Chirality Transfer in Phase-Transfer Processes: Preparation of Homochiral Substituted Cyclopentenones†

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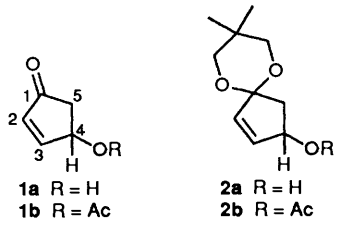
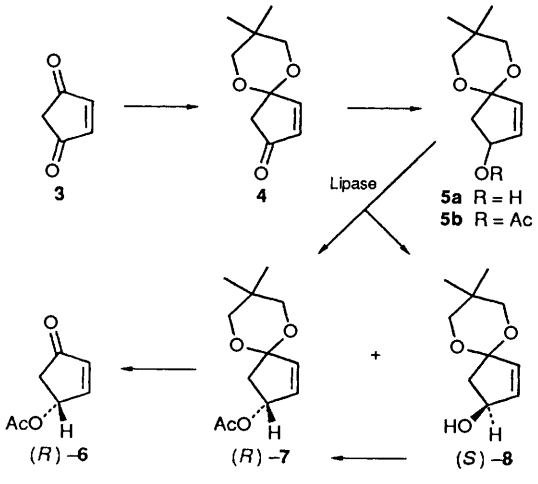
A very efficient phase transfer reaction for the preparation of the homochiral substituted cyclopentenones **13, 15** and **17** from (*R*)-4-acetoxycyclopent-2-enone **1** in a chirality transfer process is reported. The synthetic applications of the reaction products are demonstrated.

Derivatives of 4-hydroxycyclopentenone **1a** have been shown to be highly flexible building blocks in organic synthesis.[1] This had led to the elaboration of a number of routes leading to both enantiomers in optically pure form, either from enantiomerically pure starting materials or *via* enantioselective synthesis.[1]



Scheme 1

Holding the carbonyl group responsible for the tendency of **1a** to racemize, we focused on ketals **2a** and **2b** as the most promising candidates for this venture. This was particularly tempting as monoketal **4** is easily available from the well known diketone **3** and additionally can be reduced in high yield using the Luche[2] procedure to provide the allylic alcohol **5a** which gives rise to a quantitative yield of acetate **5b** on conventional acetylation.

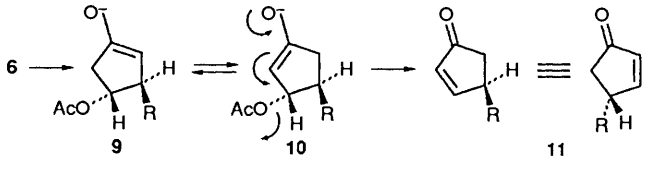


Scheme 2

This product was considered the substrate of choice for an enzymatic hydrolysis with kinetic resolution. Highly satisfactory results were indeed obtained with lipase type P (Amano Pharm Co. Ltd.) and the products obtained this way, proved to be the (*R*)-acetate **7** and the (*S*)-alcohol **8**, which can easily be separated by chromatography.[2] Acid catalyzed hydrolysis of **7** generates (*R*)-acetoxycyclopentenone **6** without any loss of optical purity.[3]

At this stage we decided on a very general check of the configurational stability of ketone **6** and proved that storage at room temperature in ether solution or treatment with a catalytic amount of toluene-*p*-sulphonic acid in tetrahydrofuran solution for 1 week left the configuration at C-4 absolutely untouched.

Since in recent years we had developed various routes to natural products, using the 1,4-addition–elimination tandem **9** → **10** → **11** to prepare substituted cyclopentenones, we were, of course, very much interested in the chirality transfer for these processes, since starting from one pure enantiomer this transformation amounts to a substitution with retention.



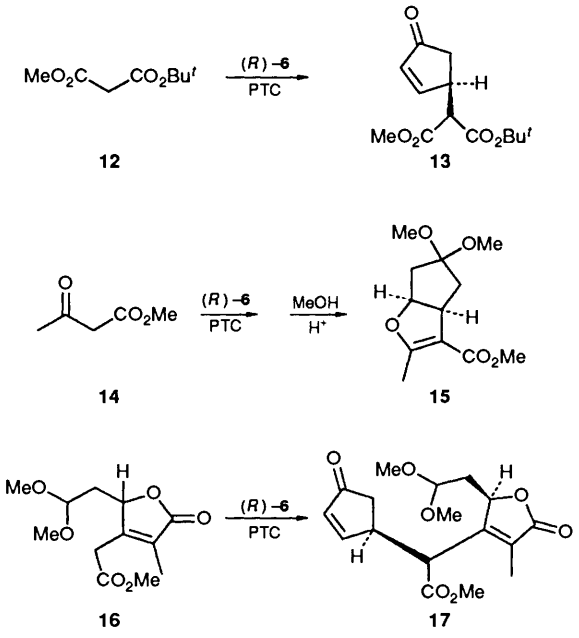
Scheme 3

Since, additionally, compounds **13**,[4] **15**[5] and **17**[6] have been of particular interest as synthetic intermediates[7] we investigated the chirality transfer for conjugate additions with **12, 14** and **16** first.

Although various reaction conditions have been used for the 1,4-addition–elimination sequence, a systematic investigation proved a phase transfer process using solid potassium carbonate and a crown ether (18-crown-6) in toluene to be the most reliable procedure. Consistently high yields were obtained with a very broad array of Michael donors.

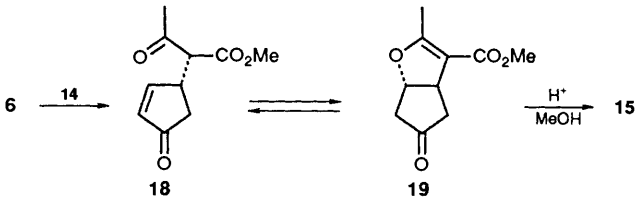
When the mixed malonate **12** was added under these conditions, the cyclopentenone **13** was obtained in 82% chemical yield and by NMR-shift experiments, done with (+)-HFC‡ on the olefinic protons, the optical purity was determined as 93.3% ee starting with a sample of ketal **7** which showed 95% ee; this proved that both steps, the hydrolysis as well as the Michael addition, proceeded, within the limits of error, without any loss of configurational purity. The formation of the dihydrofuran **15** has been investigated in detail in the racemic series[4] where it was shown that the results obtained

† Submitted to mark the 150th anniversary of the Chemical Society/Royal Society of Chemistry.
‡ HFC = Tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III).



Scheme 4

with *tert*-butoxy acetoacetate hold quite well for β-keto esters in general. The proton acceptor used in this case was to be lithium hydride and under these conditions an equilibrium mixture of the ring opened β-keto ester **18** and the dihydrofuran **19** were obtained.

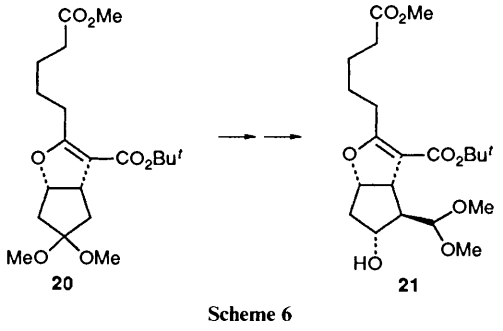


Scheme 5

Since for further preparative work as well as for shift-measurements this represents a severe drawback, the addition sequence for simplicity's sake was generally followed by a ketalization step ($MeOH/H^+$); this shifts the equilibrium completely to one side, thus focussing the material into the bicyclic dihydrofuran **15**. Since this is stable and easy to purify, its optical purity was again checked with (+)-HCF in deuteriated benzene. In this case there was, however, a small but reproducible drop in optical purity with lithium hydride as the proton accepting species. Starting with an ee of 95% for the ketal **7**, an 80% ee was obtained for the final product **15**. To find the configurational leak we first of all proved the configurational stability of **15** under acidic conditions. This led us to conclude that racemization can only take place at stage **18** *via* base catalysed enolization of the cyclopentenone. Expecting a higher selectivity from our phase transfer system we ran this transformation with potassium carbonate and 19-crown-6, and were pleased to note that under these conditions perfect chirality transfer took place again.

As the same holds for ketal **20**, which has been regio-selectively and stereoselectively converted into the acetal **19**,[8] this opens an enantioselective route to acceptor-stabilized prostacyclines.

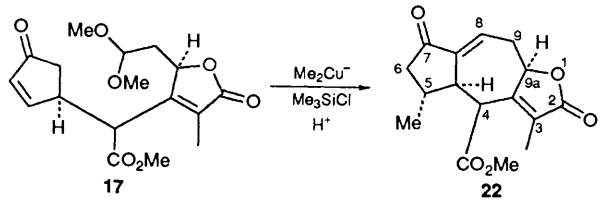
As an entry into the hydroazulene series we investigated the butenolide donor **16**, again using the PTC-addition technique. As in the racemic series, the pair of epimeric esters **17** were obtained in 90% chemical yield and in subsequent shift measurements with (+)-HFC using the nicely separated OCH_3



Scheme 6

resonances of the acetal group, a complete chirality transfer was easily proven. This addition is of synthetic value since in our earlier experiments in the racemic series we had converted **17** into hydroazulenes of type **22** with excellent stereoselectivity.[6]

Whilst with the adducts **15** and **17** the application in organic synthesis is fairly obvious and has been demonstrated,[5,6] use of the diesters of type **13** becomes particularly visible if one realizes that simple decarboxylation[1] gives rise to the monoester **23**—an enantiomerically pure δ-keto ester that was recently prepared in a multi-step procedure by E. J. Corey and his collaborators[9] as an intermediate *en route* to brefeldin A. Besides that, alkylation generates compounds of type **24** which, after ozonization, can be very useful for aldol-annellation as Helquist demonstrated in the saturated series.[10,11]



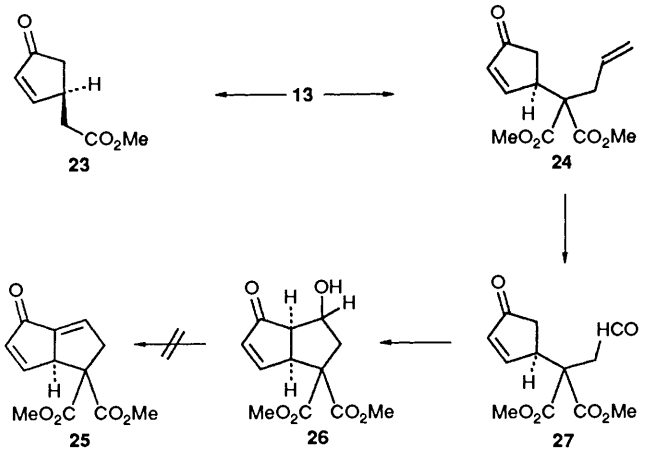
Scheme 7

Since the aldehyde **27** looks like an ideal precursor for various unsaturated bicyclooctanones, we set out to investigate the ozonolysis of **24** as well as subsequent cyclizations. The expectation was to generate the β-hydroxy ketone **26** this way or, maybe, even the corresponding cross-conjugated dienone **25**. The most important aspect for ozonolysis is certainly chemoselectivity, but since the cyclopentenone double bond is less electron rich no particular problems were expected with this step.

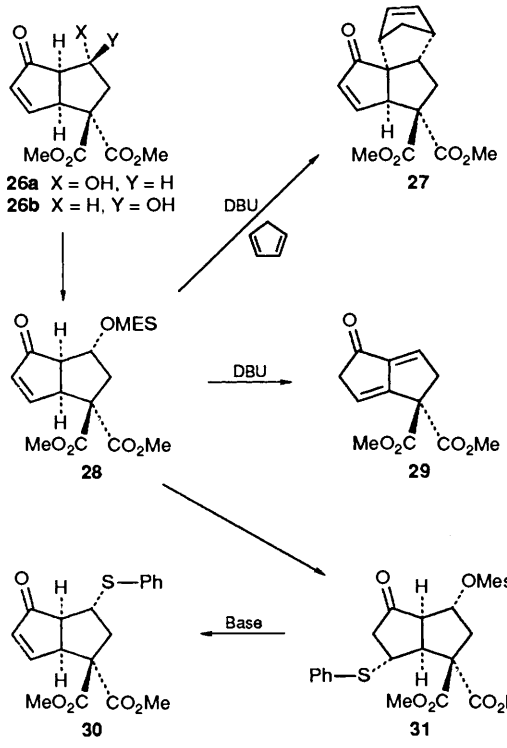
In the event, selective ozonisation in the presence of the dye Sudan III did provide the aldehyde **27** in 89% yield. As in the saturated series, cyclization was achieved easily under acidic conditions giving rise to a 3:1 mixture of the epimers **26a** and **26b**. The two diastereoisomers were separated and and the major one, **26a**, was converted into the mesylate **28*** for elimination studies. Although the elimination in the presence of DBU worked very well, there was no trace of the cross conjugated material **25** in the reaction product, the deconjugated dienone **29** proving to be the only unsaturated compound present.

Obviously the accumulation of 5 sp^2 centres in this combination of five-membered rings imposes severe strain on the cross-conjugated system **25**, which is certainly diminished by inserting one sp^3 centre in the deconjugation process. The very high tendency to avoid the cross-conjugated arrangement

* To investigate the synthetic potential of these compounds the reactions described here were, for simplicity's sake, run with racemic material.



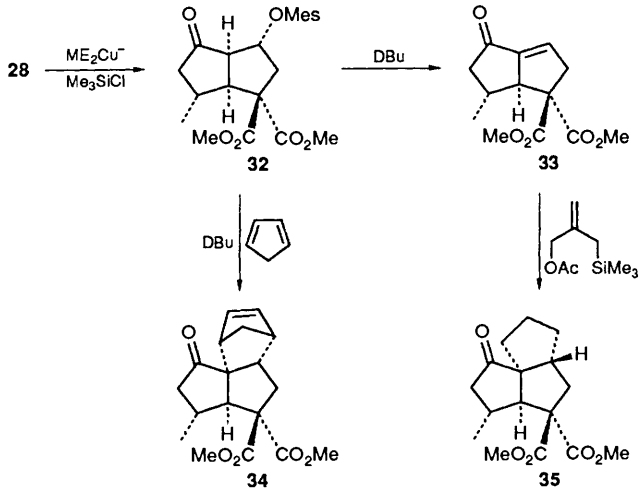
Scheme 8



Scheme 9

makes this ketone behave like a chemical chameleon and this can be nicely demonstrated with thiophenol adduct **31**. This thioether was initially prepared with the aim of inverting the sequence of double bond formation. The mesylate being the better leaving group, it was expected to be eliminated first, this time allowing the possibility of the second double bond being introduced in a purely thermal manner, not by a deconjugating sulphoxide elimination.* Whatever mild conditions one chose however, for the first elimination, the second obviously could not be stopped and the product isolated under various conditions turned out always to be thioether **30**. Its formation can be explained by readdition of thiophenol to either **25** or **29**, which, however, by no means proves the existence of the cross-conjugated isomer **25**, since **29** after picking up the nucleophile could easily reconjugate to form **30**. The remarkable regioselectivity in the readdition process may rather be considered as a strong argument in favour of **29** as an intermediate.

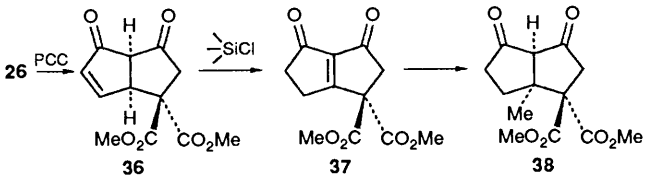
The same arguments hold for the selective formation of the Diels–Alder adduct with cyclopentadiene (see **27**). Although it looks like a product from the interception of **25** by the diene, the selectivity in favour of the more sterically hindered double bond again argues strongly in favour of the deconjugated isomer **29** as the real intermediate. Although **25** could not be prepared one still can use the mesylate **28** as its synthetic equivalent, since cuprate additions to this material give rise to **32** which in a subsequent elimination generates the conjugated ketone **33**.



Scheme 10

This enone may be considered the product of a chemoselective cuprate addition to **25** and its interesting potential for further cycloaddition chemistry can be nicely demonstrated by the Diels–Alder adduct **34** and by Trost's[12] palladium-catalysed three-carbon annelation process to yield the tricyclic ketone **35**.

The results reported here prove that the cyclization product **26** is the synthetic equivalent of the cross-conjugated dienone **25**. To demonstrate that the scope for this molecule can be expanded even into a broader set of applications, we investigated the PCC oxidation of this alcohol.



Scheme 11

Although the diketone **36** was easily obtained, its further applications are very much limited by a fast isomerization reaction. Even mild Lewis acids such as trimethylchlorosilane very quickly generate the isomer **37** albeit as an achiral molecule, with a highly substituted double bond. In spite of this, dimethylcuprate additions may still be used to form the 1,3-diketone **38**, with two adjacent quaternary carbon atoms.

The results described prove that all three ketones **13**, **15** and **17** are useful intermediates for the preparation of homochiral cyclopentenone derivatives, compounds which open up a variety of routes to biologically active compounds of this type.

Experimental

M.p.s were recorded on a Büchi melting point microscope. UV spectra were measured in methanol on a Beckman 3600

* The corresponding seleno elimination was just recently reported for the unsubstituted model diene. S. Yamazaki, M. Hama and S. Yamabe, *Tetrahedron Lett.*, 1990, **31**, 2917.

instrument and IR spectra on a Perkin-Elmer 581 spectrometer, ^{1}H NMR spectra on Bruker WP 200 and Bruker AM 300 instruments, and ^{13}C spectra on the Bruker AM 300, too. δ-Values are given relative to tetramethylsilane. *J* Values in Hz. Mass spectra were determined with a Finnigan MAT 312 instrument at 70 eV. For flash chromatography, silica gel (30–60 ξm) (Baker) was used at 0.3 bar and all solvents were dried by the usual methods. Elemental analyses were obtained with a CHN rapid instrument (Heraeus). Ether refers to diethyl ether and petroleum to light petroleum (b.p. 50–70 °C).

General Procedure for Chirality Transfer.—Acetoxycyclopentenone (0.022 mol), $[\alpha]_D^{22}$ + 89 (*c* 3.00, MeOH), and the corresponding Michael donor (0.022 mol) were dissolved in toluene (30 ml). Under nitrogen, potassium carbonate (0.023 mol) and 18-crown-6 (0.46 mmol) were added to the mixture which was then stirred for 18 h at 0 °C. For work-up, the mixture was diluted with water and extracted with dichloromethane. The dichloromethane extract was dried ($MgSO_4$) and evaporated and the product purified by chromatography (silica, petroleum–ether, 1:2). Yields were in the range 80–90%.

(R)-tert-*Butyl Methyl* (4-*Oxocyclopent*-2-*enyl*)*malonate* **13**.[4]—The optical purity was determined with HFC in hexadeuteriobenzene. The optical rotation was taken with the monoester **23**, $[\alpha]_D^{22}$ + 122 (*c* 1.00, CH_2Cl_2).

(R)-*Methyl* cis-3a,5,6,6a-*Tetrahydro*-5,5-*dimethoxycyclopenta*[b]*furan*-3-*carboxylate* **15**.[5]—The optical purity was determined with HFC in hexadeuteriobenzene, $[\alpha]_D^{22}$ + 112 (*c* 1.50, MeOH).

(R)-*Methyl* [2-(2,2-*Dimethoxyethyl*)-2,5-*dihydro*-4-*methyl*-5-*oxo*-3-*furyl*]-4-*oxocyclopent*-2-*enylacetate* **17**.—The optical purity was determined with HFC in hexadeuteriobenzene.

Dimethyl 4-*Oxocyclopent*-2-*enyl*(*allyl*)*malonate* **24**.—This compound was prepared in a phase transfer process as described above as a colourless oil (77%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3021, 1730, 1715, 1630 and 1205; $\delta_H(CDCl_3$, 200 MHz) 7.77 (1 H, dd, *J* 6 and 2), 6.18 (1 H, dd, *J* 6 and 2), 5.5–5.8 (1 H, m), 5.1–5.2 (2 H, m), 3.75 (3 H, s), 3.69 (3 H, s), 3.60–3.80 (1 H, m), 2.72 (2 H, tr, *J* 7), 2.51 (1 H, dd, *J* 19 and 6.5) and 2.29 (1 H, dd, *J* 19 and 3.5). The same compound was obtained from **13** after standard transesterification (MeOH, MeONa) and phase transfer alkylation (conditions *vide supra*). Without further characterization this material was taken through an ozonization–reduction sequence to form the aldehyde **27**.

Dimethyl 4-*Oxocyclopent*-2-*enyl*(*formylmethyl*)*malonate* **27**.—The allyl compound **24** (500 mg, 2 mmol) was dissolved in freshly distilled methanol (20 ml) and one crystal of Sudan III was added. This mixture was treated with ozone until the colour changed when excess of ozone was purged by nitrogen. Dimethyl sulphide (6 mmol) was added to the mixture which was kept at −30 °C for 1 h and then evaporated. The product was purified by flash chromatography (ether–petroleum, 1:1) to yield the aldehyde **27** as a colourless oil (440 mg, 89%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730, 1430 and 1080; $\delta_H(CDCl_3$, 200 MHz) 9.79 (1 H, s), 7.70 (1 H, dd, *J* 6 and 2.5), 6.34 (1 H, dd, *J* 6 and 2), 3.79 (3 H, s), 3.77 (3 H, s), 3.4–3.6 (1 H, m), 3.06 (1 H, dd, *J* 19 and 1), 2.88 (1 H, dd, *J* 19 and 1), 2.48 (1 H, dd, *J* 18 and 7) and 2.20 (1 H, dd, *J* 18 and 3); *m*/*z* 254 (M^+) (Found: M^+, 254.0789. $C_{15}H_{14}O_6$ requires *M*, 254.0790).

Dimethyl (3aβ,6aβ)-3-*Hydroxy*-4-*oxo*-1,2,3,3a,4,6a-*hexahydropentalene*-1,1-*dicarboxylate* **26**.—The aldehyde **27** (1.16 g, 4.5 mmol) was dissolved in dry benzene and after addition of a few mg of toluene-*p*-sulphonic acid this solution was refluxed for 1 h. (TLC-control, reaction time is critical.) The solvent was evaporated and the residue separated by chromatography (silica, petroleum–ether, 1:1).

α-*Carbinol* **26a**. White crystals (603 mg, 52%), m.p. 129 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3300–3600, 1730, 1715, 1435 and 1260; $\delta_H(CD_2Cl_2$, 200 MHz) 7.45 (1 H, dd, *J* 6 and 2.5), 6.29 (1 H, dd, *J* 6 and 2), 4.33 (1 H, dd, *J* 11 and 5.5), 4.09 (1 H, m, *J* 5.5 and 3), 3.78 (3 H, s), 3.75 (3 H, s), 2.95 (1 H, dd, *J* 9.5 and 5.5), 2.41 (1 H, dd, *J* 13 and 1) and 2.07 (1 H, dd, *J* 13 and 11) (Found: C, 56.45; H, 5.55. $C_{12}H_{14}O_6$ requires C, 56.69; H, 5.52%).

β-*Carbinol* **26b**. Colourless oil (224 mg, 19%), $\nu_{max}(CHCl_3)/cm^{-1}$ 3300–3500, 1730, 1715, 1430 and 1265; $\delta_H(CD_2Cl_2$, 200 MHz) 7.32 (1 H, dd, *J* 6 and 2.5), 6.18 (1 H, dd, *J* 6 and 2), 4.42 (1 H, d, *J* 5.5), 4.30 (1 H, m), 3.76 (3 H, s), 3.74 (3 H, s), 2.83 (1 H, m), 2.38 (1 H, dd, *J* 14 and 1), 2.14 (1 H, dd, *J* 14 and 4.5); *m*/*z* 254 (M^+) (Found: M^+, 254.0809. $C_{15}H_{14}O_6$ requires *M*, 254.0790).

The subsequent experiments were exercised with the α-carbinol **26a** exclusively.

Formation of the mesylate **28**. The hydroxy compound **26a** (1 mmol) dissolved in dry dichloromethane (10 ml) was treated with triethylamine (1.1 mmol) followed by methanesulphonyl chloride (3 mmol). After 5 h at room temperature the solvent was evaporated and the residue filtered through silica to yield the pure mesylate **28** as a white foam (79%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730, 1720, 1590, 1350 and 1280; $\delta_H(CDCl_3$, 200 MHz) 7.45 (1 H, dd, *J* 6 and 2), 6.34 (1 H, dd, *J* 6 and 2), 5.16 (1 H, dd, *J* 10 and 6), 4.03 (1 H, m), 3.81 (3 H, s), 3.80 (3 H, s), 3.24 (1 H, dd, *J* 10 and 6), 3.15 (3 H, s), 2.62 (1 H, dd, *J* 14 and 6) and 2.45 (1 H, dd, *J* 14 and 10.5); *m*/*z* 332 (M^+) (Found: M^+, 332.0566. $C_{13}H_{16}O_8S$ requires *M*, 332.0566).

Dimethyl 4-*Oxo*-1,2,4,5-*tetrahydropentalene*-1,1-*dicarboxylate* **29**.—The mesylate **28** (16 mg, 0.044 mmol) was dissolved in dichloromethane (2 ml). After the addition of DBU (0.1 mmol), the mixture was left at room temperature for 5 h and then evaporated. The product was purified by chromatography to yield a white foam (4 mg, 33%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1740, 1730, 1697, 1600, 1040 and 860; $\delta_H(CDCl_3$, 200 MHz) 6.61 (2 H, m), 3.80 (6 H, s) and 2.8–2.99 (4 H, m); *m*/*z* 236 (M^+).

Dimethyl (3aβ,6aβ)-4-*Oxo*-3-*phenylthio*-1,2,3,3a,4,6a-*hexahydropentalene*-1,1-*dicarboxylate* **30**.—The mesylate **28** (560 mg, 1.68 mmol) was dissolved in dry dichloromethane (20 ml) and after addition of thiophenol (202 mg) the mixture was left at room temperature for 30 min. It was then washed with aqueous sodium hydrogen carbonate, dried ($MgSO_4$) and evaporated. On chromatography of the residue the adduct **31** was isolated (18%, 140 mg) together with the cyclopentenone **30** (34%, 254 mg) (spectroscopic data *vide infra*). Compound **31**: $\nu_{max}(CHCl_3)/cm^{-1}$ 1740, 1730, 1260 and 1180; $\delta_H(CDCl_3$, 200 MHz) 7.3–7.6 (5 H, m), 3.82 (3 H, s), 3.72 (3 H, s), 3.7–3.8 (1 H, m), 3.37 (1 H, dd, *J* 16 and 7), 3.27 (1 H, m), 3.02 (3 H, s), 2.82 (1 H, dd, *J* 18 and 2), 2.71 (1 H, dd, *J* 15 and 5), 2.52 (1 H, dd, *J* 15 and 7) and 2.44 (1 H, dd, *J* 18 and 1). With this structural information available, at a later stage the mixture obtained in the first step was directly treated with DBU (1 equiv.) in dry dichloromethane (20 ml) for 15 min, after which the solution was washed with saturated aqueous ammonium chloride and evaporated to yield the cyclopentenone **30** (80%): $\nu_{max}(CHCl_3)/cm^{-1}$ 1730, 1715 and 1590; $\delta_H(CDCl_3$, 200 MHz) 7.2–7.5 (6 H, m), 6.26 (1 H, dd, *J* 6 and 2), 4.57 (1 H, ddd, *J* 6, 5 and 2.5), 3.90 (1 H, m), 3.85 (3 H, s), 3.78 (3 H, s), 2.89 (1 H, dd, *J* 6 and 2) and 2.51 (2 H, m); *m*/*z* 346 (M^+) (Found: M^+, 346.0873. $C_{18}H_{18}O_5S$ requires *M*, 346.0875).

Diels–Alder Adduct **27**.—The mesylate **28** (300 mg, 0.9 mmol)

dissolved in dry toluene (10 ml) was treated with cyclopentadiene (1 ml) and DBU (1 mmol). After 2 h the mixture was evaporated and the residue purified by chromatography to give the adduct **27** as a white foam (20 mg, 7%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3040 and 1730; $\delta_H(CDCl_3$, 200 MHz) 7.46 (1 H, dd, *J* 6 and 2), 6.35 (2 H, m), 6.06 (1 H, dd, *J* 6 and 2), 3.75 (3 H, s), 3.56 (3 H, s), 3.51 (1 H, dd, *J* 4.5 and 1.5), 3.09 (1 H, ddd, *J* 12, 8 and 4), 2.87 (1 H, m), 2.65 (1 H, m), 2.57 (1 H, dd, *J* 14 and 8.5), 2.42 (1 H, m) and 1.55 (2 H, m); *m/z* 302 (M^+) (Found: M^+, 302.1153. $C_{17}H_{18}O_5$ requires *M*, 392.1154).

Dimethyl (6aβ)-1,2,4,5,6,6a-*Hexahydropentalene*-1,1-*dicarboxylate* **33**.—The cyclopentenone **27** (200 mg, 0.6 mmol) was dissolved in dry tetrahydrofuran (7 ml) and treated with trimethylchlorosilane (195 mg). The mixture was cooled to −78 °C and treated with a lithium dimethylcuprate solution (1.5 equiv.) whilst the temperature was slowly allowed to rise to −20 °C. After 30 min, the solution was poured into saturated aqueous ammonium chloride and the mixture extracted with ether. The combined organic phases were washed with brine and evaporated to give the mesylate **32** (194 mg, 93%); $\delta_H(CDCl_3$, 200 MHz) 1.06 (3 H, d, *J* 6.5); *m/z* 348 (M^+). This material was immediately redissolved in dry dichloromethane (20 ml) and treated with DBU (100 mg). The elimination was finished in 15 min (TLC-control) and after evaporation of the mixture purification of the residue by chromatography gave the enone **33** (83%, 132 mg); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730, 1435, 1365 and 1175; $\delta_H(CDCl_3$, 200 MHz) 6.36 (1 H, m), 3.7–3.9 (1 H, m), 3.79 (3 H, s), 3.74 (3 H, s), 3.54 (1 H, ddd, *J* 18, 3 and 2), 2.68 (1 H, dd, *J* 18 and 2), 2.38 (1 H, dd, *J* 18 and 11), 1.7–1.9 (1 H, m) and 1.23 (3 H, d, *J* 6.5); *m/z* 252 (M^+) (Found: M^+, 252.1309. $C_{13}H_{16}O_5$ requires *M*, 252.13 H).

Diels–Alder Adduct **34**.—The adduct (38%) was prepared as described for **27**; $\nu_{max}(CHCl_3)/cm^{-1}$ 3020, 2960, 1730 and 1430; $\delta_H(CDCl_3$, 200 MHz) 5.86 (2 H, m), 3.78 (3 H, s), 3.74 (3 H, s), 3.39 (1 H, tr, *J* 8), 2.92 (1 H, m), 2.50 (1 H, dd, *J* 17 and 10), 1.9–3.3 (6 H, m), 1.24 (1 H, d, *J* 9), 1.15 (1 H, d, *J* 9) and 1.07 (3 H, d, *J* 6.5); *m/z* 318 (M^+) (Found: M^+, 318.1467. $C_{18}H_{22}O_5$ requires *M*, 318.1467).

Dimethyl (3aβ)-7-*Methylene*-1-*oxodecahydrocyclopenta*[c]-*pentalene*-3,4-*dicarboxylate* **35**.—The elimination product **33** (33 mg, 0.13 mmol) dissolved in dry tetrahydrofuran (3 ml) was treated with tetrakis(triphenylphosphine)palladium (9 mg) and 1,2-bis(diphenylphosphino)ethane (1 mg). After the addition of 2-acetoxymethylallyl(trimethyl)silane (30 mg) the mixture was refluxed for 3 h, evaporated, and the product purified by flash chromatography to give the ketone **35** (10 mg, 25%) as a colourless oil; $\nu_{max}(CHCl_3)/cm^{-1}$ 1735, 1730, 1650 and 1270; $\delta_H(CDCl_3$, 200 MHz) 5.8–5.9 (2 H, m), 3.78 (3 H, s), 3.77 (3 H, s), 3.61 (1 H, d, *J* 8), 3.38 (1 H, m), 2.5–1.9 (9 H, m) and 1.07 (3 H, *J* 6.5); *m/z* 306 (M^+) Found: 306.1465. $C_{17}H_{22}O_5$ requires 306.1467.

Dimethyl (3aβ,6aβ)-*Dioxo*-1,2,3,3a,4,6a-*hexahydropentalene*-1,1-*dicarboxylate* **36**.—Compound **26** (50 mg, 0.18 mmol) and pyridinium chlorochromate (61 mg, 0.26 mmol) were stirred in dichloromethane (2 ml) for 3 h. The solution was then filtered through silica to yield the diketone **36** (29 mg, 65%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1765, 1745, 1710, 1590, 1310 and 1270; $\delta_H(CDCl_3$, 200 MHz) 7.61 (1 H, dd, *J* 6 and 2), 6.31 (1 H, dd, *J* 6 and 2), 4.33 (1 H, m), 3.87 (3 H, s), 3.82 (3 H, s), 3.42 (1 H, dd, *J* 6 and 0.5), 3.06 (1 H, d, *J* 18.5) and 2.74 (1 H, dd, *J* 18.5 and 0.5); *m/z* 252 (M^+) (Found: M^+, 252.0633. $C_{12}H_{12}O_6$ requires *M*, 252.0633).

Dimethyl 3,4-*Dioxo*-1,2,3,3a,4,6-*hexahydropentalene*-1,1-*dicarboxylate* **37**.—The diketone **36** (825 mg, 0.32 mmol) in dry dichloromethane (50 ml) was treated with triethylamine (0.64 mmol) and trimethylchlorosilane (353 mg, 0.35 mmol) at 0 °C for 5 h. Evaporation of the mixture and flash chromatography of the residue gave the diketone **37** (285 mg, 35%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1750, 1735, 1710, 1620 and 1380; $\delta_H(CDCl_3$, 200 MHz) 3.86 (6 H, s), 3.44 (2 H, s) and 2.8–3.2 (4 H, s).

As described for compound **32** this compound was treated with dimethylcuprate to yield the diketone **38** (38%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1770, 1730, 1440, 1260 and 1125; $\delta_H(CDCl_3$, 200 MHz) 3.84 (3 H, s), 3.78 (3 H, s), 3.15 (1 H, d, *J* 1.5), 2.94 (2 H, m), 2.1–2.5 (4 H, m) and 1.48 (3 H, s); *m/z* 268 (M^+) (Found: M^+, 268.0947. $C_{13}H_{16}O_6$ requires *M*, 268.0947).

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