Allylic Oxidation and First Transformations of a Key Intermediate in the Total Synthesis of Agarofuran Sesquiterpenes[‡]

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This paper describes the synthesis of polyhydroxylated decalinic systems through oxidative furan ring opening of 3-(2′-furyl)-2-methoxycarbonylcyclohexadione-4-monoethylene ketal **12** using dimethyl dioxirane (DMDO). The functionalisation of the decalinic product **5**, aimed at the synthesis of antifeedant agarofuran sesquiterpenes according to our previously reported strategy, is demonstrated to occur with good stereochemical control of the introduced oxygenated functions, using as a key step an original allylic oxidation by DMDO.

Introduction

Agarofuran sesquiterpenes are polyesters of various tricyclic polyols, the general structure of which (**1**) is formed around the agarofuran backbone **2**, which can be related to the eudesmane family with an ether linkage between carbon atoms C-4a and C-11, thus forming a tetrahydrofuran ring, fused to the *trans* decalinic system A/B (Figure 1). Hydroxy groups can be present on this skeleton on almost any carbon atom, with various stereochemistries. This last feature, added to the diversity of the organic acids involved in the esterification of the hydroxy groups, generates a great diversity in this type of sesquiterpene.

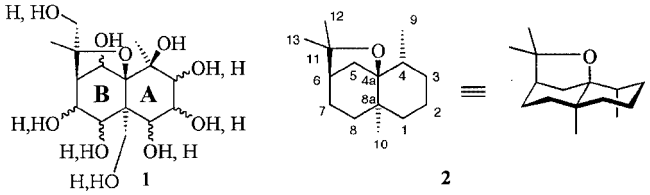

Figure 1. General structure of the agarofurans of the *Celestraceae*

More than 200 representatives of this class of compounds have been isolated and identified, mainly from plants of the *Celastraceae* family. Crude extracts of these plants have been used for a long time to protect plants against insect attacks and in traditional medicine for treatment of various diseases. In some cases, identification of the active principles has allowed a biological activity to be correlated with a definite agrofuran ester.[1,2] However, their low abundance in the crude extracts and difficulties in their isolation have generally impeded studies on their mode of action, even if some structure−activity relationships have been established and reported in the literature, particularly in the case of the antifeedant activity.[1]

In our biological studies devoted to the understanding of the transduction cascade at a molecular level in the case of the gustatory receptor of insects,[3] we focused on this family of compounds. Indeed, our decision to investigate the biological activity of these compounds was due to their structural diversity and their low toxicity for insects, compared to that of other well-known antifeedant substances like azadirachtine. We were therefore prompted to design flexible synthetic strategies towards agarofuran sesquiterpenes.

Some interesting syntheses of agarofurans have already been reported in the literature.[4] Owing to the difficulty of designing an easily accessible unique precursor incorporating the proper structural features for the further flexible and stereoselective introduction of the contiguous oxygenated groups on the decalinic system, most reported syntheses of agarofurans are devoted to the synthesis of the less hydroxylated ones and use the standard strategies of "eudesmane chemistry". We have already reported our approaches in that field, taking advantage of the straightforward "cyperone route".[5,6] Some strategies have nevertheless been designed, mainly by White's and Spivey's teams,[7] to synthesise the most hydroxylated agarofurans and are based

[‡] Synthesis of Agarofuran Antifeedants, IV. Part III: Ref.[13]

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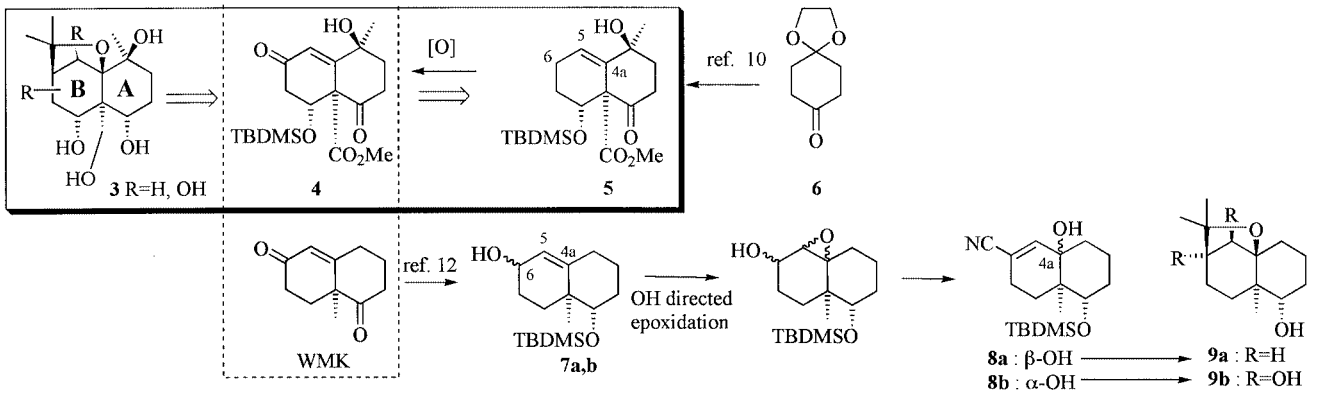
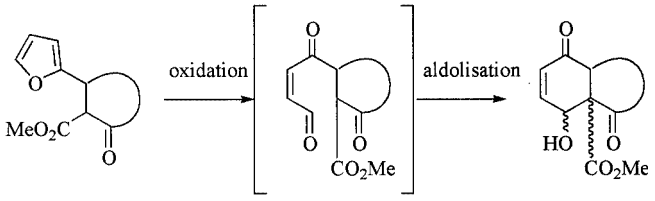


Scheme 1

on the early construction of a decalinic precursor, which is thereafter transformed in order to introduce the remaining carbon and oxygen atoms.

Our retrosynthetic analysis of this type of molecule (Scheme 1) was essentially derived from the same principle, but based on the efficiency of the intramolecular aldol condensation of (*Z*)-2,3-unsaturated 1,4-dicarbonylated compounds generated in situ by oxidative ring opening of a furan ring attached to a conveniently carbonylated compound (Scheme 2). This process was first reported by Lallemand's group in his approach to the clerodanes diterpenes.[8,9]



Scheme 2

In the first paper of the series[10] we mentioned the possible straightforward synthesis of decalinic compound **5** starting from the commercially available 1,4-cyclohexanedione derivative **6**.[11] On the other hand, we also focused our efforts on designing new versatile methods for the construction of the tetrahydrofuran ring of the agarofuran sesquiterpenes using alcohols **7**, derived from Wieland−Miescher ketone (WMK), as model compounds.[12] Thus we have reported the syntheses of agarofuran analogues **9**, via γ-hydroxy nitriles **8**. The characteristic feature of this latter strategy was to show the correlation between the configuration of the hydroxy group at C-4a in nitrile **8**, which was dependent on the configuration of the hydroxy group in its precursor **7**, and the possibilities of functionalisation of the final agarofuran skeleton.

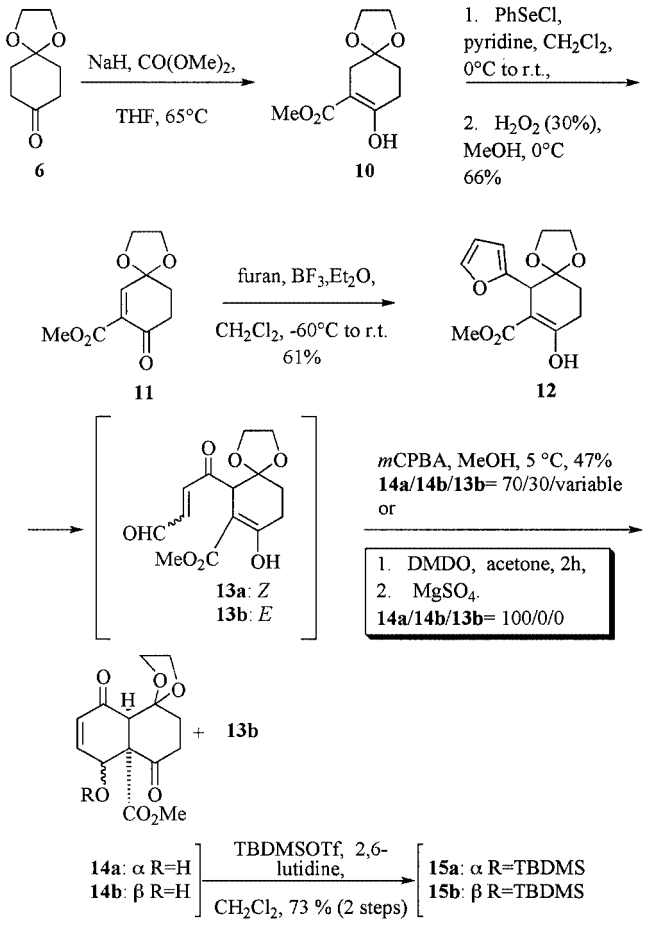
In this paper, we report the detailed synthesis of our designed precursor **5**, its allylic oxidation, leading to α,β-unsaturated ketone **4**, similar to WMK, and the first transformations of this compound required to prove the compatibility of our two strategies described above. Indeed, the high level of substitution of our WMK analogue **4** should induce new stereochemical features, which may change the course of the transformations designed in the case of WMK. The most critical factor to manage was the configuration of the oxygenated function at C-4a, which has to be introduced in the early steps of the synthetic sequence through the stereoselective epoxidation of the $\Delta^{4a,5}$ double bond. In our previous model studies, this epoxidation step was only controlled by the configuration of the hydroxy group at C-6, which had to be inverted through a Mitsunobu reaction to give access to both configurations at C-4a in nitrile **8**. In the case of precursor **4**, the presence of a supplementary tertiary hydroxy group at C-4 may allow new opportunities of controlling this key transformation. Moreover, another important aspect of these stereochemical studies, also related to the control of the configuration of the ring junction of the decalinic system, is the possible entry in the *pyrano*-agarofuran series of compounds, that we reported in the previous paper of the series.[13]

Results and Discussion

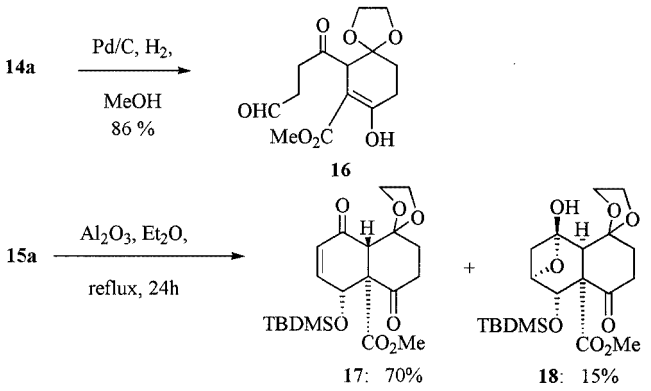
Synthesis of Decalin 5

The starting material, the commercially available cyclohexanedione monoethylene ketal **6** was first carboxymethylated to the β-keto ester **10**, which was subsequently converted into the α,β-unsaturated keto ester **11** by standard selenium chemistry. Lewis-acid mediated condensation with furan was then performed according to previously described procedures[8,9] and gave adduct **12** in good yield (61%) in multigram quantities (Scheme 3).

The first attempts at oxidative opening of the furan ring by *m*-CPBA resulted as expected in the formation of a (*Z*)-dicarbonylated intermediate **13a**, which underwent spontaneous intramolecular aldolisation. However, the configuration of the aldol was not completely controlled in these conditions and this experimental procedure afforded both *cis* decalins **14a** and **14b** (**14a/14b**, 7:3) in 47% yield. These compounds have been fully characterised as their silyl ether derivatives **15**. However, isolation difficulties, and formation as a by-product of the (*E*)-dicarbonylated compound **13b**,



Scheme 3



Scheme 4

prompted us to look for a more suitable oxidizing reagent. Dimethyl dioxirane (DMDO) was selected[14] because of the neutrality of the reaction mixture, which should decrease the amount of isomerisation of the kinetic aldol formed in the course of the reaction. Indeed, in these conditions compound **12** only gave the *cis* decalin **14a** as a crystalline product (Scheme 3).

An important aspect of the workup was the mandatory drying step of the reaction ($MgSO_4$) before evaporation of the solvent, as the presence of traces of water in the reaction medium may allow the formation of the (*E*)-dicarbonylated compound **13b** in a catalytic process involving 1−4 addition of water, which allows a retroaldolisation process to take place, followed by an unselective dehydration. Indeed, the presence of the double bond is crucial in the stabilisation of the closed form of the aldol, since hydrogenation of decalin **14a** in standard conditions resulted in the formation of keto ester **16** in good yield (86%, Scheme 4).

The *cis* configuration of decalins **14** was first assumed from mechanistic considerations, related to the necessary minimisation of the steric interactions between the dioxolane and the furan rings in the starting material, which induces the six-membered ring to adopt the conformation where the furan is in the axial position. Later, configurations of the asymmetric centers in both decalins were fully established by NMR studies on their *tert*-butyldimethylsilyl derivatives **15**. The presence in both isomers of a small ^4J coupling constant between H-4a and H-3_{eq} clearly indicates the equatorial position of the former on ring A, which is only compatible with a *cis* decalinic compound (Figure 2). Configuration of the hydroxyl group at C-8 was derived in the case of **15b** from a NOE effect between H-4a and H-8 resulting from their 1,3-diaxial relative position on ring B. Moreover, careful recrystallisation of unprotected decalin **14a** allowed its analysis by X-ray diffraction, confirming our previous stereochemical assignments (Figure 3, top-left).[15]

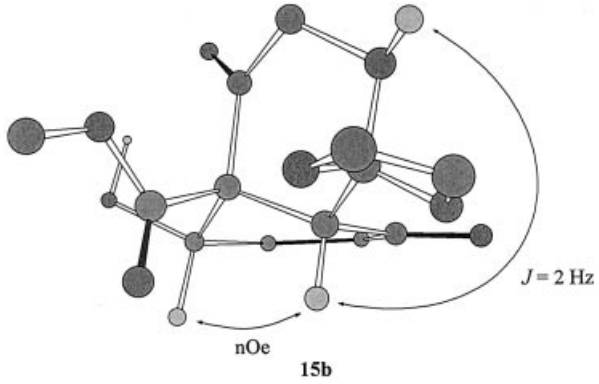


Figure 2. Conformation of **15b**

An unexpected result was, however, the nonisomerisation of ring junction in unprotected decalins **14**. Previous studies on this type of intramolecular aldol reaction leading to closely related compounds have indeed reported the possible thermodynamic equilibration of the reaction mixture through a retroaldolisation−aldolisation process, finally affording the more thermodynamically stable *trans* decalins.[9] This discrepancy can be explained by the fact that, in our case, the isomerisation process would have required, as a key step, the change of the pseudo-chair conformation of the cyclohexene ring (ring A) in the dicarbonylated intermediate **13a**, which is prohibited by the stabilisation of its conformation by stereoelectronic effects due to its peculiar dioxaspiro bicyclic structure. The conformation of this intermediate is therefore fixed by steric factors in its precursor

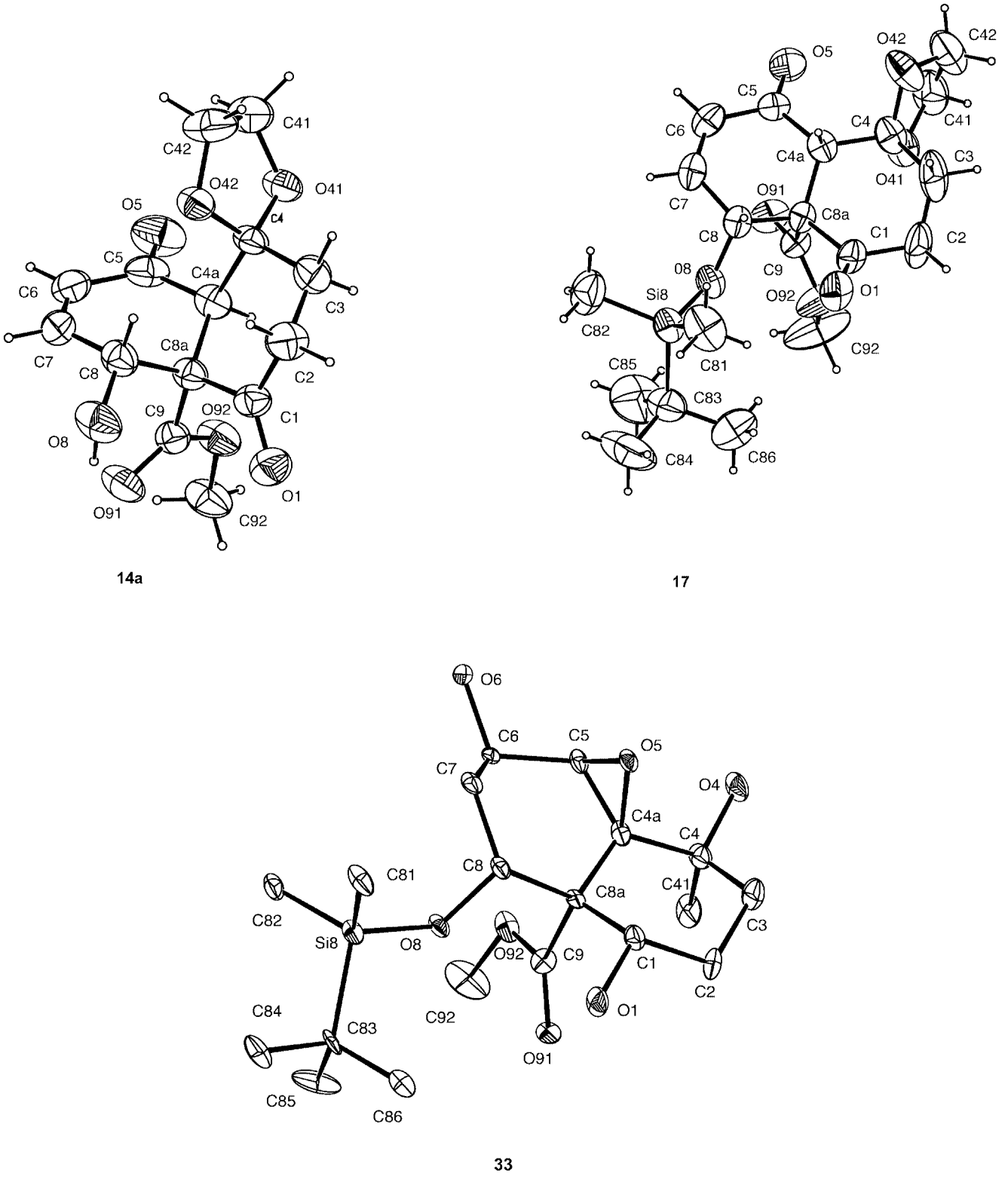


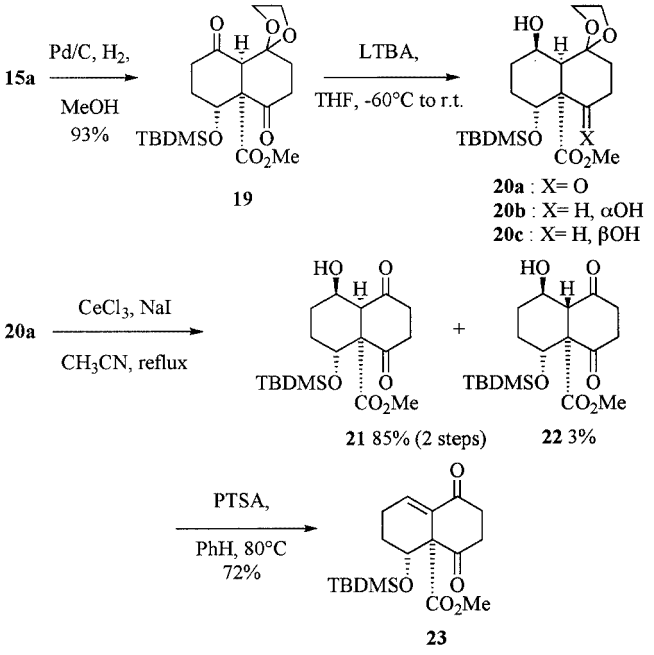
Figure 3. X-ray diagram of compounds **14**, **17** and **33**

12. Nevertheless, in order to test the reactivity of the *trans* decalins in our further transformations, we performed isomerisation of the ring junction on silyl ether **15a**, taking advantage of the presence of the carbonyl group in the α position relative to the hydrogen at C-4a. Using basic alumina, the expected compound **17** was obtained in 70% yield and characterised by X-ray diffraction (Figure 3, top-right)[15] with ketal **18** (15%) as a by-product, formation of

which was due to residual water and confirmed the easy 1−4 addition of water to the enone system of the *cis* decalinic compounds **14** and **15** (Scheme 4).

Functional Fittings on Decalin 15a

The *tert*-butylsilyl derivative **15a** was first hydrogenated (Pd/C in methanol) to the saturated compound **19** in 93% yield (Scheme 5). Regio and stereoselective reduction of the carbonyl at C-5 was then performed using lithium tri-*tert*-butoxyaluminohydride (LTBA, −60 °C, THF) and gave **20a**, where the hydroxy group thus obtained is axial on ring B. Other reducing reagents ($LiAlH_4$, $NaBH_4$) gave mixtures of **20a** and both isomeric diols **20b** and **20c**. Carbonyl deprotection to give the β-hydroxy ketone **21** was only possible in good yield (85%) using $CeCl_3$ and NaI in CH_3CN[16] with formation of minor amounts (3%) of *trans*-β-hydroxy ketone **22**. The stable β-hydroxy ketone **21** can be further dehydrated by treatment with PTSA in benzene to yield enone **23** (72%) while *trans*-β-hydroxy ketone **22** afforded, in these conditions, the same enone **23** in moderate yield (37%).

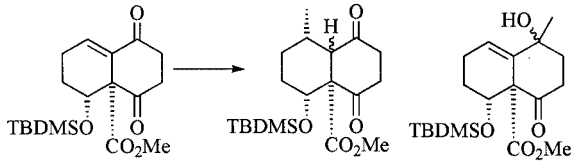


Scheme 5

A further important feature of the synthesis was the stereoselective introduction of a supplementary methyl group at C-4 by reaction of an appropriate organometallic reagent with the carbonyl group to form the methyl carbinol encountered in the natural compounds.

This transformation, which seemed at first to be easy, was in fact quite surprising. The most difficult aspect to manage was not the stereochemical course of the organometallic addition but its regiochemistry. Whereas the carbonyl group at C-1 remained untouched under all conditions, organolithium reagents were found to add not only in a 1−2 process to the carbonyl group at C-4 but also in a 1−4 process, leading to the corresponding β-methyl ketones **24**. The peculiar behaviour of organolithium reagents in this case is probably related to their potential chelation by the axial methoxycarbonyl group at C-8a on the α face of the molecule, which forces the organometallic species to be in a position where 1−4 addition is favoured. This supposition is supported by the fact that 1−4 addition occurred only from the α face of the molecule, even if the quenching of the enolate was thereafter unselective, leading to a mixture of ketones **24**.

The best results were, however, obtained by the action of methyllithium (Et_2O, −70 °C) and led to the regioselective formation of a (95:5) mixture of both isomers **5a** (32%) and **5b** (1.7%) and diketones **24a** (26%) and **24b** (8%). Interestingly, the stereochemical course of the 1−2 addition could be inverted using methylcerium.[17] In that case, the organometallic species reacted regioselectively giving a (15:85) mixture of **5a** and **5b** without any 1−4 addition. Extensive studies are reported on Scheme 6.



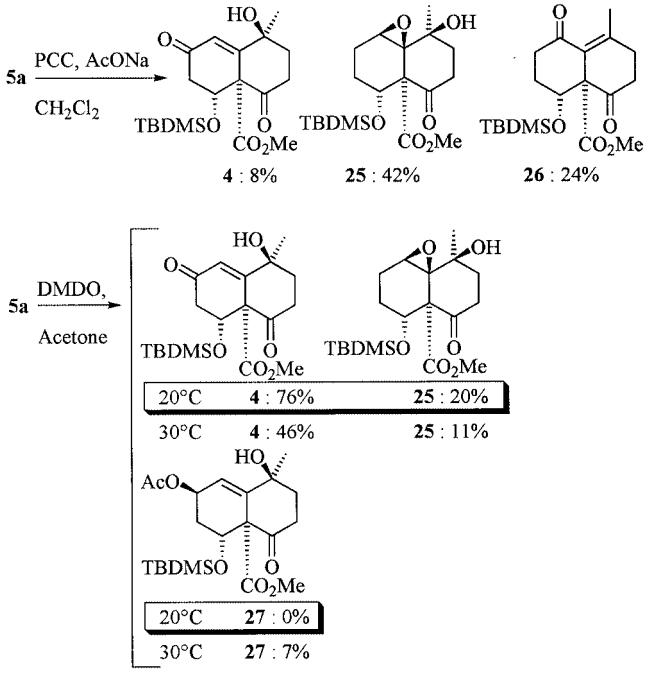
conditions	24 [%]	5 [%](5a:5b)
MeLi-LiBr 2.25 equiv./Et_2O,–70°C to 0°C	80	20 *(80:20)*
MeLi 3 equiv./Toluene,–70°C to 0°C	24	25 *(60:40)*
MeMgBr 2.25 equiv./Et_2O,–70°C to 0°C	80	0
MeMgBr-$CeCl_3$ 2.25 equiv./Et_2O, 0°C	0	70 *(20:80)*
MeLi 2.25 equiv./Et_2O,–70°C to 0°C	34	33.5 *(95:5)*

Scheme 6

Oxidation of the Decalinic System

After we had achieved the synthesis of our designed precursor **5** in a stereocontrolled manner, the next challenging step was its oxidation. Indeed, oxidative treatment of such a tertiary allylic alcohol could lead either to allylic oxidation or to an allylic rearrangement giving access to a carbonyl group at C-5. Both processes could be valuable in the course of agarofuran syntheses. However, the second one would have invalidated our previously designed strategy for tetrahydrofuran ring construction.

Several reagents were tried on **5a** (Scheme 7). The peculiar behaviour of **5a** upon oxidative treatment was demonstrated by its oxidation by pyridinium chlorochromate (PCC), when the major products were derived from either oxidation of the double bond (**25**) or allylic rearrangement (**26**). However, in this case, allylic oxidation was observed in 8% yield, giving the first access to our designed precursor **4**. In the search for more suitable oxidizing agents, we found



Scheme 7

that DMDO in large excess at room temperature was able to achieve the allylic oxidation of **5a** in good yield (76%) with a small amount of epoxide **25** (20%) and without any rearranged products. But minor changes in the decalinic system impeded any oxidation with DMDO. Moreover, the course of the reaction was very temperature sensitive. When conducted on alcohol **5a** at higher temperature (>30 °C, room temperature of a quite hot summer day!), acetate **27** was obtained as the major by-product, beside compounds **4** and **25**. The precise mechanism of formation of **27** was not clearly established, but its production enabled us to fully investigate the stereochemical features of the $\Delta^{4a,5}$ epoxidation step as described below. Indeed, reduction ($LiAlH_4$ 1 M in THF) of enone **4** and acetate **27** gave respectively triols **28** and **32** similar to alcohols **7a,b** used in our previous study (Scheme 1).[12]

As shown in Figure 4 for compound **28**, both hydroxy groups at C-4 and C-6 may have a directing role in the following epoxidation step; however, epoxidation in peracidic conditions has been reported[18] to be controlled more efficiently by the configuration of secondary than by tertiary hydroxy groups in the α position. Therefore *m*-CPBA-mediated epoxidation should occur from the more sterically hindered α face of the molecule. Indeed, epoxidation of triol **28** by using *m*-CPBA furnished epoxide **29** in high yield (Scheme 8). The stereochemical course of the epoxidation was unambiguously determined by X-ray analysis of a derivative.[13]On the other hand, epoxidation of triol **28** using [$VO(acac)_2$/*t*BuOOH] was controlled by the tertiary equatorial hydroxy group at C-4, and epoxide **31** was obtained as the major product of the reaction (Scheme 8); the minor product of the reaction, namely enone **30** could be recycled through reduction to triol **28**.

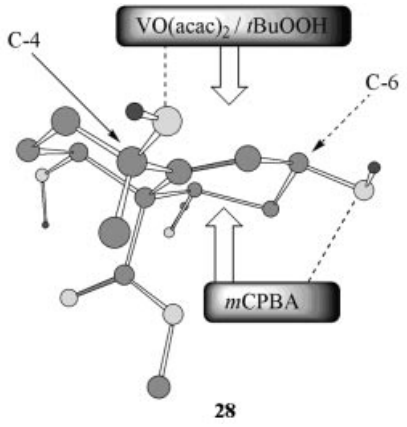
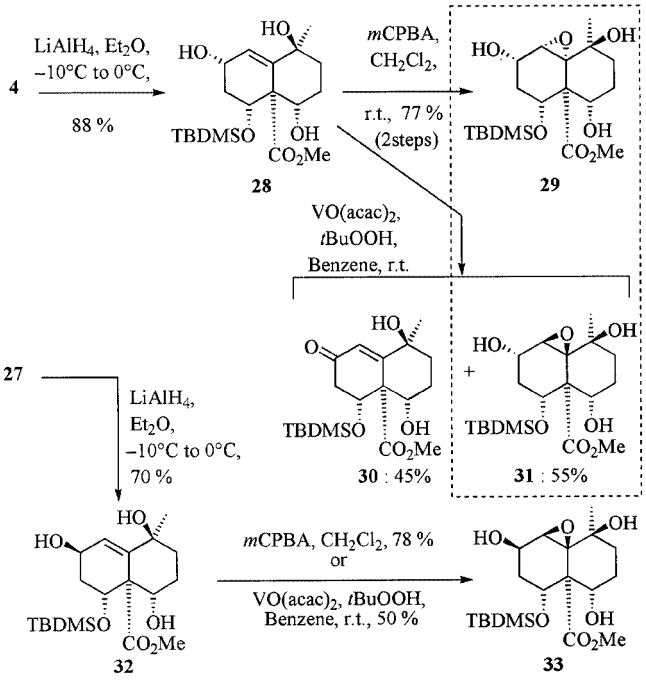


Figure 4. Model for the directed epoxidation of dihydroxy alkene **28**



Scheme 8

In order to confirm the influence of the configuration of the hydroxy group at C-6 in these reactions, epoxidation of triol **32** was performed by *m*-CPBA and [$VO(acac)_2$/*t*BuOOH]. In both cases, epoxide **33** was obtained, X-ray analysis of which confirmed unambiguously the stereochemical assignment of the three contiguous quaternary stereogenic centers (Figure 3, bottom).[15]

Conclusion

The most important feature of this study is that we have demonstrated the compatibility of our two previously reported strategies through the efficient synthesis of triol **28**, epoxidation of which can be efficiently controlled, giving access to either of the epoxides **29** or **31** exhibiting the op-

posite configuration at C-4a. As the stereocontrolled introduction of an oxygenated function at the ring junction has been demonstrated to be the key feature for further construction of the heterocycle of the agarofurans, we should be able to synthesise several promising agarofuran polyols for biological investigations. As a preliminary result, we report in the next paper the synthesis of a *pyrano*-agarofuran tetraol.

Experimental Section

General Remarks: Melting points, recorded on a Büchi 510 apparatus are uncorrected. NMR spectroscopic data (^{1}H: 300 MHz; ^{13}C: 75.5 MHz) were recorded on a VARIAN Gemini 300 instrument. All NMR spectra were recorded in deuteriochloroform ($CDCl_3$). Chemical shifts are reported in δ ppm relative to $CHCl_3$ ($CDCl_3$) as internal reference: δ = 7.27 ppm for ^{1}H (δ = 77.14 ppm for ^{13}C). Coupling constants (*J*) are given in Hertz (Hz). Multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet) and br (broad). X-ray data recordings at room temperature were performed with a Philips PW 1100 diffractometer (Cu-*Kα* radiation, λ = 1.5418 Å) and at low temperature by using the W32 wiggler beam line at the LURE synchrotron facility, Orsay, France.[19] Mass spectra (MS) were obtained on a Nermag R10−10C (DCI or DEI) or linked to a Varian 3300 GC. Ionisation was obtained either by electronic impact (EI) or chemical ionisation with ammonia (CI, NH_3). Mass spectroscopic data are reported as *m*/*z*. High resolution mass spectra were recorded by Institut de Chimie des Substances Naturelles, Mass Spectrometry Laboratory, Gif sur Yvette, France. Infrared spectra (IR) were obtained on a Nicolet Avatar 320 FT-IR and are reported in terms of frequency of absorption ($\tilde{\nu}$, cm^{-1}). Microanalyses were performed by Institut de Chimie des Substances Naturelles, Microanalytical Laboratory, Gif-sur-Yvette, France. All reactions were monitored by thin layer chromatography (TLC) carried out on precoated silica-gel 60F 254 plates (E. Merck, ref. # 5554). Visualization was accomplished with UV light, then 7−10% ethanolic phosphomolybdic acid solution and $KMnO_4$ solution were used as developing agents followed by heating. Diethyl ether (Et_2O) was distilled from sodium benzophenone, dichloromethane (CH_2Cl_2) and hexamethylphosphorictriamide (HMPA) from calcium hydride.

β-Keto Ester 10: Freshly distilled anhydrous dimethyl carbonate (250 mL, 2.96 mol) and a solution of 1,4-cyclohexanedione monoethyleneacetal **6** (40 g, 0.25 mol) in anhydrous THF (130 mL) were added successively to a suspension of NaH (8.5 g, 95% powder, 0.35 mol) in anhydrous THF (250 mL) under argon and with mechanical stirring. After the addition was complete, the mixture was refluxed for 5 h. The resulting brownish mixture was cooled to 0 °C and acetic acid (400 mL of a 10% aqueous solution) was added. The organic layer was separated and the aqueous phase further extracted with Et_2O (3 × 300 mL). The combined organic layers were washed with aqueous saturated sodium hydrogen carbonate solution (300 mL) and brine (300 mL), dried ($MgSO_4$) and concentrated in vacuo to give crude keto ester **10** as a yellow solid, which was recrystallized from 95% ethanol to furnish **10** (39.2 g, 73%) as white crystals. M.p. 64−65 °C, ref.,[20] M.p. 60−61 °C.

α,β-Unsaturated β-Keto Ester 11: Anhydrous pyridine (10 mL) was added dropwise to a solution of phenylselenyl chloride (20 g, 100 mmol) in anhydrous CH_2Cl_2 (350 mL) at 0 °C. After 15 minutes, a solution of keto ester **10** (19.8 g, 934.5 mmol) in anhydrous CH_2Cl_2 (120 mL) was added dropwise to the orange solution, and the resulting solution was stirred for 3 h at 0 °C and overnight at room temperature. Aqueous HCl (10% solution) was added to the mixture and the organic layer was separated and cooled to −5 °C. Hydrogen peroxide (30 wt% in water; 30 mL) was added dropwise in six portions at 15-min intervals and stirred for 1 h until complete decoloration of the reaction mixture. The resulting mixture was diluted with water (175 mL) and the organic layer was separated. The separated organic layer was washed with aqueous saturated sodium hydrogen carbonate solution (300 mL) and brine (300 mL), dried ($MgSO_4$), and concentrated in vacuo to give **11** as a yellow solid (18.8 g, 88%) which was used in the next step without further purification. An analytical sample can be obtained by recrystallization in cold methanol (−10 °C) to give pure **11** as yellow plates. M.p. 43 °C. ^{1}H NMR: δ = 7.10 (t, *J* = 1 Hz, 1 H), 4.10−4.00 (m, 4 H), 3.80 (s, 3 H), 2.72−2.67 (m, 2 H), 2.24−2.19 (m, 2 H). ^{13}C NMR: δ = 193.8 (s), 164.4 (s), 149.4 (d), 132.6 (s), 103.7 (s), 65.3 (t), 52.4 (q), 36.2 (t), 32.8 (t). GC analysis (AT-5, 0.32 mm id. × 30 m, 80−300 °C, 10 °C/min), retention time 7.33 min. EI MS: *m*/*z* (%) = 212 (5) [M^+], 184 (15), 170 (20), 126 (40), 98 (50), 53 (100). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2955, 2894, 1718, 1690, 1615.

Furan 12: Freshly distilled furan (120 mL, 1.6 mol) and distilled $BF_3{\cdot}Et_2O$ (1.6 mL, 17.4 mmol) were added dropwise to a solution of **11** (20 g, 94.33 mmol) in CH_2Cl_2 (500 mL) at −60 °C under argon. The resulting solution was warmed to room temperature (4 h). The reaction mixture was treated with aqueous saturated sodium hydrogen carbonate solution (40 mL) and the organic layer was separated. The separated organic layer was washed with brine (100 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give crude **12** (19.6 g) as a brown oil which was purified by chromatography (EtOAc/cyclohexane, 40:60) to give **12** (16.2 g, 61%) recrystallized from methanol as white plates. M.p. 83−84 °C. ^{1}H NMR: δ = 12.10 (s, 1 H), 7.30 (dd, *J* = 2, 1 Hz, 1 H), 6.30 (dd, *J* = 3, 2 Hz, 1 H), 6.00 (dd, *J* = 3, 1 Hz, 1 H), 4.20−4.10 (m, 4 H), 3.90 (s, 1 H), 3.60 (s, 3 H), 2.80−2.40 (m, 2 H), 2.15 (ddd, *J* = 13, 12, 7 Hz, 1 H), 1.60 (m, 1 H). ^{13}C NMR: δ = 172.8 (s), 172.3 (s), 155.2 (s), 141.6 (d), 110.3 (d), 108.3 (d), 107.3 (s), 97.7 (s), 65.0 (t), 64.7 (t), 51.8 (q), 41.6 (d), 27.8 (t), 26.9 (t). GC analysis (AT-5, 0.32 mm id. × 30 m, 80−300 °C, 10 °C/min), retention time 9.94 min. EI MS: *m*/*z* (%) = 280 (50) [M^+], 248 (M^+ − MeOH, 47), 162 (60), 99 (100), 87 (25), 55 (30). CI MS: *m*/*z* (%) = 298 ([M + NH_4]$^+$, 90), 281 ([MH]$^+$, 100). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2952, 2885, 1749, 1716, 1653, 1613, 1276, 1228, 1195, 1059. $C_{14}H_{16}O_6$ (280.29): calcd. C 59.99, H 5.80; found C 59.85, H 5.75.

Aldol 14a: A solution of dimethyldioxirane[21] in acetone (1110 mL) was added dropwise to a solution of **12** (20.5 g, 73.21 mmol) in acetone (1110 mL) under argon. The resulting solution was stirred for 2 h at room temperature, dried for 2 h ($MgSO_4$), and concentrated under reduced pressure to give crude **14a** (21.03 g) as a slightly yellow solid which was used in the next step without further purification. An analytical sample can be obtained by recrystallization in cold methanol (−10 °C) to give pure **14a** as white crystals. M.p. 176−178 °C. ^{1}H NMR: δ = 7.10 (dd, *J* = 10, 2 Hz, 1 H), 5.92 (ddd, *J* = 10, 2, 1 Hz, 1 H), 5.66 (td, *J* = 12, 2 Hz, 1 H), 4.62 (d, *J* = 12 Hz, OH, 1 H), 4.00−3.80 (m, 4 H), 3.75 (s, 3 H), 3.70 (s, 1 H), 3.10 (ddd, *J* = 15, 8, 3 Hz, 1 H), 2.53 (td, *J* = 15, 3 Hz, 1 H), 2.16−2.09 (m, 2 H). ^{13}C NMR: δ = 202.2 (s), 192.4 (s), 171.3 (s), 154.4 (d), 128.4 (d), 108.2 (s), 68.7 (d), 68.3 (s), 66.4 (t), 65.1 (t), 56.8 (d), 53.4 (q), 35.5 (2C, t). GC analysis (AT-5, 0.32 mm id. × 30 m, 220−320 °C, 10 °C/min), retention time 3.20 min. EI MS: *m*/*z* (%) = 296 (10) [M^+], 237 (10), 181 (12), 100 (100), 99 (90), 55 (27). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3499, 2961, 2897, 1726, 1709, 1675, 1615,

1257, 1235, 1157, 1038, 1021. $C_{14}H_{16}O_7$ (296.29): calcd. C 56.37, H 6.08; found C 56.31, H 5.93.

Ketoaldehyde 16: A solution of alcohol **14a** (555 mg, 1.87 mmol) in methanol (40 mL) was hydrogenated for 3 h under atmospheric pressure in the presence of 10% palladium on charcoal. The suspension was filtered through Celite and the resulting solution concentrated under reduced pressure. The residue (520 mg) was purified by chromatography (EtOAc/cyclohexane, 40:60) to give **16** (480 mg, 86%) which was recrystallized from a mixture of diethyl ether/pentane (50:50) as white crystals. M.p. 120 °C. ^{1}H NMR: δ = 12.18 (s, 1 H), 9.81 (s, 1 H), 4.12−4.09 (m, 4 H), 3.80 (s, 1 H), 3.70 (s, 3 H), 3.00 (q, *J* = 7 Hz, 2 H), 2.80 (t, *J* = 7 Hz, 1 H), 2.70 (t, *J* = 7 Hz, 1 H), 2.50 (m, 2 H), 2.10 (td, *J* = 13, 7 Hz, 1 H), 1.10 (m, 1 H). ^{13}C NMR: δ = 207.8 (d), 200.9 (s), 174.0 (s), 172.0 (s), 107.5 (s), 96.0 (s), 65.2 (t), 64.5 (t), 53.7 (d), 51.8 (q), 37.4 (t), 37.1 (t), 27.7 (t), 27.2 (t). EI MS: *m*/*z* (%) = 298 (5) [M^+], 280 (18) [$M^+ - H_2O$], 181 (100), 109 (32), 99 (40). CI (NH_3) MS: *m*/*z* (%) = 316 ([M + NH_4]$^+$, 90), 299 (MH^+, 100), 281 ($MH^+ - H_2O$, 3). IR (neat, cm^{-1}): ṽ = 3510, 2935, 2898, 2728, 1730, 1712, 1660, 1617, 1282, 1228, 1194.

Silyl Ether 15a: Lutidine (34.5 mL, 292 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (32 mL, 146 mmol) were added dropwise to a solution of crude alcohol **14a** (21.03 g, 71.00 mmol) in CH_2Cl_2 (530 mL) at 0 °C under argon. The resulting solution was warmed to room temperature and stirred for 1 h, then HCl (400 mL of 1 N solution) was added. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 400 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by chromatography (EtOAc/cyclohexane, 30:70) to give 21.88 g (73%, 2 steps) of **15a** which was recrystallized from pentane as white plates. M.p. 75−76 °C. ^{1}H NMR: δ = 6.90 (dd, *J* = 10, 4 Hz, 1 H), 5.90 (d, *J* = 10 Hz, 1 H), 5.00 (d, *J* = 4 Hz, 1 H), 4.10−3.93 (m, 4 H), 3.92 (s, 1 H), 3.72 (s, 3 H), 2.80−2.50 (m, 2 H), 2.20−1.90 (m, 2 H), 0.80 (s, 9 H), 0.10 (s, 6 H). ^{13}C NMR: δ = 203.8 (s), 194.1 (s), 168.3 (s), 149.4 (d), 129.6 (d), 108.0 (s), 66.6 (s), 66.3 (d), 65.9 (t), 64.7 (t), 53.6 (d), 53.0 (q), 36.4 (t), 32.7 (t), 25.7 (q), 17.9 (s), −4.0 (q), −5.0 (q). GC analysis (AT-5, 0.32 mm id. × 30 m, 160−300 °C, 10 °C/min), retention time 11.16 min. EI MS: *m*/*z* (%) = 410 (1) [M^+], 353 ($M^+ - t$Bu, 40), 321 ($M^+ - t$Bu − CH_3OH, 57), 293 (21), 277 (18), 249 (18), 221 (13), 99 (100), 89 (40), 73 (50), 55 (29). IR (neat, cm^{-1}): ṽ = 2954, 2928, 2257, 1750, 1720, 1681, 1228, 1088. $C_{20}H_{30}O_7Si$ (MW, 410.55): calcd. C 58.50, H 7.37; found C 58.15, H 7.29.

Silyl Ether 15b: A solution of dry *m*-CPBA (1.9 g, 7.7 mmol) in methanol (20 mL) was added dropwise to a solution of furan **12** (1.2 g, 4.28 mmol) in dry methanol (40 mL) at 0 °C. The resulting solution was stirred for 5 h at 0 °C and for 48 h between 5 and 10 °C. Methanol was evaporated under reduced pressure, the residue was diluted with CH_2Cl_2 (30 mL), and KF (0.5 g, 8.60 mmol) was added to the resulting mixture. The suspension was stirred for 12 h at 5 °C, filtered, and the solution was evaporated under reduced pressure. The residue was purified by chromatography (EtOAc/cyclohexane, 50:50) to give **14a** and **14b** (382 mg, 47%; 70:30). Lutidine (0.56 mL, 4.86 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.69 mL, 3.0 mmol) were added successively to a 0 °C solution of **14a** and **14b** (382 mg, 1.29 mmol) in CH_2Cl_2 (6 mL) under argon. The same procedure was used as described above. The residue was purified by preparative TLC on silica gel (EtOAc/cyclohexane, 40:60) to give silyl ether **15a** (189 mg, 36%) and silyl ether **15b** (126 mg, 24%) as a colorless oil. ^{1}H NMR: δ = 6.92 (dd, *J* = 10, 3 Hz, 1 H), 5.90 (dd, *J* = 10, 2 Hz, 1 H), 4.97 (dd, *J* = 3, 2 Hz, 1 H), 4.10−3.90 (m, 4 H), 3.71 (s, 3 H), 3.50 (d, *J* = 2 Hz, 1 H), 2.99 (ddd, *J* = 15, 13, 6 Hz, 1 H), 2.50 (dt, *J* = 15, 6 Hz, 1 H), 2.30 (td, *J* = 13, 6 Hz, 1 H), 2.00−1.90 (m, 1 H), 0.80 (s, 9 H), 0.10 (s, 6 H). ^{13}C NMR: δ = 203.0 (s), 193.2 (s), 170.4 (s), 151.3 (d), 128.2 (d), 107.9 (s), 66.7 (s), 65.7 (d), 65.9 (t), 63.8 (t), 55.5 (q), 53.1 (d), 38.7 (t), 33.0 (t), 26.4 (q), 18.0 (s), −4.0 (q), −5.0 (q). GC analysis (AT-5, 0.32 mm id. × 30 m, 160−300 °C, 10 °C/min), retention time 12.00 min. EI MS: *m*/*z* (%) = 410 (2) [M^+], 353 ($M^+ - t$Bu, 38), 321 ($M^+ - t$Bu − CH_3OH, 55), 293 (25), 277 (20), 221 (13), 99 (100), 89 (40), 73 (50), 55 (29). IR (neat, cm^{-1}): ṽ = 2956, 2930, 2258, 1749, 1718, 1228, 1090.

Enone 17 and Acetal 18: Al_2O_3 (800 mg) was added to a solution of enone **15a** (130 mg, 0.31 mmol) in Et_2O (6 mL) and the resulting mixture was refluxed for 23 h. The mixture was cooled to room temperature, filtered, and the solvent evaporated under reduced pressure. The residue was purified by chromatography on silica gel (EtOAc/cyclohexane, 30:70) to give **17** (91 mg, 70%) as a white solid, starting material **15a** (10 mg, 7%) and **18** (20 mg, 15%) as colorless oils. **17:** M.p. 150−151 °C (MeOH). ^{1}H NMR: δ = 6.34 (dd, *J* = 10.5, 2 Hz, 1 H), 5.90 (dd, *J* = 10.5, 2 Hz, 1 H), 4.90 (t, *J* = 2 Hz, 1 H), 4.49−4.41 (m, 1 H), 4.31−4.23 (m, 1 H), 4.07−3.96 (m, 2 H), 3.67 (s, 3 H), 3.18 (td, *J* = 15, 5.5 Hz, 1 H), 2.94 (s, 1 H), 2.43 (ddd, *J* = 15, 5.5, 3 Hz, 1 H), 2.02−1.92 (m, 1 H), 2.30 (td, *J* = 15, 4.5 Hz, 1 H), 0.82 (s, 9 H), 0.19 (s, 3 H), 0.16 (s, 3 H). ^{13}C NMR: δ = 203.4 (s), 192.0 (s), 168.6 (s), 145.1 (d), 129.5 (d), 106.4 (s), 68.6 (d), 67.6 (s), 67.0 (t), 66.0 (t), 55.6 (q), 52.2 (d), 37.6 (t), 37.2 (t), 25.6 (q), 18.0 (s), −4.5 (q), −4.8 (q). **18:** − ^{1}H NMR: δ = 5.42 (s, 1 H), 5.03 (d, *J* = 10 Hz, 1 H), 4.52−4.48 (m, 1 H), 4.29−4.22 (m, 1 H), 4.08−3.89 (m, 2 H), 3.74 (s, 3 H), 3.75−3.69 (m, 1 H), 3.32 (d, *J* = 2 Hz, 1 H), 2.60−2.48 (m, 2 H), 2.11−2.02 (m, 2 H), 1.82−1.68 (m, 1 H), 1.61−1.53 (m, 1 H), 0.82 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H). ^{13}C NMR: δ = 203.8 (s), 174.2 (s), 107.1 (s), 102.6 (s), 73.9 (d), 73.8 (d), 65.2 (t), 63.8 (t), 56.7 (s), 52.9 (d), 52.6 (q), 43.5 (t), 32.9 (t), 30.9 (t), 25.5 (q), 17.9 (s), −4.9 (q), −5.4 (q). CI (NH_3) MS: *m*/*z* (%) = 446 ([M + NH_4]$^+$, 40), 429 (MH^+, 70), 428 (80) [M^+], 411 ($MH^+ - H_2O$, 3).

Diketone 19: A solution of enone **15a** (12.0 g, 29.26 mmol) in methanol (600 mL) was hydrogenated for 2 h under atmospheric pressure in the presence of 10% palladium on charcoal (50 mg). The suspension was filtered through Celite and the resulting solution was concentrated under reduced pressure. The resulting solid was purified by chromatography (EtOAc/cyclohexane, 30:70) to give **19** (11.25 g, 93%) as white crystals. M.p. 91−92 °C (pentane). ^{1}H NMR: δ = 4.58 (dd, *J* = 7, 3 Hz, 1 H), 4.05−3.80 (m, 4 H), 3.72 (s, 3 H), 2.86−2.72 (dd, *J* = 7, 3 Hz, 1 H), 2.60−2.32 (m, 3 H), 2.26−1.94 (m, 4 H), 0.80 (s, 9 H), 0.00 (s, 6 H). ^{13}C NMR: δ = 207.3 (s), 204.5 (s), 168.6 (s), 107.2 (s), 68.9 (d), 66.3 (s), 65.6 (t), 64.2 (t), 55.4 (d), 53.0 (q), 37.2 (t), 36.2 (t), 31.5 (t), 28.8 (t), 25.6 (q), 17.9 (s), −4.6 (q), −5.1 (q). GC analysis (AT-5, 0.32 mm id. × 30 m, 150−325 °C, 10 °C/min), retention time 11.78 min. EI MS: *m*/*z* (%) = 412 (3) [M^+], 397 (1), 381 (1), 355 ($M^+ - t$Bu, 100), 295 (50), 251 (35), 205 (27), 99 (90), 75 (95), 59 (50), 41 (25). CI MS: *m*/*z* (%) = 430 ([M + NH_4]$^+$, 16), 413 (MH^+, 100). IR (neat, cm^{-1}): ṽ = 2951, 2886, 2855, 1744, 1722, 1255, 1103. $C_{20}H_{32}O_7Si$ (412.57): calcd. C 58.21, H 7.83; found C 57.75, H 7.82.

Alcohol 20a: Lithium tri-*tert*-butoxyaluminohydride (73 mL of a 1.1 M solution in THF, 80.3 mmol) was added dropwise to a solution of diketone **19** (19.1 g, 46.35 mmol) in THF (1000 mL) at − 60 °C under argon. The reaction mixture was warmed to room temperature, stirred overnight, and diluted with Et_2O (500 mL). The resulting solution was treated with saturated aqueous am-

monium chloride solution (100 mL), filtered through Celite, dried ($MgSO_4$), and concentrated under reduced pressure to give crude **20a** (17.53 g) as a white solid which was used in the next step without further purification. An analytical sample can be obtained by recrystallization in 95% ethanol as a white solid. M.p. 119−120 °C. ^{1}H NMR: δ = 4.64 (dd, *J* = 7, 3 Hz, 1 H), 4.20 (td, *J* = 7, 3 Hz, 1 H), 4.05−3.95 (m, 4 H), 3.71 (s, 3 H), 3.02 (d, *J* = 3 Hz, 1 H), 2.65−2.41(m, 3 H), 2.31−2.20 (m, 1 H), 2.00−1.80 (m, 2 H), 1.62−1.50 (m, 3 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.03 (s, 3 H). ^{13}C NMR: δ = 205.4 (s), 169.5 (s), 109.4 (s), 68.7 (d), 65.6 (d), 64.7 (t), 64.2 (t), 62.2 (s), 52.5 (q), 48.0 (d), 35.7 (t), 31.9 (t), 26.8 (t), 24.2 (t), 25.8 (q), 17.9 (s), −4.7 (q), −5.2 (q). GC analysis (AT-5, 0.32 mm id. × 30 m, 220−300 °C, 10 °C/min), retention time 6.78 min. EI MS: *m*/*z* (%) = 414 (14) [M$^+$], 357 (M$^+$ − *t*Bu, 13), 307 (43), 99 (95), 89 (30), 75 (100), 55 (34), 41(17). IR (neat, cm^{-1}): ṽ = 3525, 2950, 2923, 2893, 1735, 1718, 1246, 1107. $C_{20}H_{34}O_7Si$ (414.59): calcd. C 57.94, H 8.27; found C 57.94, H 8.41.

***cis*-β-Hydroxy Ketone 21:** Cerium chloride heptahydrate (46.72 g, 127.70 mmol) and sodium iodide (1.3 g, 8.36 mmol) were added to a solution of crude alcohol **20a** (17.53 g, 42.34 mmol) in dry acetonitrile (584 mL) under argon. The reaction mixture was heated to reflux for 3 h, cooled to room temperature, and diluted with Et_2O (450 mL). The resulting solution was washed with HCl (240 mL of a 0.5 N solution), saturated aqueous sodium hydrogen carbonate solution (240 mL), and brine (240 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by chromatography (MeOH/CH_2Cl_2, 1:99 to 2:98) to give **21** (13.37 g, 85%, 2 steps) and **22** (0.514 g, 3%) as white solids. **21:** M.p. 113−114 °C (95% ethanol). ^{1}H NMR: δ = 4.80 (br. s, 1 H), 4.47 (br. s, 1 H), 3.71 (s, 3 H), 3.25 (d, *J* = 3 Hz, 1 H), 2.91−2.79 (m, 1 H), 2.70−2.48 (m, 3 H), 2.22 (br. s, 1 H), 2.15−2.00 (m, 1 H), 1.97−1.82 (m, 1 H), 1.56−1.49 (m, 2 H), 0.83 (s, 9 H), 0.07 (s, 3 H), 0.00 (s, 3 H). ^{13}C NMR: δ = 210.5 (s), 203.2 (s), 169.5 (s), 69.2 (d), 68.5 (d), 63.4 (s), 53.3 (q), 51.6 (d), 36.3 (t), 34.9 (t), 26.8 (t), 23.6 (t), 25.7 (q), 17.9 (s), −4.0 (q), −5.4 (q). GC analysis (AT-5, 0.32 mm id. × 30 m, 175−325 °C, 10 °C/min), retention time 8.50 min. EI MS: *m*/*z* = 313 (30), 295 (35), 281 (10), 263 (30), 235 (50), 227 (45), 89 (70), 75 (100), 59 (30). CI MS: *m*/*z* (%) = 388 ([M + NH_4]$^+$, 100), 371 (MH$^+$, 75), 353 (45), 256 (10), 239 (75). IR (neat, cm^{-1}): ṽ = 3478, 2928, 2856, 1740, 1712, 1246. $C_{18}H_{30}O_6Si$ (370.53): calcd. C 58.34, H 8.16; found C 57.85, H 8.41.

***trans*-β-Hydroxy Ketone 22:** M.p. 122−123 °C (Et_2O). ^{1}H NMR: δ = 4.73 (br. s, 1 H), 3.75 (s, 3 H), 3.60−3.50 (m, 1 H), 3.23 (d, *J* = 11.5 Hz, 1 H), 3.04 (d, *J* = 1.5 Hz, 1 H), 2.80−2.60 (m, 4 H), 1.85−1.67 (m, 4 H), 0.85 (s, 9 H), 0.08 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR: δ = 208.5 (s), 202.1 (s), 168.4 (s), 68.6 (d), 68.5 (d), 67.0 (s), 54.5 (q), 53.5 (d), 35.9 (t), 35.6 (t), 27.7 (t), 27.5 (t), 25.7 (q), 18.0 (s), −4.0 (q), −5.3 (q). IR (neat, cm^{-1}): ṽ = 3427, 2953, 2885, 2856, 1741, 1718, 1244. $C_{18}H_{30}O_6Si$ (370.53): calcd. C 58.34, H 8.16; found C 58.31, H 8.18.

α, β-Unsaturated Ketone 23: PTSA (660 mg, 3.47 mmol) was added to a solution of alcohol **21** (13.37 g, 36.13 mmol) in benzene (870 mL). The reaction mixture was dehydrated under azeotropic distillation (Dean Stark) for 3 h, cooled to room temperature, and diluted with CH_2Cl_2 (80 mL). The resulting solution was washed with water (150 mL) and brine (150 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by chromatography (EtOAc/cyclohexane, 40:60) to give enone **22** (9.3 g, 72%) as a white solid. M.p. 118−119 °C (MeOH). ^{1}H NMR: δ = 7.20 (dd, *J* = 8, 4 Hz, 1 H), 4.67 (dd, *J* = 8, 3 Hz, 1 H), 3.72 (s, 3 H), 2.97−2.86 (m, 1 H), 2.81−2.41 (m, 4 H), 2.29−2.25 (m, 1 H), 2.06−1.92 (m, 1 H), 1.58−1.48 (m, 1 H), 0.85 (s, 9 H), 0.12 (s, 3 H), 0.05 (s, 3 H). ^{13}C NMR: δ = 201.3 (s), 193.3 (s), 168.8 (s), 142.3 (d), 131.5 (s), 67.9 (d), 65.8 (s), 53.3 (q), 35.2 (d), 35.0 (t), 27.5 (t), 25.7 (q), 22.5 (t), 17.9 (s), −4.0 (q), −5.4 (q). GC analysis (AT-5, 0.32 mm id. × 30 m, 175−325 °C, 10 °C/min), retention time 6.89 min. EI MS: *m*/*z* (%) = 295 (M$^+$ − *t*Bu, 50), 277 (10), 263 (50), 245 (15), 235 (100), 217 (20), 207 (10), 89 (50), 75 (80), 59 (40). CI MS: *m*/*z* (%) = 370 ([M + NH_4]$^+$, 85), 353 (MH$^+$, 100). IR (neat, cm^{-1}): ṽ = 2927, 2855, 1740, 1720, 1628, 1243. $C_{18}H_{28}O_5Si$ (352.51): calcd. C 61.33, H 8.00; found C 61.42, H 8.15.

Tertiary Alcohol 5a: Methyllithium (37.2 mL of a 1.6 M solution in Et_2O, 59.52 mmol) was added dropwise to a solution of enone **23** (9.3 g, 26.42 mmol) in anhydrous Et_2O (372 mL) at −78 °C. The reaction mixture was stirred for 30 min, warmed to 0 °C, and water (100 mL) added. The organic phase was separated and the aqueous phase was extracted with Et_2O (2 × 300 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and the solvents evaporated under reduced pressure. The crude product was purified by chromatography on silica gel (EtOAc/cyclohexane, 30:70) to give **5a** (3.160 g, 32%), **5b** (155 mg, 1.7%), **24a** (2.48 g, 26%), and **24b** (765 mg, 8%) as white solids.**5a:** M.p. 74−75 °C (*n*-hexane). ^{1}H NMR: δ = 6.30 (dd, *J* = 5, 2 Hz, 1 H), 4.40 (dd, *J* = 8, 3 Hz, 1 H), 3.69 (s, 3 H), 2.70 (td, *J* = 10, 3 Hz, 1 H), 2.56−2.42 (m, 1 H), 2.30−2.19 (m, 1 H), 2.12−2.58 (m, 6 H), 1.40 (s, 3 H), 0.80 (s, 9 H), 0.10 (s, 3 H), 0.05 (s, 3 H). ^{13}C NMR: δ = 204.6 (s), 169.9 (s), 139.7 (s), 128.9 (d), 71.3 (s), 69.0 (d), 65.3 (s), 52.9 (q), 36.0 (t), 35.5 (t), 30.6 (q), 27.4 (t), 23.5 (t), 25.7 (q), 18.0 (s), −4.0 (q), −5.4 (q). CI MS: *m*/*z* (%) = 386 ([M + NH_4]$^+$, 7), 369 (MH$^+$, 20), 351 (MH$^+$ − H_2O, 100), 319 (13). IR (neat, cm^{-1}): ṽ = 3456, 2931, 2855, 1740, 1715, 1657, 1256, 1218. HRMS calcd. for $C_{19}H_{33}O_5Si$ [MH$^+$] 257.20973, found 257.20520. $C_{19}H_{32}O_5Si$ (368.55): calcd. C 61.92, H 8.75; found C 61.92, H 8.79.

Tertiary Alcohol 5b: M.p. 100−102 °C (*n*-hexane). ^{1}H NMR: δ = 6.00 (dd, *J* = 7, 2 Hz, 1 H), 4.40 (dd, *J* = 8, 3 Hz, 1 H), 3.69 (s, 3 H), 3.30 (td, *J* = 10, 3 Hz, 1 H), 2.34−2.26 (ddd, *J* = 14, 5, 3 Hz, 1 H), 2.25−1.92 (m, 4 H), 1.79−1.76 (m, 1 H), 1.68−1.55 (m, 2 H), 1.42 (s, 3 H), 0.82 (s, 9 H), 0.12 (s, 3 H), 0.09 (s, 3 H). ^{13}C NMR: δ = 205.0 (s), 172.0 (s), 140.0 (s), 127.0 (d), 71.4 (s), 69.0 (d), 65.3 (s), 52.3 (q), 39.0 (t), 37.0 (t), 29.5 (q), 27.0 (t), 25.7 (q), 23.5 (t), 18.0 (s), −4.0 (q), −5.4 (q). CI MS: *m*/*z* (%) = 386 ([M + NH_4]$^+$, 2), 369 (MH$^+$, 20), 351 (MH+ − H_2O, 100), 337 (20), 319 (20). $C_{19}H_{32}O_5Si$ (368.55): calcd. C 61.92, H 8.75; found C 62.03, H 8.83.

β-Methyl Ketone 24a: M.p. 73 °C (EtOH 95%). ^{1}H NMR: δ = 4.73 (t, *J* = 3 Hz, 1 H), 3.71 (s, 3 H), 2.98 (d, *J* = 11 Hz, 1 H), 2.68−2.61 (m, 4 H), 1.80−1.65 (m, 2 H), 1.50−1.38 (m, 3 H), 0.94 (d, *J* = 6 Hz, 3 H), 0.84 (s, 9 H), 0.06 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR: δ = 206.7 (s), 203.1 (s), 169.3 (s), 68.7 (d), 67.0 (s), 55.8 (d), 53.2 (q), 36.8 (d), 35.4 (t), 32.1 (t), 29.5 (t), 28.0 (t), 25.8 (q, 2 C), 25.7 (q), 19.6 (q), 18.0 (s), −4.0 (q), −5.3 (q). $C_{19}H_{32}O_5Si$ (368.55): calcd. C 61.92, H 8.75; found C 62.23, H 8.86.

β-Methyl Ketone 24b: M.p. 114−115 °C (EtOH 95%). ^{1}H NMR: δ = 4.10 (dd, *J* = 12, 5 Hz, 1 H), 3.70 (s, 3 H), 2.90−2.85 (m, 1 H), 2.68−2.54 (m, 3 H), 2.51−2.43 (m, 1 H), 2.37 (d, *J* = 5 Hz, 1 H), 2.08−1.92 (m, 1 H), 1.70−1.58 (m, 2 H), 1.53−1.43 (m, 1 H), 1.18 (d, *J* = 7 Hz, 3 H), 0.85 (s, 9 H), 0.12 (s, 3 H), 0.11 (s, 3 H). ^{13}C NMR: δ = 206.4 (s), 202.7 (s), 169.5 (s), 71.3 (d), 62.9 (s), 55.4 (2 C), 52.3 (q), 36.7 (d), 34.8 (t), 29.6 (t), 27.1 (t), 26.9 (q), 25.8 (q, 3C), 18.0 (s), −4.4 (q), −4.8 (q). GC analysis (AT-5, 0.32 mm id. × 30 m, 225−325 °C, 10 °C/min), 311 (M$^+$ − *t*Bu, 55), 293 (M$^+$ − *t*Bu − H_2O), 251 (M$^+$ − *t*Bu − H_2O − CH_3COOH, 80), 223

(50), 131 (30), 89 (50), 75 (100), 59 (50), 41 (50). CI MS: *m/z* (%) = 369 (MH^+, 100). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2928, 2855, 1754, 1720, 1245. $C_{19}H_{32}O_5Si$ (368.55): calcd. C 61.92, H 8.75; found C 61.88, H 8.77.

Enone 4: An acetone solution of dimethyldioxirane[21] (650 mL) was added to a solution of alkene **5a** (930 mg, 2.52 mmol) in acetone (8.25 mL). The resulting solution was stirred for 60 h at 15 °C and concentrated under reduced pressure. The residue was diluted with Et_2O. The organic phase was separated and the aqueous phase extracted with Et_2O (2 × 100 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and the solvents evaporated under reduced pressure. The crude product was purified by chromatography (EtOAc/cyclohexane, 30:70) to give **4** (731 mg, 76%) and **25b** (192 mg, 20%) as white crystals. **4:** M.p. 163−164 °C (pentane). ^1H NMR: δ = 6.48 (s, 1 H), 4.75 (dd, *J* = 12, 6 Hz, 1 H), 3.78 (s, 3 H), 2.90−2.83 (m, 2 H), 2.67−2.60 (m, 2 H), 2.20−2.10 (m, 1 H), 2.00−1.83 (m, 2 H), 1.54 (s, 3 H), 0.82 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H). ^{13}C NMR: δ = 201.4 (s), 197.7 (s), 167.7 (s), 160.6 (s), 127.2 (d), 71.5 (s), 68.3 (d), 65.9 (s), 53.0 (q), 43.7 (t), 36.7 (t), 36.4 (t), 28.8 (q), 25.8 (q), 18.0 (s), −4.6 (q), −5.0 (q). GC analysis (AT-5, 0.32 mm id. × 30 m, 200−320 °C, 10 °C/min), retention time 6.97 min. EI MS: *m/z* (%) = 307 (100), 275 (20), 247 (18), 231 (25), 207 (60), 75 (62). CI MS: *m/z* (%) = 400 ($[M + NH_4]^+$, 88), 383 (MH^+, 100), 367 (60). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3450, 2952, 2929, 2856, 1738, 1724, 1673, 1622, 1249. $C_{19}H_{30}O_6Si$ (382.53): calcd. C 59.66, H 7.90; found C 59.87, H 8.12.

Epoxide 25: M.p. 101−102 °C (pentane). ^1H NMR: δ = 4.32 (dd, *J* = 11, 5 Hz, 1 H), 3.72 (s, 3 H), 3.44 (d, *J* = 3.5 Hz, 1 H), 2.79 (ddd, *J* = 16, 11, 6 Hz, 1 H), 2.52−2.41 (m, 1 H), 2.40 (s, 1 H), 2.25−2.15 (m, 1 H), 2.08−1.48 (m, 5 H), 1.35 (s, 3 H), 0.76 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 3 H). ^{13}C NMR: δ = 202.4 (s), 168.7 (s), 69.9 (s), 68.8 (s), 68.2 (d), 63.6 (s), 56.7 (d), 52.2 (q), 37.2 (t), 36.7 (t), 25.7 (q), 25.4 (t), 24.4 (q), 21.5 (t), 18.0 (s), −4.6 (q), −5.0 (q). GC analysis (DB5MS, 0.32 mm id. × 30 m, 200−300 °C, 10 °C/min), retention time 5.17 min. EI MS: *m/z* (%) = 327 ($[M^+ - t\text{Bu}]$, 100), 309 (30), 291 (40), 227 (10). CI MS: *m/z* (%) = 402 ($[M + NH_4]^+$, 25), 385 (MH^+, 60), 367 (60), 270 (15), 253 (100). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3495, 2950, 2855, 1723, 1258, 1103. $C_{19}H_{32}O_6Si$ (384.54): calcd. C 59.34, H 8.39; found C 59.21, H 8.46.

Acetate 27: Prepared from **5a** by the same procedure as for enone **4** but at 30 °C (yield 7%). M.p. 100−101 °C (*n*-hexane/EtOAc). ^1H NMR: δ = 6.33 (d, *J* = 5 Hz, 1 H), 5.40 (q, *J* = 5 Hz, 1 H), 4.65 (dd, *J* = 11.5, 4 Hz, 1 H), 3.71 (s, 3 H), 2.77 (td, *J* = 17, 6 Hz, 1 H), 2.61−2.51 (ddd, *J* = 17, 9, 5 Hz, 1 H), 2.60−1.70 (m, 4 H), 2.03 (s, 3 H), 1.47 (s, 3 H), 0.82 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H). ^{13}C NMR: δ = 203.1 (s), 170.6 (s), 168.7 (s), 145.5 (s), 125.1 (d), 71.4 (s), 66.7 (d), 65.7 (d), 65.5 (s), 52.5 (q), 36.1 (t), 36.0 (t), 35.7 (t), 33.3 (q), 30.0 (q), 25.7 (q), 18.0 (s), −4.6 (q), −4.8 (q). CI MS: *m/z* (%) = 444 ($[M + NH_4]^+$, 60), 427 (MH^+, 10), 409 (10), 367 (55), 209 (100). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3466, 2951, 2928, 2895, 2855, 1718, 1371, 1238, 1110.

Alcohol 28: A solution of enone **4** (860 mg, 2.25 mmol) in Et_2O (75 mL) was added dropwise to a solution of $LiAlH_4$ (560 mg, 14.70 mmol) in Et_2O (100 mL) at −10 °C under argon. The reaction mixture was stirred at −10 °C for 2 h, warmed to 0 °C, quenched with water (0.56 mL), NaOH (0.56 mL of a 15% solution), and water (1.68 mL), and stirred for 1 h. The resulting mixture was filtered and the solid residue was washed with diethyl ether. The solvent was removed under reduced pressure to give **28** (800 mg, 88%) as a colorless oil. The product was used without purification in the next step but can be purified by flash chromatography (EtOAc/cyclohexane, 90:10) to give **28** as a white solid. M.p. 78−80 °C (EtOAc/cyclohexane). ^1H NMR: δ = 6.20 (br. d, *J* = 1 Hz, 1 H), 4.30 (br. dd, *J* = 9, 6 Hz, 1 H), 4.07 (dd, *J* = 12, 4 Hz, 1 H), 3.85 (d, *J* = 10 Hz, 1 H, OH), 3.70 (s, 3 H), 3.30 (td, *J* = 10, 5 Hz, 1 H), 2.20−1.30 (m, 6 H), 1.20 (s, 3 H), 0.85 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H). ^{13}C NMR: δ = 173.5 (s), 141.6 (s), 127.5 (d), 79.8 (d), 75.4 (d), 72.7 (s), 65.7 (d), 57.0 (s), 51.6 (q), 39.8 (t), 38.1 (t), 30.2 (t), 27.3 (q), 25.9 (q), 18.0 (s), −3.7 (q), −4.8 (q). CI MS: *m/z* (%) = 404 ($[M + NH_4]^+$, 40), 387 (MH^+, 40), 369 ($MH^+ - H_2O$, 60), 299 (80). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3400, 2950, 2929, 2856, 1718, 1660, 1248, 1114, 836.

Epoxide 29: *m*-CPBA (1.277 g, 7.41 mmol, 75% with H_2O) was added portionwise to a solution of crude alkene **28** (800 mg, 2.07 mmol) in CH_2Cl_2 (60 mL). The reaction mixture was stirred for 1 h at room temperature and KF (1.280 g, 22.06 mmol) was added. The mixture was stirred for 30 min at room temperature, filtered, and the solvents evaporated under reduced pressure. The residue was purified by chromatography (EtOAc/cyclohexane, 90:10) to give epoxide **29** (700 mg, 77%, 2 steps) as a colorless oil. ^1H NMR: δ = 4.10−4.00 (m, 3 H), 3.76 (s, 3 H), 3.72 (br. s, 1 H, OH), 3.32 (m, 1 H), 2.10−1.40 (m, 6 H), 1.20 (s, 3 H), 0.84 (s, 9 H), 0.08 (s, 3 H), 0.05 (s, 3 H). ^{13}C NMR: δ = 173.6 (s), 78.8 (d), 75.0 (d), 70.6 (s), 67.3 (s), 65.6 (d), 58.7 (d), 55.1 (s), 51.6 (q), 35.5 (t), 34.4 (t), 29.3 (t), 25.7 (q), 24.1 (q), 17.9 (s), −4.4 (q), −4.8 (q). CI MS: *m/z* (%) = 420 ($[M + NH_4]^+$, 30), 403 (MH^+, 100), 385 (10), 371 (10). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3429, 2952, 2928, 2916, 2849, 1711, 1263, 1111, 907, 836, 732.

Epoxide 31: $VO(acac)_2$ (7.1 mg, 0.026 mmol) was added to a solution of alkene **28** (50 mg, 0.129 mmol) in benzene (1.5 mL) under argon, followed by dropwise addition of a solution of *t*BuOOH (0.24 mL of a 5−6 M solution in decane, 1.2 mmol). The reaction mixture was stirred for 1 h 30 min at room temperature and the benzene evaporated under reduced pressure. The residue was purified by chromatography (EtOAc/cyclohexane, 0:100 to 30:70) to give enone **30** (23 mg, 45%) and epoxide **31** (29 mg, 55%) as white solids. **Epoxide 31:** M.p. 157−158 °C (Et_2O/*n*-hexane, 1:1). ^1H NMR: δ = 4.30−4.19 (m, 2 H), 3.84−3.77 (m, 1 H), 3.82 (s, 3 H), 3.53 (d, *J* = 2 Hz, 1 H), 3.10−2.80 (br. s, 1 H, OH), 2.33 (ddd, *J* = 14.5, 9, 6 Hz, 1 H), 2.00−1.50 (m, 5 H), 1.17 (s, 3 H), 0.84 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H). ^{13}C NMR: δ = 172.4 (s), 76.2 (d), 73.4 (d), 69.4 (s), 68.6 (s), 64.4 (d), 57.6 (d), 55.1 (s), 52.2 (q), 37.7 (t), 37.5 (t), 30.0 (t), 25.8 (q), 23.1 (q), 17.9 (s), −3.5 (q), −4.6 (q). GC analysis (MDN5S, 0.32 mm id. × 30 m, 180−300 °C, 8 °C/min), retention time 10.95 min. CI MS: *m/z* (%) = 420 ($[M + NH_4]^+$, 0.5), 403 (MH^+, 100), 385 (30), 371 (10). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3428, 2950, 2928, 2895, 2857, 1719, 1248, 1095, 831, 777.

Enone 30: ^1H NMR: δ = 6.58 (s, 1 H), 4.45 (dd, *J* = 11, 7.5 Hz, 1 H), 3.90 (d, *J* = 12 Hz, 1 H, OH), 3.75 (s, 3 H), 3.50 (td, *J* = 12, 4 Hz, 1 H), 2.90 (dd, *J* = 15, 11 Hz, 1 H), 2.65 (dd, *J* = 15, 7.5 Hz, 1 H), 2.15−1.30 (m, 4 H), 1.28 (s, 3 H), 0.84 (s, 9 H), 0.12 (s, 3 H), 0.10 (s, 3 H). ^{13}C NMR: δ = 198.0 (s), 171.4 (s), 162.7 (s), 125.4 (d), 79.9 (d), 75.6 (d), 69.3 (s), 55.6 (s), 52.1 (q), 44.5 (t), 38.8 (t), 29.8 (t), 27.7 (q), 25.9 (q), 18.0 (s), −3.7 (q), −4.8 (q). GC analysis (MDN5S, 0.32 mm id. × 30 m, 180−300 °C, 8 °C/min), retention time 11.35 min. CI NH_3 MS: *m/z* (%) = 402 ($[M + NH_4]^+$, 90), 385 (MH^+, 1), 205 (100).

Alcohol 32: Prepared from acetate **27** by the same procedure as for alcohol **28** (yield 70%). Colorless oil. ^1H NMR: δ = 6.29 (d, *J* = 5.5 Hz, 1 H), 4.39−4.34 (m, 2 H), 3.96 (d, *J* = 10 Hz, 1 H, OH), 3.63 (s, 3 H), 3.39 (td, *J* = 10, *J* = 4 Hz, 1 H), 2.20−1.50 (m, 6 H), 1.10 (s, 3 H), 0.81 (s, 9 H), 0.08 (s, 3 H), 0.05 (s, 3 H). ^{13}C

Table 1. X-ray diffraction data

	14a	**17**	**33**
Empirical formula	$C_{14}H_{16}O_7$	$C_{20}H_{30}O_7Si$	$C_{19}H_{34}O_7Si$
Molecular mass	296.29	410.54	402.56
Crystal system	Tetragonal	Monoclinic	Monoclinic
Space group	$P4_12_12$	$P2_1/c$	$P2_1/c$
Parameters (Å)	a = 13.319(2) b = 13.319(2) c = 14.922(2)	a = 22.502(5) b = 8.317(2) c = 11.726(4) β = 91.81(5)°	a = 11.728(2) b = 7.841(2) c = 23.023(3) β = 92.08(8)°
Volume (Å^3)	2647.1(9)	2193.4(10)	2115.8(7)
Z	8	4	4
Density (calcd.)	1.487	1.243	1.264
μ (mm^{-1})	0.120	1.261	0.147
Diffractometer/detector	Synchrotron/Image plate MAR345	Philips PW1100	Synchrotron/Image plate MAR345
Radiation (Å)/monochromator	0.9678/Si(111)	1.5418/graphite	0.9530/Si(111)
Temperature (K)	193	293	113
Crystal size (mm)	0.2 × 0.2 × 0.1	0.5 × 0.3 × 0.2	0.1 × 0.1 × 0.05
Data collecting mode	Rotation	θ/2θ	Rotation
Number of measured reflections	13136	5652	9733
Completeness (%)	99.0	84.5	89.5
Number of independent reflections	1169	2951	2137
Number of observed reflections with $F \geq 2\sigma(F)$	1160	2641	2134
Rw (on F^2), all data	0.163	0.207	0.095
Rw (on F^2), observed data	0.162	0.200	0.094
R factor, all data	0.054	0.085	0.036
R factor, observed data	0.053	0.076	0.036
Parameter/F_o ratio	6.0	11.5	8.4
CCDC deposition number	194784	194785	194786

NMR: δ = 173.1 (s), 144.2 (s), 123.9 (d), 79.5 (d), 72.7 (2 C, s + d), 63.3 (d), 56.9 (s), 51.4 (q), 39.4 (t), 37.4 (t), 30.0 (t), 27.2 (q), 25.9 (q), 18.0 (s), −3.7 (q), −4.7 (q).

Epoxide 33: *m*-CPBA (650 mg, 3.77 mmol, 75% with H_2O) was added portionwise to a solution of alkene **32** (379 mg, 0.98 mmol) in CH_2Cl_2 (50 mL). The reaction mixture was stirred for 1 h at room temperature and KF (700 mg, 12 mmol) was added. The mixture was stirred for 30 min at room temperature, filtered, and the solvents evaporated under reduced pressure. The residue was purified by chromatography (EtOAc/cyclohexane, 90:10) to give epoxide **33** (310 mg, 78%) as a white solid. M.p. 151 °C (EtOAc). ^{1}H NMR: δ = 4.45−4.39 (m, 1 H), 4.32 (dd, J = 8, 6.5 Hz, 1 H), 3.86 (br. s, 1 H, OH), 3.79−3.72 (m, 1 H), 3.73 (s, 3 H), 3.72 (d, J = 2.5 Hz, 1 H), 3.40−2.80 (br. s, 2 H, OH), 2.05−1.72 (m, 5 H), 1.62−1.50 (m, 1 H), 1.14 (s, 3 H), 0.82 (s, 9 H), 0.09 (s, 3 H), 0.07 (s, 3 H). ^{13}C NMR: δ = 171.5 (s), 76.5 (d), 73.4 (d), 69.6 (s), 69.5 (s), 65.1 (d), 58.6 (d), 54.8 (s), 51.7 (q), 38.3 (t), 37.7 (t), 30.2 (t), 25.9 (q), 22.8 (q), 17.9 (s), −3.6 (q), −4.7 (q). CI MS: *m/z* (%) = 420 ([M + NH_4]$^+$, 1), 403 (MH^+, 100), 345 (10). IR (neat, cm^{-1}): ν̃ = 3427, 2951, 2856, 1722, 1249, 1092, 833, 779.

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