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Efficient Trapping of Ketone Enolates with Acrylate and β-Sulfonylacrylate Thioesters, β-Sulfonyl-, β-Sulfinyl- and β-Chloro-vinyl Ketones; Facile Preparation of a Hydrindanone, *cis*-Dimethyloctalone, and Unsaturated 1,5-Dicarbonyl Compounds

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Abstract

Tandem conjugate addition–ring closure involving reaction of the lithium enolate arising from conjugate addition of lithiated (*E*)-but-2-enyldiphenylphosphine oxide to 2-methyl-cyclopent-2-enone with two moles of t-butylthioacrylate generates a hydrindanol, and, in the presence of copper(I), a lactone derived from the hydrindanol. β-Sulfonylacrylate phenyl and t-butyl thioesters, β-chlorovinyl, β-sulfonyl- and β-sulfinyl-vinyl ketones react with the foregoing enolate, and with the enolate generated through conjugate addition of a methylcuprate to 2-methylcyclohexenone to give unsaturated 1,5-dicarbonyl compounds. The β-chlorovinyl ketones in particular react rapidly and in high yield. 2-Methylcyclohexenone has thereby been converted into a *cis*-dimethyl octalone; the conversion illustrates the effectiveness of β-chlorovinyl methyl ketone in the Robinson annelation. Reactions of the lithium enolate and titanium enol of 2,6-dimethylcyclohexanone with the β-substituted enones to give the corresponding unsaturated 1,5-dicarbonyl compounds and other products are also recorded.

Introduction

We have pointed out elsewhere how the problem associated with the use of methyl vinyl ketone in a Robinson annelation sequence initiated under aprotic conditions can be efficiently overcome through the use of vinyl ketones bearing β-sulfonyl substituents.[1,2] Thus, the reaction of the lithiated phosphine oxide (1) with 2-methylcyclopent-2-enone in tetrahydrofuran at −70° generates the enolate (2), which upon brief treatment with the β-sulfonyl enone (3) at −30° gives the unsaturated 1,5-dicarbonyl compound (or vinylogous β-diketone) (4) in 53% yield from the phosphine oxide (1). The product is easily hydrogenated to provide the 1,5- or δ-diketone required for aldol cyclization.[1,2] β-Sulfonyl enones thus have a clear advantage over other reagents prescribed as equivalents to methyl vinyl ketone and its homologues for use under aprotic conditions.[1] A specific advantage in the present case is that the conjugate addition–enolate trapping provides in one chemical operation a product which, in possessing relative configurations at C2, C3 and C1′ identical with those at C13, C17 and

[1] Haynes, R. K., and Vonwiller, S. C., *J. Chem. Soc., Chem. Commun.*, 1987, 92; Haynes, R. K., Vonwiller, S. C., and Hambley, T. W., *J. Org. Chem.*, 1989, **54**, 5162.
[2] Vonwiller, S. C., Ph.D. Thesis, University of Sydney, 1987.

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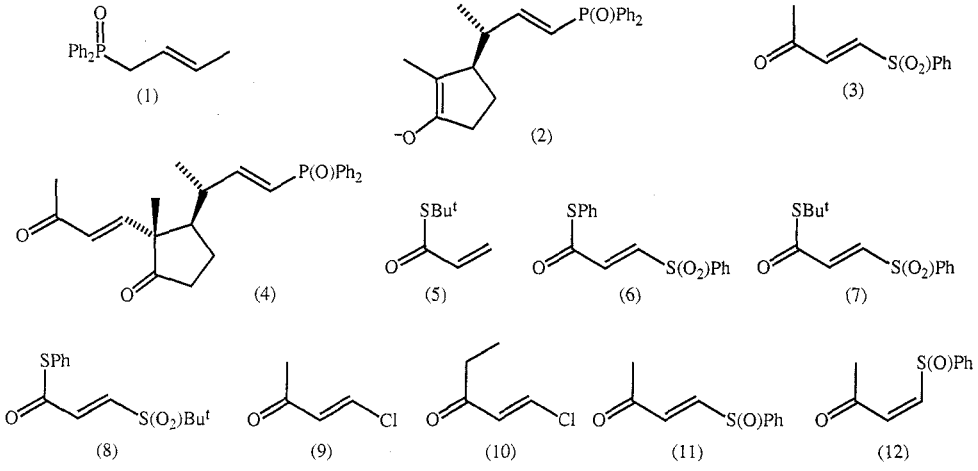
C 20 in vitamin D derivatives, is a most useful precursor to such derivatives.[1,2]

In preliminary work leading to the use of the β-sulfonyl enones, we carried out exploratory reactions of the enolate (2) with the acrylate thioester (5) and the β-sulfonylacrylate thioesters (6)–(8).[2] It was necessary also to establish if β-sulfonyl enones react with enolates generated under somewhat different conditions, and indeed whether the β-halo- and β-sulfinyl-vinyl ketones (9)–(12) should react in the same way as the β-sulfonyl enones. We now describe in detail the results of these experiments.



Discussion

The preparation of compounds (3) and (6)–(8) has been described elsewhere.[3] The β-chloro enones (9)[4] and (10)[5] were obtained from acetylene and the appropriate acid chloride in the presence of aluminium chloride. The β-sulfinyl enone (11) was obtained by oxidation of the corresponding sulfide.[3] It was isomerized to the (*Z*)-compound (12) through irradiation from a mercury lamp.

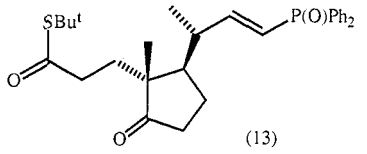
The purpose of using the thioacrylate (5) in the enolate trapping was to generate the monoadduct (13).[1,2] However, treatment of the enolate (2) in tetrahydrofuran at −10° with 1 equiv. of the thioacrylate (5) gave a mixture of the adducts (16) and (17) (52%) arising from enolate (2), a 9 : 1 mixture of two diastereomers of a hydrindanol diadduct (20%), and polymeric material. The high-field ^{1}H n.m.r. data of the major diastereomer (15) of the hydrindanol (Experimental section) indicate that the thioester groups at C4 and C6 (hydrindanol numbering) are *cis* and equatorial. The signals from H4 and H6, at δ 2·605 and 2·672 respectively, are readily identified; both protons display *trans* diaxial coupling of 12·5 Hz to H5β. H6 has an additional *trans* diaxial coupling of 12·5 Hz to H7β. The compound arises through tandem addition of 2 equiv. of the thioacrylate to the enolate via the intermediate ester enolate

[3] Haynes, R. K., Vonwiller, S. C., Stokes, J. P., and Merlino, L. M., *Aust. J. Chem.*, 1988, **41**, 881.

[4] Benson, W. R., and Pohland, A. E., *J. Org. Chem.*, 1964, **29**, 385.

[5] Hills, P. R., and McQuillin, F. J., *J. Chem. Soc.*, 1953, 4060.

(14). The stereochemical outcome of the conjugate addition–enolate trapping is such that the newly introduced substituents are *trans*;[1] these relatively large substituents will also be pseudo-equatorial. Thus, the pseudo-axial methyl group will direct the ring closure of the intermediate (14) to take place through the α-face of the cyclopentanone to generate the *cis*-fused hydrindanol (15).



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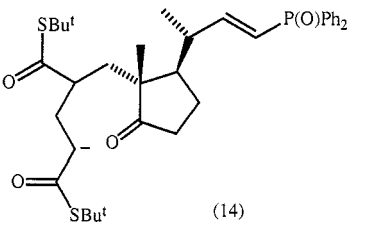
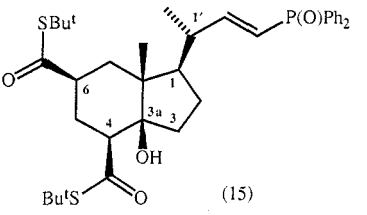
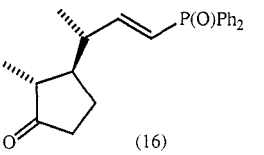


(14)



(15)



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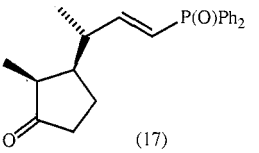
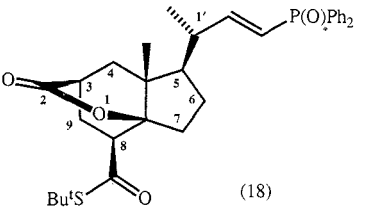


(17)



(18)

This mode of formation of the hydrindanol is unique, although there have appeared a number of concurrent reports describing formation of six-membered rings in tandem addition–ring closure reactions involving cyclohexanone enolates and acrylate electrophiles.[6] Thus, the diaddition of unsaturated carbonyl compounds to generate six-membered rings is strikingly favoured. In the present case, the monoadduct (13) could never be detected. In an attempt to attenuate the reactivity of the putative ester enolate precursor of the monoadduct, the enolate (2) was treated with cuprous cyanide prior to treatment with the thioacrylate. Rather than a monoadduct, a new product, the lactone diadduct (18), was now obtained in 34% yield together with the hydrindanol (15) and polymeric material. Constitution of the lactone (18) follows from the ^{13}C n.m.r. spectrum which contained signals due to thioester (δ 199·1) and lactone groups (90·1, 175·7) the infrared spectrum, with signals at 1682 and 1754 cm^{-1}, and the ^1H n.m.r. spectrum which contained well-defined signals from a set of six protons in a cyclohexane ring. The bridging lactone requires H3 to be equatorial, and the cyclohexane ring to be boat-like. This is indicated by the signal due to H3 at δ 2·721, which displays

[6] Posner, G. H., and Lu, S.-B., *J. Am. Chem. Soc.*, 1985, **107**, 1424; Posner, G. H., Lu, S.-B., Asirvatham, E., Silversmith, E., and Schuliman, E. M., *J. Am. Chem. Soc.*, 1986, **108**, 511; Posner, G. H., Lu, S.-B., *Tetrahedron Lett.*, 1986, **27**, 659; Posner, G. H., and Asirvatham, E., *Tetrahedron Lett.*, 1986, **107**, 663; Posner, G. H., Webb, K. S., Asirvatham, E., Jew, S.-S., and Innocenti, A. D., *J. Am. Chem. Soc.*, 1988, **110**, 4754.

trans-diequatorial couplings of 5·5 Hz to H4β and 2·5 Hz to H9β and the signal for H8 at 3·021, which displays a *trans*-diaxial coupling of 10·25 Hz to H9β. The lactone arises by copper(I)-activated intramolecular nucleophilic attack by the alkoxide on the thioester produced from intermediate (14) by ring closure. Related conversions of hydroxy thioesters into lactones have been described previously.[7] Use of dicyclopentadienyltitanium dichloride, titanium tetraisopropoxide or cuprous iodide also gave the diadducts (15) and (18) in overall yields of 30–40% based on the phosphine oxide; in no case could any monoadduct be detected. As our aim was to obtain the monoadduct, the formation of the diadducts was never optimized, and in all the reactions, 1 equiv. or less of electrophile was used.

To prevent the ester enolate, arising by conjugate addition of the ketone enolate (2) to the acrylate thioester, from reacting with a second mole of the thioester, the use of unsaturated ester electrophiles bearing a leaving group attached to the β-carbon atom was considered. The intermediate ester enolate will internally displace the group to provide a neutral unsaturated product. Related reactions are known, and moderate success has been achieved by treatment of α,β-unsaturated ketones bearing β-leaving groups such as halide,[8] ammonium[4] and sulfenyl[9] with simple alkyl organometallic nucleophiles. The reactions of enolates with methyl β-chloropropenoate[10] and the β-chlorovinyl ketone (9)[5] have been reported also. Cyclic β-sulfinyl enones undergo addition–elimination with malonate nucleophiles,[11] and acyclic β-chlorovinyl ketones react in similar fashion with enolates of β-dicarbonyl compounds.[12]

Treatment of the enolate (2), generated in the usual way, with the β-phenylsulfonyl phenylthioacrylate (6) at −15° for 5 min gave the adduct (19) in 48% yield. When an excess of butyllithium was used to generate the carbanion of the phosphine oxide (1), cleavage of the phenylthioester, as evidenced by the formation of the β-phenylthio phenyl thioacrylate (20), also took place. However, the use of the β-phenylsulfonyl t-butyl thioacrylate (7) overcame the problem, and enolate trapping provided the adduct (21) in 54% yield. In contrast, use of the β-t-butylsulfonyl phenyl thioacrylate (8) gave the adduct (19) in 39% yield. Although the yields of the products are relatively modest, they are acceptable in view of the failure of the thioacrylate (5) to deliver a monoadduct. Such a compound can in principle be obtained by selective

[7] Masamune, S., Hayase, Y., Schilling, W., Chan, W. K., and Bates, G. S., *J. Am. Chem. Soc.*, 1977, **99**, 6756.

[8] Leyendecker, F., Drouin, J., and Conia, J. M., *Tetrahedron Lett.*, 1974, 2391; Clark, R. D., and Heathcock, C. H., *J. Org. Chem.*, 1976, **41**, 636; Wender, P. A., and Eck, S. L., *Tetrahedron Lett.*, 1977, 1245; Coke, J. L., Williams, C. H., and Natarajan, S., *J. Org. Chem.*, 1977, **42**, 2380; Piers, E., and Morton, H. E., *J. Chem. Soc., Chem. Commun.*, 1978, 1033; Piers, E., and Morton, H. E., *J. Org. Chem.*, 1979, **44**, 3437.

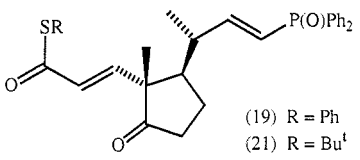
[9] Posner, G. H., and Brunelle, D. J., *J. Chem. Soc., Chem. Commun.*, 1973, 907; Kobayashi, S., Takei, T., and Mukaiyama, T., *Chem. Lett.*, 1973, 1097; Kobayashi, S., and Mukaiyama, T., *Chem. Lett.*, 1974, 705; Kobayashi, S., and Mukaiyama, T., *Chem. Lett.*, 1974, 1425; Dieter, R. K., Silks, L. A., Fishpaugh, J. R., Kastner, M. E., *J. Am. Chem. Soc.*, 1985, **107**, 4679; Dieter, R. K., Silks, L. A. *J. Org. Chem.*, 1986, **51**, 4687.

[10] House, H. O., Roelofs, W. L., and Trost, B. M., *J. Org. Chem.*, 1966, **31**, 646; Boeckmann, R. K., Bershas, J. P., Clardy, J., and Solheim, B., *J. Org. Chem.*, 1977, **42**, 3630.

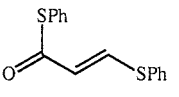
[11] Bryson, T. A., Dardis, R. E., and Gammill, R. B., *Tetrahedron Lett.*, 1978, 743.

[12] Kochetkov, N. K., Kudryashov, L. J., and Gottich, B. P., *Tetrahedron*, 1961, **12**, 63.

reduction of the enone double bond in products (19) or (21). In seeking to convert the adduct (19) into a diketone such as (4) suitable for conversion into a vitamin D precursor, we embarked on a model study involving compound (22).[2] The conversion of thioesters into ketones through use of organocopper[13] or Grignard reagents[14] is well known, but the study revealed that unsaturated thioesters cannot be converted into the corresponding ketones in this manner.[2] We therefore turned to β-sulfonylvinyl ketones for the enolate trapping; as noted in the Introduction, these very effectively trap the enolate (2) to generate vinylogous β-diketones such as (4) in yields greater than 50% from the phosphine oxide (1).[1,2]



(19) R = Ph
(21) R = Bu^t



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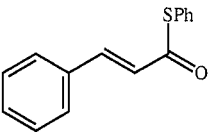
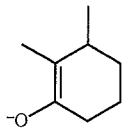


(22)

In turning to the β-chloro enones, we note that the thermodynamic lithium enolate of 2-methylcyclohexanone in liquid ammonia was reported some time ago to react over a period of three days with the β-chloro enone (9) to give approximately 20% of product.[5] It is apparent from the present work that the conditions used were far from optimum. When the enolate (2) was treated with the β-chloro enone (9) at −30° and quenched after 5 min, the vinylogous diketone (4) was isolated in 76% yield, based on the amount of the phosphine oxide (1) used in the generation of enolate (2). Thus, in this particular case, the β-chloro enone is a superior reagent to the β-sulfonyl enone (3). The enolate (23), generated by the conjugate addition of the organocopper reagent derived from methylmagnesium bromide and copper(I) cyanide in ether, reacts with the β-chloro enone (9) to give the cyclohexanone (24) as a single diastereoisomer in 90% yield. Initially formed solely as the (*E*)-isomer, the compound partially isomerized to the (*Z*)-isomer during chromatographic purification. The *cis*-disposition of the methyl groups was indicated by the results of n.O.e. experiments as set out in the Experimental section. This was further confirmed by hydrogenation of the compound to the δ-diketone (25) and acid-catalysed aldol ring closure of the latter to the known octalone (26);[14] the final product was obtained in an overall yield of 66% from 2-methylcyclohexenone. The ethyl β-chloro enone (10) also reacted in similar fashion to give the ethyl analogue (27) (52%). The lithium enolate of 2,6-dimethylcyclohexanone at −30° reacted rapidly with the β-chloro enone (9) to give a 4 : 1 mixture of the adducts (28) and (29) (90%). As in the case with compound (24), isomerization of the double bond took place during chromatography of this mixture so that mixtures also containing the *cis* compounds (30) and (31) were ultimately obtained. A similar reaction took place with the β-chloro enone (10) to give the mixtures of the ethyl analogues

[13] Anderson, R. J., Henrick, C. A., and Rosenblum, L. D., *J. Am. Chem. Soc.*, 1974, **96**, 3654.
[14] Araki, M., Sakata, S., Takei, H., and Mukaiyama, T., *Bull. Chem. Soc. Jpn*, 1974, **47**, 1777; Cardellicchio, C., Fiandanese, V., Marchese, G., and Ronzini, L., *Tetrahedron Lett.*, 1985, **26**, 3595.

(32)–(35) of the foregoing products. Stereochemical features in the products were established from high-field ^{1}H n.m.r. n.O.e. experiments, as described in the Experimental section.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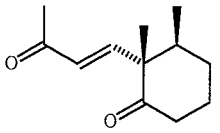
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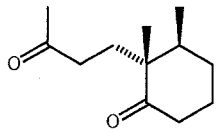
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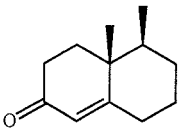
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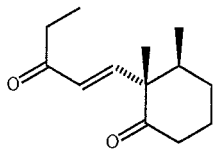
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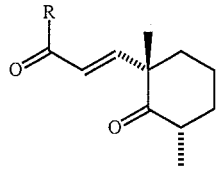
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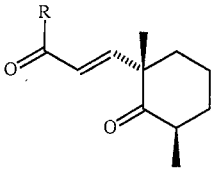
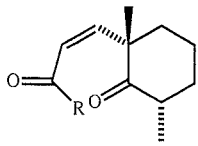
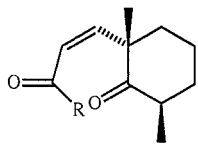
(32) R = Et


(29) R = Me
(33) R = Et


(30) R = Me
(34) R = Et


(31) R = Me
(35) R = Et

With the β-sulfonyl enone (3), a slower reaction took place with the lithium enolate of 2,6-dimethylcyclohexanone to give a similar mixture of products (28) and (29), although in somewhat lower yield (80%). Significantly, the β-sulfinyl enone (11) also reacted cleanly to give these products (84%). As we have noted elsewhere,[1] the addition–elimination which generates the vinylogous β-diketones is not concerted. Thus, the (*Z*)-β-sulfinyl enone (12) provided a mixture of compounds (28)–(31) enriched in (*E*)-isomers (28) and (29). In an attempt to render the reactions more stereoselective, the lithium enolate was treated with chlorotitanium triisopropoxide at –30° prior to treatment with the sulfonyl and sulfinyl enones (3) and (11). Titanium enols prepared in this manner react stereoselectively with carbonyl compounds in aldol[15] and related reactions.[15,16] In the present case it was expected that the titanium in the enol would preferentially coordinate with the polar sulfone or sulfoxide group, rather than with the carbonyl group in the enones (3) or (11), and thus direct the enol to react with improved stereoselectivity at the β-carbon atom of the respective enone. However, the reaction displayed this regiochemistry only for the sulfoxide. Whereas the β-sulfonyl enone gave an unstable aldol product, the sulfoxide gave a 4 : 1 mixture of the normal conjugate adducts (28) and (29), although in a relatively low yield (35%).

[15] Reetz, M. T., and Peter, R., *Tetrahedron Lett.*, 1981, **22**, 4691; Reetz, M. T., Steinback, R., Westerman, J., Urg, R., Wenderoth, B., and Peter, R., *Angew. Chem., Int. Ed. Eng.*, 1982, **21**, 135.

[16] Reetz, M. T., *Top. Curr. Chem.*, 1982, **106**, 1; Seebach, D., in 'Organic Synthesis: an Interdisciplinary Challenge' (Eds J. Streith, H. Prinzbach and G. Schill) pp. 77–99, and references therein (Blackwell Scientific Publications: Oxford 1985).

Concluding Comments

We have described here a new tandem conjugate addition–cyclization reaction with a thioacrylate electrophile which represents a facile means of constructing hydrindanols in stereoselective fashion. The reaction, which was not optimized, will be useful in the construction of the highly functionalized hydrindanols required for the synthesis of vitamin D and related compounds. We shall describe elsewhere how the yields of related compounds can be dramatically increased through use of excess of the appropriate electrophiles under carefully controlled conditions.

We have shown that β-chloro and β-sulfinyl enones can be used in place of the sulfonyl enones described earlier[1] as reagents which are superior to methyl vinyl ketone and alkyl (α-trimethylsilyl)vinyl ketones in those Robinson annelation sequences whose first step must be carried out under aprotic conditions. The reagents are also far more reactive than is methyl (α-trimethylsilyl)vinyl ketone; thus, under the conditions used in the present work, only 25% of the latter ketone is consumed in a reaction with the enone (2) to generate the δ-diketone corresponding to compound (4) in low yield.[1,2] It is stressed that the β-sulfur and β-halo enones are complementary reagents; it is a relatively easy matter to prepare β-sulfinyl and sulfonyl enones,[2] but not β-chloro enones, bearing functional groups. It is also noted that the current method of preparing unsaturated 1,5-dicarbonyl compounds (vinylogous β-diketones) from the β-substituted enones and the ketone enolates is considerably more direct than that described hitherto.[17]

The reagents provide an economical and simpler alternative to methyl (α-trimethylsilyl)vinyl ketone[18] for the preparation of octalones bearing *cis*-vicinal methyl groups characteristic of eremophilane sesquiterpenes.[19–22] It is worth noting that under protic conditions, methyl vinyl ketone reacts with the thermodynamic enolate of 2,3-dimethylcyclohexanone to generate mixtures of the *trans*- and *cis*-dimethyl octalones in low yields,[20,21] and prior to the advent of methyl (α-trimethylsilyl)vinyl ketone and of the β-substituted enones of the present work, less convenient, indirect methods had to be used to prepare the pure *cis*-dimethyl compound (24).[21–23]

Finally, it is pointed out that the addition–elimination reactions of these reagents with ketone enolates is not general. Thus, whereas the tertiary enolates described here react efficiently, secondary enolates, such as that derived from cyclohexanone, react in quite different fashion, as shall be described later. However, we expect that products analogous to those described here will be obtained when suitably masked forms of primary and secondary enolates, for example, silyl enol ethers or enamines, are used.

[17] Khan, H. A., and Paterson, I., *Tetrahedron Lett.*, 1982, **23**, 2399.
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Experimental

^{1}H n.m.r. spectra were recorded on Bruker WM400 (400 MHz) and AC200F (200 MHz), and Varian XL400, XL100 and EM390 spectrometers, with samples dissolved in $CDCl_3$ containing tetramethylsilane as internal reference. ^{13}C n.m.r. spectra were recorded from $CDCl_3$ solutions on Bruker AC200F, Varian CFT20 and Jeol FX60Q spectrometers. Infrared spectra were recorded on Perkin Elmer 221 and 710B spectrometers or a Digilab FTS 20/80 Fourier transform spectrometer from the neat liquid (sodium chloride plates) or solutions in chloroform as indicated. Mass spectrometry was carried out on AEI MS9 (e.i.) or AEI MS30 (c.i., methane) spectrometers equipped with a DS 90 data-handling system. Microanalyses were performed by the Australian Mineral Development Laboratories, Melbourne and at the University of New South Wales facility. In those cases where satisfactory microanalyses were unable to be obtained, characterization was made by means of high-resolution mass spectroscopy and high-field ^{1}H n.m.r. spectroscopy. Melting points were recorded on a Reichert melting point stage and are uncorrected.

All chromatographic separations were carried out by flash chromatography with Merck silica gel 60 (230–400 mesh ASTM). Merck silica gel (60 PF_{254}) was used for preparative centrifugal (radial) chromatography with a Chromatotron model 7924 from Harrison Research, U.S.A. Analytical thin-layer chromatography (t.l.c.) was carried out with Merck precoated aluminium t.l.c. plates coated with silica gel 60 F 254 (0·2 mm). Solvents and commercially available reagents were purified in the standard manner.

Preparation of Electrophiles

The preparation of the electrophiles (3), (5)–(9)[3] and (10)[5] has been described elsewhere. (*E*)-4-Phenylsulfonylbut-3-en-2-one (3) was also conveniently prepared in the following way. A solution of (*E*)-4-chlorobut-3-en-2-one (300 mg, 2·88 mmol, 1·0 equiv.) in methanol (25 ml) containing sodium phenylsulfinate (520 mg, 3·17 mmol, 1·1 equiv.) was stirred for 3 h at room temperature. The solvent was removed under reduced pressure, and the residue partitioned between ether (25 ml) and water (30 ml). The aqueous layer was extracted with ether (2×20 ml), and the combined ether layers were washed successively with sodium carbonate solution (2×20 ml, 10%) and brine (20 ml) and then dried (Na_2SO_4). The solvent was removed to give the (*E*)-sulfonyl enone (4·7 g, 78%), as needles, m.p. 61–62° from ether/pentane.[3]

(*E*)-4-(Phenylsulfinyl)but-3-en-2-one (11) was prepared in the following way. To a stirred solution of (*E*)-4-(phenylthio)but-3-en-2-one (1 g, 5·1 mmol, 1·0 equiv.) in glacial acetic acid (25 ml) at 20° was added hydrogen peroxide (0·64 ml, 27·5% containing 0·175 g, 5·1 mmol, 1·0 equiv.). The solution was stirred for 6 h and then treated with water (20 ml) and extracted with ethyl acetate (3×20 ml). The combined organic extracts were washed successively with sodium hydrogen carbonate solution (3×20 ml, 10%) and brine (20 ml), and then dried (Na_2SO_4). The solvent was removed to give the crude sulfoxide (1·05 g). Purification by flash chromatography (ethyl acetate/light petroleum, 1 : 1) gave *(E)-4-(phenylsulfinyl)but-3-en-2-one* (557 mg, 65%) as off-white needles, m.p. 69–71° from ethyl acetate/light petroleum. During chromatography of the crude material, it was noted that some isomerization to the less polar (*Z*)-isomer (12) took place (Found: C, 61·7; H, 5·2. $C_{10}H_{10}O_2S$ requires C, 61·8; H, 5·2%). ν_{max} ($CHCl_3$) 2999w, 1724s, 1698s, 1595m, 1447m, 1361m, 1326m, 1286s, 1241s, 1234s, 1148s, 1087s, 1055m, 958w, 687m, 597m cm^{-1}. ^{1}H n.m.r. (200 MHz) δ 2·17, 3H, s, H1; 6·97, 1H, d, $J_{4,3}$ 15·0 Hz, H4; 7·36, 1H, d, $J_{3,4}$ 15·0 Hz, H3; 7·45–7·70, m, Ph. ^{13}C n.m.r. (50 MHz) δ 29·26, C1; 124·8, C_{ortho}, 129·9, C_{meta}, 130·7, C_{para}, 141·4, C_{ipso}, Ph; 131·9, C3; 149·3, C4; 195·0, C2. Mass spectrum *m/z* 194 (M, 7%), 178 (4), 163 (10), 152 (48), 146 (50), 140 (29), 131 (25), 126 (17), 109 (35), 78 (25), 77 (29), 65 (11), 51 (36), 50 (13), 43 (100), 39 (11).

The (*Z*)-4-(phenylsulfinyl)but-3-en-2-one (12) was prepared by isomerization of the (*E*)-isomer. A solution of the (*E*)-isomer (5·4 g, 25·7 mmol) in dry chloroform (600 ml) under nitrogen was stirred at room temperature under illumination from a 125 W medium-pressure mercury lamp for 3 days. The solvent was then removed by evaporation under reduced pressure to leave the sulfoxide mixture which was shown by ^{1}H n.m.r. spectroscopy to consist of a 1 : 2 mixture of (*E*)- and (*Z*)-isomers and other unidentified material. Purification by flash chromatography (ethyl acetate) gave the (*E*)-sulfoxide (2·4 g, 44%) and then (*Z*)-

4-(phenylsulfinyl)but-3-en-2-one (12) (509 mg, 9%) as a white semicrystalline mass. The compound is unstable, and attempts to purify it resulted in isomerization into the (*E*)-isomer. ^{1}H n.m.r. (90 MHz) δ 2·32, H1; s, 6·55, 1H, d, $J_{3,4}$ 9 Hz, H3; 6·67, 1H, d, $J_{4,3}$ 9 Hz, H4; 7·27–7·92, 5H, m, Ph.

Enolate Trapping Reactions

With 2-Methylcyclopent-2-enone and S-t-Butyl Propenethioate

Butyllithium was added to a stirred solution of (*E*)-but-2-enyldiphenylphosphine oxide (1)[20] (452 mg, 1·76 mmol) in tetrahydrofuran (15 ml) at –80° until the first permanent orange colour due to the anion appeared. More butyllithium (0·81 ml, 1·85 mmol, 2·3 M in hexane) was added at –80° to effect complete deprotonation. The resulting orange-red solution was stirred for a further 10 min and then treated dropwise with a solution of 2-methylcyclopent-2-enone (178 mg, 1·85 mmol) in tetrahydrofuran (2 ml) such that the temperature remained between –75 and –70°. The reaction mixture was then warmed to –10° and treated with a solution of *S*-t-butyl propenethioate (5) (381 mg, 2·65 mmol) in tetrahydrofuran (4 ml) for 5 min. Butan-1-ol (0·5 ml) was added and the whole was stirred at 0° for 5 min before being extracted with ether (2×75 ml). The combined extracts were washed with brine (10 ml) and dried (Na_2SO_4). Removal of the solvent by evaporation under reduced pressure left a viscous oil containing the product and some non-polar polymeric material. This was submitted to flash chromatography with ethyl acetate/light petroleum (9 : 1) to give *S,S'-di-t-butyl 1-[3'-(diphenylphosphinoyl)-1'-methylprop-2'-enyl]-3a-hydroxy-7a-methyl-octahydro-1H-indene-4,6-dicarbothioate* as a white powder [226 mg, 20%, R_F 0·42 (ethyl acetate)] and as a 9 : 1 mixture of diastereomers. The major epimer (15), assigned the (1*RS*,1'*SR*,2'*E*,3a*SR*,4*SR*,6*RS*,7a*RS*) configuration, was isolated by radial chromatography as a white solid, m.p. 207–215° (dec.) (Found: C, 67·9; H, 8·0. $C_{36}H_{49}O_4PS_2$ requires C, 67·5; H, 7·7%). ν_{max} ($CHCl_3$) 3596–3328s(br) (OH), 3051s, 2968s, 2928s, 1675sh s (C=O), 1653s (C=O), 1456w, 1438m, 1367m, 1247m, 1166s, 1122m, 1028w, 1004m, 982m cm^{-1}. ^{1}H n.m.r. (400 MHz) δ 0·919, 3H, s, 7a-Me; 1·180, 3H, d, $J_{1'\text{-Me},1'}$ 6·6 Hz, 1'-Me; 1·444, 1·456, s, 18H, 2×Bu^t; 1·62–1·83, 6H, m, H1,2α,2β,3α,3β,7β; 1·85–1·92, 2H, m, H5α,7α; 2·009, 1H, ddd, $J_{5\beta,6\alpha}$ 12·6, $J_{5\beta,4\alpha}$ 12·6, $J_{5\beta,5\alpha}$ 12·6 Hz, H5β; 2·450, ddq, $J_{1',2'}$ 8·9, $J_{1',1}$ 8·9, $J_{1',1'\text{-Me}}$ 6·6 Hz, H1'; 2·605, 1H, dd, $J_{4\alpha,5\beta}$ 12·5, $J_{4\alpha,5\alpha}$ 3·3 Hz, H4α; 2·672, 1H, ddt, $J_{6\alpha,5\beta}$ 12·5, $J_{6\alpha,7\beta}$ 12·5, $J_{6\alpha,5\alpha} \approx 3·6$, $J_{6\alpha,7\alpha} \approx 3·6$ Hz, H6α; 4·24, 1H, s, OH; 6·200, 1H, dd, $J_{3',P}$ 24·6, $J_{3',2'}$ 16·8 Hz, H3'; 6·584, 1H, ddd, $J_{2',P}$ 19·4, $J_{2',3'}$ 16·8, $J_{2',1'}$ 8·8 Hz, H2'; 7·44–7·73, 10H, m, 2×Ph. Mass spectrum *m/z* 641 (M+1, <1%), 640 (M, <1), 552 (14), 551 (37), 495 (20), 461 (14), 389 (18), 257 (17), 256 (77), 255 (16), 202 (31), 201 (25), 131 (20), 91 (14), 57 (100), 55 (18), 41 (59), 39 (14), 29 (27).

Also obtained after flash chromatography was a mixture of the conjugate adducts (16) and (17) (321 mg, 52%). The compounds were prepared as follows. (*E*)-But-2-enyldiphenylphosphine oxide (500 mg, 1·0 equiv.) in tetrahydrofuran (20 ml) under nitrogen at –78° was deprotonated with butyllithium as described above. After 15 min a solution of 2-methylcyclopent-2-enone (187 mg, 1·94 mmol) in tetrahydrofuran (1 ml) was added dropwise between –78 and –70°. The deep red colour of the phosphine oxide anion faded immediately. The reaction mixture was stirred for a further 15 min and then quenched with saturated ammonium chloride solution (10 ml). The aqueous layer was then extracted with ethyl acetate (2×50 ml) and the combined organic layers were washed with brine (100 ml) and dried (Na_2SO_4). Removal of the solvent under reduced pressure left the crude product as a viscous oil. This was submitted to flash chromatography with methanol/ethyl acetate (1 : 49) to give a 1·38 : 1 mixture of the compounds as a viscous gum (669 mg, 98%). This mixture was submitted to h.p.l.c. (methanol/ethyl acetate, 3 : 400; Whatman Partisil 10 M20 column, 6·0 ml/min, 600 p.s.i.) to give firstly (*1'*RS,*2*SR,*2'*E,*3*SR)-*3-[3'-(diphenylphosphinoyl)-1'-methylprop-2'-enyl]-2-methylcyclopentanone* (16) (R_t 98 min), as a white microcrystalline solid, m.p. 127–128·5° (Found: C, 74·9; H, 7·2. $C_{22}H_{25}O_2P$ requires C, 75·0; H, 7·15%). ν_{max} ($CHCl_3$) 3081w, 2972s, 2935m, 2877m, 1736s (C=O), 1692w, 1457w, 1438s, 1173s (P=O), 1122s, 988w, 695s cm^{-1}. ^{1}H n.m.r. (400 MHz) δ 1·08, 3H, d, $J_{2\text{-Me},2}$ 6·5 Hz, 2-Me; 1·212, 3H, d, $J_{1'\text{-Me},1'}$ 7·0 Hz, 1'-Me; 1·488–1·573, 1H, m, H4β; 1·743–1·83, 1H, m, H3; 1·80–1·895, 1H, m, H2; 1·980–2·045, 1H, m, H4α; 2·100, 1H, ddd, $J_{5\alpha,5\beta}$ 18·0, $J_{5\alpha,4\beta}$ 9·5, $J_{5\alpha,4\alpha}$ 8·5 Hz, H5α; 2·328, 1H, ddd, $J_{5\beta,5\alpha}$ 18·0, $J_{5\beta,5\beta}$ 8·0, $J_{5\beta,4\alpha}$ 1·5 Hz, H5β; 2·684, 1H, dddq, $J_{1',2'}$ 8·5, $J_{1',1'\text{-Me}}$ 7·0, $J_{1',3}$ 4·5, $J_{1',3'}$ 1·0 Hz, H1'; 6·313, 1H, ddd, $J_{3',P}$ 24·5, $J_{3',2'}$ 17·0, $J_{3',1'}$ 1·0 Hz,

H3′; 6·756, 1H, ddd, $J_{2',P}$ 19·5, $J_{2',3'}$ 17·0, $J_{2',1'}$ 8·5 Hz, H2′; 7·433–7·718, 10H, m, 2×Ph. N.O.e. difference experiments: preirradiation at δ 1·08 (2-Me), enhancements at 1·74–1·90 (H2,H3, 2·9%); preirradiation at δ 1·21 (1′-Me), enhancements at 1·74–1·90 (H2,3, 1·9%), 2·68 (H1′, 1·9%). ^{13}C n.m.r. (100·6 MHz) δ 13·3, 2-Me; 17·4, 1′-Me; 23·0, C5; 36·7, C4; 40·6, 47·3, 49·3, C2,3,1′; 123·2, C3′; 128·4, 131·0, 131·6, 133·1, Ph; 153·4, C2′; 201·9, C1. Mass spectrum *m/z* 352 (M, 2·3%), 337 (M−Me, 1·9), 256 (93), 202 (100), 183 (13), 155 (10), 131 (17), 125 (10), 91 (11), 77 (20), 55 (17), 47 (15), 41 (17).

The (1′*RS*,2*SR*,2′*E*,3*SR*)-isomer (17) (R_t 109 min) was eluted next as a colourless viscous gum, for which satisfactory combustion analyses could not be obtained (Found; $M^{+\bullet}$, 352·1587. $C_{22}H_{25}O_2P$ requires $M^{+\bullet}$, 352·1592). ν_{max} ($CHCl_3$) 3081w, 2974s, 2942m, 2878m, 1736s (C=O), 1633w, 1466w, 1438s, 1172s (P=O), 1122s, 987w, 695s cm^{-1}. ^{1}H n.m.r. (400 MHz) δ 1·004, 3H, d, $J_{2\text{-Me},2}$ 8·0 Hz, 2-Me; 1·132, 3H, d, $J_{1'\text{-Me},1'}$ 7·2 Hz, 1′-Me; 1·603, 1H, dddd, $J_{4\beta,4\alpha}$ 12·5, $J_{4\beta,3}$ 11·0, $J_{4\beta,5\beta}$ 9·0, $J_{4\beta,5\alpha}$ 9·0 Hz, H4β; 1·911–2·00, 1H, m, H4α; 2·01–2·10, 1H, m, H3; 2·144, 1H, ddd, $J_{5\alpha,5\beta}$ 18·0, $J_{5\alpha,4\beta}$ 9·5, $J_{5\alpha,4\alpha}$ 8·5 Hz, H5α; 2·299, 1H, ddd, $J_{5\beta,5\alpha}$ 19·5, $J_{5\beta,4\beta}$ 9·0, $J_{5\beta,4\alpha}$ 1·5 Hz, H5β; 2·348–2·403, 1H, m, H2; 2·45, 1H, dddq, $J_{1',3}$ 9·0, $J_{1',2'}$ 8·5, $J_{1',1'\text{-Me}}$ 7·2, $J_{1',3'}$ 1·0 Hz, H1′; 6·291, 1H, ddd, $J_{3',P}$ 24·5, $J_{3',2'}$ 17·0, $J_{3',1'}$ 1·0 Hz, H3′; 6·646, 1H, ddd, $J_{2',P}$ 19·5, $J_{2',3'}$ 17·0, $J_{2',1'}$ 8·5 Hz, H2′; 7·441–7·730, 10H, m, 2×Ph. ^{13}C n.m.r. (100·6 MHz) δ 9·8, 2-Me; 18·5, 1′-Me; 25·0, C5; 37·3, C4; 40·1, 44·6, 45·7, C2,3,1′; 121·9, C3′; 128·5, 131·1, 131·7, 133·6, Ph; 155·1, C2′; 220·7, C1. Mass spectrum *m/z* 352 (M, 1·2%), 337 (M−Me, 1·2), 256 (40), 202 (100), 183 (8), 155 (5), 131 (10), 125 (7), 91 (8), 77 (16), 55 (14), 47 (13), 41 (16).

With 2-Methylcyclopent-2-enone and S-t-Butyl Propenethioate in the Presence of Copper(I) Cyanide

The lithium enolate was generated as described above at −80° from (*E*)-but-2-enyldiphenylphosphine oxide (410 mg, 1·60 mmol), butyllithium (0·73 ml, 1·68 mmol, 2·3 M in hexane) and 2-methylcyclopent-2-enone (90) (161 mg, 1·68 mmol). After 5 min cuprous cyanide (216 mg, 2·40 mmol) was added in one portion with stirring and the mixture was warmed to −10° over 30 min. A solution of *S*-t-butyl propenethioate (346 mg, 2·40 mmol) in tetrahydrofuran (4 ml) was added dropwise and after 10 min butan-1-ol (0·5 ml) was added. The insoluble copper salts were removed by filtration and the filtrate was worked up as described above to give a clear viscous oil. This was dissolved in ethyl acetate (2 ml) and applied to a short column of alumina to remove residual copper salts and polymeric material. The oil remaining after evaporation of the solvent was then submitted to flash chromatography with ethyl acetate to give *S-t-butyl (1′*RS,*2′*E,*3*SR,*4a*SR,*5*SR,*7a*RS,*8*RS*)-5-[3′-(diphenylphosphinoyl)-1′-methylprop-2′-enyl]-4a-methyl-2-oxo-hexahydro-3,7a-ethano-2*H*-cyclopenta[b]pyran-8-carbothioate* (18) as a white microcrystalline solid (298 mg, 34%, R_F 0·23), m.p. 197–199° from ethyl acetate (Found: C, 69·9; H, 7·2. $C_{32}H_{39}O_4PS$ requires C, 69·8; H, 7·1%). ν_{max} ($CHCl_3$) 2977s, 1754vs (lactone C=O), 1682s (thioester C=O), 1438m, 1248sh m, 1173s, 1122s, 1038s, 1006s cm^{-1}. ^{1}H n.m.r. (400 MHz) δ 0·932, 3H, s, 4a-Me; 1·066, 3H, d, $J_{1'\text{-Me},1'}$ 6·5 Hz, 1′-Me; 1·475, 9H, s, Bu^t; 1·566, 1H, d, $J_{4\alpha,4\beta}$ 13·2, H4α; 1·668, 1H, ddd, $J_{5,6\alpha}$ 10·4, $J_{5,6\beta}$ 10·4, $J_{5,1'}$ 8·8 Hz, H5; 1·779, 1H, ddd, $J_{4\beta,4\alpha}$ 13·2, $J_{4\beta,3}$ 5·5, $J_{4\beta,9\beta}$ 2·4 Hz, H4β; 1·85–1·97, 3H, m, H6α,6β,7α; 2·036, 1H, ddd, $J_{9\alpha,9\beta}$ 13·2, $J_{9\alpha,8}$ 10·2, $J_{9\alpha,3}$ 3·2 Hz, H9α; 2·05–2·14, 2H, m, H9β,7β; 2·435, ddq, $J_{1',2'} \approx 9$, $J_{1',5} \approx 9$, $J_{1',1'\text{-Me}}$ 6·5 Hz, H1′; 2·721, 1H, ddd, $J_{3,4\beta}$ 5·5, $J_{3,9\alpha}$ 3·2, $J_{3,9\beta}$ 2·5 Hz, H3; 3·021, 1H, dd, $J_{8,9\alpha}$ 10·25, $J_{8,9\beta}$ 7 Hz, H8; 6·269, 1H, dd, $J_{3',P}$ 25, $J_{3',2'}$ 16·9 Hz, H3′; 6·642, 1H, ddd, $J_{2',P}$ 19·1, $J_{2',3'}$ 16·8, $J_{2',1'}$ 8·4 Hz, H2′; 7·45–7·73, 10H, m, 2×Ph. N.O.e. difference experiment: preirradiation at δ 0·932 (4a-Me), enhancements at 2·44 (H1′, 4·1%) and at 1·78 (H4β, 2·0%). ^{13}C n.m.r. (100·6 MHz) 17·7, 18·6, 1-Me, 4a-Me; 26·7, 26·9, 29·8, C4,6,9; 29·7, C**Me**$_3$; 36·5, C5; 38·1, C7; 42·4, $J_{C,P}$ 16 Hz, C1′; 48·7, 49·4, C3,8; 46·8, 49·2, **C**Me$_3$, C4a; 90·1, C7a; 121·4, d, $J_{C,P}$ 101 Hz, C3′; 128·6, d, $J_{C,P}$ 11 Hz, C_{ortho}; 131·2, d, $J_{C,P}$ 10 Hz, C_{meta}; 131·8, C_{para}; 133·2, C_{ipso}; 155·3, C2′; 175·7, C2; 199·1, **C**OSBu^t. Mass spectrum *m/z* 550 (M, 4%), 493 (20), 462 (35), 461 (M−Bu^tS, 100), 434 (27), 419 (11), 407 (7), 256 (47), 202 (35), 201 (25), 131 (14), 91 (12), 77 (14), 57 (Bu^t, 47), 41 (20), 29 (12).

Also obtained was the hydrindanol (15) (72 mg, 7%). The predominant formation of compound (18) in this particular experiment was not reproducible; the hydrindanol and compound (18) were obtained in approximately equal amounts from other experiments run under the above conditions.

With 2-Methylcyclopent-2-enone and S-Phenyl (E)-3-(Phenylsulfonyl)propenethioate (6)

Butyllithium (0·29 ml, 0·69 mmol, 2·40 M in hexane) was added dropwise to a stirred solution of (*E*)-but-2-enyldiphenylphosphine oxide (177 mg, 0·69 mmol) in tetrahydrofuran (15 ml) at −60° under nitrogen. The resulting orange-red solution was then stirred for 5 min before a solution of 2-methylcyclopent-2-enone (66 mg, 0·69 mmol) in tetrahydrofuran (2 ml) was added dropwise. The colour of the solution changed to a pale yellow after 1 equiv. of the enone had been added. The reaction mixture was warmed to −20° and then a solution of *S*-phenyl (*E*)-3-(phenylsulfonyl)propenethioate (252 mg, 0·83 mmol) in tetrahydrofuran (6 ml) was added dropwise to cause formation of an orange-red coloured solution. The rate of the addition was regulated so as to maintain the reaction temperature between −20 and −15°. Stirring was continued within this temperature range for 5 min during which time the red colour slowly intensified. Saturated ammonium chloride solution (10 ml) was added and then the mixture was extracted with ethyl acetate (2×75 ml). The combined extracts were washed with brine and dried (Na_2SO_4) and then the solvents were removed under reduced pressure to leave an orange viscous oil. This was then prepurified by flash chromatography with methanol/ethyl acetate 1 : 99 to give a pale oil (251 mg) containing the product which coeluted with a yellow impurity. Attempts to curb the formation of, or to remove, the yellow impurity by using *N,N*-dimethylaniline in the reaction mixture, by carrying out an oxidative workup by washing the reaction mixture with aqueous sodium hypochlorite or by washing the ether/dichloromethane extracts of the product with acidic or basic solutions were ineffective. However, upon allowing the ethyl acetate extracts to stand for 2 days, decomposition of the impurities to baseline material according to t.l.c. analysis with methanol/ethyl acetate (1 : 99) took place, thus obviating the need for a second chromatography. Further purification was achieved by radial chromatography with methanol/ethyl acetate (1 : 99) to give *S-phenyl (1′RS,1″SR,2″E,3E,5′SR)-3-{5′-[3″-(diphenylphosphinoyl)-1″-methylprop-2″-enyl]-1′-methyl-2′-oxocyclopentyl}propenethioate* (19) as a white powder (172 mg, 48%), m.p. 152·5–155° (Found: C, 72·1; H, 6·0. $C_{31}H_{31}O_3PS$ requires C, 72·4; H, 6·1%). ν_{max} ($CHCl_3$) 3008sh s, 2982s, 1967w, 1920w, 1817w, 1743s (C=O), 1687s (C=O, unsat.), 1624s, 1479w, 1438s, 1174s, 1122s, 1105m, 1070m, 1028w, 1022s, 1002w, 975m, 833m cm^{-1}. ^1H n.m.r. (400 MHz) δ 1·077, 3H, d, $J_{1''\text{-Me},1''}$ 6·6 Hz, 1″-Me; 1·155, 3H, s, 1′-Me; 1·573, 1H, dddd, $J_{4'\beta,4'\alpha}$ 12, $J_{4'\beta,3'\alpha}$ 12, $J_{4'\beta,5'}$ 11·5, $J_{4'\beta,3'\beta}$ 7·8 Hz, H4′β; 2·03–2·10, 1H, m, H4′α; 2·157, 1H, ddd, $J_{5',4'\beta}$ 11·5, $J_{5',1''}$ 9·9, $J_{5',4'\alpha}$ 6·3 Hz, H5′; 2·258, 1H, ddd, $J_{3'\alpha,3'\beta}$ 19, $J_{3'\alpha,4'\beta}$ 11·7, $J_{3'\alpha,4'\alpha}$ 9 Hz, H3′α; 2·463, 1H, dd, $J_{3'\beta,3'\alpha}$ 19·3, $J_{3'\beta,4'\beta}$ 8 Hz, H3′β; 2·509, 1H, ddq, $J_{1'',5'}$ 9·5, $J_{1'',2''}$ 8·5, $J_{1'',1''\text{-Me}}$ 6·6 Hz, H1″; 6·279, 1H, d, $J_{2,3}$ 15·5 Hz, H2; 6·308, 1H, dd, $J_{3'',P}$ 24, $J_{3'',2''}$ 17 Hz, H3″; 6·669, 1H, ddd, $J_{2'',P}$ 19, $J_{2'',3''}$ 17, $J_{2'',1''}$ 8·5 Hz, H2″; 6·824, 1H, d, $J_{3,2}$ 15·5 Hz, H3; 7·37–7·77, 15H, m, 3×Ph. Mass spectrum (c.i.) *m/z* 543 (M+Et, 15%), 515 (M+1, 31), 406 (22), 405 (86), 379 (20), 372 (23), 340 (37), 201 (20), 169 (100), 107 (37), 71 (27), 59 (84), 41 (100), 29 (100).

With 2-Methylcyclopent-2-enone and S-t-Butyl (E)-3-t-(Butylsulfonyl)propenethioate (8)

The lithium enolate was generated at −60° as previously described from (*E*)-but-2-enyldiphenylphosphine oxide (207 mg, 0·81 mmol), butyllithium (0·42 ml, 0·81 mol, 1·91 M in hexane) and 2-methylcyclopent-2-enone (78 mg, 0·81 mmol). A solution of *S*-t-butyl (*E*)-3-(t-butylsulfonyl)propenethioate (256 mg, 0·97 mmol) was added at −20° as previously described to give an orange-red solution. Workup followed by flash chromatography and then radial chromatography (methanol/ethyl acetate, 1 : 99) afforded *S-t-butyl (1′RS,1″SR,2″E,3E,5′SR)-3-{5′-[3″-(diphenylphosphinoyl)-1″-methylprop-2″-enyl]-1′-methyl-2′-oxocyclopentyl}propenethioate* (21) as a highly viscous oil which upon trituration with ether solidified to a white powder (215 mg, 54%), m.p. 175–180° (Found: C, 70·3; H, 7·15. $C_{29}H_{35}O_3PS$ requires C, 70·4; H, 7·1%). ν_{max} ($CHCl_3$) 2970s, 1965w, 1900w, 1820w, 1741 (C=O), 1662s (C=O, unsat.), 1620s, 1455m, 1438m, 1365m, 1280w, 1168s, 1120s, 1105sh m, 1060w, 1030m, 1012m, 973m cm^{-1}. ^1H n.m.r. (400 MHz) δ 1·071, 3H, d, $J_{1''\text{-Me},1''}$ 6·5 Hz, 1″-Me; 1·110, 3H, s, 1′-Me; 1·491, 9H, s, Bu^t; 1·551, dddd, $J_{4'\beta,4'\alpha}$ 12, $J_{4'\beta,3'\alpha}$ 12, $J_{4'\beta,5'}$ 10·6, $J_{4'\beta,3'\beta}$ 7·8 Hz, H4′β; 2·02–2·11, 1H, m, H4′α; 2·123, 1H, ddd, $J_{5',4'\beta}$ 11·5, $J_{5',1''}$ 9·5, $J_{5',4'\alpha}$ 6·3 Hz, H5′; 2·237, 1H, ddd, $J_{3'\alpha,3'\beta}$ 19·0, $J_{3'\alpha,4'\beta}$ 11·7, $J_{3'\alpha,4'\alpha}$ 8·9 Hz, H3′α; 2·440, 1H, dd, $J_{3'\beta,3'\alpha}$ 18·8, $J_{3'\beta,4'\beta}$ 8 Hz, H3′β; 2·492, 1H, ddq, $J_{1'',5'}$ 9·5, $J_{1'',2''}$ 8·6, $J_{1'',1''\text{-Me}}$ 6·5 Hz, H1″; 6·091, 1H, d, $J_{2,3}$ 15·7 Hz, H2; 6·288, 1H, ddd, $J_{3'',P}$ 24·4, $J_{3'',2''}$ 16·8, $J_{3'',1''}$ 0·7 Hz, H3″; 6·659, 1H, d, $J_{3,2}$ 15·5 Hz, H3;

6·664, 1H, ddd, $J_{2'',P}$ 19·2, $J_{2'',3}$ 16·8, $J_{2'',1''}$ 8·6 Hz, H2''; 7·45–7·73, 4H, m, 2×Ph. Mass spectrum *m/z* 494 (M, 13%), 405 (41), 256 (100), 202 (41), 201 (68), 77 (31), 57 (25), 41 (25), 28 (70).

With 2-Methylcyclopent-2-enone and (E)-Chlorobut-3-en-2-one (9)

The lithium enolate was generated at −40° from (*E*)-but-2-enyldiphenylphosphine oxide (6·66 g, 26 mmol) in tetrahydrofuran (200 ml), butyllithium (11·92 ml, 1·1 equiv., 2·4 M in hexane) and 2-methylcyclopent-2-enone (2·52 g, 1·02 equiv.) in tetrahydrofuran (2 ml). The reaction mixture was allowed to warm to −30° and then a solution of (*E*)-4-chlorobut-3-en-2-one (2·99 g, 1·1 equiv.) in tetrahydrofuran (2 ml) was added dropwise so as to maintain the temperature between −35 and −30°. During the addition the solution became yellow-orange in colour. The reaction mixture was stirred for 15 min and was then quenched with saturated ammonium chloride solution (100 ml). The resulting mixture was extracted with ethyl acetate (3×200 ml), and the extracts were dried (Na_2SO_4) and evaporated to leave an orange oil. Immediate purification by flash chromatography (methanol/ethyl acetate, 1 : 24) followed by radial chromatography gave the adduct (4) containing *c.* 5% of the (*Z*)-isomer as a brittle foam (7·56 g, 70%) after thorough drying at high vacuum. The characterization of compound (4) is described elsewhere.[1]

With 2-Methylcyclohex-2-enone and (E)-4-Chlorobut-3-en-2-one (9); Preparation of the Octalone (26)

A solution of the Grignard reagent prepared from magnesium turnings (0·33 g, 13·7 mg-atom, 1·5 equiv.) and methyl iodide (0·68 ml, 1·55 g, 10·9 mmol, 1·2 equiv.) in dry ether (20 ml) was transferred by cannula to a flask containing a stirred suspension of copper(I) cyanide (0·98 g, 10·9 mmol, 1·2 equiv.) in dry ether (20 ml) at 20° under nitrogen. The suspension was stirred for 15 min before a solution of 2-methylcyclohex-2-enone (1 g, 9·1 mmol, 1·0 equiv.) in ether (10 ml) was added. After a further 15 min 4-chlorobut-3-en-2-one (1·2 g, 11·8 mmol, 1·3 equiv.) in ether (20 ml) was added, and the resulting mixture was stirred for 10 min before being quenched with a saturated solution of ammonium chloride (20 ml). The mixture was filtered, and the organic layer was separated from the filtrate. The aqueous layer was extracted with ether (20 ml) and the combined ether extracts were washed successively with water (2×30 ml) and brine (30 ml) and then dried (Na_2SO_4). The solvent was removed under reduced pressure to leave an oil which was submitted to flash chromatography with ethyl acetate/light petroleum (1 : 4) to give *(1'E,2RS,3RS)-2,3-dimethyl-2-(3'-oxobut-1'-enyl)cyclohexanone* (24) (1·57 g, 90%) as a clear oil (Found: C, 74·1; H, 9·1. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%). ν_{max} (liquid film) 2964m, 2938m, 2876w, 1709s, 1674s, 1627m, 1459w, 1428w, 1360m, 1257s, 1162m, 961w, 945w cm^{-1}. ^1H n.m.r. (400 MHz) δ 0·88, 3H, d, $J_{Me,3}$ 7·2 Hz, 3-Me; 1·21, 3H, s, 2-Me; 1·58–1·68, 1H, m, H4; 1·68–1·79, 1H, m, H5α; 1·79–1·87, 1H, m, H4α; 1·97–2·09, 1H, m, H5β; 2·02, 1H, dqd, $J_{3\alpha,4\beta}$ 9·6, $J_{3\alpha,Me}$ 7·2, $J_{3\alpha,4\alpha}$ 3·6 Hz, H3α; 2·30, 3H, s, 4'-Me; 2·38, 1H, dddd, $J_{6\alpha,6\beta}$ 13·8, $J_{6\alpha,5\beta}$ 4·8, $J_{6\alpha,5\alpha}$ 4·8, $J_{6\alpha,4\alpha}$ 1·2 Hz, H6α; 2·52, 1H, ddd, $J_{6\beta,6\alpha}$ 13·8, $J_{6\beta,5\alpha}$ 10·8, $J_{6\beta,5\beta}$ 6·00 Hz, H6β; 6·02, 1H, d, $J_{1',2'}$ 16·8 Hz, H1'; 6·89, 1H, d, $J_{2',1'}$ 16·8 Hz, H2'. N.O.e. difference experiments: preirradiation at δ 0·88 (3-Me), enhancements at 1·21 (2-Me, 0·9%) and 1·97–2·09 (H5α, 1·6%); preirradiation at 1·21 (2-Me), enhancements at 0·88 (3-Me, 0·8%), 2·52 (H6β, 0·8%), 6·02 (H1', 1·9%); preirradiation at 2·30 (4'-Me), enhancements at 6·02 (H1', 1·0%), 6·89 (H2', 2·4%). ^{13}C n.m.r. (100·6 MHz) δ 15·56, 15·72, 2-Me, 3-Me; 24·62, C4; 26·99, C3; 28·75, C5; 37·94, C6; 40·64, C4'; 55·39, C2; 130·6, C2'; 151·2, C1'; 198·2, C3'; 212·8, C1. Mass spectrum *m/z* 194 (M, 17%), 179 (3), 151 (25), 123 (54), 109 (36), 98 (88), 97 (55), 95 (46), 43 (100).

A solution of the unsaturated ketone (24) (2·0 g, 1·0 mmol) in dry ethanol containing a catalytic quantity of palladium on charcoal (10%) was shaken under hydrogen gas at 5 atm for 3 days. The mixture was filtered, and the filtrate was evaporated to dryness to give the product in quantitative yield; distillation at 115°/0·35 mm (Kugelrohr) gave the diketone (25) as a colourless oil. Although the compound has been cited in the literature,[22] it does not appear to have been previously characterized (Found: C, 73·6; H, 10·4. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·3%). ν_{max} (film) 2962m, 2937m, 2875w, 1705vs, 1464w, 1428w,

1356m, 1170w, 946w cm^{-1}. ^1H n.m.r. (200 MHz) δ 0·93, 3H, d, $J_{Me,3\alpha}$ 9·4 Hz, 3-Me; 1·02, 3H, s, 2-Me; 1·53–2·04, 6H, m, H4,5,1′; 2·16, 3H, s, H4′; 2·21–2·57, 4H, m, H2′,6. Mass spectrum *m/z* 196 (M, 0·3%), 181 (6), 178 (9), 163 (7), 153 (6), 135 (17), 126 (31), 125 (21), 121 (23), 111 (49), 107 (33), 97 (28), 95 (35), 93 (32), 91 (19), 83 (29), 82 (38), 79 (30), 77 (20), 71 (16), 69 (47), 67 (37), 55 (93), 43 (100), 41 (96), 39 (38), 32 (30).

The saturated diketone (25) (100 mg, 0·51 mmol) and a few crystals of *p*-toluenesulfonic acid in dry benzene (30 ml) were heated under reflux with azeotropic removal of water during 3 days. The solvent was then evaporated under reduced pressure, and the residue was taken up into ether (30 ml). The ether solution was washed with aqueous sodium carbonate (20 ml, 10%), and brine (20 ml), and then dried (Na_2SO_4). Evaporation of solvent left an orange oil, which was submitted to flash chromatography with ethyl acetate/light petroleum (1 : 9) to give (4a*RS*,5*SR*)-4a,5-dimethyl-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (26)[18–20] (60 mg, 66% from 2-methylcyclohex-2-enone) as a pale yellow oil. ^1H n.m.r. spectrum (400 MHz) δ 0·92, 3H, d, $J_{Me,5}$ 6·4 Hz, 5-Me; 1·11, 3H, s, 4a-Me; 1·41–1·63 and 1·85–1·93, 5H, m, H5,6,7; 1·76, 1H, ddd, $J_{4\alpha,3\beta}$ 14·0, $J_{4\alpha,4\beta}$ 13·5, $J_{4\alpha,3\alpha}$ 5·0 Hz, H4α; 2·06, 1H, ddd, $J_{4\beta,4\alpha}$ 13·5, $J_{4\beta,3\beta}$ 5·1, $J_{4\beta,3\alpha}$ 3·4 Hz, H4β; 2·23–2·32, 2H, m, H8; 2·35, 1H, dddd, $J_{3\alpha,3\beta}$ 17·0, $J_{3\alpha,4\alpha}$ 5·0, $J_{3\alpha,4\beta}$ 3·4, $J_{3\alpha,1}$ 0·4 Hz, H3α; 2·44, 1H, ddd, $J_{3\beta,3\alpha}$ 17·0, $J_{3\beta,4\alpha}$ 14·3, $J_{3\beta,4\beta}$ 5·1 Hz, H3β; 5·74, 1H, ddd, $J_{1,8\alpha}$ 1·5, $J_{1,3\alpha}$ 0·9, $J_{1,8\beta}$ 0·6 Hz, H1. N.O.e. difference experiments: preirradiation at δ 0·92 (5-Me), enhancements at 1·11 (10-Me, 0·5%), 1·42–1·48 (1·6%) and 2·06 (H4β, 1·2%); preirradiation at 1·11 (10-Me), enhancements at 0·92 (5-Me, 0·5%), 1·42–1·52 (1·1%), 2·06 (H4β, 0·6%), and 2·44 (H3β, 1·7%). ^{13}C n.m.r. (50 MHz) δ 14·85, 4a-Me; 15·62, 5-Me; 26·14, 30·07, 33·0, 33·59, C3,4,6,7,8; 38·64, C4a, 42·78, C5; 123·6, C1; 171·4, C8a; 199·6, C2.

With 2-Methylcyclohex-2-enone and (E)-1-Chloropent-1-en-3-one (10)

A solution of the Grignard reagent prepared from magnesium turnings (0·33 g, 13·7 mg-atom, 1·5 equiv.) and methyl iodide (0·68 ml, 1·55 g, 10·9 mmol, 1·2 equiv.) in dry ether (20 ml) was transferred by cannula to a flask containing a stirred suspension of copper(I) cyanide (0·98 g, 10·9 mmol, 1·2 equiv.) in dry ether (20 ml) at 20° under nitrogen. The suspension was stirred for 15 min before a solution of 2-methylcyclohex-2-enone (1·0 g, 9·1 mmol, 1·0 equiv.) in ether (10 ml) was added. After a further 15 min a solution of 1-chloropent-1-en-3-one (1·4 g, 11·8 mmol, 1·3 equiv.) in ether (20 ml) was added, and the solution was stirred for 10 min before being quenched with saturated aqueous ammonium chloride (20 ml). The mixture was worked up as described above to give a 3 : 2 mixture of the product (27) and starting β-chlorovinyl ethyl ketone. The mixture was submitted to flash chromatography with ethyl acetate/light petroleum (1 : 4) to give *(1′E,2RS,3RS)-2,3-dimethyl-2-(3′-oxopent-1′-enyl)cyclohexanone* (27) (0·98 g, 52%) as a clear oil (Found: C, 75·0; H, 10·1. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·7%). ν_{max} (liquid film) 2073s, 2939s, 2877m, 1704vs, 1675s, 1629m, 1457m, 1356w, 1183w, 1123w, 983w, 945w cm^{-1}. ^1H n.m.r. (400 MHz) δ 0·88, 3H, d, $J_{Me,3}$ 7·0 Hz, 3-Me; 1·11, 3H, t, $J_{5',4'}$ 7·5 Hz, H5′; 1·21, 3H, s, 2-Me; 1·57–1·68, 1H, m, H4α; 1·70–1·80, 1H, m, H5β; 1·70–1·88, 1H, m, H4β; 1·99–2·09, 1H, m, H5α; 2·02, 1H, dqd, $J_{3\alpha,4\beta}$ 9·6, $J_{3\alpha,Me}$ 7·0, $J_{3\alpha,4\alpha}$ 3·6 Hz, H3α; 2·39, 1H, dddd, $J_{6\alpha,6\beta}$ 14·0, $J_{6\alpha,5\alpha}$ 5·0, $J_{6\alpha,5\beta}$ 5·0, $J_{6\alpha,4\alpha}$ 1·2 Hz, H6α; 2·51, 1H, ddd, $J_{6\beta,6\alpha}$ 14·0, $J_{6\beta,5\alpha}$ 10·0, $J_{6\beta,5\beta}$ 6·0 Hz, H6β; 2·61, 1H, dq, J_{gem} 18·0, $J_{4',5'}$ 7·5 Hz, H4′; 2·63, 1H, dq, J_{gem} 18·0, $J_{4',5'}$ 7·5 Hz, H4′; 6·04, 1H, d, $J_{2',1'}$ 16·9 Hz, H2′; 6·92, 1H, d, $J_{1',2'}$ 16·9 Hz, H1′. N.O.e. difference experiment: preirradiation at δ 0·88 (3-Me), enhancements at 1·21 (2-Me, 3·8%) and at 2·02 (H3α, 3·5%). ^{13}C n.m.r. (15 MHz) δ 7·86, C5′; 15·3, 3-Me; 16·1, 2-Me; 24·1, C4; 28·7, C5; 33·2, C4′; 37·9, C6; 40·6, C3; 55·3, C2; 129, C2′; 150, C1′; 200, C3′; 211, C1. Mass spectrum *m/z* 208 (M, 16%), 151 (20), 137 (25), 123 (19), 112 (100), 95 (35), 81 (25), 69 (13), 57 (39), 41 (30), 29 (35).

Reaction of the Enolate of 2,6-Dimethylcyclohexanone with 4-Chlorobut-3-en-2-one (9)

2,6-Dimethylcyclohexanone (200 mg, 1·6 mmol, 1 equiv.) in tetrahydrofuran (5 ml) was added to a solution at −78° of lithium diisopropylamide, prepared from diisopropylamine (0·25 ml, 17·5 mg, 1·75 mmol, 1·1 equiv.) and butyllithium (7·3 ml, 2·4 M in hexane, 1·75 mmol, 1·1 equiv.) in tetrahydrofuran (10 ml) under nitrogen. After 30 min, the solution was warmed to −40° and then treated with a solution of 4-chlorobut-3-en-2-one (183 mg,

9·7 mmol, 1·1 equiv.) in tetrahydrofuran (20 ml). After 30 min the solution was quenched with saturated aqueous ammonium chloride (30 ml) and extracted into ether (2×30 ml). The combined ether extracts were washed successively with water and brine and then dried (Na_2SO_4). The solvent was removed under reduced pressure to give a yellow-brown oil (344 mg), ^{1}H n.m.r. analysis of which indicated that it consisted solely of a 4 : 1 mixture of the *trans* and *cis* products (28) and (29). This was submitted to flash chromatography with ethyl acetate/light petroleum (1 : 4) to give firstly an inseparable 5 : 3 mixture of the (1′*E*,2*RS*,6*RS*)- and (1′*Z*,2*RS*,6*RS*)-isomers (28) and (30) of *2,6-dimethyl-2-(3′-oxobut-1′-enyl)cyclohexanone* (224 mg, 72%) as a pale yellow oil, b.p. 125°/11 mm (Found: C, 74·3; H, 9·7. $C_{12}H_{18}O_2$ requires C, 74·2; H 9·3%). ν_{max} (liquid film) 2970m, 2932s, 2859w, 1718s, 1715s, 1707s, 1696m, 1685m, 1675s, 1617m, 1457w, 1452w, 1374w, 1359w, 1257w, 1180w, 1124w, 999w, 986w cm^{-1}. ^{1}H n.m.r. (400 MHz) (*E*)-isomer (28) δ 1·03, 3H, d, $J_{Me,6}$ 6·0 Hz, 6-Me; 1·19, 3H, s, 2-Me; 1·25–2·20, 6H, m, H3,4,5; 2·26, 3H, s, H4′; 2·59, 1H, dqd, $J_{6\beta,5\alpha}$ 13·0, $J_{6\beta,Me}$ 6·0, $J_{6\beta,5\alpha}$ 5·8 Hz, H6β; 6·02, 1H, d, $J_{2',1'}$ 16·3 Hz, H2′; 6·91, 1H, d, $J_{1',2'}$ 16·3 Hz, H1′. N.O.e. difference experiments: preirradiation at δ 1·19 (2-Me), enhancements at 6·02 (H2′, 1·1%), 6·91 (H1′, 2·2%); preirradiation at 2·59 (H6β), enhancements at 1·03 (6-Me, 3·5%), 6·02 (H2′, 1·7%), 6·91 (H1′, 2·3%); preirradiation at 6·02 (H2′), enhancements at 1·03 (6-Me, 9·8%), 1·19 (2-Me, 3·4%), 2·26 (H4′, 6·0%); preirradiation at 6·91 (H1′), enhancements at 1·03 (6-Me, 11·0%), 1·19 (2-Me, 8·0%), 2·26 (H4′, 9·4%). ^{1}H n.m.r. (400 MHz) (*Z*)-isomer (30) δ 1·01, 3H, d, $J_{Me,6}$ 6·0 Hz, 6-Me; 1·16, 3H, s, 2-Me; 1·25–2·20, 6H, m, H3,4,5; 2·16, 3H, s, H4′; 2·64, 1H, dqd, $J_{6\beta,5\alpha}$ 13·0, $J_{6\beta,Me}$ 6·0, $J_{6\beta,5\beta}$ 5·8 Hz, H6β; 6·11, 1H, d, $J_{2',1'}$ 12·0 Hz, H2′; 6·22, 1H, d, $J_{1',2'}$ 12·0 Hz, H1′. N.O.e. difference experiments: preirradiation at δ 2·16 (H4′), enhancements at 6·11 (H2′, 1·6%), 6·22 (H1′, 1·5%); preirradiation at 6·11 (H2′), enhancements at 1·01 (6-Me, 18%), 2·16 (H4′, 4·0%). ^{13}C n.m.r. (100·6 MHz) (*E*)-isomer δ 14·88, 6-Me; 22·07, C4; 24·00, 2-Me; 27·73, C4′; 36·64, C5; 40·64, C3; 43·02, C6; 52·05, C2; 130·0, C2′; 150·1, C1′; 197·4, C3′; 212·0, C1. (*Z*)-isomer δ 14·88, 6-Me; 22·23, 2-Me; 22·72, C4; 30·80, C4′; 38·20, C5; 42·26, C6; 45·64, C3; 52·88, C2; 126·7, C2′; 151·0, C1′; 197·4, C3′; 211·2, C1. Mass spectrum *m/z* 194 (M, 4·8%), 179 (1·8), 166 (18), 151 (33), 96 (19), 95 (90), 93 (20), 81 (36), 79 (11), 67 (30), 55 (26), 43 (100), 41 (52), 39 (21), 29 (16), 27 (17).

The next fraction consisted of an inseparable 3 : 2 mixture of the (1′*E*,2*RS*,6*SR*)- and (1′*Z*,2*RS*,6*SR*)-isomers (29) and (31) of *2,6-dimethyl-2-(3′-oxobut-1′-enyl)cyclohexanone* (56 mg, 18%) as a pale yellow oil (Found: C, 74·3; H, 9·7. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%). ^{1}H n.m.r. (400 MHz) (*E*)-isomer (29) δ 1·03, 3H, d, $J_{Me,6}$ 6·4 Hz, 6-Me; 1·25–2·18, 6H, m, H3,4,5; 1·39, 3H, s, 2-Me; 2·32, 3H, s, H4′; 2·74, 1H, dqd, $J_{6\alpha,5\beta}$ 12·8, $J_{6\alpha,Me}$ 6·4, $J_{6\alpha,5\alpha}$ 6·4 Hz, H6α; 6·00, 1H, d, $J_{2',1'}$ 16·6 Hz, H2′; 7·23, 1H, d, $J_{1',2'}$ 16·6 Hz, H1′. N.O.e. difference experiments: preirradiation at δ 1·03 (6-Me), enhancements at 2·74 (H6α, 1·6%), 6·00 (H2′, 1·9%); preirradiation at 2·74 (H6α), enhancement at 7·23 (H1′, 3·5%). ^{1}H n.m.r. (400 MHz) (*Z*)-isomer (31) δ 1·02, 3H, d, $J_{Me,6}$ 6·4 Hz, 6-Me; 1·25–2·18, 6H, m, H3,4,5; 1·25, 3H, s, 2-Me; 2·26, 3H, s, H4′; 2·5–2·8, 1H, m, H6; 6·11, 1H, d, $J_{2',1'}$ 10·5 Hz, H2′; 6·20, 1H, d, $J_{1',2'}$ 10·5 Hz, H1′.

Reaction of the Enolate of 2,6-Dimethylcyclohexanone with (E)-1-Chloropent-1-en-3-one (10)

2,6-Dimethylcyclohexanone (1·0 g, 7·94 mmol, 1 equiv.) in tetrahydrofuran (20 ml) was added to a solution at −78° of lithium diisopropylamide, prepared from diisopropylamine (1·22 ml, 882 mg, 8·7 mmol, 1·1 equiv.) and butyllithium (4·6 ml, 1·9 M in hexane, 8·7 mmol, 1·1 equiv.) in tetrahydrofuran (100 ml) under nitrogen. After 30 min, the solution was warmed to −40° and then treated with a solution of 1-chloropent-1-en-3-one (1·03 g, 9·7 mmol, 1·1 equiv.) in tetrahydrofuran (20 ml). After 30 min the solution was quenched with saturated aqueous ammonium chloride (30 ml) and extracted into ether (2×30 ml). The combined ether extracts were washed successively with water and brine and then dried (Na_2SO_4). The solvent was removed under reduced pressure to give a yellow-brown oil (1·96 g), ^{1}H n.m.r. analysis of which indicated that it consisted solely of a 4 : 1 mixture of the *trans* and *cis* products (32) and (34). The mixture was submitted to flash chromatography with ethyl acetate/light petroleum (1 : 9) to give an 8 : 1 mixture of the (1′*E*,2*RS*,6*RS*)- and (1′*Z*,2*RS*,6*RS*)-isomers (32) and (34) of *2,6-dimethyl-2-(3′-oxopent-1′-enyl)cyclohexanone* (790 mg, 48%) as a clear oil, b.p. 130°/0·6 mm (Kugelrohr) (Found: M$^{+\bullet}$, 208·1477. $C_{13}H_{20}O_2$ requires M$^{+\bullet}$, 208·1458). ν_{max} (liquid film) 2974m, 2933s, 2860w, 1712vs, 1676s, 1619m, 1456m, 1376w, 1123m,

1000m, 985·6w cm^{-1}. ^1H n.m.r. (400 MHz) (*E*)-isomer (32) δ 1·02, 3H, d, $J_{Me,6}$ 6·5 Hz, 6-Me; 1·10, 3H, t, $J_{5',4'}$ 7·5 Hz, H5′; 1·19, 3H, s, 2-Me; 1·30–2·18, 6H, m, H3,4,5; 2·56, 2H, q, $J_{4',5'}$ 7·5 Hz, H4′; 2·59, 1H, dqd, $J_{6\beta,5a}$ 15·0, $J_{6\beta,Me}$ 7·5, $J_{6\beta,5\beta}$ 7·5 Hz, H6β; 6·04, 1H, d, $J_{2',1'}$ 16·8 Hz, H2′; 6·96, 1H, d, $J_{1',2'}$ 16·8 Hz, H1′. N.O.e. difference experiments: preirradiation at δ 1·19 (2-Me), enhancements at 6·04 (H2′, 0·5%), 6·96 (H1′, 0·7%); preirradiation at 2·56 (H4′), enhancements at 1·02 (6-Me, 3·0%), 6·04 (H2′, 1·9%), 6·96 (H1′, 2·0%); preirradiation at 6·04 (H2′), enhancement at 2·56 (H4′, 3·7%); preirradiation at 6·96 (H1′), enhancement at 6·04 (H2′, 6·7%). ^1H n.m.r. (400 MHz) (*Z*)-isomer (34) δ 1·00, 3H, d, $J_{Me,6}$ 6·5 Hz, 6-Me; 1·03, 3H, t, $J_{5,4}$ 7·5 Hz, H5′; 1·16, 3H, s, 2-Me; 1·27–2·18, 6H, m, H3,4,5; 2·45, 2H, q, $J_{4',5'}$ 7·5 Hz, H4′; 2·64, 1H, m, H6; 6·12, 1H, d, $J_{2',1'}$ 12·0 Hz, H2′; 6·22, 1H, d, $J_{1',2'}$ 12·0 Hz, H1′. ^{13}C n.m.r. (100·6 MHz) (*E*)-isomer (32) δ 7·932, C5′; 14·87, 2-Me; 22·05, C4; 23·97, 6-Me; 36·70, C5; 40·79, C3; 43·02, C6; 45·74, C4′; 52·04, C2; 129·1, C2′; 149·1, C1′; 200·3, C3′; 212·6, C1. (*Z*)-isomer (34) δ 7·686, C5′; 14·75, 2-Me; 22·15, 6-Me; 22·73, C4; 34·35, C5; 38·30, C3; 42·22, C6; 45·74, C4′; 52·99, C2; 126·5, C2′; 151·0, C1′; C1 and C3′ not detected. Mass spectrum *m/z* 208 (M, 13%), 180 (41), 165 (60), 151 (43), 123 (81), 112 (85), 109 (71), 95 (94), 81 (80), 67 (77), 57 (88), 55 (84), 53 (47), 43 (76), 41 (96), 39 (54), 29 (100), 27 (61).

The next fraction eluted was a 6 : 1 mixture of compounds tentatively identified as the *cis*-dimethyl compounds (33) and (35) (220 mg, 13%) as a colourless oil, b.p. 130°/0·3 mm (Kugelrohr), for which satisfactory microanalyses could not be obtained. ^1H n.m.r. (90 MHz) δ 1·00, 3H, d, *J* 6 Hz, 6-Me; 1·07, 3H, t, *J* 6·8 Hz, H5′; 1·35, 3H, s, 2-Me; 1·2–2·4, 6H, H3,4,5; 2·63, 2H, q, *J* 6·8 Hz, H4′; 2·52–2·91, 1H, m, H6; 5·93, 1H, d, *J* 16·5 Hz, H2′; 7·15, 1H, d, *J* 16·5 Hz, H1′.

Reaction of the Enolate of 2,6-Dimethylcyclohexanone with (E)-4-Phenylsulfonylbut-3-en-2-one (3)

2,6-Dimethylcyclohexanone (200 mg, 1·59 mmol) was deprotonated with lithium diisopropylamide (1·1 equiv.) in tetrahydrofuran (15 ml) as described above. At –30°, a solution of 4-phenylsulfonylbut-3-en-2-one (368 mg, 1·75 mmol, 1·1 equiv.) in tetrahydrofuran (20 ml) was added and the resulting solution stirred for 30 min. The solution was quenched and worked up as above to give a yellow-brown oil (414 mg), which according to ^1H n.m.r. analysis consisted of a 4 : 1 mixture of the *cis*- and *trans*-isomers (28) and (29) contaminated with phenylsulfinic acid. Purification by flash chromatography enabled the product mixture, now additionally containing the compounds (30) and (31), to be isolated (247 mg, 80% overall).

Reaction of the Enolate of 2,6-Dimethylcyclohexanone with (E)-4-Phenylsulfinylbut-3-en-2-one (11)

A solution of (*E*)-4-phenylsulfinylbut-3-en-2-one (171 mg, 0·88 mmol, 1·1 equiv.) in tetrahydrofuran (10 ml) was added to a solution at –30° of the enolate of 2,6-dimethylcyclohexanone, prepared from the ketone (100 mg, 0·80 mmol) and lithium diisopropylamide (1·1 equiv.) in tetrahydrofuran (15 ml). After 30 min, the solution was quenched and worked up to give a dark brown oil (187 mg), which according to ^1H n.m.r. analysis consisted of a 5 : 1 mixture of the products (28) and (29) contaminated with a small quantity of a phenylsulfur impurity. Purification by flash chromatography gave the product mixture containing additionally the (*Z*)-isomers (30) and (31) as a light yellow oil (130 mg, 84% overall).

Reaction of the Enolate of 2,6-Dimethylcyclohexanone with (Z)-4-Phenylsulfinylbut-3-en-2-one (12)

From (*Z*)-4-phenylsulfinylbut-3-en-2-one (171 mg, 0·88 mol) and the ketone (100 mg, 0·80 mol) according to the foregoing conditions was obtained a pale yellow oil (414 mg), which according to ^1H n.m.r. analysis consisted of a mixture containing the (*E*)-isomers (28) and (29) (7 : 1) and the (*Z*)-isomers (30) and (31).

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