (0.560 g), and water (1.0 mL) were taken in DMF (7 mL) and oxygen was bubbled into the reaction mixture for 20 min. A solution of the compound **13** (0.7 g, 2.8 mmol) in DMF (17 mL) was added to the reaction mixture and the contents were stirred at room temperature in an oxygen atmosphere. After 12 h, the reaction mixture was quenched with HCl (10%) and it was extracted with ether (3×25 mL). The combined organic layers were washed with brine (25 mL) and dried over anhydrous sodium sulfate. Removal of solvent followed by column chromatography (petroleum ether–ethyl acetate 85:15) of the residue furnished the diketo ester **19** (0.558 g, 75%) as a colorless solid, which was recrystallized from petroleum ether–ethyl acetate mixture, mp: 64–66 °C. UV (MeOH) λ_{max}: 300 (s) nm. IR ν_{max} (film): 1717 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.45 (d of superimposed dd, J_1=J_2=7.0 Hz, J_3=1.2 Hz, 1H, γH of β,γ-enone moiety), 6.18 (d of superimposed dd, J_1=J_2=7.0 Hz, J_3=1.2 Hz, 1H, βH of β,γ-enone moiety),

3.66 (s, 3H, –COOCH_3), 3.38–3.30 (m, 2H), 2.64 (part of an AB system, J_{AB}=16.8 Hz, 1H), 2.44 (part of an AB system, J_{AB}=16.8 Hz, 1H), 2.36 (dd, J_1=16.8 Hz, J_2=3 Hz, 1H), 2.06 (s, 3H, methyl H), 1.84 (dd, J_1=14.2 Hz, J_2=2.1 Hz, 1H), 1.28 (s, 3H, methyl H), and 1.24 (s, 3H, methyl H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 215.1 (CO), 206.6 (CO), 176.5 (*C*OOCH$_3$), 139.7, 138.2 (olefinic carbons), 128.2, 56.9, 52.4, 51.0, 47.2, 46.2, 39.7, 31.8, 25.8, and 19.6. Mass (*m*/*z*): 264 (M^+). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63%. Found: C, 67.97; H, 8.48%.

4.1.8. Photoreaction of 19: 2-acetonyl-2,7-dimethyl-7-carbomethoxy tricyclo[3.3.0.0^{4,6}]oct-3-one (14). A solution of **19** (0.1 g, 0.37 mmol) in degassed acetone (110 mL, solvent as well as sensitizer) was irradiated with mercury vapor lamp (125 W, Applied Photophysics) in a Pyrex immersion well for 1.5 h, under nitrogen. Acetone was evaporated under vacuum and the residue was chromatographed. Elution with petroleum ether–ethyl acetate (88:12) gave some unreacted starting material (0.020 g). Further elution with petroleum ether–ethyl acetate (84:16) furnished the product **14** (0.042 g, 42%) as a colorless solid, which was found to be identical with the compound prepared by Wacker oxidation of **18**.

4.1.9. 2-Acetonyl-2,7-dimethyl-7-carbomethoxytricyclo[3.3.0]oct-3-one (20). To a solution of **14** (0.5 g, 1.9 mmol) in dry benzene (100 mL) were added tri-*n*-butyltin hydride (1 mL, 3.1 mmol) and AIBN (0.310 g, 1.8 mmol) under nitrogen atmosphere and refluxed for 12 h. After 12 h, the reaction mixture was washed with 1% ammonia solution (3×30 mL) and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography. Elution with petroleum ether first gave tin impurities. Continued elution with petroleum ether–ethyl acetate (85:15) furnished the bicyclic compound **20** (0.302 g, 60%) as a colorless liquid. IR ν_{max} (neat): 1732 and 1722 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.7 (s, 3H, –COOCH_3), 2.82–2.5 (br m, 6H), 2.3 (m, 1H), 2.2–2.0 (s merged with m, total 4H, methyl proton of COCH$_3$+1H), 1.4–1.2 (s merged with m, total 5H), and 1.0 (s, 3H, methyl H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 222.6 (CO), 205.9 (CO), 177.7 (*C*OOCH$_3$), 53.6, 52.2, 51.9, 49.2, 48.7, 45.7, 43.9, 39.6, 35.9, 30.5, 25.2, and 20.9. HRMS (EI) (*m*/*z*): Found 289.1401 (M^++Na); Calcd for $C_{15}H_{22}O_4$: 289.1410 (M^++Na).

4.1.10. 1,4-Dimethyl-4-carbomethoxytricyclo[6.3.0.0^{2,6}]-undec-8-ene-10-one (15). To a solution of the compound **20** (0.120 g, 0.45 mmol) in tertiary butanol (1.5 mL) was added potassium tertiary butoxide (0.035 g, 0.31 mmol) at room temperature under nitrogen for 15 min. The reaction mixture was stirred for 15 min at room temperature and quenched with a saturated solution of ammonium chloride and the aqueous layer was extracted with ethyl acetate (3×15 mL). The combined extract was washed with brine (15 mL) and dried over anhydrous sodium sulfate. Removal of solvent followed by column chromatography (petroleum ether–ethyl acetate 86:14) of the residue furnished the compound **15** (0.073 g, 70%). IR ν_{max} (neat): 1727 and 1709 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$+CCl_4) δ: 5.65 (s, 1H, olefinic H), 3.65 (s, 3H, –COOCH_3), 2.83–2.63 (m, 2H), 2.52 (dd, J_1=12 Hz, J_2=6.5 Hz, 1H), 2.44–2.28 (m, 3H), 2.24 (s, 2H), 1.50–1.39 (m, 1H), 1.34 (s, 3H), 1.24 (t, J=11.6 Hz, 1H), and 1.11 (s, 3H, methyl H). ^{13}C NMR (75 MHz, $CDCl_3$+CCl_4) δ: 208.9 (CO), 177.2 (*C*OOCH$_3$), 193.2, 122.6 (two olefinic carbons), 54.7, 52.5, 51.9, 50.7, 49.1, 46.4, 44.5, 37.2, 32.5, 24.6, and 24.5. HRMS (EI) (*m*/*z*): Found 248.1425 (M^+); Calcd for $C_{15}H_{20}O_3$: 248.1412 (M^+).

4.1.11. 2,7-Dimethyl-7-carbomethoxy-tricyclo-[3.3.0.0^{4,6}]octan-3-one (11). A solution of the compound **17** (0.1 g, 0.480 mmol) in dry acetone (100 mL) was irradiated under nitrogen with a mercury vapor lamp (125 W, Applied Photophysics) in a Pyrex immersion well for about 1.15 h. The solvent was removed in vacuo and the residue was chromatographed on silica gel. Elution with petroleum ether–ethyl acetate (96:4) gave some unreacted starting material (0.12 g, 12%). Further elution with petroleum ether–ethyl acetate (94:6) furnished the compound **11** as a colorless liquid (0.061 g, 61%). IR (film) ν_{max}: 1727 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.73 (s, 3H), 3.04–2.96 (m, 1H), 2.86 (q, J=5 Hz, 1H), 2.62–2.41 (cluster of m, 3H), 1.96 (dd, J_1=10 Hz, J_2=5 Hz, 1H), 1.73 (d, J=14 Hz, 1H), 1.23 (s, 3H), 1.01 (d, J=7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 215.7, 177.7, 52.3, 51.7, 51.5, 43.5, 41.8, 40.0, 36.4, 35.3, 23.0, and 10.6. HRMS (ESI) (*m*/*z*): Found 209.1181 (M^++H); Calcd for $C_{12}H_{17}O_3$: 209.1178 (M^++H).

4.1.12. 2,7-Dimethyl-7-carbomethoxybicyclo[3.3.0]-octan-3-one (21). To a solution of the compound **11** (0.750 g, 3.6 mmol) and tributyltin hydride (1.3 mL, 4.46 mmol) in dry benzene (200 mL) was added AIBN (catalytic) and reflux for 14 h under nitrogen atmosphere. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography. Elution with petroleum ether first gave tin impurities. Elution with petroleum ether–ethyl acetate (95:5) furnished the compound **21** (0.480 g, 63.4%) as a colorless liquid. IR (film) ν_{max}: 1734 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.69 (s, 3H), 2.80–2.62 (m, 3H), 2.61–2.42 (m, 1H), 2.37–2.12 (m, 2H), 2.02–1.80 (m, 2H), 1.43–1.24 (m, 1H), 1.35 (s, 3H), 1.08 (d, J=7 Hz, 3H) (signals due to major isomer). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 221.5, 178.3, 52.1, 50.3, 47.9, 45.4, 44.0, 42.8, 37.3, 25.7, 14.3, and 10.3. HRMS (ESI) (*m*/*z*): Found 211.136 (M^++H); Calcd for $C_{12}H_{19}O_3$: 211.1334 (M^++H).

4.1.13. 2-Allyl-2,7-dimethyl-7-carbomethoxy-3-vinyl-bicyclo[3.3.0]octan-3-ol (12). Sodium hydride (0.030 g of 60% w/w suspension in oil, 1.25 mmol) was placed in a two-necked flask and washed with dry petroleum ether. A solution of ketone **21** (0.1 g, 0.476 mmol) in anhydrous DME (2 mL) was added slowly to the reaction mixture at 0 °C. The resulting suspension was stirred at room temperature for 1 h, followed by the addition of allyl bromide (0.5 mL) at 0 °C. The reaction mixture was stirred for 3 h at room temperature after which it was quenched by the addition of saturated aq NH_4Cl. It was extracted with ether (3×10 mL) and combined extracts were washed with brine and dried over anhydrous sodium sulfate. Removal of solvent followed by chromatography (petroleum ether–ethyl acetate 97:3) gave monoallylated compound [(0.075 g, 63%). IR (film) ν_{max}: 1731 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.76–5.60 (complex m, 1H), 5.11–5.00 (m, 2H),

3.69 (s, 3H), 2.84–2.67 (m, 3H), 2.56–2.47 (m, 1H), 2.23 (dd, J_1=13 Hz, J_2=7 Hz, 1H), 2.23–2.07 (m, 2H), 1.97–1.87 (m, 1H), 1.31 (s, 3H), 1.27–1.10 (cluster of m, 2H), and 0.97 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 222.0, 178.2, 133.2, 118.5, 52.8, 52.2, 51.2, 50.4, 45.2, 44.3, 43.4, 40.8, 34.3, 25.6, and 17.2. HRMS (ESI) (*m/z*): Found 251.1640 (M^++H); Calcd for $C_{15}H_{23}O_3$: 251.1647 (M^++H)].

The allylated compound thus obtained was subjected to Grignard reaction as described below.

Cerium trichloride heptahydrate (0.1 g, 0.268 mmol) was heated to 150 °C under high vacuum. The resulting white powder was cooled under nitrogen, suspended in THF (1.5 mL) and stirred at room temperature for 2 h under nitrogen. Vinyl magnesium bromide (0.3 mL of a 1 M solution in THF, 0.3 mmol) was added to the suspension at −78 °C and stirred for 30 min. A solution of alkylated compound obtained as above (0.05 g, 0.2 mmol) in THF was added, after that the reaction mixture was warmed to ambient temperature. After stirring for 1 h, the reaction mixture was refluxed for 2 h. The reaction mixture was quenched with water and extracted with ether (3×10 mL). The combined extracts were washed with brine (5 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to give an yellow oil. Purification by column chromatography (petroleum ether–ethyl acetate 96:4) gave the product **12** (0.035 g, 63%). IR (film) ν_{max}: 3509 and 1721 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.92 (dd, J_1=17 Hz, J_2=11 Hz, 1H), 5.74–5.66 (m, 1H), 5.15 (dd, J_1=17 Hz, J_2=1.5 Hz, 1H), 5.05 (dd, J_1=11 Hz, J_2=1.5 Hz, 1H), 4.96–4.88 (m, 2H), 3.58 (s, 3H), 2.53–2.36 (br m, 3H), 2.10–1.97 (m, 2H), 1.86–1.70 (m, 3H), 1.44 (dd, J_1=13.7 Hz, J_2=3.3 Hz, 1H), 1.34–1.24 (m, 2H), 1.22 (s, 3H), and 0.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.7, 141.6, 135.8, 117.2, 113.1, 87.6, 53.0, 51.8, 50.7, 49.9, 46.1, 44.1, 43.6, 40.7, 39.2, 24.4, and 15.4. HRMS (ESI) (*m/z*): Found 301.1773 (M^++Na); Calcd for $C_{17}H_{26}O_3Na$: 301.1780.

4.1.14. 4-Carbomethoxy-1,4-dimethyl-tricyclo-[6.3.0.0^{2,6}]undec-9-en-8-ol (22). To a degassed solution of diene **12** (0.03 g, 0.107 mmol) in dichloromethane (2 mL) was added second generation Grubbs' catalyst (5 mg, 0.005 mmol) and the reaction mixture was stirred at ambient temperature under nitrogen for 30 min. Removal of solvent followed by chromatography (petroleum ether–ethyl acetate 88:12) of the residue gave the compound **22** (0.019 g, 70%). IR (film) ν_{max}: 3458 and 1724 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.79–5.76 (m, 1H), 5.56–5.54 (m, 1H), 3.65 (s, 3H), 2.52–2.46 (m, 1H), 2.30–2.15 (cluster of m, 6H), 1.60–1.42 (cluster of m, 2H), 1.43 (br s, 1H), 1.34 (s, 3H), 1.25 (dd, J_1=14 Hz, J_2=4 Hz, 1H), and 1.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.0, 136.2, 132.8, 95.2, 56.8, 52.1, 52.0, 50.3, 50.1, 45.5, 43.3, 40.25, 40.23, 26.3, and 19.5. HRMS (ESI) (*m/z*): Found 273.1470 (M^++Na); Calcd for $C_{15}H_{22}O_3Na$: 273.1467.

4.1.15. Oxidation of 22 with PCC: 1,4-dimethyl-4-carbomethoxy-tricyclo[6.3.0.0^{2,6}]undec-8-en-10-one (15). To a stirred solution of compound **22** (0.015 g, 0.06 mmol) in dichloromethane (1 mL) was added PCC (0.05 g, 0.23 mmol) and stirred at ambient conditions till completion of reaction (TLC, 1.5 h). The dichloromethane was removed and the reaction mixture was purified by flash chromatography (petroleum ether–ethyl acetate 87:13) to furnish the compound **15** (0.012 g, 80.6%), which was found to be identical with the compound obtained previously.

4.1.16. 2,7-Dimethyl-2,4,4-triallyl-7-carbomethoxy-bicyclo[3.3.0]octan-3-one (23) and 2,4-diallyl-2,7-dimethyl-7-carbomethoxy-bicyclo[3.3.0]octan-3-one (7). Sodium hydride (0.114 g of 60% w/w suspension in oil, excess) was placed in a two-necked flask and washed with dry petroleum ether and tetrahydrofuran (0.5 mL) was added to it. A solution of ketone **21** (0.1 g, 0.476 mmol) in tetrahydrofuran (2 mL) was added slowly to the reaction mixture and reaction mixture was refluxed for 15 min. The reaction mixture was cooled and allyl bromide (0.5 mL) was added and further refluxed for 1.5 h. The reaction mixture was cooled and quenched by addition of saturated NH_4Cl solution and it was extracted with ether (3×10 mL). The combined extracts were washed with brine and dried over anhydrous sodium sulfate. Removal of the solvent and column chromatography of the residue on silica gel (petroleum ether–ethyl acetate 99:1) first gave the trialkylated compound **23** (0.067 g, 43%). Further elution with (petroleum ether–ethyl acetate 98:2) gave the dialkylated compound **7** (0.04 g, 29%).

Data for compound **23**: IR (film) ν_{max}: 1729 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.87–5.56 (m, 3H), 5.15–4.97 (m, 6H), 3.70 (s, 3H), 2.71–2.61 (m, 1H), 2.57–2.42 (cluster of m, 4H), 2.39–2.29 (cluster of m, 5H), 1.46 (dd, J_1=13.8 Hz, J_2=6 Hz, 1H), 1.34–1.26 (m merged with s, total 4H), and 0.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 224.9, 178.5, 133.8, 133.6, 133.2, 118.6, 118.4, 118.3, 53.9, 52.1, 51.3, 50.1, 48.9, 45.8, 45.0, 40.8, 40.2, 37.9, 36.9, 24.7, and 21.7. HRMS (ESI) (*m/z*): Found 353.2085 (M^++Na); Calcd for $C_{21}H_{30}O_3Na$: 353.2093.

Data for compound **7**: IR (film) ν_{max}: 1726 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.80–5.59 (m, 2H), 5.13–4.98 (m, 4H), 3.69 (s, 3H), 2.76 (ddd, J_1=13.8 Hz, J_2=8 Hz, J_3=1 Hz, 1H), 2.59–2.40 (m, 3H), 2.28–1.96 (m, 5H), 1.42–1.18 (m merged with s, total 5H), and 0.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 223.1, 178.5, 135.8, 133.5, 118.6, 117.1, 55.5, 52.3, 52.1, 51.5, 49.2, 44.2, 42.7, 42.2, 40.9, 35.3, 26.8, and 18.6. HRMS (ESI) (*m/z*): Found 291.1959 (M^++H); Calcd for $C_{18}H_{27}O_3$: 291.1960 (M^++H).

4.1.17. 1,4-Dimethyl-4-carbomethoxy-tricyclo-[5.4.1.0^{2,6}]dodec-9-en-12-one (6). To a degassed solution of diene **7** (0.015 g, 0.051 mmol) in dichloromethane (1.5 mL) was added second generation Grubbs' catalyst (5 mg, 0.005 mmol) and stirred at ambient temperature under nitrogen for 45 min. Removal of solvent followed by chromatography of the residue (petroleum ether–ethyl acetate 97:3) gave the tricyclic compound **6** (0.009 g, 66.6%) as a colorless solid. Mp 101–103 °C. IR (film) ν_{max}: 1724 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.64–5.63 (m, 2H), 3.68 (s, 3H), 2.67–2.60 (m, 1H), 2.43–2.07 (cluster of m, 7H), 1.92–1.83 (m, 1H), 1.26 (s, 3H), and 1.14–1.00 (s merged with m, total 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 224.9, 177.9, 127.5, 127.1, 54.5, 52.2, 50.9, 49.0, 45.9, 41.8, 41.4, 40.9, 31.9, 29.8, 24.2, and 19.3. HRMS (ESI)

(*m*/*z*): Found 263.1651 (M^++H); Calcd for $C_{16}H_{23}O_3$: 263.1647 (M^++H).

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References and notes

1. (a) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668–1698; (b) Jaykumar, S.; Ishar, M. P. S.; Mahajan, M. P. *Tetrahedron* **2002**, *58*, 379–471; (c) Behforuz, M.; Ahmadian, M. *Tetrahedron* **2000**, *56*, 5259–5288.
2. (a) Boger, D. L. *Chemtracts: Org. Chem.* **1996**, *9*, 149–189; (b) Boger, D. L. *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 5, pp 451–512; (c) Weinreb, S. M. *Acc. Chem. Res.* **1985**, *18*, 16–21.
3. (a) Corey, E. J.; Cheng, X.-M. *The Logic of Chemical Synthesis*; Wiley: New York, NY, 1989; (b) Chanon, M.; Barone, R.; Baralotto, C.; Julliard, M.; Hendrickson, J. B. *Synthesis* **1998**, 1559–1583.
4. (a) Ugi, I. *Pure Appl. Chem.* **2001**, *73*, 187–191; (b) Bertozzi, F.; Gundersen, B. V.; Gustafsson, M.; Olsson, R. *Org. Lett.* **2003**, *5*, 1551–1554; (c) Mironov, M. A.; Mokrushin, V. S.; Maltsev, S. S. *Synlett* **2003**, 943–946.
5. (a) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136; (b) Hudlicky, T. *Chem. Rev.* **1996**, *96*, 3–30; (c) Winkler, J. D. *Chem. Rev.* **1996**, *96*, 167–176; (d) Malacria, M. *Chem. Rev.* **1996**, *96*, 289–306; (e) Parson, P. J.; Penkett, C. S.; Shell, A. J. *Chem. Rev.* **1996**, *96*, 195–206; (f) Wang, K. K. *Chem. Rev.* **1996**, *96*, 207–222; (g) Sheehan, S. M.; Lalic, G.; Chen, J. S.; Shair, M. D. *Angew. Chem., Int. Ed.* **2000**, *39*, 2714–2715.
6. (a) Boeck, B. D.; Harrington-Frost, N. M.; Pattenden, G. *Org. Biomol. Chem.* **2005**, *3*, 340–347; (b) Boehm, H. M.; Handa, S.; Pattenden, G.; Lee, R.; Blake, A. J.; Li, W.-S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3522–3538; (c) Harrington-Frost, N. M.; Pattenden, G. *Tetrahedron Lett.* **2000**, *41*, 403–405; (d) Curran, D. P. *Aldrichimica Acta* **2000**, *33*, 104–110.
7. Nicolaou, K. C.; Sugita, K.; Baran, P. S.; Zhong, Y.-L. *J. Am. Chem. Soc.* **2002**, *124*, 2221–2232.
8. (a) Magdziak, D.; Meek, S. J.; Pettus, T. R. R. *Chem. Rev.* **2004**, *104*, 1383–1429 and references therein; (b) Liao, C. C.; Peddinti, R. K. *Acc. Chem. Res.* **2002**, *35*, 856–866; (c) Drutu, I.; Njardarson, J. T.; Wood, J. L. *Org. Lett.* **2002**, *4*, 493–496; (d) Quideau, S.; Lebon, M.; Lamidey, A.-M. *Org. Lett.* **2002**, *4*, 3975–3978; (e) Quideau, S.; Pouysegu, L. *Org. Prep. Proced. Int.* **1999**, *31*, 617–680 and references therein; (f) Bonnarme, V.; Mondon, M.; Gesson, J.-P.; Cousson, A. *Chem. Commun.* **1999**, 1143–1144; (g) Carlini, R.; Higgs, K.; Rodrigo, R.; Taylor, N. *Chem. Commun.* **1998**, 65–66.
9. Singh, V. *Acc. Chem. Res.* **1999**, *32*, 324–333.
10. (a) Wu, Y. T.; Vidovic, D.; Magull, J.; De Meijere, A. *Eur. J. Org. Chem.* **2005**, *8*, 1625–1636; (b) Tripp, J. C.; Schiesser, C. H.; Curran, D. P. *J. Am. Chem. Soc.* **2005**, *127*, 5518–5527; (c) Banwell, M. G.; Edward, A. J.; Harfoot, G. J.; Jolliffe, K. A. *Tetrahedron* **2004**, *60*, 535–547; (d) Davis, C. E.; Duffy, B. C.; Coates, R. M. *J. Org. Chem.* **2003**, *68*, 6935–6943; (e) Dhimane, A.; Aissa, C.; Malacria, M. *Angew. Chem.* **2003**, *42*, 3284–3287; (f) Srikrishna, A.; Dethe, D. H. *Org. Lett.* **2003**, *5*, 2295–2298; (g) Mehta, G.; Murthy, A. S. K. *Tetrahedron Lett.* **2003**, *44*, 5243–5246; (h) Wang, J.-C.; Krische, M. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 5855–5857; (i) Banwell, M. G.; Edward, A. J.; Harfoot, G. J.; Jolliffe, K. A. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2439–2441; (j) Paquette, L. A.; Feng, G. *J. Am. Chem. Soc.* **2002**, *124*, 9199–9203.
11. (a) Harrowven, D. C.; Lucas, M. C.; Howes, P. D. *Tetrahedron* **2001**, *57*, 9157–9162; (b) Harrowven, D. C.; Lucas, M. C.; Howes, P. D. *Tetrahedron Lett.* **2000**, *41*, 8985–8987; (c) Ader, T. A.; Champey, C. A.; Kuznetsova, L. V.; Li, T.; Lim, Y. H.; Rucando, D.; Sieburth, S. M. *Org. Lett.* **2001**, *3*, 2165–2167.
12. (a) Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671–719; (b) Little, R. D. *Chem. Rev.* **1996**, *96*, 93–114; (c) Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry*; Springer: Berlin, 1987.
13. (a) Shim, S. H.; Swenson, D. C.; Gloer, J. B.; Dowd, P. F.; Wicklow, D. T. *Org. Lett.* **2006**, *8*, 1225–1228; (b) Rukachaisirikul, V.; Tansakul, C.; Saithong, S.; Pakawatchai, C.; Isaka, M.; Suvannakad, R. *J. Nat. Prod.* **2005**, *68*, 1674–1676; (c) Winner, M.; Gimenez, A.; Schmidt, H.; Sontag, B.; Steffan, B.; Steglich, W. *Angew. Chem., Int. Ed.* **2004**, *43*, 1883–1886; (d) Hellwig, V.; Dasenbrock, J.; Steglich, W.; Leonhardt, K.; Anke, T. *Eur. J. Org. Chem.* **1998**, 73–79.
14. (a) Mellows, G.; Mantle, P. G.; Feline, T. C.; Williams, D. J. *Phytochemistry* **1973**, *12*, 2717–2720; (b) Comer, F. W.; McCapra, F.; Qureshi, I. H.; Scott, A. I. *Tetrahedron* **1967**, *23*, 4761–4768; (c) Heatly, N. G.; Jennings, M. A.; Florey, H. W. *Br. J. Exp. Pathol.* **1947**, *28*, 35–46.
15. (a) Nishida, M.; Iseki, K.; Shibasaki, M.; Ikegami, S. *Chem. Pharm. Bull.* **1990**, *38*, 3230–3237; (b) Schuda, P. F.; Phillips, J. L.; Morgan, T. M. *J. Org. Chem.* **1986**, *51*, 2742–2751; (c) Greene, A. E.; Luche, M. J.; Serra, A. A. *J. Org. Chem.* **1985**, *50*, 3957–3962; (d) Trost, B. M.; Shuey, C. D.; DiNinno, F., Jr.; McElvain, S. S. *J. Am. Chem. Soc.* **1979**, *101*, 1284–1285; (e) Sakan, F.; Hashimoto, A.; Ichihara, A.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1971**, 3703–3706; (f) Hashimoto, H.; Tsuzuki, K.; Sakan, F.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1974**, 3745–3748. For other references on synthesis of hirsutic acid, see Ref. 12.
16. Austin, K. A. B.; Banwell, M. G.; Harfoot, G. J.; Willis, A. C. *Tetrahedron Lett.* **2006**, *47*, 7381–7384.
17. Part of the work has been reported, preliminary communication, Singh, V.; Tosh, D. K.; Mobin, S. M. *Tetrahedron Lett.* **2004**, *45*, 1729–1732.
18. (a) Mehta, G.; Singh, V. *Chem. Rev.* **1999**, *99*, 881–930; (b) Petasis, N. A.; Patane, M. A. *Tetrahedron* **1992**, *48*, 5757–5821.
19. (a) Adler, E.; Holmberg, K. *Acta Chem. Scand.* **1976**, *28b*, 465–472; (b) Singh, V.; Bedekar, A. V. *Synth. Commun.* **1989**, *19*, 107–117.
20. (a) Stork, G.; Baine, N. H. *Tetrahedron Lett.* **1985**, *26*, 5927–5930; (b) Paquette, L. A.; Ra, C. S.; Silvestri, T. W. *Tetrahedron* **1989**, *45*, 3099–3106; (c) Singh, V.; Prathap, S. *Tetrahedron* **1996**, *52*, 14287–14296.
21. (a) Zimmerman, H. E.; Armesto, D. *Chem. Rev.* **1996**, *96*, 3065–3112; (b) Demuth, M. *Organic Photochemistry*; Padwa, A., Ed.; Marcel-Dekker: New York, NY, 1991; Vol. 11, pp 37–97 and references therein; (c) Schuster, D. I. *Rearrangement in*

Ground and Excited States; de Mayo, P., Ed.; Academic: New York, NY, 1980; Vol. 3 and references therein.
22. (a) Horspool, W. M. *Organic Photochemistry*; Gilbert, A., (senior reporter), Ed.; The Royal Society of Chemistry: Cambridge, 2001; Vol. 32, pp 74–116; (b) Singh, V. *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W., Lenci, F., Eds.; CRC: 2004; pp 78-1–78-34.
23. Tsuji, J.; Shimizu, I.; Yamamoto, K. *Tetrahedron Lett.* **1976**, 2975–2976.
24. Enholm, E. J.; Jia, Z. J. *J. Org. Chem.* **1997**, *62*, 174–181.
25. (a) *Hand Book of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Weinheim, Germany, 2003; (b) *Alkene Metathesis in Organic Synthesis*; Furstner, A., Ed.; Springer: Berlin, Germany, 1998.
26. (a) Katz, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3010–3019; (b) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592–4633; (c) Schmidt, B. *Angew. Chem., Int. Ed.* **2003**, *42*, 4996–4999.