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Regioselective Pinacol Rearrangement of Unsymmetrical Cyclobutane-1,2-diols

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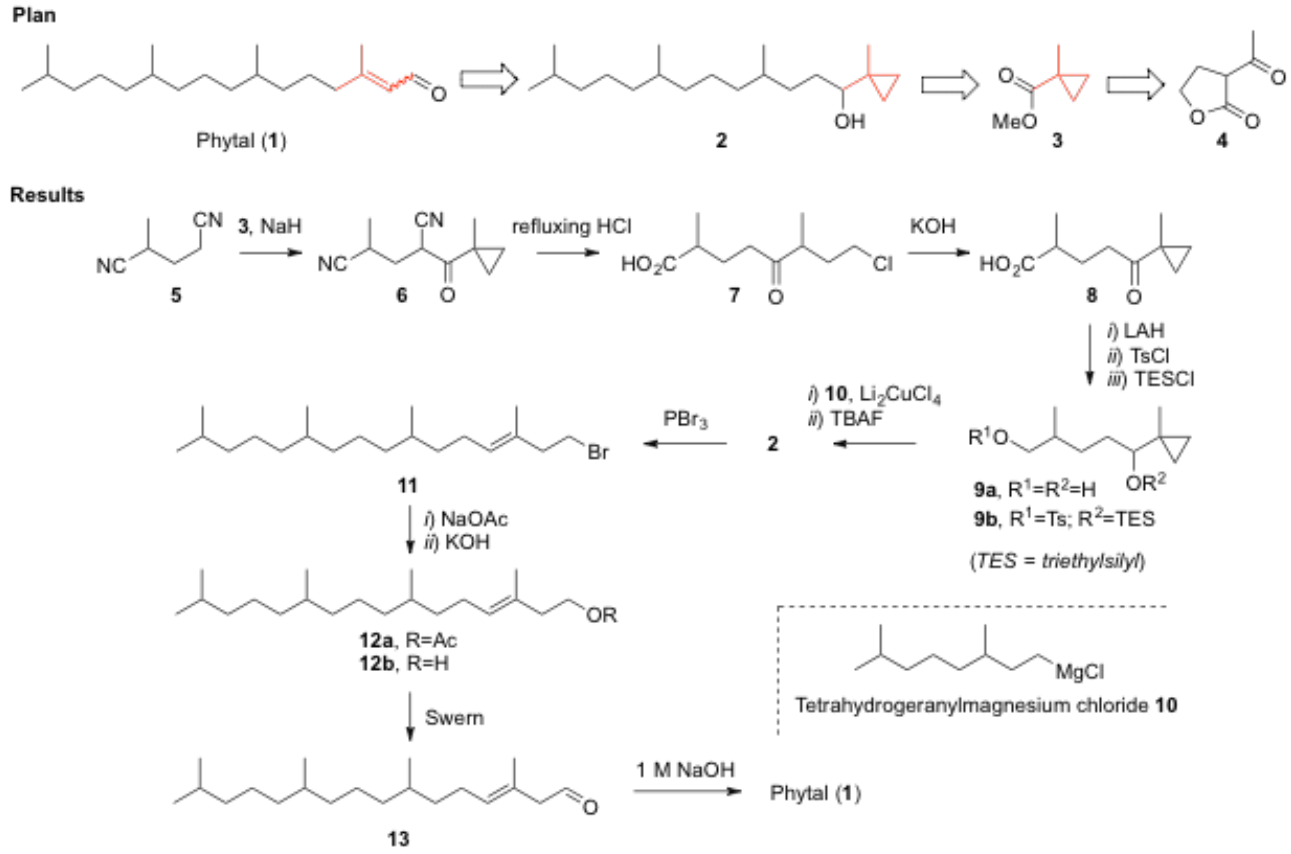
Abstract

Hydroxy-sulfone **34b**, prepared as a mixture of *trans* and *cis* isomers by condensing the *O*-silyl derivative **18c** of 2-hydroxy-2-methyl-cyclobutanone **18b** — the Norrish II photocyclisation product of 2,3-pentanedione **21** — and methyl phenyl sulfone **33** was found to rearrange selectively either to the cyclopropanic β-ketosulfone **37** or the isomeric methyl ketone **38** by using, respectively, the tosyl fluoride/DBU and the DAST reagent. The potential of this methodology has been illustrated by a synthesis of phytal **1** from geranylacetone **46**, and by the preparation from 3,4-hexanedione **51** and prenol **56** — *via* the cyclopropanic β-ketosulfone **54** (X-ray) — of an advanced fragment of the juvenile hormone molecule **59**.

1. Introduction

As exemplified in the polyprenol and the insect pheromone series, the conversion of cyclopropyl carbinols into homoallylic bromides in acid (Lewis or protic) conditions — i.e., the homoallylic rearrangement — has evolved as an efficient methodology to synthesize compounds with trisubstituted carbon-carbon double bonds.[1] With a view to designing a new access to phytal (**1**), a key intermediate to tocopherols,[2] the possibility of unveiling at a late stage of the synthesis the C1-C4 (red-coloured) residue of this aldehyde via homoallylic rearrangement of alcohol **2** had been studied (Scheme 1).[3]

To this end, ester **3**, prepared in four steps from acetobutyrolactone **4**,[4a] had been reacted with 2-methyl-glutaronitrile **5** — a facility of the Nylon 6-6 industry[5] — in basic conditions. Refluxing the keto-dinitrile **6** thus produced in conc. HCl, and then treating the resulting chloro-ketone **7** with KOH afforded the keto-acid **8**. Next, diol **9a**, formed by treatment of **8** with an excess of LAH, was sequentially reacted with tosyl chloride (TsCl) and triethylsilyl chloride (TESCl) to give tosylate **9b**, the Wurtz coupling of which with tetrahydrogeranylmagnesium chloride **10**, followed by hydrolysis of the silyl ether, furnished the cyclopropyl carbinol **2**. The latter was then converted into bromide **11** using PBr_3 under Johnson conditions.[1a] Finally, exchanging the bromine atom to an acetoxy group, hydrolyzing the acetate **12a** with KOH, and then oxidizing the resulting alcohol **12b** under Swern conditions afforded isophytal **13**, which was next isomerized to phytal (**1**) using diluted sodium hydroxide. Although our strategy was validated, in addition to the number

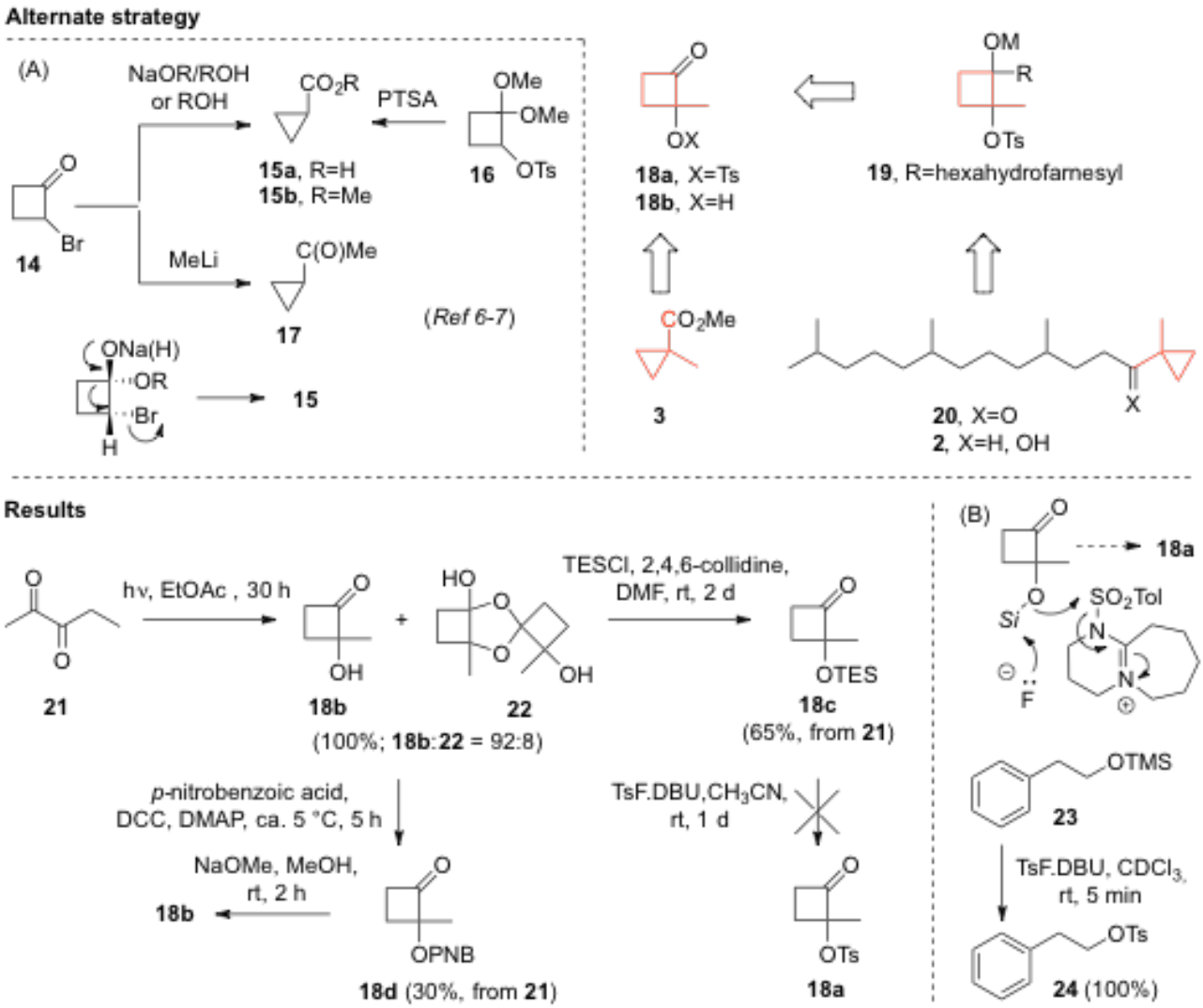


Scheme 1. Plan and synthesis of phytal (**1**) from ester **3**.

of steps and the lack of convergence, another concern was the limited availability of ester **3**. Although various preparative procedures have been designed,[4b-d] this compound is very expensive and, clearly, a more practical approach to the C_{20} alcohol **2** was desirable. To this end, the possibility of accessing this cyclopropyl carbinol by the ring-contraction process depicted in Scheme 2 was investigated, and our progress and observations along this line are reported in this publication.

2. Results and discussion

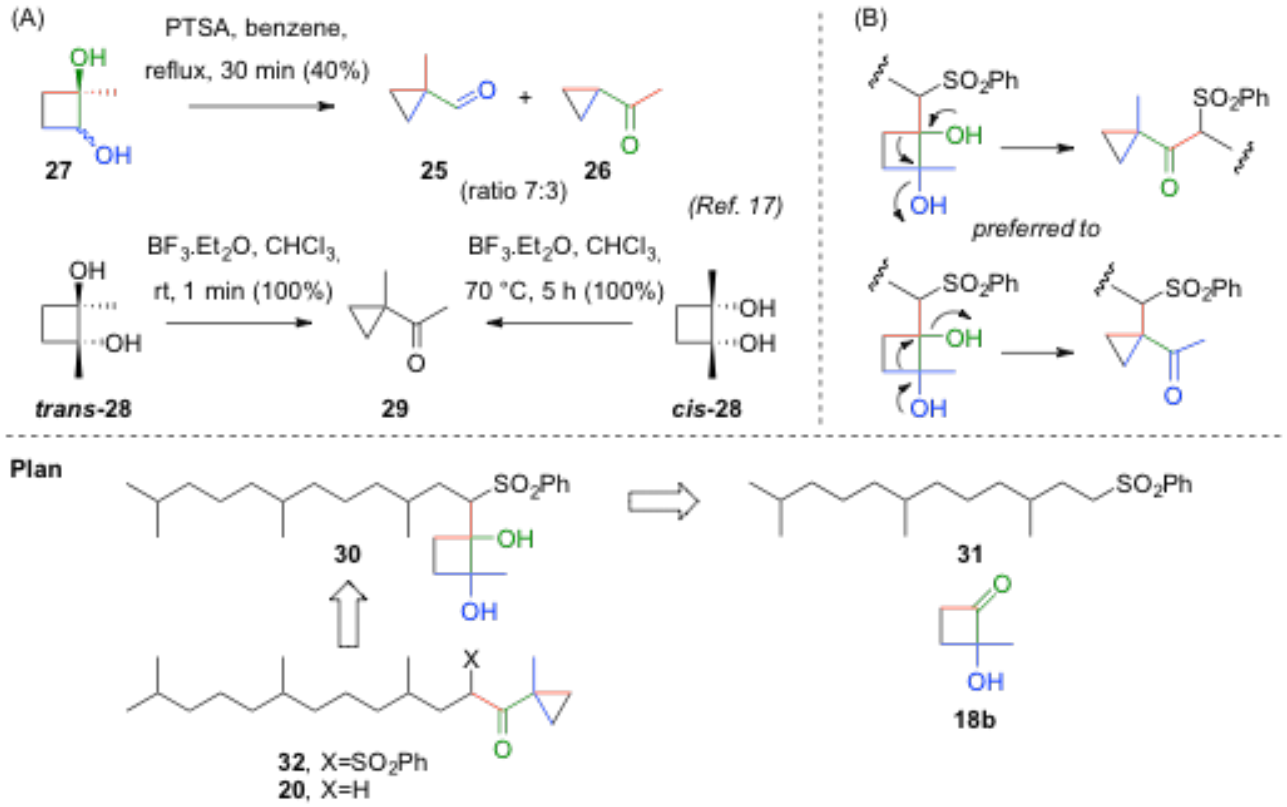
As exemplified in Scheme 2A, the Favorskii reaction of 2-halocyclobutanones (and related acetals) is well documented.[6-8] Whatever the pH conditions used, experiments in D_2O have shown that the rearrangement of 2-bromo-cyclobutanone **14** to cyclopropanecarboxylic acid **15a** does not proceed by the classical mechanism — i.e., the Loftfield cyclopropanone mechanism — but, more likely, by nucleophilic addition of D_2O (or the deuteroxide anion) to the carbonyl group followed, as indicated, by semibenzylic rearrangement of the tetrahedral intermediate;[6d,9] acceleration of this rearrangement process by added silver ion has been shown not to result from pre-dissociation of the carbon-halogen bond, thus excluding a cationic intermediate,[6f] and the rearrangement of acetal **16** into ester **15b** by treatment with *p*-toluenesulfonic acid (PTSA) is thought to proceed similarly.[7d] Interestingly, a related "pull-push" mechanism has been proposed for the formation of ketone **17** by reacting **14** with methyllithium (or the corresponding Grignard reagent);[6h] results obtained in the rearrangement in basic conditions of 2-chlorocyclobutanols with blocked configuration strongly supported this view, with only those chlorohydrins in which the chlorine atom occupies a pseudo-equatorial orientation rearranging to a cyclopropanecarboxaldehyde.[10] Keeping these observations in mind with a view to designing a convenient access to cyclopropyl carbinol **2**, the tosylate **18a** of the known[11] hydroxycyclobutanone **18b** was targeted in the hope, as depicted, that the alkoxide anion **19** formed by condensing **18a** and a hexahydrofarnesyl organometallic species would rearrange to ketone **20**, resulting in a straightforward access



Scheme 2. Alternate strategy from hydroxy-ketone **18b** and results.

to this alcohol, and thence to phytal **1** (another possibility being an access to ester **3** by methanolysis of **18a**).

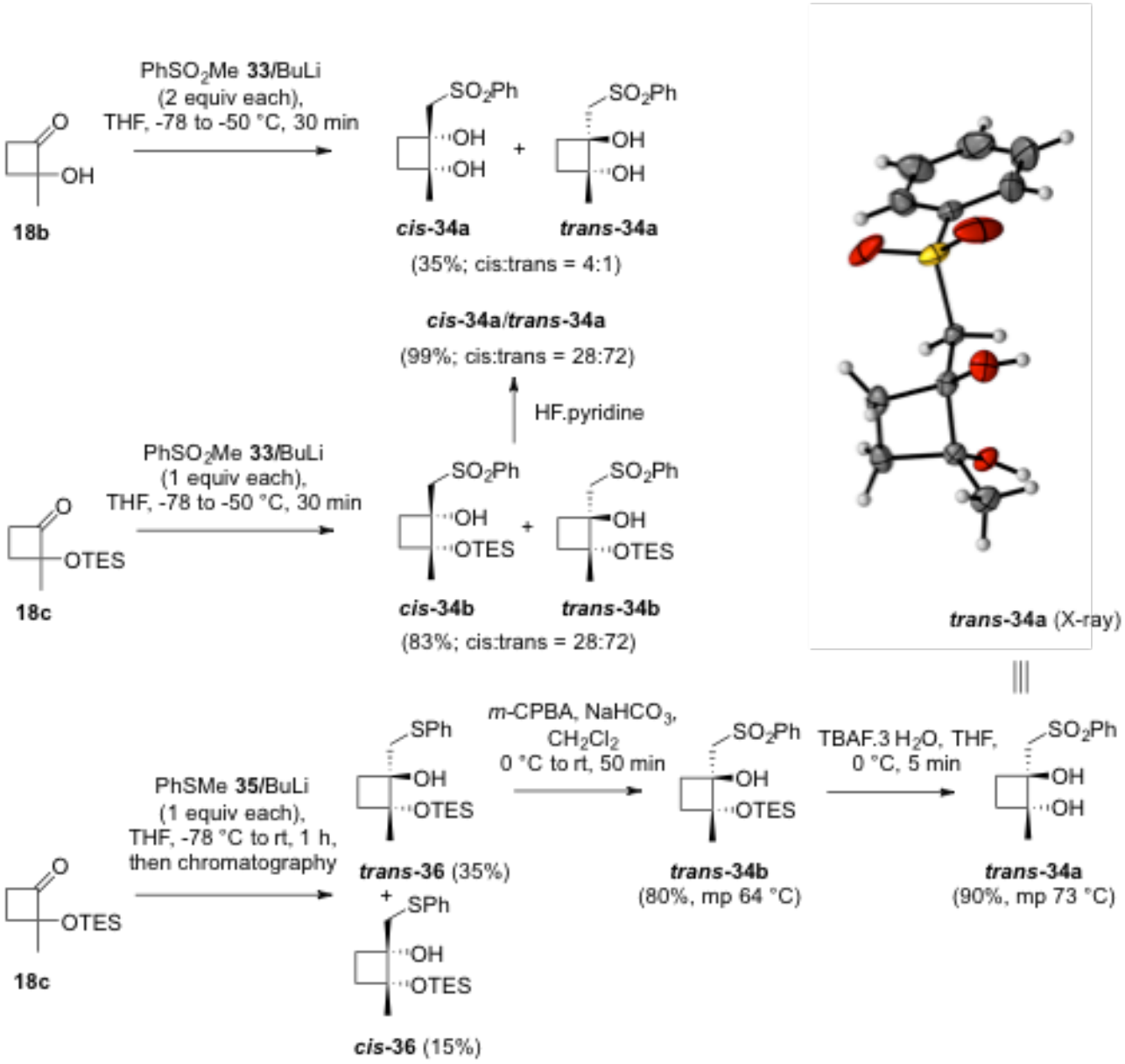
Ketone **18b** was prepared according to literature by irradiating a solution of 2,3-pentadione **21** in EtOAc (used in place of benzene[11a]) with a mercury lamp for ca. 30 h to obtain, after elimination of the solvents, a 92:8 mixture (GC) of ketone **18b** and its dimer **22**[11b] in virtually quantitative yield. Although purifying this mixture by column chromatography did furnish pure **18b**, only freshly-prepared **18b**/**22** mixtures were used owing to pronounced tendency of this ketone to give **22** on standing. Reacting **18b** with TsCl in standard conditions (in pyridine, alone or with added DMAP) resulted only in decomposition and the same observation was made using either the *N*-tosyl-*N*–methylimidazolium triflate[12a] or the TsCl•DABCO reagent,[12b] as recommended in case of hindered alcohols; no more success was encountered by treating the corresponding lithium (or potassium) alkoxide with TsCl in THF,[12c] or attempting to exchange the oxygen to a chlorine (or bromine) atom using conventional reagent conditions. The use of tosyl fluoride associated with DBU (TsF•DBU) as a reagent, and of an *O*-silyl derivative of **18b** as substrate was then considered. Nonaflyl fluoride (NFF) has proved to be a useful reagent for converting hindered alcohols into alkyl fluorides (via nonaflates) when DBU was used as a base[13] and, independently, conversion of *O*-TMS derivatives of various alcohols and enols to corresponding nonaflates has been efficiently realized by reacting these ethers with NFF in presence of tetraalkylammonium (or cesium) fluoride.[14] Although covalent catalysis was not probed in the former conditions, it could be envisioned, as depicted in Scheme 2B, that the *N*-tosylpyrimidoazepinium fluoride that TsF should



Scheme 3. Modified plan for synthesis of ketone **20** from hydroxycyclobutanone **18b**.

form with DBU would cleave the silyl ether, resulting in a fast tosylation process owing to conjunction of base and covalent catalysis. Indeed, reacting the *O*-TMS ether **23** with excess TsF and DBU in $CDCl_3$ (NMR tube experiment) afforded within a few minutes the tosylate **24** in virtually quantitative yield.[15] Accordingly, the alcohol function of **18b** was protected with a TES group (preferred to TMS owing to a better stability) by using TES chloride and added 2,4,6-collidine in DMF to obtain, after purification by column chromatography, the silyl ether **18c** in fair yield (overall 65%, from **21**); notably, using other base and solvent conditions failed to give **18c** and, in most cases, decomposition was observed. Deceptively, however, reacting **18c** with the TsF•DBU reagent in acetonitrile for a prolonged period failed to give tosylate **18a**. Attempted esterification of **18b** with carboxylic acids was no more rewarding: decomposition was observed either by reacting **18b** with *p*-nitrobenzoyl chloride or trifluroacetic anhydride and added DMAP in pyridine and, although ester **18d** could be obtained in low yield (30%) by reacting **18b** with *p*-nitrobenzoic acid and added DCC, treating this ester with NaOMe in methanol resulted in hydrolysis of the ester. This led us to modify our plan, with the pinacol rearrangement preferred to the preceding quasi-Favorskii reaction process (Scheme 3).

Consonant with observations made with 2-halocyclobutanones (vide supra), 1,2-cyclobutanediols rearrange in acidic conditions (Lewis or protic) to cyclopropylcarbonyl compounds.[6j,16,17] Except in case of phenyl substitution,[16b] and as illustrated in Scheme 3A by the formation of a 7:3 mixture of, respectively, 1-methyl-cyclopropanecarboxaldehyde **25** and cyclopropyl methyl ketone **26** by refluxing 1- methycyclobutane-1,2-diol **27** with PTSA in benzene,[17] controlling the regioselectivity of this rearrangement in case of unsymmetrical substitution was a potential problem. In addition, though of less significance, the rate of these rearrangements is dependent on stereoelectronic factors — the *trans*-diol ***trans*-28** rearranges to **29** faster than its *cis*-isomer ***cis*-28** — and controlling the stereoselectivity of the cyclobutanediol preparation process might have been desirable. As depicted in Scheme 3B, owing to strong electron-withdrawing property of the sulfonyl group, it could be surmised that the diol **30** formed by

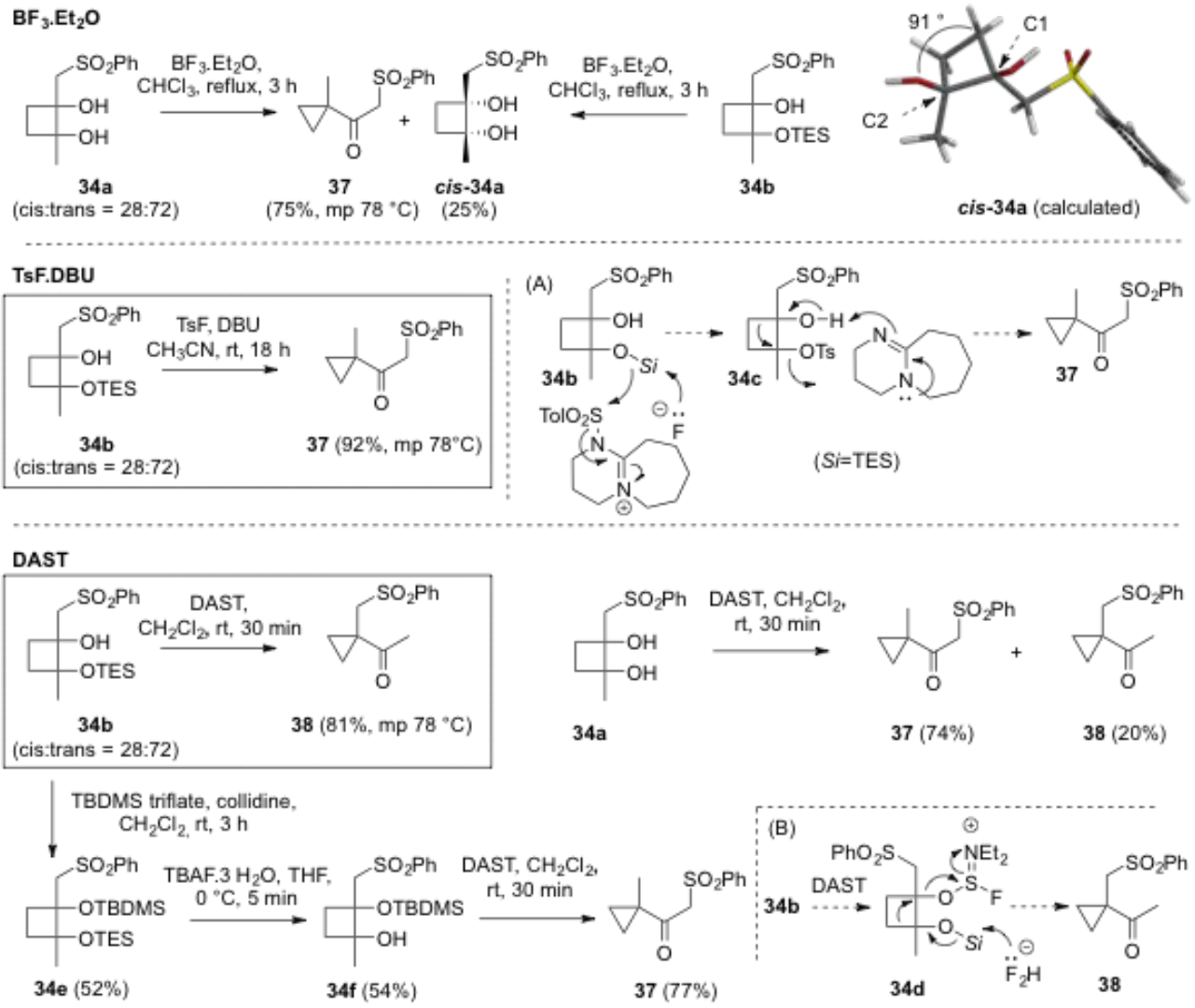


Scheme 4. Preparation of model diol-sulfones.

condensing **18b** and hexahydrofarnesyl phenyl sulfone **31** would rearrange selectively in acidic conditions into the β-ketosulfone **32**, potentially convertible into **20** by hydrogenolysis of the sulfone.

Model experiments were realized using methyl phenyl sulfone **33** (Scheme 4). *Syn*-selectivity (with regard to the methyl group) has previously been observed by reacting 1,2-cyclobutanedione with excess MeLi (or MeMgBr) in ether (or THF) to obtain, via the lithium (or magnesium) alkoxide of hydroxy-ketone **18b**, the diol ***cis*-28**,[6j,17] and indeed the *cis* diol-sulfone ***cis*-34a** was found to be the main product (***cis*-34a**:***trans*-34a** = 4:1; these structures were determined later) by reacting **18b** with the lithium anion of sulfone **33** (two-fold excess) in THF, although the yield was low (35%). A better result was registered by using the *O*-silylated ketone **18c** and a stoichiometric amount of this anion in otherwise the same conditions to obtain in good yield (83%) a 28:72 mixture (GC, ^{1}H NMR) of sulfones ***cis*-34b** and ***trans*-34b**, respectively; a ratio not significantly affected by varying the solvent, the metal, the temperature and the time conditions. Treating this silyl ether mixture with HF•pyridine afforded in high yield (99%) a mixture of the diol-sulfones ***cis*-34a** and ***trans*-34a** (same diastereomeric ratio).

Owing to their similar polarity in TLC, either separating the ***cis*-34a**/***trans*-34a** or the ***cis*-34b**/***trans*-34b** mixture by column chromatography proved unfeasible, a difficulty that



Scheme 5. Pinacol rearrangement of sulfones **34a** and **34b**.

was overcome by reacting **18c** with the lithio derivative of thioanisole **35** in similar conditions. After 1 h, TLC showed two new products, and these were efficiently separated by chromatography. Although NMR analysis strongly suggested that the minor product (15%) was ***cis*-36**, the major one (35%) thus being ***trans*-36**, a more rigorous structure assignment was secured by reacting the latter compound with *m*-CPBA to obtain sulfone ***trans*-34b** (80%, mp 64 °C), identified (by GC, ^{1}H NMR) to the main product of the **18c**-**33** condensation, and whose treatment by TBAF afforded a crystalline sulfone (90%, mp 73 °C), similarly identified as the minor component of the **18b**-**33** condensation product, and to which structure ***trans*-34a** was assigned by X-ray diffraction analysis. It thus follows that the main product of the **18c**-**35** condensation was the *trans*-sulfide ***trans*-36**, that the **18c**-**33** condensation proceeded with same *anti*-selectivity (***cis*-34b**/***trans*-34b** = 28:72), and that using hydroxyketone **18b** resulted in reversal of this selectivity, with formation of the *cis*-sulfone ***cis*-34a** as main product.

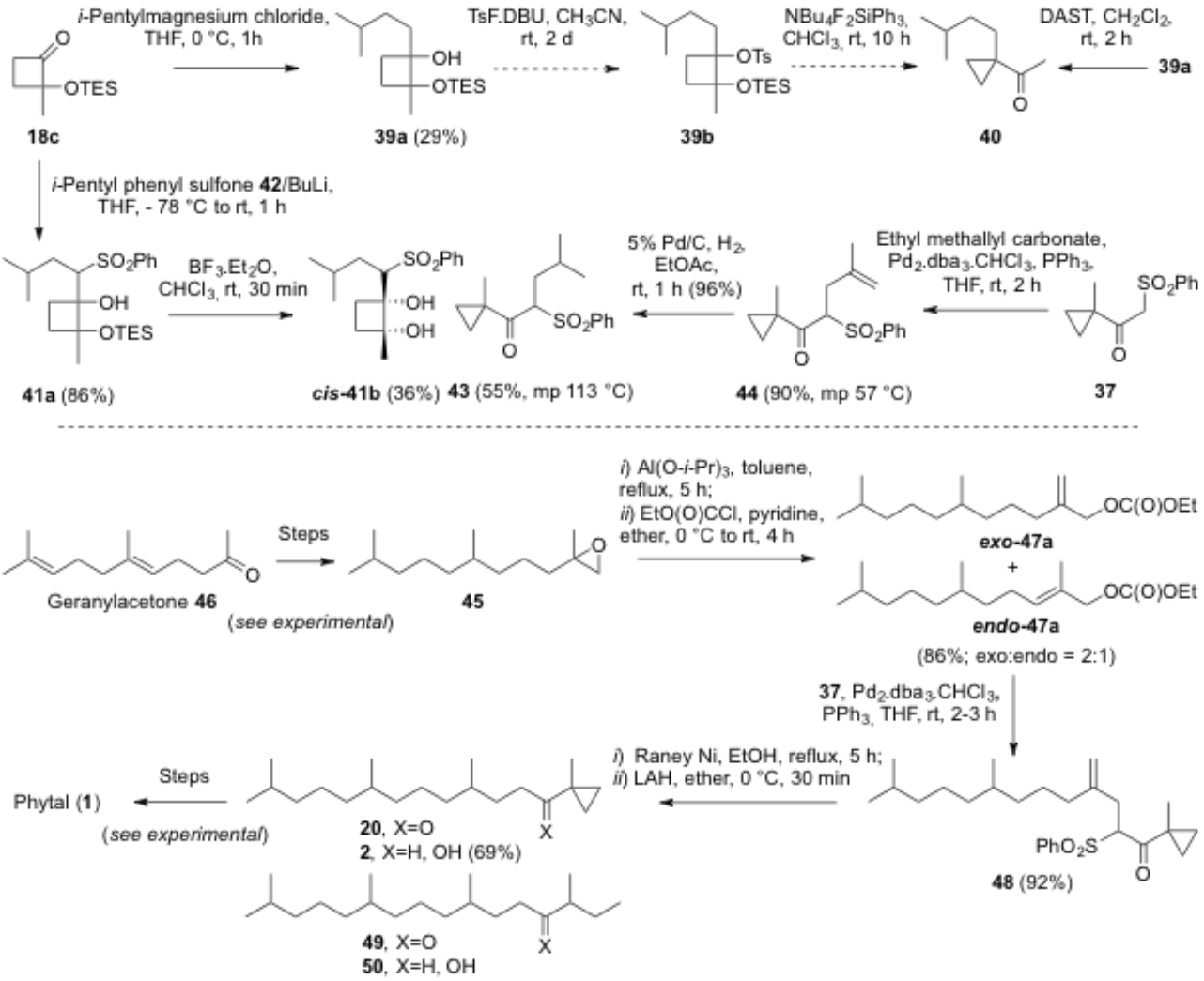
At contrast with results previously obtained with dimethylcyclobutanediol **28** (vide supra), no reaction was observed in TLC by reacting the preceding 28:72 diastereomeric diol-sulfone mixture with BF_3•Et_2O in $CHCl_3$ at room temperature. However, bringing the reaction mixture to reflux resulted in the formation of a new product, and 3 h later, when decomposition was visible, hydrolysis followed by column chromatography afforded successively the β-ketosulfone **37** (75%) as a white solid (mp 78 °C) and the pure *cis*-sulfone ***cis*-34a** (25%), the same result being obtained by using the silylated sulfone **34b** in place of **34a** (Scheme 5). In the same way, reacting the 4:1 diol-sulfone mixture in these conditions afforded **37** (24%), and ***cis*-34a**

(65%). The apparent lack of reactivity of the *cis*-isomer was confirmed either by refluxing ***cis*-34a** with BF_3•Et_2O in chloroform or PTSA in benzene: in each case, only partial decomposition was observed.

The lower reactivity of sulfone **34a**, as compared to dimethylcyclobutanediol **28** deserves a few comments. As pointed out by Conia,[17] in contrast with the *cis* isomer, in one conformation, the two OH groups of the *trans*-diol ***trans*-28** occupy a pseudoequatorial position and, accordingly, this diol should react faster, as observed. In the present case, owing to the negative inductive effect of the sulfonyl group, only the OH at C2 is displaced and sulfone ***trans*-34a** should not react as fast as ***trans*-28**, as observed. As to the observed dichotomy in reactivity of the *trans*- and the *cis*-isomer, in the solid state, the torsion angle formed by the C2-O and the C1-C4 bond of ***trans*-34a** approximates 145 °, compared with the indicated 91 ° value suggested by a modelling study of the corresponding torsion angle in ***cis*-34a**. Although the latter value rises to ca. 135 ° by linking the oxygen to BF_3, it is likely that anchimeric assistance of the C1-C4 sigma-bond electrons would hardly contribute in this case, thus explaining the lack of reactivity of ***cis*-34a** under these conditions.[18]

With control of the stereochemical fate of the **18c**-**33** condensation having proved difficult (vide supra), the only possibility for ensuring a full conversion of this diastereomeric mixture was to convert the OTES substituent into a good leaving group — "pull effect"— and, if possible, to increase the "push" ability of the C1 oxygen. To this end, the use of the TsF•DBU reagent was reconsidered. With failure to sulfonylate the hydroxyketone **18b** being imputable to strong deactivating effect (possibly electronic and steric) of the carbonyl group, it could be envisioned, as depicted in Scheme 5A, that **34b** would react with the putative *N*-tosyl-pyrimidoazepinium fluoride intermediate more easily than **18b** and, irrespective of the sulfone stereochemistry, that a fast rearrangement of the resulting tosylate **34c** would occur owing to anionisation of the C1 alcohol by DBU (pK_{BH+} 24.3). No reaction was observed by TLC upon reacting **34b** with an equivalent of TsF and DBU in acetonitrile at room temperature for 2 h. However, adding excess reagents (3 equiv. of each) to the reaction mixture resulted in the smooth formation of a new product, and 16 h later, when the reaction was completed, brief purification by chromatography of the product then isolated afforded the ketosulfone **37** in good yield (92%).

Although our goal was achieved, the possibility of reversing the regioselectivity of this rearrangement was studied. Previously, cyclobutanone cyanohydrin has been shown to rearrange, via a cyclobutonium ion, into a fluorinated cyclopropanecarbonitrile when reacted with DAST,[19] thus illustrating the remarkable ability of this reagent to amplify the leaving group ability of deactivated OH groups. Keeping in mind the preceding observations, this result strongly suggested that the sulfiminium fluoride **34d** which should form by reacting hydroxysulfone **34b** with DAST would evolve by intramolecular nucleophilic attack of the fluoride ion onto the silicon atom, with the result of a fast "push-pull" rearrangement to the methyl ketone **38** (Scheme 5B). This would extend a concept previously conceived to access the quadrone skeleton by pinacol rearrangement of a tricycloundecanediol,[20] and has now been verified in practice. As evidenced by TLC analysis, adding DAST to a solution of **34b** in CH_2Cl_2 at room temperature resulted within a few minutes in the formation of a new product and 30 min later, when the reaction was completed, a solid product (mp 78 °C) assigned by NMR as **38** was isolated in good yield (81%). The significant role of the silyl protection was evidenced by reacting the diol-sulfone **34a** with DAST to obtain, after separation by column chromatography, the β-ketosulfone **37** (74%) and the isomeric methyl ketone **38** (20%). Although of no immediate interest given the preceding result with TsF and DBU, the possibility to orient this rearrangement towards sulfone **37** was studied by reacting the lithium alkoxide formed in the **18c**/**33** condensation with *t*-butyldimethylsilyl triflate (TBDMSOTf); selective hydrolysis of the bis-silyl ether **34e** would have provided **34f**, potentially convertible into **37** by treatment with DAST. Although the planned quenching experiment did not succeed, this was realized stepwise by reacting **34b** with TBDMSOTf and added

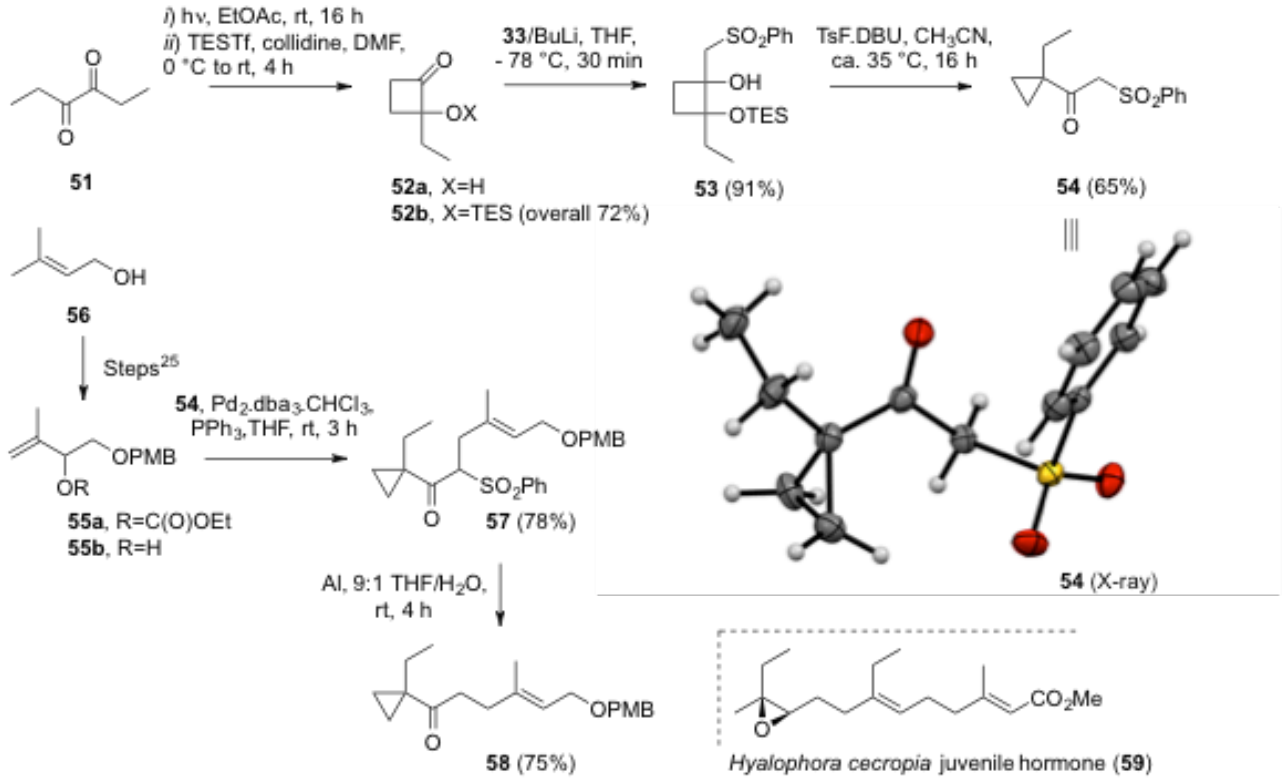


Scheme 6. Application to phytal (**1**) synthesis.

collidine in DMF to obtain **34e** (52%). Hydrolyzing selectively the TES ether of **34e** proved delicate and, using the best conditions founded so far, the *O*-TBDMS derivative **34f** was obtained in moderate yield (54%), alongside diol-sulfone **34a** (44%) by using TBAF at low temperature in THF. As expected, treating **34f** by DAST under the preceding conditions afforded the β-ketosulfone **37** (77%).

The application of these results to phytal (**1**) synthesis was then investigated (Scheme 6). Although it was later to prove otherwise, recourse to a sulfonyl group to control the selectivity of the pinacol reaction seemed unnecessary since condensing **18c** and a hexahydrofarnesyl organometallic species, and then reacting the resulting alcohol with the TsF•DBU reagent would have afforded, via alkoxide **19** (M=DBUH, in Scheme 2), the ketone **20**. This was tested by reacting **18c** with isopentylmagnesium chloride to obtain, in low yield (29%), the alcohol **39a** as a 65:35 mixture of two diastereomers (GC). Establishing the configuration of each component by ^{1}H NMR proved difficult owing to the multiplicity of signals in a narrow range of chemical shifts and, without further analyses, this alcohol product was reacted with TsF and DBU as above. NMR analysis of the complex product (TLC) thus obtained suggested it to be constituted of tosylate **39b**, alongside various unidentified impurities. Treating this product with $NBu_4F_2SiPh_3$ (NMR tube experiment) afforded a still more complex mixture, in which a methyl ketone also observed (by NMR) in the impure product issued from treatment of **39a** with DAST and to which the structure **40** was tentatively assigned by ^{13}C NMR. Modelling study revealed severe hindrance of the TES residue by the isopentyl substituent and it is likely that this discrepancy originates from the greater reactivity of the free OH as compared to the OTES substituent.

Results obtained with sulfone **41a**, which was prepared in



Scheme 7. Application to synthesis of a fragment of *Hyalophora cecropia* juvenile hormone (**59**).

good yield (86%) as a mixture of *only two* diastereomers [GC-MS, NMR; relative configuration of the C-*SO₂Ph* carbon atom was not determined] by condensing the lithium anion of isopentyl phenyl sulfone **42** and **18c**, also suggest that the steric factor is critical in this series. Practically no reaction was observed in TLC on reacting **41a** with the TsF•DBU reagent for a prolonged period. The desired ketosulfone **43** could be obtained by using BF_3•Et_2O as a reagent, however. Notably, the rearrangement proceeded in this case at room temperature and after a few hours, separation by column chromatography afforded unreacted diol-sulfone ***cis*-41b** (36%) and **43** (55%, mp 113 °C), as established by NMR; reacting further ***cis*-41b** with BF_3•Et_2O resulted in decomposition. Finally, an attempt was made to condense **18c** with the lithium anion of hexahydrofarnesyl phenyl sulfone **31** but, as previously observed with long-chain alkyl sulfones,[21] only decomposition of this sulfone was observed. A convenient solution to these difficulties was found by homologating the ketosulfone **37**, which was first reacted with ethyl methallyl carbonate under Tsuji allylation conditions[22] (with added [Pd_2dba_3•$CHCl_3$] and PPh_3 in THF) for 2 h at room temperature to obtain in good yield (90%) the sulfone **44** as a white solid (mp 57 °C). Hydrogenating **44** (H_2, 5% Pd/C) then afforded **43** (96%).

Next, homologation of **37** to phytal (**1**) was realized as indicated. Oxirane **45**, prepared in three steps (overall 77%) from geranylacetone **46** by a hydrogenation, a methylenation, and an epoxidation (see experimental), was heated under reflux with Al(O-*i*-Pr)$_3$ in toluene for 5 h. Treating the resulting alcohol mixture (2:1 by GC and NMR) with ethyl chloroformate in ether with added pyridine then afforded the carbonates ***exo*-47a** and ***endo*-47a** (overall 86%, from **45**; exo:endo = 2:1). Surprisingly, reacting this carbonate product with **37** under Tsuji conditions as above afforded in high yield (92%) the sulfone **48** as the *sole* product; this is possibly the result of equilibration of the π-allylpalladium intermediates, owing to reversibility of the palladation process.[23]

Although removing the sulfonyl group using aluminium would have been more appropriate (vide infra), straightforward conversion of **48** to ketone **20** was attempted by heating this sulfone with Raney nickel in EtOH.[24] This gave an over-hydrogenated product with the same polarity as **20** in TLC, later identified as **49** by GC-mass. Reducing this hydrogenation product with LAH, and then separating the

resulting two-component mixture (TLC) by column chromatography afforded successively the alcohol **50** (29%) and the cyclopropyl carbinol **2** (69%; identified by GC-mass and NMR), which was subsequently converted into phytal (**1**) by using the same sequence as depicted in Scheme 1 (overall 52% from **2**).

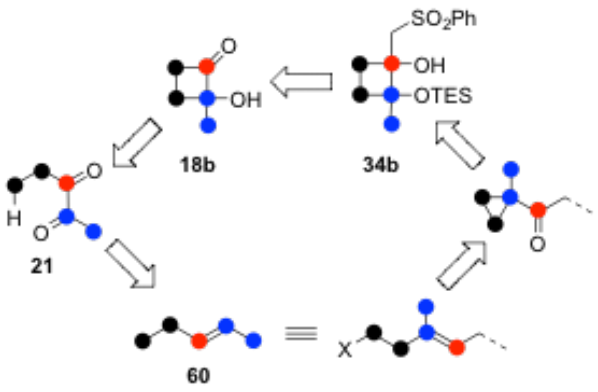
Finally, the scope of this emerging methodology was briefly explored by irradiating a solution of 3,4-hexanedione **51** in EtOAc (Scheme 7). As previously observed,[11c] owing to the symmetry of the molecule, the reaction proceeded faster as compared with dione **21**, and on completion after 16 h (TLC), elimination of the solvent afforded quantitatively the ketone **52a**, which was silylated with TESOTf to give, after purification by column chromatography, the pure (by NMR) ketone **52b** in good yield (overall 72%, from **51**). Reacting **52b** with the lithium anion of sulfone **33** then gave the hydroxysulfone **53** (91%) as a mixture of two diastereomers (by NMR). Without further purification, this condensation product was reacted with the TsF•DBU reagent in acetonitrile. Though proceeding more slowly, as compared with **34b**, after 16 h heating at ca. 35 °C the reaction was completed (by TLC) and the usual processing, followed by recrystallization from Et_2O/hexane afforded **54** (65%) as white crystals whose structure **54** was confirmed by X-ray analysis. Reacting this sulfone with the carbonate **55a** of alcohol **55b** (prepared in three steps from prenol **56** as described[25]) under Tsuji conditions, and then treating the resulting sulfone **57** (78%) with aluminium in moist THF[26] furnished in good yield (75%) the C1-C9 fragment **58** of *Hyalophora cecropia* juvenile hormone (**59**).

3. Conclusion

Initially conceived for the use of dinitrile **5** in the synthesis of phytyl derivatives, this study has evolved into a convenient synthesis of aldehyde **1** from 2,3-pentanedione **21** and geranylacetone **46**. Crucial in this approach was the selective pinacol rearrangement of an unsymmetrical cyclobutane glycol, a challenging task that was solved by taking advantage of the electron-withdrawing properties of the sulfonyl group, another key feature being the protection of the remote alcohol with a TES group. Thus, reacting sulfone **34b** with the TsF•DBU reagent has afforded the β-ketosulfone **37** with a perfect selectivity, which could be reversed simply by using DAST in place of this reagent. Although not explicitly probed, in each case this efficiency is likely to result from the conjunction of base and covalent catalysis, facilitated by the use of a fluorinated reagent and a silyl protection.

More straightforward conversion of cyclopropyl alcohol **2** to isophytal (**1**) — not investigated in this study — would be desirable. Nevertheless, the results presented in this publication are not without interest. In addition to being transposable to the synthesis of an advanced fragment of juvenile hormone **59** from dione **51**, the strategy we used to prepare the key cyclopropyl-carbinol intermediate **2** should be applicable to the synthesis of a variety of cyclopropane derivatives and of unsaturated compounds. The ready availability of diones **21** and **51** combined with the mildness of the conditions used in the allylation step, and in the elimination of the sulfonyl group, makes β-ketosulfones **37** and **54** a valuable alternative to the commonly-used pathway starting from γ-butyrolactone **4** and proceeding via corresponding β-ketoesters, thereby improving significantly the already valuable olefination methodology developed by Johnson.

Finally, ironically, since gem-diones are accessible by oxidation of 2-alkenes,[27] as illustrated below (Scheme 8), the Norrish II/pinacol/homoallylic rearrangement sequence that has been used in present work makes 2-pentene **60** a formal synthetic equivalent of an isopentene residue, an analogy that suggests possible applications in the isotopic labelling of isoprenyl derivatives.



Scheme 8.

4. Experimental

General. Infrared (IR) spectra were recorded in KBr pellets on a Perkin Elmer Spectrum One apparatus. Excepted otherwise indicated ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-300 apparatus at 300 and 75 MHz, respectively; Bruker DPX-400 for 400 MHz ^{1}H NMR experiments. Chemical shifts (δ) are reported in parts per million relative to the solvent resonance as the internal standard [$CD(H)Cl_3$, 7.26 and 77 ppm respectively]. Signal multiplicity is described as s, singlet; d, doublet; t, triplet; m, multiplet; br, broad. Melting points (mp) have been measured on an Electrothermal apparatus. Elemental analyses were realized at the laboratory of analyses of the Faculty of Chemistry of the University of Strasbourg. GC-MS analyses were performed on a Shimadzu-QP5050 GCMS apparatus. GC analyses were performed on a HP 6890 apparatus equipped with a HP-5 crosslinked 5% Ph-Me Siloxane (30 m x 0.32 m x 0.25 mm). TLC analyses were performed on silica gel (60 GF254 Merck); with spot visualisation by exposure to UV light (254 nm) or treatment with the H_2SO_4/vanillin reagent, alkaline $KMnO_4$ or iodine vapour. Column chromatography refers to the Stille method using Merck 60H silica gel; unless it is otherwise stated, a slow gradient of solvents was realized. All experiments were performed in dried glassware, under an argon atmosphere with magnetic stirring. All solvents used were freshly distilled from an appropriate reagent [Na.benzophenone (ether, THF, toluene); Mg (MeOH, EtOH), CaH_2 (CH_2Cl_2, DMF); K_2CO_3 (EtOAc); CaH_2, then P_4O_{10} (CH_3CN); P_4O_{10} (pentane, hexane, $CHCl_3$)]. Pyridine, triethylamine and 2,4,6-collidine were distilled from CaH_2. CH_2I_2 was stirred for 2 d with K_2CO_3 and added copper bronze, filtered on neutral alumina, and then distilled from CaH_2 (Bp 55-60 °C at 10 Torr). Tosyl chloride and PPh_3 were re-crystallized from hexane. Methallyl alcohol, ethyl chloroformate, oxalyl chloride, thioanisole, $TiCl_4$ and BF_3•Et_2O were distilled from CaH_2. Tosyl fluoride was prepared using a protocol adapted from literature.[28] In an argon atmosphere, KF ("spray dried" grade; 11.6 g, 200 mmol) was added to a solution of TsCl (19.06 g, 100 mmol) in CH_3CN (100 mL) and the resulting mixture was stirred at rt for 30 h. The residue left by evaporation of the solvents in a vacuum was diluted with CH_2Cl_2 and the solids were eliminated by filtration on a sintered funnel. Concentration of the filtrate in a vacuum then afforded TsF (16.4 g, 94%) as a white solid (mp 40 °C). [Pd_2dba_3•$CHCl_3$] was freshly prepared from $PdCl_2$ as described in Ref. 29. Ethyl methallyl carbonate (prepared according to literature[30]) was distilled before use (Bp 59 °C at 10 Torr). Diones **21** and **51**, geranylacetone **46**, prenol **56**, *t*-butyldimethylsilyl chloride, *t*-butyldimethylsilyl triflate, trietylsilyl triflate, DBU, diethylaminosulfur trifluoride, Al(O-*i*-Prop)$_3$ were used as received (all reagents from Fluka-Sigma-Aldrich). All other reagents were available. *n*-BuLi solutions (in hexane; only freshly opened bottles were used) were titrated with *N*-pivaloyl-*o*-toluidine.[31] Aluminium (ca. 4xcm^2 pieces of aluminium foil) was activated just before use by treatment with 2% aqueous $HgCl_2$ as described in Ref. 26b. Raney® nickel was activated *in situ* by stirring vigorously the commercial slurry (in water) in EtOH for a few hours and then siphoning off the supernatant, these operations being repeated twice. Zinc powder was activated *in situ* by treatment with TMSCl as previously reported.[32] pH 2 tartaric buffer was prepared by adding NaOH pellets to 0.7 M tartaric acid (Universal paper as an indicator). For all hydrogenation experiments, 5% Pd/C (ca. 4-5 mg/mmol) was added to a degassed solution of the substrate in EtOAc (ca. 4 mL/mmol). The resulting mixture was stirred at rt in a H_2 atmosphere, and then filtered on a bed of Celite® (washings

with CH_2Cl_2). The residue left by evaporation of the solvents was purified by column chromatography. Irradiations were performed using a Philipps HPK-125 UV lamp. X-ray analyses: the crystals were placed in oil, and a single crystal was selected, mounted on a glass fibre and placed in a low-temperature N_2 stream. X-ray diffraction data collection was carried out on a Nonius Kappa-CCD diffractometer equipped with an Oxford Cryosystem liquid N_2 device, using Mo-Kα radiation (λ = 0.71073 Å). The crystal-detector distance was 36 mm. The cell parameters were determined (Denzo software[33a]) from reflections taken from one set of 10 frames (1.0° steps in phi angle), each at 20 s exposure. The structures were solved by Direct methods using the program SHELXS-97.[33b] The refinement and all further calculations were carried out using SHELXL-2013.[33c] The H-atoms were included in calculated positions and treated as riding atoms using SHELXL default parameters. The non-H atoms were refined anisotropically, using weighted full-matrix least-squares on F^2.

2-Hydroxy-2-methylcyclobutan-1-one 18b: In a 1-L round-bottom flask connected to an argon/vacuum line, and equipped with a 10 cm-long Pyrex finger containing the lamp, EtOAc (950 mL) was thoroughly degassed (two freeze/pump/thaw cycles). Dione **21** (10 g, 100 mmol), diluted with EtOAc (ca. 30 mL) was added with a syringe and, after the flask was tightly wrapped in a foil of aluminium, the resulting yellow solution was irradiated with gentle stirring until the reaction was complete (30 h), as indicated by disappearance of the yellow colour, almost as a titration. The solvents were eliminated in a vacuum to give a 92/8 mixture (GC) of **18b** and **22** respectively as a pale-yellow oil (10 g, 100%); IR (neat, cm^{-1}): 3418, 1788; ^{13}C NMR ($CDCl_3$): δ 22.1, 28.1, 39.2, 88.3, 212.2; MS (CI-NH_3): *m*/*z* 118 (M + NH_4^+), 101 (M + H^+), 83, 72, 55. Dimer **22**: MS (CI-NH_3): *m*/*z* 218 (M + NH_4^+), 201 (M + H^+), 183, 141, 127, 116, 99.

2-Methyl-2-[(triethylsilyl)oxy]cyclobutan-1-one 18c: In a flask connected to an argon line, 2,4,6-collidine (4.6 mL, 35 mmol) was diluted with DMF (10 mL) and, with stirring, and cooling (ice bath), TESCl (5.8 mL, 35 mmol) and the preceding **18b**/**22** mixture (2 g, 20 mmol), diluted with DMF (10 mL) were added sequentially with a syringe. The cooling bath was removed and the reaction mixture was further stirred at rt for 2 d before being diluted with 1 M HCl (40 mL) and hexane (30 mL). After vigorous stirring, the aqueous layer was extracted with hexane (3 x 15 mL) and the pooled organic phases were washed with brine (3 x 20 mL), and dried ($MgSO_4$). The coloured residue left by evaporation of the solvents was purified by column chromatography (hexane/EtOAc) to give, after thorough elimination of the solvents in a vacuum, **18c** as a colourless oil (2.79 g, overall 65% from **21**); TLC (hexane:ether = 4:1) R_f = 0.58; IR (neat, cm^{-1}): 1956, 1877, 1790, 1270, 1214, 1039, 1013, 816, 744; ^1H NMR ($CDCl_3$): δ 0.57-65 (m, 6H), 0.91-0.96 (m, 9H), 1.43 (s, 3H), 2.02-2.09 (m, 2H), 2.66-2.87 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 5.9 (CH_2Si), 6.8 (CH_3CH_2), 23.9 (CH_3), 29.4 ($C3H_2$), 38.8 ($C4H_2$), 89.3 (C2), 210.5 (C=O); MS (CI-NH_3): *m*/*z* 232 (M + NH_4^+), 215 (M + H^+), 185, 157, 131, 115, 102; Anal. Found: C, 61.87; H, 10.25 %. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34 %

1-Methyl-2-oxocyclobutyl 4-nitrobenzoate 18d: In a flask connected to an argon line, with stirring, DMAP (425 mg, 6.96 mmol) and DCC (718.4 mg, 6.96 mmol) were added sequentially to a cooled (ice bath) solution of hydroxyketone **18b** (232.6 mg, 2.32 mmol) and *p*-nitrobenzoic acid (426.0 mg, 2.55 mmol) in CH_2Cl_2 (5 mL). After a further 6 h stirring at 0 °C, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and 0.2 M HCl (6 mL). The organic phase was washed with 0.2 M HCl (2 x 6 mL), brine (3 x 7 mL), and dried ($MgSO_4$). The solvents were evaporated and the coloured residue was chromatographed on silica gel (hexane/EtOAc) to give ester **18d** (176.2 mg, 30%) as a white solid; TLC (hexane:ether = 1:1) R_f = 0.56; mp 141 °C; IR (KBr, cm^{-1}): 1791, 1728, 1346, 1284, 1207, 1103, 1013, 843, 716; ^1H NMR ($CDCl_3$): δ 1.63 (s, 3H, CH_3), 2.12-2.21 (m, 1H), 2.65-2.75 (m, 1H), 2.91-3.03 (m, 1H), 3.23-3.35 (m, 1H), 8.16-8.19 (m, 2H), 8.26-8.29 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 20.3 (CH_3), 26.4 ($C3H_2$), 39.8 ($C4H_2$), 90.2 (C2), 123.8/131.1/134.5/150.9 (C_{arom}), 163.6 [C=O(O)], 205.5

(C=O); Anal. Found: C, 57.72; H, 4.80%. Calcd for $C_{12}H_{11}NO_5$: C, 57.83; H, 4.45%.

General protocol for cyclobutanone/sulfone condensation experiments. All these experiments were similarly realized and only that with ketone **18c** and methyl phenyl sulfone **33** is described.

2-Methyl-1-[(phenylsulfonyl)methyl]-2-[(triethylsilyl)oxy]cyclobutan-1-ol 34b: In a flask connected to an argon/vacuum line, a solution of sulfone **33** (156 mg, 1 mmol) in THF (4 ml) was thoroughly degassed (three freeze/pump/thaw cycles). The flask was immersed in a dry-ice/acetone bath and, with stirring, 1.6 M (in hexane) *n*-BuLi (625 µL) was added with a syringe. After 30 min stirring, a degassed solution of ketone **18c** (92.5 mg, 0.43 mmol) in THF (2 mL) was added with a cannula. The temperature was then allowed to rise gradually to -50 °C. After 30 min stirring, the cooling bath was removed and the reaction mixture was diluted with ether (3 mL) and water (4 mL). The aqueous layer was extracted with ether (3 x 5 mL) and the pooled organic phases were washed with water (6 mL), brine (2 x 6 mL), and dried ($MgSO_4$). The solvents were evaporated in a vacuum and the solid residue was chromatographed on silica gel (hexane/EtOAc) to give, after thorough elimination of the solvents in a good vacuum, a 28:72 (GC) mixture of, respectively, ***cis*-34b** and ***trans*-34b** (133 mg, 83%) as a white solid; TLC (hexane:ether = 1:1) R_f = 0.33; mp 64 °C; ^{1}H NMR ($CDCl_3$): δ 0.47-0.62 (m, 6H, $SiCH_2$), 0.85-0.95 (m, 9H, $SiCH_2CH_3$), 1.33/1.35 (2 s, 3H, CH_3), 1.56-2.35 (m, 4H, CH_2), 3.32-3.86 (m, 3H, SO_2CH_2, OH), 7.50-7.70 (m, 3H), 7.91-7.98 (m, 2H); ^{13}C NMR ($CDCl_3$, signals of the *trans* isomer in red): δ 6.1/6.3 ($SiCH_2$), 6.9/7.0 ($SiCH_2CH_3$), 22.4/23.7 (CH_3), 27.5/28.1 (CH_2), 31.2/34.9 (CH_2), 60.0/62.1 (SO_2CH_2), 77.9/77.9 (C2), 79.5/79.5 (C1), 127.7/128.5 (C_{arom}), 129.0/129.3 (C_{arom}), 133.5/133.81 (C_{arom}), 141.2/141.3 (C_{arom}); MS (CI-NH_3): *m*/*z* 338 (M + NH_4^+), 371 (M + H^+), 256, 239, 229, 216, 173, 132, 97.

1-Benzenesulfonylmethyl-2-methyl-cyclobutane-1,2-diol 34a: General protocol for cyclobutanone/sulfone condensation experiments. In THF (80 mL). From hydroxycyclobutanone **18b** (1 g, 10 mmol) and sulfone **33** (3.12 g, 20 mmol). Isolated: 4:1 mixture (GC, NMR) of, respectively, sulfones ***cis*-34a** and ***trans*-34a** (914 mg, 35%) as a thick colourless oil; TLC (hexane:ether = 1:1) R_f = 0.08; ^{1}H NMR ($CDCl_3$): δ 1.35 (s, 2.4 H, CH_3), 1.45 (s, 0.6H, CH_3), 1.62-2.32 (m, 4H), 3.32-3.70 (m, 2H), 2.47/3.22/3.86/4.15 (4 s, 2H, 2 OH), 7.54-7.70 (m, 3H), 7.91-7.97 (m, 2H); ^{13}C NMR ($CDCl_3$, signals of the *trans* isomer in red): δ 22.5/22.7 (CH_3), 27.7/28.4 (CH_2), 29.1/34.5 (CH_2), 60.6/60.9 (SO_2CH_2), 74.5/75.8 (C2), 76.7/77.2 (C1), 127.6/127.7 (C_{arom}), 129.3/129.4 (C_{arom}),133.9/134.0 (C_{arom}), 140.6/140.8 (C_{arom}); MS (CI-NH_3): *m*/*z* 274 (M + NH_4^+), 257 (M + H^+), 256, 239, 216, 174, 132, 115, 97. **By hydrolysis of sulfone 34b:** In an argon atmosphere, HF.pyridine (20 µL, 0.588 mmol) was added to a stirred solution of the 28/72 mixture of ***cis*-34b** and ***trans*-34b** (219 mg, 0.590 mmmol) in CH_2Cl_2 (2 mL). After 5 min stirring at rt, the reaction mixture was diluted with 1 M HCl (2 mL) and CH_2Cl_2 (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL) and the pooled organic phases were washed with brine (3 x 3 mL), and dried (K_2CO_3). Purification of the residue left by evaporation of the solvents by column chromatography (hexane/EtOAc) afforded, after thorough elimination of the solvents in a good vacuum, a 28/72 (GC, NMR) mixture of, respectively, ***cis*-34a** and ***trans*-34a** as a thick colourless oil (150 mg, 99%).

***Trans*-2-methyl-1-[(phenylthio)methyl]-2-[(triethylsilyl)oxy]cyclobutan-1-ol *trans*-36 and *cis*-2-methyl-1-[(phenylthio)methyl]-2-[(triethylsilyl)oxy]cyclobutan-1-ol *cis*-36:** In a flask connected to an argon/vacuum line, a solution of thioanisole **35** (62 µL, 0.54 mmol) in THF (1.2 mL) was thoroughly degassed and then cooled to –78 °C (dry ice/acetone bath). With stirring, 1.6 M (in hexane) *n*-BuLi (337 µL, 0.81 mmol) was added with a syringe and the resulting mixture was stirred 2 h at –78 °C, and then 20 h at rt before being cooled to ca. 0 °C (ice bath). A solution of ketone **18c** (77.5 mg, 0.36 mmol) in THF (1.5 mL) was added with a syringe and, after stirring 1 h at rt, the reaction mixture was diluted with ether (2 mL) and water (3 mL). The aqueous layer was extracted

with ether (3 x 3 mL) and the pooled organic phases were washed with 1 M HCl (3 mL), brine (3 x 4 mL), and dried ($MgSO_4$). The coloured residue left by evaporation of the solvents in vacuo was chromatographed on silica gel (hexane/ether) to give successively the *trans* cyclobutanol ***trans*-36** (42 mg, 35%) and the *cis* isomer ***cis*-36** (18 mg, 15%). ***trans*-36**: TLC (hexane:ether = 1:1) R_f = 0.74; ^{1}H NMR ($CDCl_3$): δ 0.56 (q, J = 7.8 Hz, 6H), 0.91 (t, J = 7.8 Hz, 9H), 1.32 (s, 3H), 1.60-1.89 (m, 3H), 2.03-2.15 (m, 1H), 3.05 (d, J = 1.2 Hz, 2H), 3.73 (s, 1H, OH), 7.05-7.10 (m, 1H), 7.16-7.21 (m, 2H), 7.31-7.35 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 6.2 ($SiCH_2$), 6.9 (CH_2CH_3), 23.3 (CH_3), 28.9 (CH_2), 33.4 (CH_2), 41.4 (SCH_2), 78.3 (C2), 79.1 (C1), 125.7 (C_{arom}), 128.7 (C_{arom}), 129.3 (C_{arom}), 137.9 (C_{arom}); MS (CI-NH_3): m/z 339 (M + H^+), 229, 207, 173, 132, 115, 97. ***cis*-36**: TLC (hexane:ether = 1:1) R_f = 0.65; ^{1}H NMR ($CDCl_3$): δ 0.54 (q, J = 8.0 Hz, 6H), 0.90 (t, J = 8.0 Hz, 9H), 1.30 (s, 3H), 1.56-1.80 (m, 4H), 2.70 (s, 1H, OH), 3.12 (d, J = 13.4 Hz, 1H), 3.45 (dd, J = 13.4, 1.0 Hz, 1H), 7.06-7.23 (m, 3H), 7.32-7.37 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 6.3 ($SiCH_2$), 7.0 (CH_2CH_3), 23.1 (CH_3), 27.7 (CH_2), 31.0 (CH_2), 42.6 (SCH_2), 78.7 (C2), 79.1 (C1), 128.1 (C_{arom}), 128.9 (C_{arom}), 129.5 (C_{arom}), 137.9 (C_{arom}); MS (CI-NH_3): m/z 339 (M + H^+), 229, 207, 173, 132, 115, 97.

***Trans*-2-methyl-1-[(phenylsulfonyl)methyl]-2-[(triethylsilyl)oxy]cyclobutan-1-ol *trans*-34b:** With stirring, $NaHCO_3$ (60 mg, 0.71 mmol) and *m*-CPBA (62 mg, 0.472 mmol) were added sequentially to a cooled (ice bath) solution of sulfide ***trans*-36** (40 mg, 0.118 mmol) in CH_2Cl_2 (350 µL). The resulting mixture was further stirred for 40 min at 0 °C, and then 1 h at rt before being diluted with CH_2Cl_2 (5 mL) and 0.25 M $Na_2S_2O_3$ (2 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL) and the pooled organic phases were washed with 10% $NaHCO_3$ (6 mL), brine (6 mL), and dried ($MgSO_4$). The solid residue left by evaporation of the solvents was purified by column chromatography (hexane/EtOAc) to give, after elimination of the solvents in a vacuum, sulfone ***trans*-34b** (34.9 mg, 80%) as a white solid; TLC (hexane:ether = 1:1) R_f = 0.33; mp 64 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.53 (q, J = 8.0 Hz, 6H), 0.88 (t, J = 8.0 Hz, 9H), 1.35 (s, 3H), 1.56-1.82 (m, 3H), 2.20-2.30 (m, 1H), 3.44 (dd, J = 14.0, 1.1 Hz, 1H), 3.54 (d, J = 15.0 Hz, 1H), 3.84 (s, 1H, OH), 7.55-7.69 (m, 3H), 7.93-7.96 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 6.3 ($SiCH_2$), 7.0 (CH_2CH_3), 22.4 (CH_3), 27.5 (CH_2), 31.2 (CH_2), 60.0 (SO_2CH_2), 77.9 (C2), 79.5 (C1), 127.7 (C_{arom}), 129.3 (C_{arom}), 133.8 (C_{arom}), 141.2 (C_{arom}); MS (CI-NH_3): m/z 388 (M + NH_4^+), 371 (M + H^+), 256, 239, 229, 216, 173, 132, 97; Anal. Found: C, 58.23, H, 8.38 %. Calcd for $C_{18}H_{30}O_4SSi$: C, 58.34; H, 8.16 %.

***Trans*-1-methyl-2-[(phenylsulfonyl)methyl]cyclobutane-1,2-diol *trans*-34a:** In a flask connected to an argon line, with stirring, TBAF.3 H_2O (22 mg, 0.067 mmol) was added to a cooled (ice bath) solution of sulfone ***trans*-34b** (25 mg, 0.067 mmol) in THF (200 µL). After 5 min stirring, the reaction mixture was diluted with ether (2 mL) and 1 M $KHSO_4$ (1 mL). The aqueous phase was extracted with ether (3 x 1 mL) and the pooled organic phases were washed with brine (3 x 2 mL), and dried ($MgSO_4$). The residue left by evaporation of the solvents was purified by column chromatography (hexane/EtOAc) to give, after elimination of the solvents in a vacuum, diol-sulfone ***trans*-34a** as a white solid (15.4 mg, 90%); TLC (hexane:EtOAc = 1:1) R_f = 0.08; mp 73 °C [monocrystals obtained by slow diffusion (in a NMR tube) of cyclohexane into a solution of ***trans*-34a** in $CDCl_3$]; ^{1}H NMR ($CDCl_3$): δ 1.45 (s, 3H), 1.70-1.94 (m, 3H), 2.14-2.22 (m, 1H), 2.48 (s, 1H, OH), 3.52 (d, J = 14.1 Hz, 1H), 3.67 (d, J = 14.1 Hz, 1H), 3.86 (s, 1H, OH), 7.54-7.70 (m, 3H), 7.91-7.97 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 22.5 (CH_3), 28.4 (CH_2), 29.1 (CH_2), 60.6 (SO_2CH_2), 74.5 (C2), 76.7 (C1), 127.6 (C_{arom}), 129.4 (C_{arom}), 134.0 (C_{arom}), 140.6 (C_{arom}); MS (CI-NH_3): m/z 274 (M + NH_4^+), 257 (M + H^+), 256, 239, 216, 174, 132, 115, 97; crystal data $C_{12}H_{16}O_4S$, MW= 256.31, 0.06 x 0.04 x 0.04 mm, Monoclinic, space group P $2_1/c$, T = 173 K, a = 9.3097(2), b = 16.8291(5), c = 7.8017(2) Å, β = 90.234(5)°, V = 1222.31(5) Å^3, λ (Mo-Kα) = 0.71073 Å, μ = 0.265 mm^{-1}. A total of 6370 reflections were measured and 3562 were independent. Final = $R1$ = 0.0469, $wR2$ = 0.1361 (2677 refs; $I > 2\sigma(I)$), and GOF = 1.074 (for all data, $R1$ = 0.0687, $wR2$ = 0.1543).

General protocol for BF_3-mediated rearrangement experiments. All these experiments were similarly realized and only that with sulfone **34a** is described.

1-(1-Methylcyclopropyl)-2-(phenylsulfonyl)ethan-1-one 37: In a flask equipped with a condenser connected to an argon line, $BF_3.Et_2O$ (73 µL, 0.57 mmol) was added with a syringe to a stirred solution of the 28:72 mixture of diol-sulfones ***cis*-34a** and ***trans*-34a** (178 mg, 0.48 mmol) in $CHCl_3$ (415 µL). The reaction mixture was heated with stirring at 70 °C (oil bath) for 3 h before being cooled, and poured into a stirred mixture of 10 M NH_4Cl (2 mL) and CH_2Cl_2 (3 mL). The aqueous phase was extracted with CH_2Cl_2 (2 x 4 mL) and the pooled organic extracts were washed with 10 M NH_4Cl (4 x 1 mL), brine (2 x 4 mL), and dried ($MgSO_4$). The residue left by elimination of the solvents was chromatographed on silica gel (hexane/EtOAc) to give successively ketosulfone **37** (89.4 mg, 75%) as a white solid, and a thick colourless oil identified as ***cis*-34a** by GC-mass and NMR (30 mg, 25%); TLC (hexane:EtOAc = 2:1) R_f = 0.43; mp 78 °C; ^{1}H NMR ($CDCl_3$): δ 0.84 (m, 2H, 2 C*H*H), 1.30 (m, 2H, 2 CH*H*), 1.35 (s, 3H, CH_3), 4.17 (s, 2H, SO_2CH_2), 7.55-7.70 (m, 3H), 7.89-7.92 (m, 2H; ^{13}C NMR ($CDCl_3$): δ 19.0 (2 CH_2), 19.4 (CH_3), 28.1 (*C*CH_3), 61.8 (SO_2CH_2), 128.9 (C_{arom}), 129.3 (C_{arom}), 134.1 (C_{arom}), 139.1 (C_{arom}), 199.3 (C=O); MS (CI-NH_3): *m*/*z* 256 (M + NH_4^+), 239 (M + H^+), 116, 99, 72; Anal. Found: C, 60.53; H, 5.88%. Calcd. for $C_{12}H_{14}O_3S$: C, 60.48; H 5.92%. ***cis*-34a**: ^{1}H NMR ($CDCl_3$): δ 1.34 (s, 3H), 1.65-1.83 (m, 2H), 1.85-1.95 (m, 1H), 2.16-2.29 (m, 1H), 3.26 (brs, 1H, OH), 3.36 (d, *J* = 14.4 Hz, 1H), 3.47 (d, *J* =14.4 Hz, 1H), 4.15 (brs, 1H, OH), 7.54-7.68 (m, 3H), 7.90-7.95 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 22.7 (CH_3), 27.7 (CH_2), 34.5 (CH_2), 60.9 (SO_2CH_2), 75.8 (C2), 77.2 (C1), 127.7 (C_{arom}), 129.3 (C_{arom}), 133.9 (C_{arom}), 140.8 (C_{arom}); MS (CI-NH_3): *m*/*z* 274 (M + NH_4^+), 257 (M + H^+), 256, 239, 216, 174, 132, 115, 97; Anal. Found: C, 56.37; H, 6.42%. Calcd for $C_{12}H_{16}O_4S$: C, 56.23; H, 6.29%. **Using the 4:1 *cis*-34a/*trans*-34a mixture:** In $CHCl_3$ (1 mL), with added $BF_3.Et_2O$ (107 µL, 0.84 mmol). From **34a** (145 mg, 0.565 mmol). Isolated: ketosulfone **37** (39 mg, 24%) as a white solid (mp 78 °C), and the *cis* diol-sulfone ***cis*-34a** (94 mg, 65%) as a thick oil.

General protocol for TsF•DBU-mediated rearrangement experiments. All these experiments were similarly realized and only that with hydroxysulfone **34b** is described.

1-(1-Methylcyclopropyl)-2-(phenylsulfonyl)ethan-1-one 37: In a flask connected to an argon line, the 28:72 ***cis*-34b**/***trans*-34b** mixture (157 mg, 0.423 mmol) and tosyl fluoride (296 mg, 1.7 mmol) were diluted with CH_3CN (1.6 mL). With stirring, DBU (245 µL, 1.7 mmol) was added with a syringe. Within a few minutes, the yellow colour initially developed changed to orange. After 18 h stirring at rt, when the reaction was completed in TLC, the reaction mixture was diluted with CH_2Cl_2 (11 mL) and 0.1 M HCl (8 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the pooled organic extracts were washed with 0.1 M HCl (7 mL), brine (2 x 7 mL), and dried ($MgSO_4$). The solvents were evaporated and the coloured residue was purified by column chromatography (hexane/EtOAc) to give, after thorough elimination of the solvents in a good vacuum, a white solid (mp 78 °C) identified as ketosulfone **37** by NMR (92.7 mg, 92%).

General protocol for DAST-mediated rearrangement experiments. All these experiments have been realized using the same protocol and only that with hydroxysulfone **34b** is described.

1-{1-[(Phenylsulfonyl)methyl]cyclopropyl}ethan-1-one 38: In a plastic tube capped with a septum, and connected to an argon line, the 28:72 mixture of sulfones ***cis*-34b** and ***trans*-34b** (46 mg, 0.124 mmol) was diluted with CH_2Cl_2 (400 µL) and, with stirring, DAST (17 µL, 0.136 mmol) was added with a syringe. The resulting orange mixture was stirred 30 min at rt before being diluted with CH_2Cl_2 (1 mL) and 10% aqueous $NaHCO_3$ (2 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL) and the pooled organic phases were washed with brine (2 x 3 mL), and dried ($MgSO_4$). The residue left by elimination of the solvents in a vacuum was purified by column chromatography (hexane/EtOAc) to give ketone **38** (24 mg, 81%) as a white solid; TLC (1:1 hexane:EtOAc) R_f = 0.23; mp 78 °C; ^{1}H NMR ($CDCl_3$): δ 1.19-1.23 (m, 2H, 2 C*H*H), 1.35-1.40 (m, 2H, 2 CH*H*), 1.90

(s, 3H, CH_3), 3.58 (s, 2H, SO_2CH_2), 7.52-7.68 (m, 3H), 7.89-7.92 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 15.2 (2 CH_2), 23.9 (CH_3), 27.5 (C), 59.9 (SO_2CH_2), 128.5 (C_{arom}), 129.2 (C_{arom}), 133.9 (C_{arom}), 139.7 (C_{arom}), 204.2 (C=O); MS (CI-NH_3): *m*/*z* 256 (M + NH_4^+), 239 (M + H^+), 125, 97, 77; Anal. Found: C, 60.51; H, 5.99%. Calcd for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92%.

DAST-mediated rearrangement of diol-sulfone 34a: General protocol. In CH_2Cl_2 (900 µL), with added DAST (39 µL, 0.295 mmol). From the 28:72 diastereomeric mixture (75.4 mg, 0.294 mmol). Isolated: β-ketosulfone **37** (52 mg, 74%; mp 78 °C) and methyl ketone **38** (13.8 mg, 20%; mp 78 °C), both identified by GC and NMR.

***t*-Butyldimethyl{2-methyl-1-[(phenylsulfonyl)methyl]-2-[(triethylsilyl)oxy]cyclobutoxy}silane 34e:** With stirring, TBDMS triflate (204 µL, 0.890 mmol) and 2,4,6-collidine (197 µL, 1.485 mmol) were added sequentially to a cooled (ice bath) solution of the 28:72 ***cis*-34b/*trans*-34b** mixture (220 mg, 0.593 mmol) in DMF (600 µL). After 3 h stirring at rt, the reaction mixture was processed as usual to give, after purification by column chromatography (hexane/EtOAc) followed by elimination of the solvents in a good vacuum, sulfone **34e** (same diastereomeric ratio as **34b**; by GC) as a thick colourless oil (150 mg, 52%); TLC (hexane:EtOAc = 17:3) R_f = 0.46; ^{1}H NMR ($CDCl_3$): δ 0.21/0.29 (2 s, 6H, 2 $SiCH_3$), 0.47-0.56 (m, 6H, 3 $SiCH_2$), 0.82-0.89 (m, 9H, 3 $SiCH_2C\mathit{H}_3$), 0.93 [s, 9H, $C(CH_3)_3$], 1.30/1.32 (2 s, 3H, $C2CH_3$), 1.60-2.95 (m, 4H, 2 CH_2), 3.23/3.35 (2 dd, *J* = 14.8, 1.2 Hz, 1H, $SO_2C\mathit{H}H$), 3.64/3.81 (2 d, *J* = 14.8 Hz, 1H, $SO_2CH\mathit{H}$), 7.51-7.65 (m, 3H), 7.90-7.96 (m, 2H); ^{13}C NMR ($CDCl_3$): δ -2.3 ($SiCH_3$), -2.0 ($SiCH_3$), 6.3/6.4 ($SiCH_2$), 7.0/7.2 ($CH_2\mathit{C}H_3$), 20.2 [$\mathit{C}(CH_3)$], 25.6/25.7 ($C2\mathit{C}H_3$), 26.1/26.2 [$C(\mathit{C}H_3)$], 28.2/28.3 ($C3H_2$), 34.9/35.2 ($C4H_2$), 62.6/62.7 (SO_2CH_2), 79.4/79.7 (C2/C3), 127.5/129.2/133.3.141.5 (C_{arom}); MS (CI-NH_3): *m*/*z* 485 (M + H^+), 455, 427, 353, 227, 211, 199, 115, 104, 87, 59.

2-[(*t*-Butyldimethylsilyl)oxy]-1-methyl-2-[(phenylsulfonyl)methyl]cyclobutan-1-ol 34f: With stirring, TBAF.3 H_2O (62 mg, 0.19 mmol) was added to a cooled (ice bath) solution of sulfone **34e** (94.5 mg, 0.19 mmol) in THF (3 mL). After 5 min stirring, the reaction mixture was diluted with 1 M $KHSO_4$ (1 mL) and ether (2 mL). The aqueous phase was extracted with ether (3 x 1 mL) and the pooled organic extracts were washed with brine (3 x 2 mL), and dried ($MgSO_4$). The residue left by elimination of the solvents in a vacuum was chromatographed on silica gel (hexane/EtOAc) to give, successively: the sulfone **34f** (39.1 mg, 54%) as a white solid and the diol-sulfone **34a** (22 mg, 44%); TLC (hexane/EtOAc = 3 :1) R_f = 0.25; mp 115 °C; ^{1}H NMR: δ 0.17/0.18 (2 s, 3H, 2 $SiCH_3$), 0.93 [s, 9H, $C(CH_3)$], 1.42 (s, 3H, $C2CH_3$), 1.80-2.17 (m, 4H, 2 CH_2), 3.48 (d, *J* = 13.8, 1H), 3.68 (d, *J* = 13.8 Hz, 1 H), 3.87 (s, 1H, OH), 7.52-7.67 (m, 3H), 7.92-7.98 (m, 2H); ^{13}C NMR ($CDCl_3$): δ -0.7 ($SiCH_3$), 0.0 ($SiCH_3$), 20.2 [$\mathit{C}(CH_3)$], 25.3 ($C2\mathit{C}H_3$), 27.9 [$C(\mathit{C}H_3)$], 30.6/30.9 ($C3H_2$/$C4H_2$), 64.8 (SO_2CH_2), 80.6 (C1), 83.2 (C2), 129.4/131.3/135.5/143.8 (C_{arom}); MS (CI-NH_3): *m*/*z* 353 (M – OH), 313, 255, 229, 199, 185, 171, 135, 73; Anal. Found: C, 58.60; H, 7.97%. Calcd for $C_{18}H_{30}O_4SSi$: C, 58.34; H, 8.16%.

1-(1-Methylcyclopropyl)-2-(phenylsulfonyl)ethan-1-one 37 by DAST-mediated rearrangement of sulfone 34f: General protocol (see above). In CH_2Cl_2 (322 µL), with added DAST (13 µL, 0.093 mmol). From the *O*-TBDMS derivative **34f** (30 mg, 0.085 mmol). Isolated: β-ketosulfone **37** (15.6 mg, 77%) as a white solid (mp 78 °C).

2-Methyl-1-[3-methyl-1-(phenylsulfonyl)butyl]-2-[(triethylsilyl)oxy]cyclobutan-1-ol 41a: General protocol for cyclobutanone/sulfone condensation experiments. In THF (8 mL); -78 °C to rt (1 h). From ketone **18c** (230 mg, 1.07 mmol) and isopentyl phenyl sulfone **42** (394.5, 1.86 mmol). Isolated: **41a** (62/38 mixture of the *cis*- and the *trans*-isomer by GC and NMR) as a white solid (402.3 mg, 86%); TLC (hexane:EtOAc = 2:1) R_f = 0.33; mp 94 °C; ^{1}H NMR ($CDCl_3$): δ 0.50-1.06 (2m, 22H), 1.35 (s, 1.8H), 1.51 (s, 1.2H), 1,55-2,25 (m, 6H), 3.25 (dd, *J* = 10.5, 2.2 Hz, 0.6H), 3.31 (s, 0.6H), 3.66 (s, 0.4H), 3.89 (dd, *J* = 7.7, 3.3 Hz, 0.4H), 7.48-7.66 (m, 3H), 7.86-7.98 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 6.0/6.3 ($SiCH_2$), 6.9/7.2 ($SiCH_2\mathit{C}H_3$), 21.3/21.5 (CH_3), 22.6/23.2 ($C2CH_3$), 24.1/24.8 (CH_3), 25.9/26.5 (CH), 29.2/30.6 (CH_2), 31.3/34.3 (CH_2), 34.3/35.8 (CH_2), 64.5/68.4 ($CHSO_2$), 76.8/79.6 (C2), 81.1/84.2 (C1),

127.8/128.5/129.0/129.5/133.5/133.9/141.2/141.3 (C_{arom}).

4-Methyl-1-(1-methylcyclopropyl)-2-(phenylsulfonyl)pentan-1-one 43: General protocol for BF_3-mediated pinacol rearrangement experiments. In $CHCl_3$ (200 μL), with added $BF_3.Et_2O$ (34 μL, 0.27 mmol). From sulfone **41a** (96.2 mg, 0.225 mmol). Isolated: ketosulfone **43** (36.4 mg, 55%) as a white solid, and the *cis* diol-sulfone ***cis*-41b** (25.3 mg, 36%) as a thick oil; TLC (hexane:EtOAc = 1:1) R_f = 0.53; mp 113 °C; ^{1}H NMR ($CDCl_3$): δ 0.83 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H), 1.24-1.44 (m, 4H), 1.45 (s, 3H), 1.64-1.84 (m, 2H), 4.55 (dd, J = 10.5, 3.6 Hz, 1H), 7.51-7.58 (m, 2H), 7.64-7.70 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 20.1 (CH_3), 20.5 (2 CH_2), 21.9 (CH*C*H$_3$), 23.2 (CH*C*H$_3$), 26.1 (*C*HMe$_2$), 28.4 (C), 37.3 (SO_2CHCH_2), 67.7 (SO_2CH), 128.8/129.9/134.2/136.7 (C_{arom}), 204.2 (C=O); MS (CI-NH_3): m/z 295 (M + H^+), 171, 153, 143, 127, 109, 95, 77, 55; Anal. Found: C 65.41; H 7.38%. Calc for $C_{16}H_{22}O_3S$: C 65.28; H, 7.53%. ***cis*-1-Methyl-2-[3-methyl-1-(phenylsulfonyl)butyl]cyclobutane-1,2-diol *cis*-41b**: TLC (hexane:EtOAc = 1:1) R_f = 0.35; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.78 (d, J = 6.4 Hz, 3H), 0.86 (d, J = 8 Hz, 3H), 1.29 (s, 3H), 1.45-2.25 (m, 7H), 3.39 (dd, J = 10.0, 1.8 Hz, 1H) 3.48 (s, 1H, OH), 3.91 (s, 1H, OH), 7.56-7.61 (m, 2H), 7.65-7.70 (m, 1H), 7.88-7.92 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 21.5 (2 CH_3), 23.8 (C2*C*H$_3$), 25.6 (*C*HMe$_2$), 29.4 (SO_2CHCH_2), 34.1 (CH_2), 36.8 (CH_2), 67.1 (SO_2CH), 75.7 (C2), 80.5 (C1), 128.5 (C_{arom}), 129.5 (C_{arom}), 134.1 (C_{arom}), 140.4 (C_{arom}); MS (CI-NH_3): m/z 330 (M + NH_4^+), 313 (M + H^+), 295, 171, 151, 143, 127, 114, 99; Anal. Found: C, 61.19; H, 8.02%. Calcd for $C_{16}H_{24}O_4S$: C, 61.51; H, 7.74%.

General protocol for Tsuji allylation experiments. All these experiments were similarly realized and only the homolagation of ketosulfone **37** to **44** using ethyl methallyl carbonate is described.

4-Methyl-1-(1-methylcyclopropyl)-2-(phenylsulfonyl)pent-4-en-1-one 44: With stirring, in a flask equipped with a tube containing PPh_3 (11 mg, 36.0 mmol), and connected to an argon/vacuum, [$Pd_2dba_3.CHCl_3$] (6.4 mg, 5.4 mmol) was diluted with THF (450 μL). The resulting solution was thoroughly degassed before adding sequentially PPh_3 and, with a syringe, a degassed solution of ketosulfone **37** (43 mg, 0.18 mmol) and ethyl methallyl carbonate (52 mg, 0.36 mmol) in THF (300 μL). After 2 h stirring at rt, when the reaction was completed in TLC, the reaction mixture was filtered on Celite® (washings with CH_2Cl_2). The filtrates were concentrated in a vacuum and the residue was purified by column chromatography (hexane/EtOAc) to give a white solid (47 mg, 90%) identified as **44** by NMR; TLC (hexane:EtOAc = 3:1) R_f = 0.37; mp 57 °C; ^{1}H NMR ($CDCl_3$): δ 0.76 (m, 1H, C*H*H), 0.86 (m, 1H, C*H*H), 1.28 (m, 1H, CH*H*), 1.38 (m, 1H, CH*H*), 1.41 (s, 3H, C(O)CCH_3), 1.65 (s, 3H, C=CC*H*$_3$), 2.47-2.62 (m, 2H, SO_2CHCH_2), 4.58 (dd, J = 10.2, 4.3 Hz, 1H, SO_2CH), 4.59 (m, 1H, C=C*H*H), 4.76 (m, 1H, C=CH*H*), 7.52-7.59 (m, 2H), 7.64-7.71 (m, 1H), 7.76-7.80 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 19.9 (C=C*C*H$_3$), 20.0 (CH_2), 20.1 (CH_2), 22.6 [C(O)C*C*H$_3$], 28.6 [C(O)*C*CH$_3$], 36.5 (SO_2CHCH_2), 67.7 (SO_2CH), 114.3 (C=*C*H$_2$), 128.9 (C_{arom}), 130.0 (C_{arom}), 134.3 (C_{arom}), 136.7 (*C*=CH$_2$), 139.9 (C_{arom}), 203.3 (CO); MS (CI-NH_3): m/z 293 (M + H^+), 151, 95, 83, 55; Anal. Found: C, 66.02; H, 7.14%. Calcd for $C_{16}H_{20}O_3S$: C, 65.73; H, 6.89%. Hydrogenation (5% Pd/C, 1 atm H_2) of sulfone **44** (26 mg, 88.9 mmol) in EtOAc afforded, after the usual processing, sulfone **43** (25.1 mg, 96%) as a white solid (mp and mixed mp: 113 °C).

2,6,10-Trimethylundec-1-ene 61: Wittig methylenation of tetrahydrogeranylacetone **62** to **61** has previously been reported.[34] An improved procedure using Hoshima reagent conditions[35] is described below.

Geranylacetone **46** was hydrogenated to **62** (5% Pd/C, EtOAc, 1 atm H_2); TLC (hexane:ether = 3:1) R_f = 0.45; ^{1}H RMN ($CDCl_3$): δ 0.76 (d, J = 6.4 Hz, 3H); 0.86 (d, J = 6.6 Hz, 6H); 1.00-1.66 (m, 12H); 2.13 (s, 3H); 2.39 (t, J = 7.5 Hz, 2H); ^{13}C RMN ($CDCl_3$): δ 19.4, 21.4, 22.4, 22.5, 24.6, 27.9, 29.5, 32.6, 36.5, 37.1, 39.3, 208.3; MS (CI-NH_3): m/z 216 (M + NH_4^+), 199 (M + H^+), 140, 124, 109, 95, 85, 71, 58. In a flask connected to an argon/vacuum line, activated zinc powder (5.9 g, 90.7 mmol) was covered with THF (120 mL) and the resulting mixture was thoroughly degassed (three freeze/pump/thaw cycles). With stirring, CH_2I_2 (4.1 mL, 50.4 mmol) was added dropwise with a syringe and, 30 min later,

the flask was immersed in a dry ice/methanol bath. With good stirring, $TiCl_4$ (4.45 mL, 440.3 mmol) was added progressively with a syringe. The cooling bath was removed and after 30 min stirring a degassed solution of **62** (2 g, 10.08 mmol) in THF (20 mL) was transferred dropwise into the flask with a cannula. The reaction mixture was stirred at rt for a further 1 h before being diluted with ether (50 mL) and 1 M HCl (100 mL). The solids were eliminated by filtration on a sintered funnel (washings with ether) and the aqueous layer was extracted with ether (3 x 40 mL). The pooled organic phases were washed with water (2 x 50 mL), brine (50 mL), and dried ($MgSO_4$). The residue left by evaporation of the solvents was purified by column chromatography (hexane) to give, after thorough elimination of the solvents in a vacuum, **61** as a colourless oil (1.404g, 71%); TLC (hexane:ether = 9:1) R_f = 0.9; ^{1}H NMR ($CDCl_3$): δ 0.86 (d, J = 6.5 Hz, 3H), 0.87 (d, J = 6.6 Hz, 6H), 1.05-1.50 (m, 12H), 1.72 (m, 3H), 1.99 (t, J = 7.6 Hz, 2H), 4.66-4.69 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 19.7 (CH_3), 22.4 (CH_3), 22.6 (CH_3), 22.7 (CH_3), 24.8 (CH_2), 25.1 (CH_2), 28.0 (CH), 32.7 (CH), 36.7 (CH_2), 37.3 (CH_2), 38.2 (CH_2), 39.4 (CH_2), 109.5 (C=*C*H_2), 146.3 (C); MS (CI-NH_3): m/z 214 (M + NH_4^+), 197 (M + H^+), 179, 138, 123, 109, 95, 81, 71, 59.

2-(4,8-Dimethylnonyl)-2-methyloxirane 45: With stirring, *m*-CPBA (2.05 g, 9.15 mmol) was added progressively to a cooled (ice bath) solution of olefin **61** (1.2 g, 6.11 mmol) in CH_2Cl_2 (60 mL). After 30 min, the cooling bath was removed and the reaction mixture was stirred for a further 30 min before being poured into 10% $NaHCO_3$ (60 mL). Na_2SO_3 (0.4 g) was added and the resulting mixture was vigorously stirred 10 min. The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL) and the pooled organic phases were washed with 10% $NaHCO_3$ (2 x 20 mL), brine (20 mL), and dried ($MgSO_4$). The residue left by evaporation of the solvents was diluted with CH_2Cl_2 and then filtered on silica gel (washings with CH_2Cl_2) to give, after thorough elimination of the solvents in a good vacuum, epoxide **45** (1.102 g, 85%) as a colourless oil; TLC (hexane:ether = 9:1) R_f = 0.47; ^{1}H NMR ($CDCl_3$): δ 0.84 (d, J = 6.5 Hz, 3H), 0.86 (d, J = 6.6 Hz, 6H), 1.01-1.65 (m, 14H), 1.29 (s, 3H), 2.55 (d, J = 4.9 Hz, 1H), 2.57 (d, J = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 19.6 (CH_3), 20.9 (CH_3), 22.6 (CH_3), 22.7 (CH_3), 22.7 (CH_2), 24.8 (CH_2), 27.8 (CH), 32.7 (CH), 37.0 (CH_2), 37.1 (CH_2), 37.2 (CH_2), 39.3 (CH_2), 53.9 (CH_2), 57.0 (C); MS (CI-NH_3): m/z 230 (M + NH_4^+), 213 (M + H^+), 180, 169, 137, 123, 109, 95, 85, 72, 55; Anal. Found: C, 79.22; H, 13.07%. Calcd for $C_{14}H_{28}O$: C, 79.18; H 13.29%.

6,10-Dimethyl-2-methyleneundecan-1-ol *exo*-47b and (*E*/*Z*)-2,6,10-trimethylundec-2-en-1-ol *endo*-47b: Epoxide **45** (1g, 4.7 mmol) was refluxed with aluminium isopropoxide (2.88 g, 14.1 mmol) in toluene (24 mL) for 5 h. After cooling to rt, the reaction mixture was poured into a stirred mixture of ether (50 mL) and pH 2 tartaric buffer (100 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the pooled organic phases were washed with pH 2 tartaric buffer (30 mL), brine (2 x 30 mL), and dried ($MgSO_4$). Purification of the residue left by evaporation of the solvents by column chromatography (hexane/EtOAc) afforded, after elimination of the solvents in a good vacuum, a 2:1 mixture (by GC and ^{1}H NMR) of alcohols ***exo*-47b** and ***endo*-47b** as a colourless oil (971 mg, 97%); TLC (hexane:ether = 4:1) R_f = 0.32; ^{1}H NMR ($CDCl_3$): δ 0.83-0.87 (4 s, 13.5H, CH_3), 1.02-1.58 (m, 18.5H), 1.65/1.77 (2 s, 1H, *E* and *Z*-CH=CCH_3), 1.97-2.05 (m, 2H, CH_2C=CH_2 and CH_2CH=CCH_3), 3.98/4.05/4.12 (3 s, 2H, CH_2O), 4.85/5.00 (2 s, 1.3H, C=CH_2), 5.28/5.38 (2 t, J = 7.1 Hz/J = 8.0 Hz, 0.4H, *E*- and Z-C*H*=CMe); MS (CI-NH_3): m/z 230 (M + NH_4^+), 213 (M + H^+), 194, 179, 165, 151, 139, 123, 109, 95, 81, 69.

Ethylcarbonates *exo*-47a and *endo*-47a: Pyridine (408 µL, 5 mmol) and ethyl chloroformate (444 µL, 4.62 mmol) were added sequentially with a syringe to a cooled (ice bath) solution of the preceding alcohol mixture (901 mg, 4.2 mmol) in ether (10 mL). The bath was removed and the reaction mixture was further stirred for 3.5 h at rt before being poured into 10% NH_4Cl. The aqueous phase was extracted with ether (3 x 5 mL) and the pooled organic extracts were washed with water (2 x 6 mL), brine (6 mL), and dried ($MgSO_4$). The oily residue left by elimination of the solvents was purified by column chromatography (hexane/EtOAc) to give a 2:1 mixture (by GC) of,

respectively, ***exo*-47a** and ***endo*-47a** as a colourless oil (1.07 g, 89%); TLC (hexane:EtOAc) R_f = 0.47; ^{1}H NMR ($CDCl_3$): δ 0.82-0.87 (4 s, 13.5H, CH_3), 1.08-1.53 (m, 23H), 1.66/1.77 (2 s, 1 H, C*H*$_3$C=CH), 1.97-2.10 (m, 2H, C*H*$_2$C=CH_2, C*H*$_2$CH=C), 4.09/4.19 (2 q, *J* = 7.1Hz, 2H), 4.49/4.55/4.63 (3 s, 2H, CH_2O), 4.94/5.04 (2 s, 1.4H, C=C*H*$_2$), 5.39/5.48 (2 t, *J* =7.1 Hz/*J* = 7.0 Hz, 0.4H, *E*- and Z-C*H*=C(Me); ^{13}C NMR ($CDCl_3$): δ 14.2 (CH_3), 19.6 (CH_3), 21.8 (CH_3), 22.5 (CH_3), 22.6 (CH_3), 24.9 (CH_2), 25.0 (CH_2), 27.9 (CH), 32.6 (CH), 33.3 (CH_2), 36.4 (CH_2), 36.6 (CH_2), 37.2 (CH_2), 39.3 (CH_2), 63.9 (CH_2O), 66.4 (CH_2O), 70.0 (CH_2O), 72.8 (CH_2O), 73.7 (CH_2O), 112.6 (C=*C*H$_2$), 129.0 (*C*H=C), 129.1 (*C*H=C), 131.1 (CH=*C*), 132.0 (CH=*C*), 143.7 (*C*=CH_2), 153.1 (C=O), 155.3 (C=O); MS (CI-NH_3): *m*/*z* 285 (M + H^+), 194, 179, 152, 123, 109, 95, 81, 69, 55.

8,12-Dimethyl-1-(1-methylcyclopropyl)-4-methylene-2-(phenylsulfonyl)tridecan-1-one 48: General protocol for Tsuji-allylation experiments. In THF (3.7 mL), with added [Pd_2dba_3.$CHCl_3$] (46 mg, 25.9 mmol) and PPh_3 (80.2 mg, 306 mmol). From ketosulfone **37** (365 mg, 1.53 mmol) and the ***exo*-47a**/***endo*-47a** carbonate mixture (825 mg, 3.06 mmol). Isolated: ketosulfone **48** (612.3 mg, 92%) as a colourless oil. TLC (hexane:EtOAc = 3:1) R_f = 0.5; ^{1}H NMR ($CDCl_3$): δ 0.76-0.86 (m, 11H), 0.95-1.55 (m, 17H), 1.88 (t, *J* = 7.4 Hz, 2H, C5H_2), 2.47-2.62 (m, 2H, C3H_2), 4.58 (dd, *J* = 10.2, 4.3 Hz, 1H, SO_2CH), 4.62 (m, 1H, C=C*H*H), 4.76 (m, 1H, C=CH*H*), 7.52-7.58 (m, 2H), 7.64-7.72 (m, 1H), 7.77-7.83 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 19.7 (CH_3), 19.9 (CH_3), 20.1 (CH_2), 20.2 (CH_2), 22.7 (CH_3), 22.8 (CH_3), 24.9 (CH_2), 25.1 (CH_2), 28.1 (CH), 32.7 (CH), 34.8 (CH_2), 36.2 (CH_2), 36.3 (CH_2), 36.7 (CH_2), 37.3 (CH_2), 37.4 (CH_2), 67.9 (SO_2CH), 112.9 (C=*C*H_2), 128.9 (C_{arom}), 130.0 (C_{arom}), 134.3(C_{arom}), 136.8 (*C*=CH_2) 144.2 (C_{arom}), 203.3 (C=O); MS (CI-NH_3): *m*/*z* 433 (M + H^+), 291 (M – $SO_2C_6H_5$), 194, 151, 109, 95, 83, 55; Anal. Found: C, 72.54; H, 9.67%. Calcd for $C_{26}H_{40}O_3S$: C, 72.18; H 9.32%.

4,8,12-Trimethyl-1-(1-methylcyclopropyl)tridecan-1-ol 2: In a flask equipped with a condenser connected to an argon line, with stirring, β-ketosulfone **48** (600 mg, 1.38 mmol) was heated to reflux in EtOH (12 mL) with activated Raney nickel (ca. 3 g) for 5 h. After cooling, the reaction mixture was filtered on Celite® (washings with ethanol) and the filtrates were dried ($MgSO_4$), and concentrated in a vacuum. The residue was purified by column chromatography (hexane/EtOAc) to give, after evaporation of the solvents in a vacuum, an oily product (377.3 mg) constituted of ketones **20** and **49**, as estimated by GC-mass; **20**: MS (CI-NH_3): *m*/*z* 295 (M + H^+), 266, 125, 111, 98, 83, 69, 55. **49**: MS (CI-NH_3) *m*/*z* 315 (M + NH_4^+), 297 (M + H^+), 196, 165, 126, 113, 95, 85, 72, 57. In an argon atmosphere, with stirring, LAH (42 mg, 1.1 mmol) was added to a cooled (ice bath) solution of the desulfonylation product (294.5 mg, 1.0 mmol) in ether (4.5 mL). After 1 h stirring at ca. 0 °C, the reaction mixture was diluted with ether (1 mL) and 10% aqueous Na_2SO_4 was added progressively until formation of a past (ca. 1 mL). The solids were eliminated by filtration on a sintered funnel (washings with ether) and the filtrates were washed with 0.1 M HCl (5 mL), brine (2 x 6 mL), and dried ($MgSO_4$). The residue left by elimination of the solvents was chromatographed on silica gel (hexane/ether) to give, successively: the alcohol **50** (88 mg, 29%) and the cyclopropyl carbinol **2** (207 mg, 69%), both as clear colourless oil; TLC (hexane:ether = 3:2) R_f = 0.40; ^{1}H NMR ($CDCl_3$): δ 0.26-0.35 (m, 4H), 0.82-0.88 (m, 12H), 1.01 (s, 3H, CCH_3), 1.02-1.58 (m, 20H, in which OH), 2.77 (m, 1H, CHO); ^{13}C NMR ($CDCl_3$): δ 11.4/11.5/11.8/11.9 (CH_2), 17.1/17.2 (CCH_3), 19.7/19.8 (CH_3), 31.7/33.6/33.7/37.4/37.5/39.4 (CH_2), 28.1 (C12H), 32.9/33.0/33.1 (CH), 79.5/79.7 (CHOH); MS (CI-NH_3) *m*/*z* 296 (M), 279, 268, 250, 239, 196, 165, 126, 111, 95, 85, 71, 57; HRMS found: *m*/*z* 296.3087; calcd for $C_{20}H_{40}O$: 296.3079. **50**: TLC (hexane:ether = 3:2) R_f = 0.50; ^{1}H NMR ($CDCl_3$): δ 0.84-0.95 (m, 18H), 1.01-1.65 (m, 23H, in which OH), 3.37 (m, 1H, CHO); ^{13}C NMR ($CDCl_3$): δ 11.9/12.0 (CH_3), 13.2/13.3 (CH_3), 19.7/19.8/20.0.22.8/22.9 (CH_3), 24.5/24.6/24.7/24.9/25.0/26.2/26.3 (CH_2), 28.1 [*C*(CH_3)$_2$], 31.1/33.2/33.4/33.5/33.6/33.7/37.4/37.6/39.4 (CH_2), 32.9/33.0/33.1/40.0/40.1/40.6/40.7 (CH), 75.4/75.5/76.2/76.4 (CHO); MS (CI-NH_3) *m*/*z* 280 (M-18), 241, 197, 167, 139, 125, 111, 97, 83, 69, 57; HRMS found:

m/*z* 298.3243; calcd for $C_{20}H_{42}O$: 298.3236.

(*E*)-1-bromo-3,7,11,15-tetramethylhexadec-3-ene 11: The protocol used is essentially that described by Johnson.[1a] In a flask connected to an argon line, with stirring, a solution of PBr_3 (18 μL, 0.185 mmol) in ether (870 μL) was added dropwise with a syringe to a cooled (dry-ice/acetone bath) mixture of alcohol **2** (47.2 mg, 0.16 mmol), collidine (82 μL) and LiBr (16.1 mg, 0.185 mmol) diluted with ether (870 μL). After 20 h stirring at rt, the flask was immersed in an ice bath and collidine (50 μL) was added, followed by water (3 mL). The aqueous layer was extracted with pentane (4 x 1 mL) and the pooled organic phases were washed with 10% $NaHCO_3$ (2 x 1 mL), brine (1 mL), and dried ($MgSO_4$). The residue left by evaporation of the solvents was diluted with ether (870 μL) and then added, with stirring, to a cooled (ice bath) suspension of anhydrous $ZnBr_2$ (37.0 mg, 0.164 mmol) in ether (870 μL). After 3 h stirring at ca. 0 °C, the reaction mixture was diluted with pentane (1 mL) and brine (1 mL). The aqueous layer was extracted with pentane (4 x 1 mL) and the pooled organic extracts were washed with brine (2 x 1 mL), and dried (K_2CO_3). The residue left by elimination of the solvents was purified by filtration on a column of neutral alumina (washings with pentane) to give, after thorough elimination of the solvents in a good vacuum, the bromide **11** (48.6 mg, 84%) as a colourless oil; TLC (hexane:ether = 9:1) R_f = 0.70; ^{1}H NMR ($CDCl_3$): δ 0.83-0.89 (m, 12H, 4 CH_3), 1.01-1.58 (m, 17H, 3 CH, 7 CH_2), 1.63 (s, 3H, C3CH_3), 1.92-2.08 (m, 2H, C5H_2), 2.53 (t, *J* = 7.6 Hz, 2H, C2H_2), 3.43 (t, *J* = 7.6 Hz, 2H, C1H_2), 5.22 (tq, *J* = 7.1, 1.2 Hz, 1H, C4H); ^{13}C NMR ($CDCl_3$): δ 15.5 (C3*C*H_3), 19.6/19.7 (C7*C*H_3/C11*C*H_3), 22.6/22.7 (2 C15*C*H_3), 24.4/24.8/26.5 (C5H_2/C9H_2/C13H_2), 27.9 (C15H), 32.4/32.8 (C7H/C11H), 31.7/36.9/37.3/37.4/37.5/39.4/42.9 (C1H_2/C2H_2/C6H_2/C8H_2/C10H_2/C12H_2/C14H_2), 128.4 (C4H); 131.4 (C3); MS (CI-NH_3): *m*/*z* 360 (M + H^+), 245, 196, 153, 139, 126, 111, 97, 83, 69, 57.

(*E*)-3,7,11,15-tetramethylhexadec-3-en-1-yl acetate 12a: With stirring, in a flask equipped with a condenser connected to an argon line, bromide **11** (146.4 mg, 0.408 mmol) was heated in DMF (1 mL) with NaOAc (36.8 mg, 0.449 mmol) at ca. 100 °C (bath) for 10 h. After cooling, the reaction mixture was diluted with water (10 mL) and extracted with ether (3 x 10 mL). The pooled organic phases were washed with brine (3 x 5 mL), dried ($MgSO_4$), and evaporated. Chromatography of the residue on silica gel (hexane/ether) afforded acetate **12a** as a colourless oil (114.5 mg, 83%); TLC (hexane:ether = 9.1) R_f = 0.43; ^{1}H NMR ($CDCl_3$): δ 0.82-0.88 (m, 12H, 4 CH_3), 1.02-1.58 (m, 17H, 3 CH, 7 CH_2), 1.63 (s, 3H, C3CH_3), 1.90-2.03 (m, 5H, C5H_2, C(O)CH_3), 2.28 (t, *J* = 7.0 Hz, 2H, C2H_2), 4.12 (t, *J* = 7.0 Hz, 2H, C1H_2), 5.17 (tq, *J* = 6.8, 1.3 Hz, 1H, C4H); ^{13}C NMR ($CDCl_3$): δ 15.9 (C3*C*H_3), 19.5/19.6/19.7 (C7*C*H_3/C11*C*H_3), 21.0 [C(O)*C*H_3], 22.6/22.7 (2 C15*C*H_3), 24.4/24.8/25.6 (C5H_2/C9H_2/C13H_2), 28.0 (C15H), 32.5/32.8 (C7H/C11H), 36.8/37.0/37.1/37.3/37.4/37.5/38.7/39.4 (C2H_2/C6H_2/C8H_2/C10H_2/C12H_2/C14H_2), 63.2 (C1H_2), 127.7 (C4H), 130.4 (C3), 171.1 (C=O); MS (CI-NH_3): *m*/*z* 278 [M – OC(O)CH_3], 179, 123, 109, 95, 82, 68, 57.

(*E*)-3,7,11,15-tetramethylhexadec-3-en-1-ol 12b: Acetate **12a** (50.0 mg, 0.16 mmol) was stirred in methanol with added K_2CO_3 (44.2 mg, 0.32 mmol) for 3 h at rt. The reaction mixture was concentrated in a vacuum and the residue was diluted with CH_2Cl_2. The solids were eliminated by filtration on a sintered funnel (washings with CH_2Cl_2) and the pooled filtrates were dried ($MgSO_4$), and evaporated. The residue was purified by column chromatography (hexane/ether) to give alcohol **12b** as a viscous oil (39.7 mg, 84%); TLC (hexane:ether = 7:3) R_f = 0.16; ^{1}H NMR ($CDCl_3$): δ 0.83-0.88 (m, 12H, 4 CH_3), 1.01-1.58 (m, 17H, 3 CH, 7 CH_2), 1.63 (s, 3H, C3CH_3), 1.91-2.10 (m, 2H, C5H_2), 2.24 (t, *J* = 6.2 Hz, 2H, C2H_2), 3.64 (t, *J* = 6.2 Hz, 2H, C1H_2), 5.23 (td, *J* = 7.1, 1.2 Hz, 1H, C4H); ^{13}C NMR ($CDCl_3$): δ 15.6 (C3*C*H_3), 19.6/19.7 (C7*C*H_3/ C11*C*H_3), 22.6/22.7 (2 C15*C*H_3), 24.4/24.8/25.6 (C5H_2/C9H_2/C13H_2), 28.0 (C15H), 32.5/32.8 (C7H/C11H), 37.0/37.1/37.3/37.4/39.4/42.7 (C2H_2/C6H_2/C8H_2/C10H_2/C12H_2/C14H_2), 60.1 (C1H_2), 128.6 (C4H), 130.8 (C3); MS (CI-NH_3): *m*/*z* 279 (M - OH), 196, 138, 123, 111, 95, 81, 69, 57.

(*E*)-3,7,11,15-tetramethylhexadec-3-enal 13: Swern oxidation of alcohol **12b** (35 mg, 0.118 mmol) with DMSO

(51 µL, 0.567 mmol) and 1 M (in CH_2Cl_2) $(COCl)_2$ (260 µL, 0.269 mmol) in CH_2Cl_2 (0.6 mL), with added NEt_3 (83 µL, 0.591 mmol) was realized using a protocol described in Ref. 2a. Processing the reaction mixture as usual afforded, after purification by column chromatography (hexane/ether), a colourless oil (29.1 mg, 84%) identified as aldehyde **13** by NMR and mass analyses; TLC (hexane:ether = 7:3) R_f = 0.52; ^{1}H NMR ($CDCl_3$): δ 0.83-0.88 (m, 12H, 4 CH_3), 1.02-1.58 (m, 17H, 3 CH, 7 CH_2), 1.66 (s, 3H, C3CH_3), 1.94-2.16 (m, 2H, C5H_2), 3.03 (t, J = 2.6 Hz, 2H, C2H_2), 5.31 (tq, J = 7.1, 1.4 Hz, 1H, C4H), 9.60 (t, J = 2.6 Hz, 1H, C1H); ^{13}C NMR ($CDCl_3$): δ 16.8 (C3*C*H_3), 19.5/19.7 (C7*C*H_3/ C11*C*H_3), 22.6/22.7 (2 C15*C*H_3), 24.4/24.8/25.6 (C5H_2/C9H_2/C13H_2), 28.0 (C15H), 32.5/32.8 (C7H/C11H), 37.0/37.1/37.3/37.4/38.5/39.4 (C6H_2/C8H_2/C10H_2/C12H_2/C14H_2), 54.3 (C2H_2), 125.9 (C4H); 131.4 (C3), 200.0 (C=O); MS (CI-NH_3): *m*/*z* 295 (M + H^+), 277, 194, 163, 149, 123, 111, 97, 84, 69, 55.

Phytal (1): A solution of aldehyde **13** (25 mg, 0.085 mmol) in 0.5 M (in MeOH) NaOH (0.5 mL) was stirred 2 h at rt before being diluted with ether (3 mL) and water (2 mL). The aqueous layer was extracted with ether (4 x 1 mL) and the pooled organic phases were washed with brine (3 x 2 mL), and dried ($MgSO_4$). Purification of the residue left by evaporation of the solvents by column chromatography (hexane/ether) afforded a colourless oil (22.2 mg, 89%) identified as a 7:3 mixture of *E*- and *Z*-phytal **1** respectively (GC-mass, NMR); TLC (hexane:ether = 7:3) R_f = 0.42, 0.40; ^{1}H NMR ($CDCl_3$): δ 0.81-0.89 (m, 12H, 4 CH_3), 0.95-1.65 (m, 19H, 3 CH, 8 CH_2), 1.97 (s, 0.9H, C3CH_3), 2.16 (s, 2.1H, C3CH_3), 2.18 (t, J = 7.8 Hz, 1.4H, C4H_2), 2.55 (t, J = 7.6 Hz, 0.6H, C4H_2), 5.86-5.91 (m, 1H, C2H), 9.96 (d, J = 8.2 Hz, 0.3H, C1H), 9.99 (d, J = 8.0 Hz, 0.7H, C1H); ^{13}C NMR ($CDCl_3$): δ 17.6 (C3*C*H_3), 19.6/19.7/19.8 (C7*C*H_3/C11*C*H_3), 22.7/22.8 (2 C15*C*H_3), 24.5/24.7/24.9 (C5H_2/C9H_2/C13H_2), 28.0 (C15H), 32.7/32.8 (C7H/C11H), 36.6/36.7/36.9/37.3/37.4/39.4/41.0 (C4H_2/C6H_2/C8H_2/C10H_2/C12H_2/C14H_2), 127.4/128.4 (C2H); 164.4/165.0 (C3), 190.9/191.4 (C=O); MS (CI-NH_3): *m*/*z* 295 (M + H^+), 277, 194, 163, 140, 121, 111, 97, 84, 69, 55.

2-Ethyl-2-[(triethylsilyl)oxy]cyclobutan-1-one 52b: A solution of 3,4-hexadione **51** (5.7 g, 50 mmol) in EtOAc (500 mL) was irradiated for 16 h under the conditions used with **21** to give, after thorough elimination of the solvents in a vacuum, the hydroxyketone **52a** as a pale-yellow oil (5.6 g, 98.2%); ^{13}C NMR ($CDCl_3$): δ 7.8 (CH_3), 26.5 (*C*H_2CH$_3$), 28.6 (C3H_2), 39.8 (C4H_2), 91.8 (C2), 211.4 (C=O). At 0 °C (ice bath), TES triflate (17.2 mL, 76 mmol) was added dropwise to a stirred solution of **52a** (5.1 g, 44.7 mmol) and collidine (10.1 mL, 76 mmol) in DMF (25 mL). The bath was removed and after a further 4 h stirring at rt the reaction mixture was processed as usual to give, after purification by column chromatography (hexane/ether), the TES ether **52b** as a colourless oil (7.32 g; overall 72%); TLC (hexane:ether = 4:1) R_f = 0.74; ^{1}H NMR ($CDCl_3$): δ 0.64 (m, 6H), 0.96 (m, 12H), 1,68 (q, J = 7.4 Hz, C*H*$_2$CH$_3$), 2.05 (m, 2H, C3H_2), 2.72 (m, C4H_2); ^{13}C NMR ($CDCl_3$): δ 5.9 (SiCH_2), 6.8 SiCH_2*C*H_3), 7.9 (CH_3), 27.2 (*C*H_2CH$_3$), 30.3 (C3H_2), 38.8 (C4H_2), 92.6 (C2), 211.2 (C=O); Anal. Found: C, 63.36; H, 10.47%. Calcd for $C_{12}H_{24}O_2Si$: C, 63.10; H, 10.59%.

2-Ethyl-1-[(phenylsulfonyl)methyl]-2-[(triethylsilyl)oxy]cyclobutan-1-ol 53: General protocol for cyclobutanone/sulfone condensation experiments. In THF (90 mL). From ketone **52b** (2.92 g, 12.8 mmol) and sulfone **33** (2.0 g, 12.8 mmol). Isolated: hydroxysulfone **53** (65:35 mixture of the *trans*- and the *cis*-isomer, by GC and NMR) as a pale-yellow oil (4.49 g, 91%); TLC (hexane:ether = 4:1) R_f = 0.14; ^{1}H NMR ($CDCl_3$): δ 0.6-1.1 (m, 18H), 1.48-2.30 (m, 6H), 3.40 (brs, 0.7H), 3.41 (dd, J = 14.7, 1.3 Hz, 0.65H), 3.61 (d, J = 14.7 Hz, 0.65H), 7.59 (m, 3H), 7.94 (m, 2H) ; ^{13}C NMR ($CDCl_3$): δ 6.7 (SiCH_2), 7.11 (SiCH_2*C*H_3), 8.38/8.46 (CH_3), 28.0/28.8 (C*H*$_2$CH$_3$), 29.2/29.5 (C3H_2), 29.8/31.8 (C4H_2), 60.7/62.0 (SO_2CH_2), 77.0/78.5 (C2), 81.0/82.6 (C1), 127.6/128.3/128.9/129.3/133.4/133.8/141.2/141.4 (C_{arom}); Anal. Found: C, 59.71; H, 8.73%. Calcd for $C_{19}H_{32}O_4SSi$: C, 59.34; H, 8.39%.

1-(1-Ethylcyclopropyl)-2-(phenylsulfonyl)ethan-1-one 54: General protocol for TsF/DBU-mediated rearrangement experiments. In CH_3CN (50 mL), with added TsF (7.6 g, 43.6

mmol) and DBU (6.53 mL, 43.6 mmol); 23 h at ca. 30-40 °C (bath). From sulfone **53** (4.64 g, 12 mmol). Obtained, after re-crystallisation from ether/hexane: β-ketosulfone **54** (1.98 g, 65%) as colourless crystals; TLC (hexane:ether = 3:7) R_f = 0.41; mp 67 °C; ^{1}H NMR ($CDCl_3$): δ 0.87 (m, 2H, 2 C*H*H), 0.90 (t, J = 7.3 Hz, 3H, CH_3), 1.27 (m, 2H, 2 CH*H*), 1.64 (q, J = 7.3 Hz, 2H, C*H*$_2$CH$_3$), 4.06 (s, 2H, SO_2CH_2), 7.56-7.67 (m, 3H), 7.90 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 11.6 (CH_3), 16.1 (CH_2), 26.3 (*C*H$_2$CH$_3$), 34.3 (C), 61.2 (SO_2CH_2), 128.6/129.1/134.1/139.0 (C_{arom}), 198.5 (C=O); crystal data $C_{13}H_{16}O_3S$, MW= 252.32, 0.20 x 0.20 x 0.14 mm, Monoclinic, space group P 2$_1$/*n*, T = 173 K, a = 15.1060(6), b = 5.3930(3), c = 16.1750(9) Å, β = 108.160(3)°, V = 1252.09(11) Å^3, λ (Mo-Kα) = 0.71073 Å, μ = 0.252 mm^{-1}. A total of 6345 reflections were measured and 3657 were independent. Final = R1 = 0.0419, wR2 = 0.1069 (2696 refs; $I > 2\sigma(I)$), and GOF =1.037 (for all data, R1 = 0.0662, wR2 = 0.1180).

Ethyl {1-[(4-methoxybenzyl)oxy]-3-methylbut-3-en-2-yl} carbonate 55a: Alcohol **55b** was prepared from prenol **56** as described;[25] TLC (hexane:ether = 1:1) R_f = 0.32; ^{13}C NMR ($CDCl_3$): δ 18.8 (CH_3), 55.25 (OCH_3), 73.0 (2 CH_2O), 73.9 (*C*HOH), 112.0 (C=*C*H$_2$), 113.9 (C_{arom}), 129.4 (C_{arom}), 130.0 (C_{arom}), 143.8 (*C*=CH$_2$), 159.4 (C_{arom}). **55b** (1.38 g, 6,21 mmol) was reacted with ethyl chloroformate (1.18 mL, 12.4 mmol) in ether (55 mL) with added pyridine (1.1 mL, 13.6 mmol) under the conditions used for carbonatation of the ***exo*-47b**/***endo*-47b** alcohol mixture (see above) to give, after the usual processing, followed by purification by column chromatography (hexane/ether), carbonate **55a** as a colourless oil (1.54 g, 84%); TLC (hexane:ether = 1:1) R_f = 0.58; ^{1}H NMR ($CDCl_3$): δ 1.30 (t, J = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 1.74 (s, 3H, C*H*$_3$C=CH$_2$), 3.51-3.62 (m, 2H, OCHC*H*$_2$), 3.79 (s, 3H, OCH_3), 4.18 (q, J = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 4.49 (s, 2H, OCH_2), 4.97 (brs, 1H, C=C*H*H), 5.06 (brs, 1H, C=CH*H*), 5.19 (m, 1H, C*H*OH), 6.86 (m, 2H), 7.24 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 14.2 (*C*H$_3$CH$_2$), 18.9 (*C*H$_3$C=CH$_2$), 55.3 (OCH_3), 64.0 (CH$_3$*C*H$_2$), 70.2 (CH*C*H$_2$), 72.9 (OCH_2), 79.5 [*C*HO(CO)], 113.8 (C_{arom}), 114.0 (*C*H$_2$=C), 129.3 (C_{arom}), 130.0 (C_{arom}), 140.6 (*C*=CH$_2$), 154.6 (C=O), 159.3 (C_{arom}); Anal. Found: C, 64.93; H, 7.78 %. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53 %.

(*E*)-1-(1-Ethylcyclopropyl)-6-[(4-methoxybenzyl)oxy]-4-methyl-2-[(phenylsulfonyl)methyl]hex-4-en-1-one 57: Ketosulfone **54** (400 mg, 1.58 mmol) and carbonate **55a** (930 mg, 3.16 mmol) were reacted in THF (7 mL) with added [Pd_2dba_3.$CHCl_3$] (57 mg, 55 mmol) and PPh_3 (41.5 mg, 0.158 mmol) under the general Tsuji-allylation conditions (see above). After 3 h stirring at rt, the reaction mixture was filtered on Celite® (washings with ether) and the filtrates were concentrated in a vacuum. The residue was chromatographed on silica gel (hexane/ether) to give a colourless oil (567 mg, 78%) identified as **57** by NMR analysis; TLC (hexane:ether = 1:1) R_f = 0.22; ^{1}H NMR ($CDCl_3$): δ 0.86 (m, 1H, C*H*H), 0.89 (t, J = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 1.08 (m, 1H, C*H*H), 1.51 (m, 3H, CH*H*, C*H*$_2$CH$_3$), 1.57 (s, 3H, CH$_3$C=C), 1.76 (m, 1H, CH*H*), 2.54 (m, 2H, SO_2CHC*H*$_2$), 3.78 (s, 3H, OMe), 3.88 (d, J = 6.6 Hz, 2H, C*H*$_2$OCH$_2$C$_{arom}$), 4.08 (dd, J = 10.7, 3.7 Hz, 1H, SO_2CH), 4.35 (s, 2H, OCH$_2$C$_{arom}$), 5.34 (brt, J = 6.6 Hz, 1H, C=CH), 6.64 (m, 2H, C$_{arom}$H), 7.20 (m, 2H, C$_{arom}$H), 7.54 (m, 2H, C$_{arom}$H), 7.67 (m, 1H, C$_{arom}$H), 7.77 (m, 2H, 2 C$_{arom}$H; ^{13}C NMR ($CDCl_3$): δ 11.4 (CH$_2$*C*H$_3$), 15.7 (CH_2), 16.1 (CH_2), 16.7 (*C*H$_3$C=C), 26.3 (*C*H$_2$CH$_3$), 34.9 (C), 38.7 (SO_2CH*C*H$_2$), 55.3 (OCH_3), 65.8 (C=CH*C*H$_2$O), 66.7 (SO_2CH), 71.7 (OCH_2), 113.8 (C_{arom}), 126.8 (C=*C*HCH$_2$), 128.8 (C_{arom}), 129.4 (C_{arom}), 130.0 (C_{arom}), 130.3 (C_{arom}), 133.5 (*C*=CHCH$_2$), 134.2 (C_{arom}), 136.5 (C_{arom}), 159.2 (C_{arom}), 202.3 (C=O); Anal. Found: C, 68.61; H, 7.39%. Calcd for $C_{26}H_{32}O_5S$: C, 68.39; H, 7.06%.

(*E*)-1-(1-Ethylcyclopropyl)-6-[(4-methoxybenzyl)oxy]]-4-methylhex-4-en-1-one 58:

In a flask connected to an argon line, freshly activated aluminium (420 mg) was added to ketosulfone **57** (200 mg, 0.44 mmol) diluted with 9:1 THF/H_2O (12 mL). The resulting mixture was stirred 4 h at rt, and then filtered on a sintered funnel (washings with THF). The filtrates were concentrated in a vacuum and the residue was diluted with ether (15 mL) and water (10 mL). The aqueous phase was extracted with ether (2 x 5 mL) and the pooled organic phases were washed

with brine (4 x 10 mL), and dried ($MgSO_4$). The residue left by evaporation of the solvents was purified by column chromatography (hexane/ether) to give a colourless oil (103 mg, 75%) identified as **58** by NMR; TLC (hexane:ether = 1:1) R_f = 0.68; ^{1}H NMR ($CDCl_3$): δ 0.71 (m, 2 C*H*H), 0.93 (t, *J* = 7.3 Hz, 3H, CH_2CH_3), 1.14 (m, 2H, 2 CH*H*), 1.62 (s, 3H, CH_3C=C), 1.64 (q, *J* = 7.3 Hz, 2H, CH_2CH_3), 2.25 [m, 2H, $C(O)CH_2CH_2$], 2.41 [m, 2H, $C(O)CH_2$], 3.75 (s, 3H, OCH_3), 3.97 (d, *J* = 6.7 Hz, 2H, CH_2O), 4.41 (s, 2H, OCH_2C_{arom}), 5.34 (t, *J* = 6.7 Hz, 1H, C=CH), 6.86 (m, 2H), 7.25 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 11.9 (CH_2CH_3), 15.6 (2 CH_2), 16.7 (CH_3C=C), 26.7 (CH_2CH_3), 32.9 (C), 33.6 [$C(O)CH_2CH_2$], 35.4 [$C(O)CH_2CH_2$], 55.3 (OCH_3), 66.3 (CH_2O), 71.9 (OCH_2C_{arom}), 113.8 (C_{arom}), 121.1 (C=*C*HCH_2), 129.4 (C_{arom}), 130.6 (C_{arom}), 139.2 (*C*=$CHCH_2$), 159.2 (C_{arom}), 210.2 (C=O); Anal. Found: C, 76.22; H, 9.28 %. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92%.

Crystallographic data have been deposited with Cambridge Crystallographic Data Centre: Deposition numbers CCDC-1568404 and CCDC-1568399 for compounds ***trans*-34a** and **54** respectively. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

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Supporting Information

^{1}H and ^{13}C NMR spectra. Procedures for the synthesis of alcohol **2** from ester **3** and dinitrile **5**. This material is available free of charge on J-STAGE.

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