

SESQUITERPENE LACTONES.
 A TOTAL SYNTHESIS OF (±) QUADRONE

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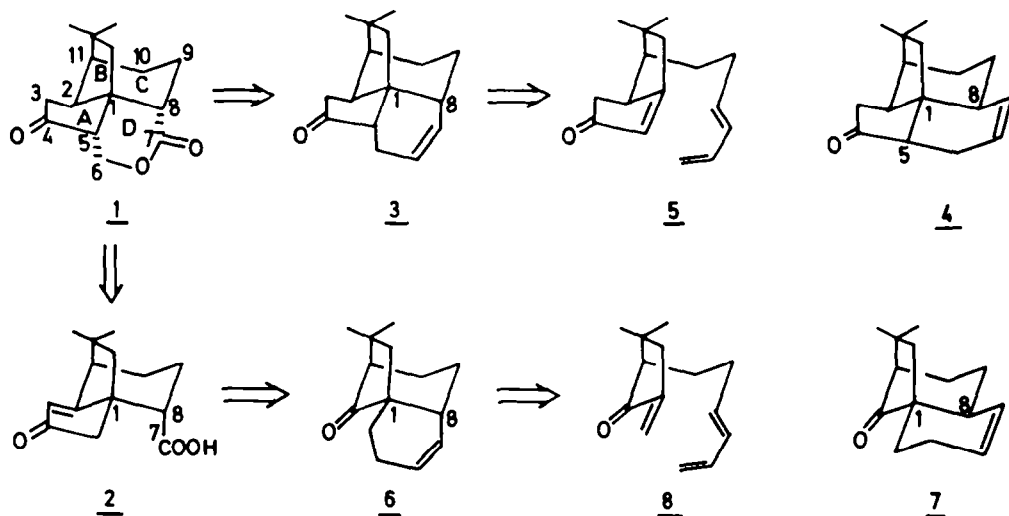
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ABSTRACT - Two routes towards (±) quadrone (1), via an intramolecular Diels-Alder reaction have been studied. The cycloaddition of 5 failed, probably because of prohibitive strain. In the alternative approach, the key step afforded a mixture of the endo- and exo-adducts 6 and 7. Both isomers were transformed into Danishefsky's intermediate 2, which has previously been converted to the title compound 1.

INTRODUCTION

Quadrone (1), a sesquiterpene lactone, has been described in 1978, as a fungal metabolite from *Aspergillus terreus* and was found to display antitumor activity¹. The biological properties and especially its novel tetracyclic skeleton have attracted much attention from synthetic organic chemists²⁻⁸. Since the first synthesis disclosed by Danishefsky² in 1981 several other groups have terminated successfully their synthetic efforts³⁻⁷. Especially the recent report of Schlessinger⁷ prompts us to describe our own results in this area.

Our strategy⁹ for assembling the basic skeleton of quadrone (1) centers around the formation of the 1,8 bond via an intramolecular Diels-Alder reaction*, hereby creating simultaneously ring C and elements of ring D (and ring A). Retrosynthetic analysis suggests that this key step could determine the viability of two approaches (scheme 1). A short and attractive route would involve the synthesis of the tetracyclic intermediate 3 (from 5) followed by conversion of the cyclohexene ring into the δ -lactone.



Scheme 1

* For reasons of consistency the quadrone numbering is used for all intermediates.

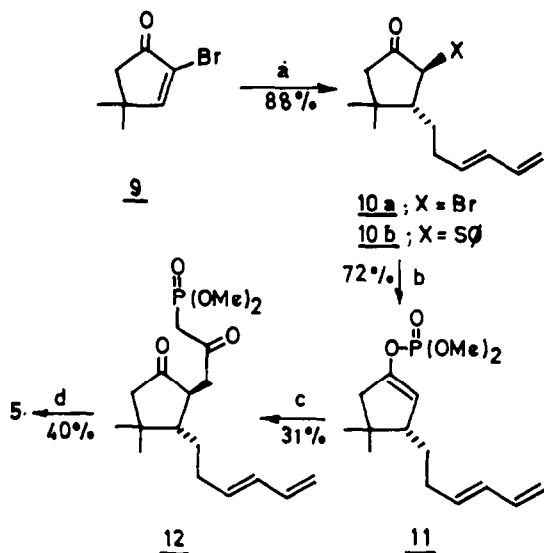
The other route, which is conceptually similar to the one recently disclosed by Schlessinger⁷, has the tricyclic ketone 6 (from 8) as a sub-target. The carbon atoms of the cyclohexene ring in 6 can subsequently be used to construct the cyclopentenone ring and the carboxylic function in 2, an intermediate already transformed by Danishefsky² into quadrone (1).

It is evident that the stereochemical outcome of the crucial Diels-Alder reactions has important consequences on the general planning, especially with regard to the configurational control at C-8. The endo-adducts 3 and 6 are ideally suited for further transformation. A priori one can however, with some confidence consider inversion of configuration at C-8 (and C-5) at a later stage in case the preferred formation of the respective exo-adducts 4 and 7 is observed.

Although the intramolecular Diels-Alder methodology is conceptually simple and could provide fast entry into the projected tetra- and tricyclic systems, we experienced severe setbacks and gained insight into intrinsic properties of some intermediates. These aspects will be discussed in the present paper.

RESULTS

Attempted synthesis of the tetracyclic ketones 3 and 4



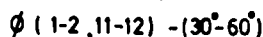
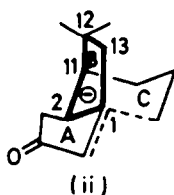
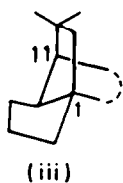
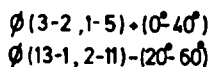
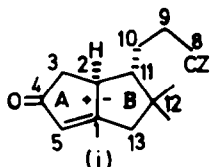
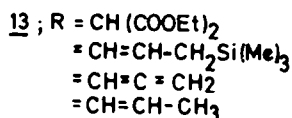
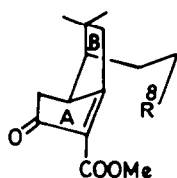
(a) C₆H₅MgBr, CuI, -40°C; (b) (MeO)₃P, Δ;
 (c) MeLi, dimethyl-2-ethoxy-3-iodo-1-propenylphosphonate; H⁺; (d) dimethylsodium, THF.

Scheme 2

The synthesis of the precursor 5 started from the readily available bromo-enone 9¹⁰ which upon CuI mediated 1,4-addition of 3,5-hexadienylmagnesium bromide¹¹ gave the cyclopentanone 10a in 88 % yield. The presence of the α-bromo atom in 9 is a determining factor; we have observed a very low yield for the analogous reaction on the less electrophilic 4,4-dimethylcyclopentenone. We originally intended to prepare 12 via 10b (from 10a and sodium thiophenoxide in DMF; 72 %); however subsequent alkylation of 10b led only to oxygen alkylated products. After considerable experimentation the route to 5 shown in scheme 2 was adopted. Although this three-step sequence had, at this exploratory level, a low efficiency it eventually enabled us to study the potentiality of the crucial Diels-Alder reaction. Perkow reaction of 10a led to the enol phosphate 11. Lithium enolate formation¹² and quenching with dimethyl-3-iodo-2-ethoxy-1-propenylphosphonate (obtained from the corresponding bromide¹³ with sodium iodide in acetone) afforded 12. Several bases were examined for the intramolecular Horner reaction¹³; however the best conditions found (scheme 2) generated precursor 5 in only low yield¹⁴. With 5 in hand we could now focus our attention on the critical cycloaddition step; however, 5 showed, under thermal and Lewis acid catalyzed conditions, no tendency to form either 3 or 4 (scheme 1).

During the course of this investigation Danishefsky¹⁵ reported the unsuccessful efforts to create the 1,8 bond upon an intramolecular Michael addition, photocycloaddition or "ene" reaction using substrates 13 with the appropriate functionalized side chain. As a consequence it seems highly probable that all routes, intending to annelate ring C, involving a rehybridization (sp² - sp³) while forming the quaternary bridgehead center, are doomed to fail. It is clear that during this internal bond formation considerable torsional strain is build up in the bicyclo[3.3.0]octene systems 5 and 13. Upon inspection of molecular models it appears that reaction is only possible when ring B adopts a geometry in which the side chain at C-11 takes an axial orientation thus allowing approach of the reacting centers 1 and 8. Although 1,8-bond length distance is difficult to realize as long C-1 is sp², one should keep in mind, that upon reaching the transition state, both the rehybridization and the C-1 - C-8 distance are related and mutually influencing each

other. Consequently, at the outset a prediction of the viability of such a process was difficult to evaluate.

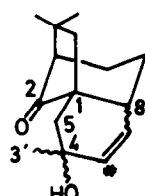
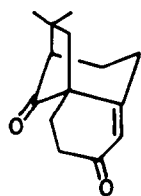
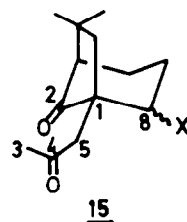
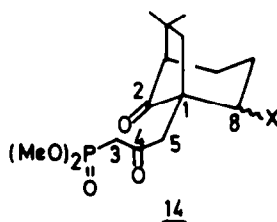
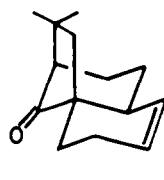
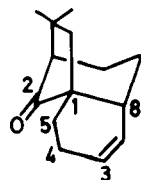


However De Clercq's torsion constraint evaluation method¹⁶ allows a more accurate description, which shows the high unlikelihood of this process. The structure of the transition state as depicted in ii implies that the five-membered ring B originally only fused with ring A (i), now becomes part of a bicyclo[3.2.1]octane system. Torsion constraint evaluation at the two adjacent bonds 1,2 and 2,11 in this five-membered ring, at the moment that C-1 is still sp²-hybridized and that C-8 has neared C-1 at bonding distance reveals the following: (i) bond 1,2 is forced by its fusion with the cyclopentene ring to adopt an endocyclic torsion angle with - sign with a magnitude between 20° and 60°; (ii) bond 2,11 also has to adopt an endocyclic torsion angle (in the same ring) of - sign with a magnitude between 30° and 60°. Overall, the ring has to accommodate a geometry conformation whereby two adjacent bonds have the same sign with a sum of 50° or more. The latter situation cannot be reached geometrically without introducing too much strain in either one of both 5-membered rings^{16b}.

It is of interest to note that in several successful syntheses^{2,3,4} of quadrone, ring C has been formed on the convex face of suitable 1,11-disubstituted bicyclo[3.3.0]octanes (iii). Because of the absence of C-1 sp² hybridization, a conformation is now available to ring B where both reacting centers can come sufficiently close for bond formation.

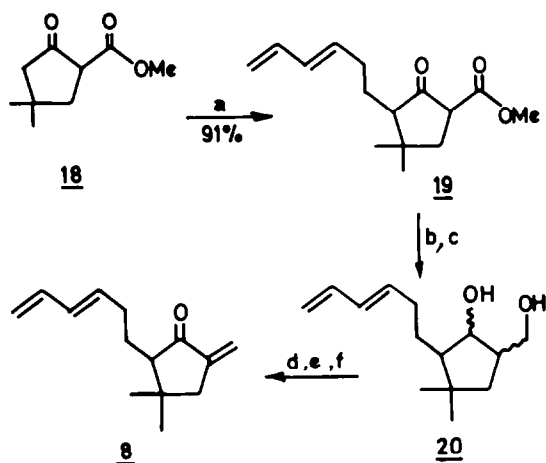
Synthetic studies via intermediates 6 and 7.

With respect to the observation that the presence of the cyclopentenone ring A in 5 is responsible for the failure of the Diels-Alder reaction, we hoped to realize ring C formation via precursor 8. Elements of the cyclohexene ring in adducts 6 and 7 can then be used to construct ring A, present in the target molecule 1, via an intramolecular Horner reaction or aldol condensation.



The β -keto phosphonate entity in 14 can be generated while retaining the carbon atoms 3, 4 and 5. Alternatively, it seems more appropriate to form the 2'-oxopropyl side chain in 15 upon introduction of an additional methyl group at C-4 (e.g. via 16) followed by oxidative elimination of the superfluous carbon atom ($\times$).

The route (scheme 3) leading to 8 starts from β -keto ester 18, readily available in two steps from dimedone¹⁷. Alkylation of the dianion¹⁸ with 3,5-hexadienyl iodide yielded 19 as a diastereoisomeric mixture. Several methods for conversion of 19 into 8 can be devised. The five-step sequence shown in scheme 3 was selected because it was reliable and fast; the overall yield was 36 %. With 8 in hand, the alternative intramolecular Diels-Alder reaction could now be studied.



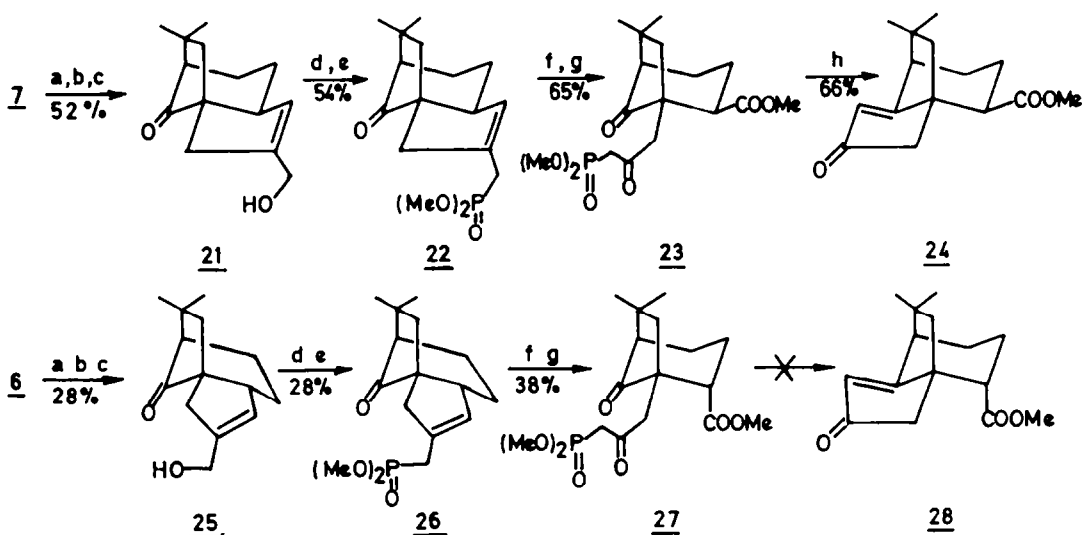
- (a) LDA, THF, C_6H_9I (b) $NaBH_4$, MeOH;
 (c) $LiAlH_4$, Et_2O ; (d) $TsCl$, Et_3N , CH_2Cl_2 ;
 (e) Jones ox.; (f) DBU, benzene.

Scheme 3

Reflux of **8** in toluene ($110^\circ C$) afforded **6** and **7** in a 1:3 ratio (60 % conversion); HPLC monitored reaction in chlorobenzene ($135^\circ C$) indicated 93 % conversion and a shift of this ratio (1:3 after 30 min) to 1:9 (2 h). On the other hand, tin tetrachloride catalyzed reaction in CH_2Cl_2 at $0^\circ C$ (1 h) led in 90 % conversion to a 1:2 ratio of **6** and **7**, after column chromatographic separation. Essentially an identical ratio was observed for reaction in water-acetonitrile (2:1) solution²⁰ at $90^\circ C$.

Independently Schlessinger⁷ observed the formation of only one isomer upon heating **8**, at $120^\circ C$, in toluene-acetonitrile solution; on ground of molecular model predictions the product was assumed to be the exo-adduct **7**. In view of our observations and structural proof (*vide infra*) this assumption was correct.

Structural assignment of the adducts could not be obtained from spectroscopic data. Considerations about the transition state conformations²¹ and comparison of the results observed for the different reaction conditions allowed tentative identification of the endo- (**6**) and exo-adduct (**7**) as respectively the minor and major product. However we felt that full structural proof was needed not only for fundamental reasons but also for the general planning. If indeed the minor product has structure **6**, the success and efficiency of our approach will become critically dependent upon our ability to include the trans decalin **7** in the synthetic scheme. In principle, one can envisage inversion at C-8, prior or subsequent to cyclohexene ring cleavage in **7**. A solution to the problem became available during work directed towards molecules of type **16**, when it was observed that CrO_3 -3,5-dimethylpyrazole²² mediated oxidation of **6** and **7** led exclusively, via the "ene" mechanism, to enone **17** (*vide infra*). It is obvious that, with **17** as an intermediate, identification of the Diels-Alder adducts is no longer possible.



- (a) O_3 , CH_2Cl_2 , $-60^\circ C$, HOAc, Zn; (b) piperidine, HOAc, benzene; (c) $NaBH_4$, MeOH; (d) PBr_3 , Et_2O ;
 (e) $(MeO)_3P$, CH_3CN , Δ ; (f) RuO_2 , $NaIO_4$, CH_3COCH_3 ; (g) CH_2N_2 ; (h) dimethylsodium, THF, DMSO, $70^\circ C$.

Scheme 4

Accordingly we focussed first on our originally projected plan which aimed at the construction of the respective key intermediates 24 and 28 (scheme 4). In addition to structural assignment, this scheme could provide information on the viability of a route involving inversion of the 8-position when adjacent to a carbomethoxy function (e.g. : 24 → 28).

Starting from 7, the three-step sequence, involving ozonolysis, aldolcondensation²³ of the unstable dialdehyde and reduction to the allylic alcohol 21 gave an overall yield of 52 %. Subsequently, the β -keto phosphonate 23 was obtained upon Michaëlis-Arbusov reaction of the corresponding allylic bromide of 21, double bond cleavage and esterification. At this moment a first indication for structures 6 and 7 became available upon comparison of the NMR data for H-8 in 23 (δ = 2.67, dd, J = 11.5 and 5 Hz) and in 27 (δ = 3.34, d, J = 6.4 Hz) when assuming a chair conformation for the cyclohexane ring.

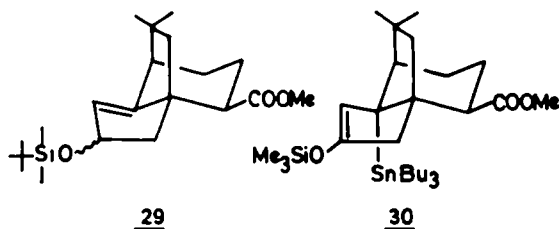
We were gratified to observe that 23 upon intramolecular Horner reaction produced the tricyclic enone 24 in 66 % yield; again as for 5, the best conditions consisted of dimethylsodium in THF. Definite proof for the equatorial orientation of the carbomethoxy group in 24 and hence of the anticipated trans decalin geometry of 7 was obtained upon comparison with 28, prepared from 2, kindly provided by Prof. Danishefsky. Epimer 24 has R_f = 0.34 (benzene-EtOAc, 8:2) and displays the NMR signal for 8-H at δ = 2.42 (dd, J = 11.2 and 5.6 Hz); the respective data for 28 are : R_f = 0.30 and δ = 2.92 (d, J = 6 Hz).

With structures 6 and 7 proven, we explored the formation of key intermediate 2 (via 28) starting from 6 (as for 7 → 24) and from the epimer 24 (via inversion at C-8). As shown in scheme 4, the yields for all steps towards 27 were significantly lower than those observed for 24. This could be related to the fact that molecules 25 and 26 with cis-hydrindane geometry are highly strained. Dreiding stereomodels²⁴ show that the combined effects of the ethano bridge and the cyclopentene ring result in a boat conformation for the cyclohexane ring, which can practically not be forced into a chair. Presumably the double bond is responsible for the excessive strain; when the fused five-membered ring is a saturated, the cyclohexane ring adopts a chair

conformation and the molecule becomes more flexible. As a consequence, formation of 25 and the subsequent substitution reactions, which could suffer from competing allylic rearrangements (SN'), will tend to give low yields. However it should be noted that also the ozonolysis of 6 and double bond cleavage in 26 led to rather complex mixtures, thus suggesting interaction of the 2-carbonyl function with the reacting site. In this context it is worthwhile mentioning that on several occasions, reaction between C-2 and C-8 axially oriented functional groups have been observed. On the other hand, the steric congested 2-carbonyl function was quite inert towards intermolecular reaction, which allowed good flexibility for manipulating the different intermediates.

Disappointingly all attempts to convert 27 into 28 met with complete failure and afforded complex reaction mixtures. With respect to the successful conversion of 23 into 24, clearly this failure is due to interference of the axial carbomethoxy group. Efforts to carry out the cyclization on the carboxylic acid stage were also unsuccessful, as this was also the case for the acid from 24; these failures could be attributed to the unsolubility of the salts.

We now faced transformation of 24 into the epimer 28, which we hoped to realize upon kinetic protonation of the C-8 carbanion or under equilibration conditions. Numerous attempts using several bases and examining different substrates were completely unsuccessful²⁵; next to 24 the process was studied on 29 and 30²⁶ having a protected enone function.



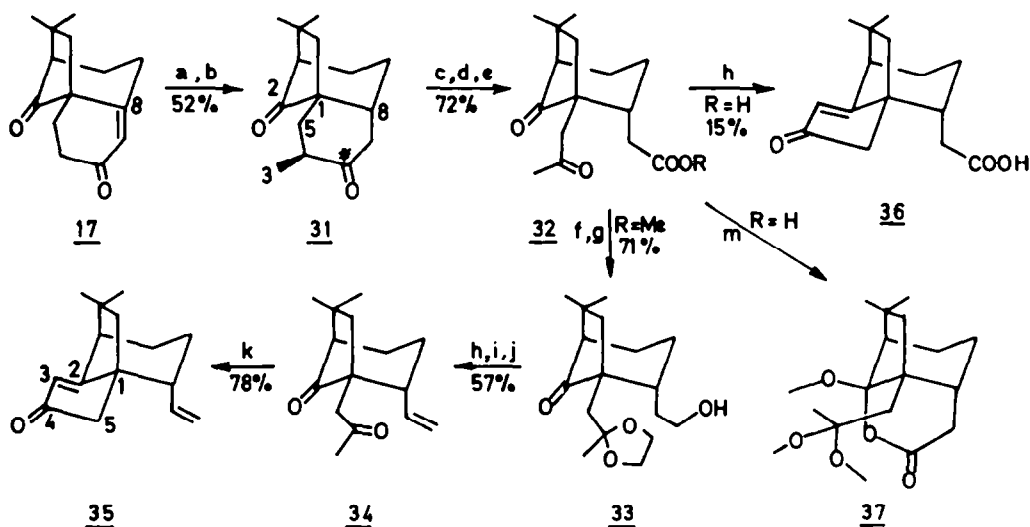
In our opinion 29 and 30 represent two opposite cases. The sp^2 hybridization of C-2, in 29, reducing the non bonding interactions for an axial substituent at C-8 could favour inversion under equilibration conditions. On the other hand one could expect that the bulky substituent in 30 would block the bottom face for kinetic protonation of a C-8 carbanion.

Having been thwarted in our attempts to realize the ringclosure of β -keto phosphonate 27

or to change the orientation of the equatorial carbomethoxy group, we turned our attention to the alternative approach based on an aldol condensation. This reaction, being less subject to steric inhibition than the Horner reaction, would tolerate better the presence of a C-8 axial substituent. Although the required 2'-oxopropyl substituent (see 15) can, in principle, be generated from the allylic alcohol 25, the very low efficiency for the formation of 25 made this approach unattractive. It was indeed much more promising to explore the synthetic potentiality of enone 17. Oxidation of 6 and 7 with CrO_3 -3,5-dimethylpyrazole afforded 17 in comparable yields (70-75 %); this reaction made separation of the Diels-Alder adducts unnecessary. Recently Schlessinger described the similar result starting from 7. The projected introduction of a C-4 methyl substituent can now be realized in combination with the generation of the cis decalin geometry (scheme 5). Methylation of 17 led in 86 % yield to a 9:1 epimeric mixture. Although this is of no consequence for further transformation, the next step was carried out on the pure major isomer (presumably with the equatorial oriented methyl group) which enabled evaluation of the stereochemical outcome. Catalytic hydrogenation afforded 31 in 60 % yield along with 13 % of the transfused isomer.

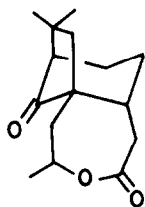
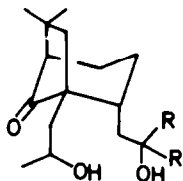
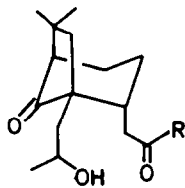
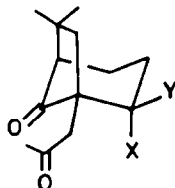
Inspection of a molecular model indicates that hydrogenation should occur preferentially from the top face of the molecule; the assumed structure 31 however became evident during its successful transformation into 2.

The stage was now set for the elaboration of the 2'-oxopropyl side chain. In order to avoid, during the cyclopentenone ring formation, reactions between the carboxylic substituent and the C-2 reacting site, we decided to use a substrate with a latent carboxylic function at C-8. However, the realization of the seemingly trivial transformation into such a precursor proved to be more difficult than expected. Several methods are conceivable, *inter alia* depending on the nature of the latent functionality (temporarily retaining - or not - the superfluous carbon ($\times$) atom in 31). Before we finally adopted the sequence outlined in scheme 5, several alternatives were explored; one looked at the outset quite promising when it was observed that lactone 38 was produced quantitatively upon mCPBA mediated Bayer-Villiger oxidation of 31. The subsequent two-step formation of a C-8 vinylic substituent via the tertiary alcohol 39 failed because the incipient organometallic reaction on 38 invariably led to unseparable mixtures of 39 and 40 ($\text{R} = \text{Me}$ or Ph), even with 10-fold excess of reagent. Methyl- and phenyllithium of magnesium-bromides were investigated. These failures may



(a) LDA, MeI; (b) Pd/C, H_2 , EtOAc; (c) TMSI, HMDS; (d) O_3 , CH_2Cl_2 , -60°C , Zn, HOAc; (e) CH_2N_2 ; (f) glycol, H^+ ; (g) LiBET_3H , THF; (h) $\text{o-NO}_2\text{C}_6\text{H}_4\text{SeCN}$, Bu_3P , THF, pyridine; (i) H_2O_2 (30 %), THF; (j) H^+ , THF; (k) NaH, *t*-AmOH, benzene, Δ ; (l) *t*-BuOK, *t*-BuOH; (m) MeOH, $\text{CH}(\text{OMe})_3$, H^+

Scheme 5

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be explained by the stability of the oxy anion of the cyclic hemi acetal. Also a remaining possibility consisting of the Bayer-Villiger oxidation on 40 (R = Me) in order to expulse the superfluous carbon atom was unsuccessful.

We then focussed on the sequence (scheme 5) starting with the ozonolysis of the trimethylsilyl ether²⁷ of 31 which produced the methyl ester 32 (R = Me). Selective mono-ketal formation and reduction of the ester function led to the primary alcohol 33 which was eliminated using Grieco's procedure²⁸, affording upon deprotection the desired precursor 34.

Alternatively, a route starting with the aldol condensation (10 eq. KOt.Bu in t.BuOH, reflux) of 32 (R = H) was explored; we were however discouraged by the low yield observed for 36 (15 %) again indicating the interference of a carboxylic acid, axially oriented at C-8. Also treatment of 32 (R = H) with trimethyl orthoformate showed the tendency for internal reaction at C-2; incidentally formation of 37 proved the cis decalin structure 31.

Aldol condensation⁶ of 34 afforded 35 in an approximately identical yield as observed on substrates of type 41 by Yoshii⁶ (41, Y = H, X = CH₂OCH₃) and Kende⁵ (41, X, Y = CH₂). In this context and with respect to the above frequently observed interference of a carboxylic function, the recent reported⁷ 45 % yield for the intramolecular aldolcondensation of 41 (Y = H, X = COOH) to 2 can be noted.

Final transformation into Danishefsky's acid 2, involved RuO₄ oxidation²⁹ (in CCl₄-acetonitrile-H₂O solution) of the double bond in 35 (86 % yield); 2 had a m.p. 143-145°C (lit.²,

142-146°C) and was found identical with an authentic sample, kindly provided by Prof. Danishefsky. Since 2 has been converted² into (±)-quadrone (1) our synthesis was therefore formally terminated.

EXPERIMENTAL SECTION

The m.p.s. are uncorrected. IR spectra were recorded on a Perkin-Elmer 337 spectrometer, mass spectra on a AEI MS-50 spectrometer. The ¹H NMR spectra were recorded at 90 MHz (Varian EM-390) or at 360 MHz (WH-Brucker) in CDCl₃ unless otherwise stated with TMS as internal standard. Chemical shifts (δ) are expressed in ppm. Rf values are quoted for Merck silicagel 60 GF₂₅₄ TLC plates of thickness 0.25 mm.

Reaction products were isolated by the addition of water and extraction with diethylether. The combined extracts were washed with brine and dried over MgSO₄. The solvent was removed from the filtered solution on a rotary evaporator. Column chromatographic separations were performed on silicagel.

2-Bromo-3-(3,5-hexadienyl)-4,4-dimethyl-cyclopentanone (10a).

To a soln of 9¹⁰ (10 g; 0.053 mol), CuI (4.04 g; 0.021 mol) and Me₂S (21.15 g; 0.341 mol) in THF (300 mL) at -40°C was added 3,5-hexadienyl magnesiumbromide (0.0795 mol) in THF (8 mL). The reaction was quenched with a sat NH₄Cl/NH₃ aq mixture. Extraction with Et₂O, work up and column chromatography (isooctane/EtOAc, 5:95) afforded 8 (12.5 g, 88 %). Rf (isooctane/EtOAc, 9:1) 0.43; IR (film) 1750, 1650, 1620 cm⁻¹; NMR 6.7-4.6 (m, 5), 4.03 (d, J = 10.5 Hz, 1), 2.32 (s, 2), 2.7-1 (m, 5), 1.22 (s, 3), 0.92 (s, 3); MS m/z 270-272 (M⁺, 1.5) 191-189 (100).

The phosphate 11.

A soln of 10a (5.43 g; 20.04 mmol) in (MeO)₂P (110 mL) was refluxed for 12 hrs. After cooling the (MeO)₂P was evaporated. The residue was extracted with Et₂O, work up and column chromatography (isooctane/EtOAc, 7:3) afforded 9 (4.32 g, 71.9 %). Rf (isooctane/EtOAc, 1:1) 0.29; IR (film) 1654, 1602 cm⁻¹; NMR 6.5-4.9 (m, 5), 5.23 (m, 1), 3.8 (d, J = 11.4 Hz, 6), 2.3 (s, 2), 2.3-1.2 (m, 5), 1.10 (s, 3), 0.97 (s, 3); MS m/z 300 (M⁺, 0.5), 245 (43), 127 (100).

The phosphonate 12.

To a soln of 11 (3.6 g; 12 mmol) in THF (25 mL) at 0°C was added MeLi (1.4 N soln; 0.0265 mol; 2.2 eq). After stirring for an additional 15 min HMPA (10 mL) was added. To this soln was added dimethyl-2-ethoxy-3-iodo-1-propenylphosphonate (7.68 g; 0.024 mol) in THF (25 mL). Stirring was continued for 7 min and the reaction was quenched with sat NH₄Cl aq. The excess of alkylating reagent was then removed on treatment with NEt₃. After evaporation, the residue was treated with HCl aq (1.75 mL; 12 N) in acetone (45 mL). Work-up and column chromatography (hexane/EtOAc, 1:3) afforded 12 (1.32 g, 31 %). Rf (Et₂O/benzene/acetone, 5:4:1) = 0.15; IR (film) 1735, 1712, 1643 cm⁻¹; NMR 6.5-4.9 (m, 5), 3.77 (d, J = 11.1 Hz, 6), 3.09 (d, J = 22.2 Hz, 2), 2.97 (d, J = 4.8 Hz, 2), 2.6-1.5 (m, 8); 1.18 (s, 3), 0.93 (s, 3); MS m/z 356 (M⁺, 11.5) 275 (43), 151 (100).

[5S⁺,6S⁺]-6-(3,5-hexadienyl)-7,7-dimethyl-bicyclo[3.3.0]oct-1-en-3-one (5).

To a soln of 12 (89 mg; 0.25 mmol) in THF (0.5 mL) at 0°C was added dimethylsodium in DMSO (0.76 M soln; 0.275 mmol; 36 μL). Stirring is continued for 7 hrs at ambient temp. The reaction was quenched with H₂O (1 mL). Extraction with Et₂O (3 x 10 mL), work up and column chromatography (isooctane/EtOAc, 8:2) afforded 5 (23 mg, 40 %). Rf (EtOAc) 0.61; UV = 228 nm; IR (film) 1700,

1620 cm^{-1} ; NMR 5.83 (d, $J = 1.8$ Hz, 1), 6.4–4.9 (m, 5), 2.52 (s, 2), 3.0–1.0 (m, 8), 1.09 (s, 3), 1.02 (s, 3); MS m/z 230 (M^+ , 16.6), 215 (15), 81 (25), 43 (100).

2-methoxycarbonyl-4,4-dimethyl-5-(3,5-hexadienyl)-cyclopentanone (19).

To a soln of LDA (0.148 mol) in THF (120 mL) at 0°C was added 2-methoxycarbonyl-4,4-dimethyl-cyclopentanone 17 (12 g; 70.6 mmol) in THF (50 mL). After adding HMPA (20 mL) stirring was continued for 2 hrs. Then a soln of 3,5-hexadienyl iodide (14.7 g; 0.0706 mol) in THF (20 mL) was added. Quenching with sat NH_4Cl aq and work-up afforded pure 19 (16.06 g, 91 %); Rf (hexane/ Et_2O , 7:3) 0.34; IR (film) 1755, 1730, 1650, 1605 cm^{-1} ; NMR 6.7–4.9 (m, 5), 3.75 (s, 3), 3.25 (t, $J = 10.5$ Hz, 1), 2.7–1.3 (m, 7), 0.8 (s, 3), 1.2 (s, 3), MS m/z 250 (M^+ , 3.6), 170 (44), 155 (100).

2-methylene-4,4-dimethyl-5-(3,5-hexadienyl)-cyclopentanone (8).

To a soln of 19 (16 g; 64 mmol) in MeOH (50 mL) was added NaBH_4 (2.8 g; 72 mmol). After work up the crude mixture is further reduced with LiAlH_4 (23 g; 60 mmol) to the diol 20.

To a soln of 20 in CH_2Cl_2 (100 mL) was added p.TsCl (17 g, 58 mmol), Et_3N (11.3 g; 113 mmol) and DMAP (0.5 g). After stirring for 48 hrs and work up, the crude product mixture was treated with Jones reagent (2 N, 18.9 mL) in acetone (150 mL).

To a soln of the crude ketosylates in benzene (140 mL) was added DBU (8.5 mL; 56 mmol). Stirring was then continued for 2 hrs at 0°C . This afforded after work-up and column chromatography (Et_2O /hexane, 2:8) 8 (4.6 g, 36 %) and 7 (450 mg, 3.5 %). Rf (hexane/ Et_2O , 8:2) = 0.55; IR 1720, 1675, 1630 cm^{-1} ; NMR 6.7–4.9 (m, 5), 6 (m, 2), 2.6–1.3 (m, 7), 1.20 (s, 3), 0.83 (s, 3); MS m/z 204 (M^+ , 27), 189 (27), 109 (100).

(1R⁺,6R⁺,9R⁺)-10,10-dimethyl-12-oxo-tricyclo[7.2.1.0^{1,6}]dodec-4-ene (6) and (1R⁺,6S⁺,9R⁺)-10,10-dimethyl-12-oxo-tricyclo[7.2.1.0^{1,6}]dodec-4-ene (7).

To a soln of 8 (5 g; 24.5 mmol) in CH_2Cl_2 (100 mL) was added SnCl_4 (1.26 g; 4.9 mmol). Stirring was then continued for 1 hr at 0°C . Work-up and column chromatography afforded 6 (1.52 g; 30.5 %). Rf (benzene/hexane, 8:2) 0.22; IR 1735, 1645 cm^{-1} ; NMR 5.72 (m, 1), 5.37 (m, 1), 2.83 (m, 1), 2.66 (m, 1), 2.19 (m, 1), 2.09–1.9 (m, 3), 1.86–1.72 (m, 2), 1.55–1.38 (m, 2), 1.82 (d, $J = 12.5$ Hz, 1), 1.42 (d, $J = 12.5$ Hz, 1), 1.21 (s, 3), 0.93 (s, 3); MS m/z 204 (M^+ , 29), 189 (8), 186 (43), 133 (100); and 7 (3.1 g, 62 %). Rf (benzene/hexane, 8:2) 0.16; IR 1735, 1640 cm^{-1} ; NMR 5.6 (m, s), 5.28 (m, 1), 2.4 (m, 1), 2.2–1.8 (m, 5), 1.87 (t, $J = 3.2$ Hz, 1), 1.83 (d, $J = 13$ Hz, 1), 1.7–1.3 (m, 3), 1.28 (d, $J = 13$ Hz, 1), 1.15 (s, 3), 0.92 (s, 3); MS m/z 204 (M^+ , 48), 189 (6.5), 133 (100).

(1S⁺,5S⁺,8R⁺)-3-hydroxymethyl-9,9-dimethyl-11-oxo-tricyclo[6.2.1.0^{1,5}]undec-3-ene (21) and (1S⁺,5R⁺,8R⁺)-3-hydroxymethyl-9,9-dimethyl-11-oxo-tricyclo[6.2.1.0^{1,5}]undec-3-ene (25).

To a soln of 7 (1.14 g; 5.6 mmol) in CH_2Cl_2 (40 mL) was added O_3 at -60°C . The mixture was then warmed to -10°C and HOAc (25 mL) and Zn (1.35 g; 20.8 mmol) were added. After stirring for 1 hr the suspension was filtered and the solvent was evaporated. The residue was dissolved in benzene (50 mL) containing piperidine (2 drops) and HOAc (3 drops). After stirring for 17 hrs the soln. was concentrated and MeOH (70 mL) and NaBH_4 (200 mg; 5.5 mmol) were added. Work-up and column chromatography (acetone/hexane, 2:8) afforded 21 (641 mg, 52 %). Rf (acetone/hexane, 25:75) 0.28; IR 3400, 1730, 1610 cm^{-1} ; NMR 5.35 (m, 1), 4.15 (s, 2), 3.1–2.65 (m, 3), 2.3–1.2 (m, 8), 1.1 (s, 3), 0.9

(s, 3); MS m/z 220 (M^+ , 3.5), 202 (18), 84 (100). Product 6 (0.57 g; 2.8 mmol) was converted into 25 (1.75 g; 28 %) in an analogous procedure. Rf (acetone/hexane, 25:75) 0.26; IR 3420, 1750, 1625 cm^{-1} ; NMR 5.3 (s, 1), 4.15 (s, 2), 3.14 (m, 1), 2.85–1.6 (m, 8), 1.99 (d, $J = 13.3$ Hz, 1), 1.66 (d, $J = 13.3$ Hz, 1), 1.21 (s, 3), 0.96 (s, 3); MS m/z 220 (M^+ , 19), 202 (11), 41 (100).

The phosphonates 22 and 26.

To a soln of 21 (386 mg; 1.75 mmol) in Et_2O (8 mL) was added PBr_3 (473 mg; 1.75 mmol) at 0°C . After stirring for 48 hrs at ambient temp the reaction was quenched with H_2O . Work-up and column chromatography afforded the corresponding bromide (377 mg, 76 %). Rf (acetone/hexane, 25:75) 0.52; IR 1735, 1630, 1450 cm^{-1} ; NMR 5.5 (s, 1), 4 (s, 2), 3.1 (m, 1), 3–1.5 (m, 8), 1.2 (d, $J = 13.5$ Hz, 1), 1.2 (s, 3), 0.92 (s, 3); MS m/z 284–282 (M^+ , 1.8), 204–202 (33.6), 203 (100). An analogous procedure was used to convert 25 (140 mg; 0.69 mmol) into the corresponding bromide (81 mg, 42 %). Rf (acetone/hexane, 25:75) 0.52; IR 1740, 1640 cm^{-1} ; NMR 5.4 (s, 1), 3.98 (s, 2), 3.3–1.3 (m, 10), 1.21 (s, 3), 0.95 (s, 3); MS m/z 284–282 (M^+ , 12), 203 (75), 91 (100).

A soln of the bromide (377 mg; 1.33 mmol) and $(\text{MeO})_3\text{P}$ (2 mL) in CH_3CN (8 mL) was refluxed for 8 hrs. This afforded after work-up and column chromatography (acetone/hexane, 4:6) 22 (295 mg, 71 %). Rf (acetone/hexane, 5:5) 0.36; IR 1735, 1625 cm^{-1} ; NMR 5.4 (s, 1), 3.7 (d, $J = 10.5$ Hz, 6), 2.66 (d, $J = 18$ Hz, 2), 3.2–1.5 (m, 9), 1.25 (d, $J = 13.5$ Hz, 1), 1.22 (s, 3), 0.94 (s, 3); MS m/z 312 (M^+ , 34), 284 (16.6), 202 (62), 131 (100).

Product 26 (51 mg; 69 %) was obtained from the corresponding bromide (70 mg, 0.24 mmol) in an analogous way. Rf (acetone/hexane, 5:5) 0.29; IR 1740, 1645 cm^{-1} ; NMR 5.3 (m, 1), 3.76 (d, $J = 10$ Hz, 6), 2.64 (d, $J = 22.3$ Hz, 2), 3.3–1.4 (m, 10), 1.2 (s, 3), 0.94 (s, 3); MS m/z 312 (M^+ , 29), 284 (12), 202 (100).

The 8-keto phosphonates 23 and 27.

To a soln of RuO_4 (from RuO_2 (20 mg) and NaIO_4 (70 mg; 0.33 mmol) in acetone (5 mL) and H_2O (1 mL) was added 22 (62 mg; 0.2 mmol) in acetone (4 mL), simultaneously with NaIO_4 (350 mg; 1.64 mmol). After stirring for 5 hrs, the reaction was quenched with isopropanol. This yielded after work-up, treatment with diazomethane and column chromatography (acetone/hexane, 1:1) 23 (48 mg, 65 %). Rf (acetone/hexane, 6:4) 0.28; IR 1730 cm^{-1} ; NMR 3.79 (d, $J = 11.2$ Hz, 3), 3.78 (d, $J = 11.2$ Hz, 3), 3.67 (s, 3), 3.15 (dd, $J = 13.2$ Hz, $J = 23$ Hz, 1), 3.09 (dd, $J = 11.2$ Hz, $J = 23$ Hz, 1), 2.93 (d, $J = 17.8$ Hz, 1), 2.75 (d, $J = 17.8$ Hz, 1), 2.67 (dd, $J = 11.5$ Hz, 5 Hz, 1), 2.33 (d, $J = 13.7$ Hz, 1), 1.75 (d, $J = 13.5$ Hz, 1), 2.16–1.70 (m, 5), 1.19 (s, 3), 1.10 (s, 3); MS m/z 374 (M^+ , 46), 359 (20), 314 (44), 151 (100). Product 26 (27 mg; 0.09 mmol) was transformed into 27 (12 mg, 38 %) using the same procedure. Rf (acetone/hexane, 5:5) 0.19; IR 1740, 1725 cm^{-1} ; NMR 3.78 (m, 6), 3.75 (s, 3), 3.34 (d, $J = 6.4$ Hz, 1), 3.14 (dd, $J = 14$ Hz, 22 Hz, 1), 3.07 (dd, $J = 14$ Hz, 22 Hz, 1), 3.04 (d, $J = 18.8$ Hz, 1), 2.64 (d, $J = 18.8$ Hz, 1), 2.12 (d, $J = 14.2$ Hz, 1), 1.81 (d, $J = 14.2$ Hz, 1), 2.5–1.5 (m, 5), 1.25 (s, 3), 1.19 (s, 3); MS m/z 374 (M^+ , 11), 359 (11), 311 (20), 151 (100).

Methyl(1R⁺,6S⁺,7R⁺)-10,10-dimethyl-4-oxo-tricyclo[4.3.2.0^{2,6}]undec-2-en-7-carboxylate (24). To a soln of 23 (25 mg; 0.07 mmol) in THF (1 mL) was added dimethylsodium (1.35 M soln. in DMSO; 0.07 mmol) at 0°C . Stirring is then continued at 70°C for 7 hrs. This yielded after quenching with NH_4Cl aq, work-up and column chromatography (acetone/hexane, 1:9) 24 (11 mg,

66.3 %, mp 79°C, Et₂O-hexane). Rf (benzene/EtOAc, 8:2) 0.34; IR 1730, 1630 cm⁻¹; NMR 5.82 (s, 1), 3.67 (s, 3), 2.55 (d, J = 18.4 Hz, 1), 2.44 (t, J = 2 Hz, 1), 2.41 (dd, J = 6 Hz, 11.2 Hz, 1), 2.29 (d, J = 18.4 Hz, 1), 2.26 (d, J = 13.6 Hz, 1), 2.1-1.5 (m, 4), 1.25 (d, J = 13.6 Hz, 1), 1.22 (s, 3), 0.84 (s, 3); HRMS m/z (61 %) 248.1386; calc. for C₁₅H₂₀O₃, 248.1412.

(1R⁺, 9R⁺)-10,10-dimethyl-12-oxo-tricyclo[7.2.1.0^{1,6}]dodec-5-en-4-one (17)

To a soln of CrO₃-DMP complex²² (0.238 mol) in CH₂Cl₂ (250 mL) at -20°C was added 7 (3 g; 51.8 mmol) in CH₂Cl₂ (100 mL). Stirring was then continued for 5 hrs at -15°C. Basic work-up and extraction with Et₂O yielded after column chromatography (acetone/hexane, 2:8) 17 (2.4 g, 75 %, mp 64°C, hexane/Et₂O). Rf (acetone/hexane, 4:6) 0.55; IR 1755, 1675, 1615 cm⁻¹; NMR 5.7 (d, J = 1.5 Hz, 1), 3-1.7 (m, 8), 2.11 (d, J = 13.5 Hz, 1), 2.10 (t, J = 3.5 Hz, 1), 1.56 (d, J = 13.5 Hz, 1), 1.24 (s, 3), 1.02 (s, 3); HRMS m/z (64 %) 218.1314; calc. for C₁₄H₁₈O₂, 218.1306.

(1R⁺, 3R⁺, 6R⁺, 9R⁺)-3,10,10-trimethyl-12-oxo-tricyclo[7.2.1.0^{1,6}]dodec-4-one (31)

To a soln of LDA (10.57 mmol) in THF (30 mL) at -78°C was added 17 (2.3 g; 10.45 mmol) in THF (15 mL). Stirring was continued for 1 hr and HMPA (2.9 g; 16.5 mmol) was added. The mixture was warmed to -30°C and MeI (7.1 g; 50 mmol) was added. After further warming up to ambient temp, the reaction was quenched with sat NH₄Cl aq. This yielded after work-up and column chromatography (acetone/hexane, 1:9) two epimeric products **a** and **b** (2.1 g, 85.8 %). **a**: Rf (EtOAc/hexane, 4:6) 0.51; UV_{max} = 250 nm; IR 1735, 1670, 1615 cm⁻¹; NMR 5.74 (d, J = 2 Hz, 1), 3.03 (m, 1), 2.77 (m, 1), 2.32 (dd, J = 15 Hz, 6 Hz, 1), 2.31 (dd, J = 13.5 Hz, 5 Hz, 1), 2.15 (m, 1), 2.08 (d, J = 13.5 Hz, 1), 2.00 (t, J = 3 Hz, 1), 1.89 (m, 1), 1.63 (t, J = 13.5 Hz, 1), 1.51 (d, J = 13.5 Hz, 1), 1.23 (s, 3), 1.10 (d, J = 6.75 Hz, 3), 1.02 (s, 3); MS m/z 232 (M⁺, 60), 204 (26), 161 (100) and **b**: Rf (EtOAc/hexane, 4:6) 0.46; UV_{max} = 250 nm; IR 1735, 1675, 1615 cm⁻¹; NMR 5.70 (d, J = 2 Hz, 1), 2.73 (m, 1), 2.45-2.25 (m, 3), 2.20-2.05 (m, 3), 2.0 (m, 1), 1.81 (d, J = 13.5 Hz, 1), 1.62 (m, 1), 1.28 (s, 3), 1.15 (d, J = 6.25 Hz, 3), 1.01 (s, 3); MS m/z 232 (M⁺, 26), 204 (19), 161 (62), 55 (100).

To a soln of the epimer **a** (750 mg; 3.2 mmol) in EtOAc (50 mL) was added Pd/C (10 %, 300 mg). This suspension was stirred under an H₂ atm. for 72 hrs. This afforded after filtration, evaporation of the solvent and column chromatography (acetone/hexane, 8:92) 31 (453 mg; 60 %, mp 62-64°C, hexane). Rf (Et₂O/hexane, 1:1) 0.39; IR 1735, 1705 cm⁻¹; NMR 3.42 (m, 1), 2.47 (m, 1), 2.3-1.86 (m, 5), 2.09 (d, J = 13 Hz, 1), 1.52 (d, J = 13 Hz, 1), 1.24 (m, 2), 1.23 (s, 3), 0.99 (d, J = 6.5 Hz, 3), 0.97 (s, 3); MS m/z 234 (M⁺, 33), 201 (52), 41 (100). Anal. calc. for C₁₅H₂₂O₂, C, 76.9; H, 9.4. Found C, 76.7; H, 9.6.

(1S⁺, 2R⁺, 5R⁺)-1-(2-oxopropyl)-2-(methoxycarbonylmethyl)-6,6-dimethyl-bicyclo[3.2.1]octan-8-one (32)

To a soln of 31 (70 mg, 0.3 mmol) in CH₂Cl₂ (5 mL) at -20°C was added HMDS (57.7 mg; 0.36 mmol) and TMSI (47 μl; 0.33 mmol). Stirring was then continued for 1 hr at ambient temp. After work up the product was immediately ozonized in CH₂Cl₂ (6 mL) at -60°C. The mixture was then flushed with N₂, the solvent evaporated and the residue was treated with Zn (0.5 g, 7.5 mmol) in HOAc (5 mL). After

stirring for 3 hrs the suspension was filtered and the solvent evaporated. Work-up and column chromatography (benzene/acetone, 7:3) afforded the acid (57 mg, 72 %). Rf (Et₂O) 0.35; IR 1735, 1720 cm⁻¹; NMR 2.78 (d, J = 17.5 Hz, 1), 2.76 (m, 1), 2.51 (d, J = 17.5 Hz, 1), 2.42 (dd, J = 16 Hz, 3 Hz, 1), 2.2-1.9 (m, 5), 2.11 (s, 3), 1.86 (t, J = 3 Hz, 1), 1.72 (d, J = 13.7 Hz, 1), 1.41 (m, 1), 1.2 (s, 3), 0.98 (s, 3); MS m/z 266 (M⁺, 1.2), 205 (20), 43 (100). The acid was then converted into 32 on treatment with CH₂N₂. Rf (Et₂O/hexane, 4:6) 0.35; IR 1735 cm⁻¹; NMR 3.65 (s, 3), 2.74 (d, J = 17.5 Hz, 1), 2.74 (m, 1), 2.49 (d, J = 17.5 Hz, 1), 2.38 (ddd, J = 15.5 Hz, 3.5 Hz, 0.7 Hz, 1), 2.13 (d, J = 13.5 Hz, 1), 2.12 (s, 3); 2.1-1.9 (m, 4), 1.84 (t, J = 3 Hz, 1), 1.71 (d, J = 13.5 Hz, 1), 1.36 (m, 1), 1.19 (s, 3), 0.97 (s, 3).

Het ketal 33.

A soln of 32 (344 mg; 1.24 mmol) glycol (1.5 mL) and p-TsOH (trace) in benzene (20 mL) is stirred at 80°C for 4 hrs, H₂O being removed with a Dean-Stork separator. Work-up and column chromatography (Et₂O/hexane, 2:8) afforded the corresponding ketal (387 mg, 97 %, mp 94°C, from hexane). Rf (Et₂O/hexane, 4:6) 0.34; IR (KBr) 1735 cm⁻¹; NMR 4-3.8 (m, 4), 3.64 (s, 3), 2.77 (m, 1), 2.63 (d, J = 16 Hz, 1), 2.37 (d, J = 15.5 Hz, 1), 2.11 (d, J = 13.5 Hz, 1), 2.1-1.9 (m, 4), 1.8 (t, J = 2.5 Hz, 1), 1.82 (d, J = 13.5 Hz, 1), 1.52 (d, J = 15.5 Hz, 1), 1.33 (m, 1), 1.28 (s, 3), 1.18 (s, 3), 0.88 (s, 3); MS m/z 324 (M⁺, 10), 309 (26), 87 (100). To a soln. of the ketal (387 mg; 1.21 mmol) in THF (7 mL) at -10°C was added super-H (2.2 eq.; 2.66 mmol). After stirring for 2 hrs, the reaction was quenched with sat NH₄Cl aq. Work-up and column chromatography (Et₂O/hexane, 55:45) yielded 33 (261 mg, 74 %). Rf (Et₂O/hexane, 7:3) 0.27; IR 3500, 1735 cm⁻¹; NMR 4-3.8 (m, 4), 3.62 (m, 1), 3.52 (m, 1), 2.49 (d, J = 15.7 Hz, 1), 2.15 (m, 1), 2.07 (d, J = 13.5 Hz, 1), 2.2-1.8 (m, 3), 1.82 (d, J = 13.5 Hz, 1), 1.79 (t, J = 2.5 Hz, 1), 1.5 (d, J = 15.7 Hz, 1), 1.4-1.17 (m, 3), 1.59 (bs, 1), 1.31 (s, 3), 1.18 (s, 3), 0.88 (s, 3); MS m/z 296 (M⁺, 0.02), 281 (0.2), 234 (5), 206 (12), 87 (100).

(1S⁺, 2R⁺, 5R⁺)-1-(2-oxopropyl)-2-vinyl-6,6-dimethyl-bicyclo[3.2.1]octan-8-one (34)

To a soln of 33 (212 mg; 0.716 mmol) and O-NO₂C₆H₄SeCN (319 mg; 1.43 mmol) in THF (2 mL) and pyridine (2 mL) was added n-Bu₃P (289 mg; 1.43 mmol) at ambient temp. After stirring for 8 hrs, the solvent was evaporated and the selenide (mp 129°C, hexane/EtOAc) was isolated after column chromatography (EtOAc/hexane, 3:7). Rf (EtOAc/hexane, 1:1) 0.42; IR 1735, 1590, 1510, 1500 cm⁻¹; NMR 8.29 (dd, J = 7.5 Hz, J = 1.2 Hz, 1), 7.55 (dd, J = 1.25 Hz, J = 7.5 Hz, 1), 7.48 (ddd, J = 7.5 Hz, J = 1.25 Hz, J = 1.2 Hz, 1), 7.31 (ddd, J = 7.5 Hz, J = 1.25 Hz, 1.2 Hz, 1), 4-3.8 (m, 4), 2.91 (m, 1), 2.8 (m, 1), 2.41 (d, J = 15.5 Hz, 1), 2.38 (m, 1), 2.05 (d, J = 13.5 Hz, 1), 2.1-1.9 (m, 4), 1.8 (t, J = 2.5 Hz, 1), 1.83 (d, J = 13.5 Hz, 1), 1.5 (d, J = 15.5 Hz, 1), 1.5 (m, 1), 1.3 (m, 1), 1.28 (s, 3), 1.19 (s, 3), 0.87 (s, 3); MS m/z 480 (M⁺, 0.3), 465 (1.2), 279 (2.6), 87 (100).

A soln of the selenide and H₂O₂ aq (30 %, 650 μL) in THF (7 mL) was stirred for 24 hrs. The mixture was then diluted with H₂O and extracted with Et₂O. The crude acetal was then hydrolysed with HCl aq (6 N, 0.5 mL) in THF (2.5 mL). Work-up and column chromatography (EtOAc/hexane, 1:9) afforded 34 (94 mg, 57 %, mp 48°C, hexane). Rf (EtOAc-hexane, 15:85) 0.33; IR 1735, 1710 cm⁻¹; NMR 5.69 (dt, J = 16.5 Hz,

10 Hz, 1), 5.06 (dd, $J = 10$ Hz, 2 Hz, 1), 4.95 (ddd, $J = 16.5$ Hz, 2 Hz, 0.5 Hz, 1), 2.88 (dd, $J = 10$ Hz, 6.3 Hz, 1), 2.74 (d, $J = 18$ Hz, 1), 2.47 (d, $J = 18$ Hz, 1), 2.3-1.95 (m, 3), 2.12 (d, $J = 13.75$ Hz, 1), 2.09 (s, 3), 1.87 (t, 3.5 Hz, 1), 1.2 (s, 3), 0.97 (s, 3); HRMS m/z (3 %) 234.1546; calc. for $C_{15}H_{22}O_2$, 234.1619.

($1R^+, 6S^+, 7R^+$)-10,10-dimethyl-7-vinyl-tricyclo[4.3.2.0^{2,6}]undec-2-en-4-one (35).

To a suspension of NaH (50 % in oil; 8.3 mg; 0.166 mmol) and t.AmOH (3 μ L, 0.03 mmol) in benzene (0.6 mL) was added 34 (30 mg; 0.133 mmol). After stirring at 80°C for 5 hrs, the reaction was quenched with sat. NH_4Cl aq.

Work-up and column chromatography (EtOAc/hexane, 1:9) afforded 35 (21.7 mg, 78 %).

Rf (EtOAc/hexane, 25:75) 0.43; $UV_{max} = 236$ nm; IR 1705, 1630 cm^{-1} ; NMR 5.85 (s, 1), 5.64 (m, 1), 5.03 (bs, 1), 4.99 (m, 1), 2.51 (dd, $J = 9.5$ Hz, 6 Hz, 1), 2.45 (t, $J = 3$ Hz, 1), 2.41 (d, $J = 18$ Hz, 1), 2.09 (m, 1), 2.06 (d, $J = 18$ Hz, 1), 1.89 (d, $J = 13$ Hz, 1), 1.9-1.7 (m, 2), 1.47 (m, 1), 1.41 (d, $J = 13$ Hz, 1), 1.24 (s, 3), 0.94 (s, 3); MS m/z 216 (M^+ , 7), 201 (18), 173 (100).

($1R^+, 6S^+, 7S^+$)-10,10-dimethyl-7-carboxy-tricyclo[4.3.2.0^{2,6}]undec-2-en-4-one (2).

To a soln. of 35 (11 mg; 0.05 mmol) in CCl_4 (200 μ L), CH_3CN (200 μ L) and H_2O (300 μ L) was added $RuO_2 \cdot xH_2O$ (1 mg) and $NaIO_4$ (100 mg; 0.46 mmol; in portions of 20 mg). After stirring for 5 hrs the reaction was quenched with isopropanol. Extraction with EtOAc, work-up and column chromatography (EtOAc/hexane/HOAc 50:50:1) afforded 2 (10 mg, 86 %, mp 143.5-145°C, EtOAc/isooctane). Rf (EtOAc/hexane/HOAc, 45:50:5) 0.37; IR 3530-2400, 1705, 1640 cm^{-1} ; NMR 5.88 (s, 1), 2.95 (d, $J = 5.1$ Hz, 1), 2.78 (d, $J = 18.3$ Hz, 1), 2.49 (t, $J = 3$ Hz, 1), 2.20 (d, $J = 18.3$ Hz, 1), 2.19-1.82 (m, 5), 1.42 (d, $J = 13.5$ Hz, 1), 1.25 (s, 3), 0.95 (s, 3H). MS m/z 234 (M^+ , 13), 219 (4.5), 206 (11), 192 (13), 147 (44), 133 (100).

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