A Synthesis of Disubstituted Acetylenes, and its Application to the Stereoselective Synthesis of Conjugated Trienes [1]

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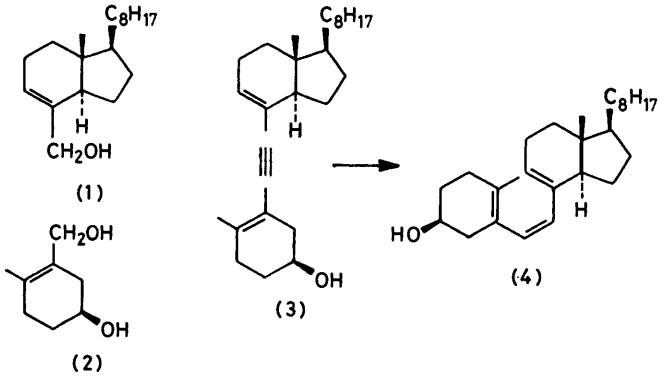
Representative β-oxo-sulphones were obtained by (a) oxidation of β-hydroxy-sulphones, (b) oxidation of α-phenylthio-ketones, and (c) reaction of metallated sulphones with saturated and αβ-unsaturated esters. The β-oxo-sulphones were converted by way of lithium (in one example, sodium) enolates into enol phosphates, which on reductive elimination provided disubstituted acetylenes in moderate to good yield. The sequence permits the preparation of acetylenes $R^1C{\equiv}CR^2$ from the primary alcohols RCH_2OH or equivalents.

The value of the method is illustrated by a highly stereoselective synthesis from (*E*)-geraniol of the conjugated *E,Z,E*-triene (34) with retention of the original *E*-geometry.

THE experiments now described were the outcome of our interest in the synthesis of 9,10-*seco*-sterols, and in particular of a wish to effect the synthesis of precalciferol$_3$ (4) † from the two primary alcohols (1) † and (2) or their equivalents. That problem is part of a more general and so far unsolved problem in the stereoselective synthesis of conjugated trienes; namely, how can two primary allylic alcohols be united by their respective α-carbon atoms to generate a conjugated triene in which (a) the original allyl geometry of both reaction partners is preserved, and (b) the new (central) disubstituted double bond has exclusively or with large predominance the *cis*- or, if it is so desired, the *trans*-configuration? For precalciferol$_3$, compliance with condition (a) is no problem; there, condition (b) is dominant. In the general case, too, existing methods will normally secure compliance with condition (a) taken alone; allylic geometry can be preserved if one of the alcohols is first converted into the corresponding phosphonium bromide [2] or diphenylphosphine oxide,[3] and then used in a Wittig or Horner reaction with the aldehyde derived from the other allylic alcohol. In that



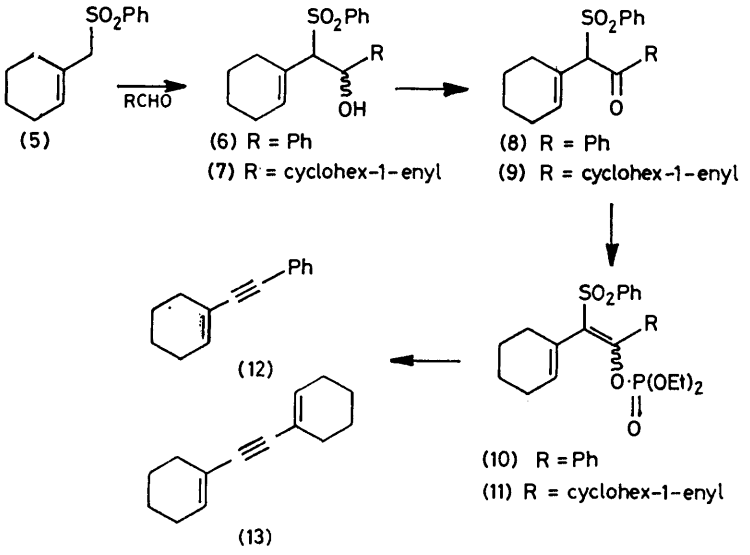
event, however, the new disubstituted double bond is usually formed partly with the *cis*-, and partly the *trans*-configuration, and the two reaction products have to be separated. It would clearly be useful to have a method leading stereoselectively to central-*cis*-trienes, and this was the objective of the present work. The reflection that the existing synthesis [4] of precalciferol$_3$ proceeds by the semihydrogenation of the conjugated enynene (3) led us to consider whether similar enynenes could be obtained with preservation of allyl geometry from two primary allylic alcohols.

Addition–elimination sequences [5] form highly effective means for obtaining olefins $R^1CH{\equiv}CHR^2$ from the alcohols RCH_2OH. Attempts [6] have been made to develop analogous routes to acetylenes $R^1C{=}CR^2$; the most successful of them [7] employs an extension of the Wittig method, in which a zwitterionic compound $^-O{-}CR^1{=}CR^2{-}PPh_3^+$ is pyrolysed in order to eliminate triphenylphosphine oxide. This method is effective for the preparation of acetylenes $R^1C{\equiv}CR^2$ where R^1 = alkyl and R^2 = aryl, where R^1 = alkyl and $R^2 = CO_2Et$, and where R^1 = alk-1-enyl and $R^2 = CO_2Et$. However, the vigorous conditions required for the reaction limit its scope, and it is not effective for dialkylacetylenes, where R^1 and R^2 = alkyl, nor for the conjugated enynenes where R^1 and R^2 = alk-1-enyl. The method now described is effective for both these classes, and uses reagents and conditions compatible with a wide range of functional groups.

M. Julia's reductive elimination [8] of β-acyloxy- and β-mesyloxy-sulphones with sodium amalgam in methanol affords a mild and potent method of generating an isolated double bond; it is also applicable [9] to the formation of conjugated olefins. Although eliminations across a double bond are usually more difficult than those across a single bond, it seemed possible that reductive elimination from an enol phosphate [10] derived from a β-oxo-sulphone might generate an acetylenic link. The reaction was first studied with the enol phosphate (10). In order to prepare this compound the lithium derivative of cyclohex-1-enylmethyl phenyl sulphone (5) was treated with benzaldehyde to give the diastereoisomeric β-hydroxy-sulphones (6) which were converted by Jones' oxidation into the β-oxo-sulphone (8). Its lithium enolate, generated by treatment with lithium diisopropylamide in tetrahydrofuran, was treated with diethyl phosphorochloridate to give (yield 90%) the enol phosphate (10). Reduction with sodium amalgam in methanol–tetrahydrofuran at 0 °C gave some of the desired acetylene (12), but it was accompanied by a considerable amount of the corresponding *trans*-disub-

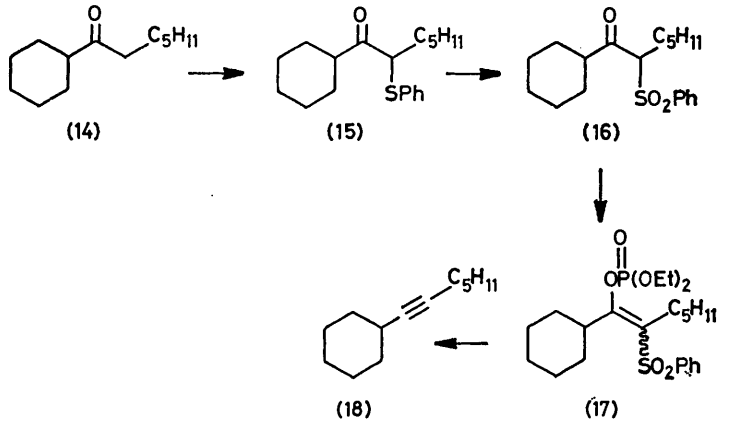
† Structures (1)—(4) inclusive represent absolute configurations; the remaining structures in this paper, so far as they are dissymmetric, represent racemates.

stituted olefin. In tetrahydrofuran alone the acetylene was formed without the olefin, but much β-oxo-sulphone (8) was regenerated (attack at P–O bond). Best results were obtained with a mixture of dimethyl sulphoxide and tetrahydrofuran at 0 °C, when again some β-oxo-sulphone was regenerated, but the acetylene (12) was obtained in 72% yield within 2 h. Similar reductive elimination conditions were used in all the acetylene syntheses here recorded; some, however, in which the favourable effect of conjugation was absent, required longer reaction times.

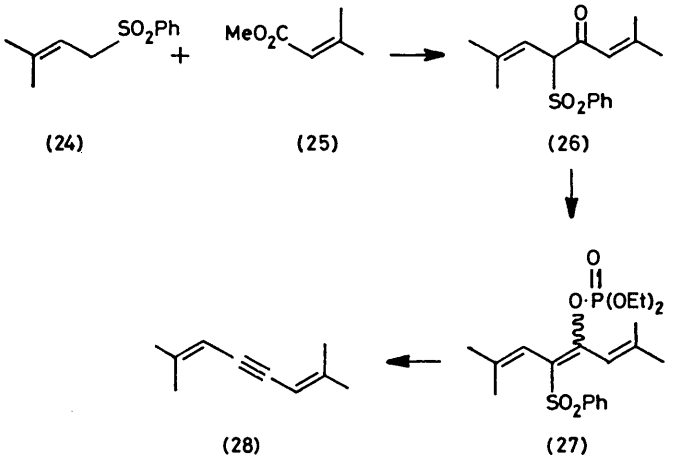


Next, di(cyclohex-1-enyl)acetylene (13) was prepared by a similar reaction sequence. The diastereoisomeric β-hydroxy-sulphones (7) were not oxidised satisfactorily by Jones' method, but Pfitzner–Moffatt oxidation [11] gave the β-oxo-sulphone (9) in *ca.* 84% yield from the starting sulphone (6). If a general method were available for the oxidation of β-hydroxy-sulphones to β-oxo-sulphones, it would probably afford the most convenient way of obtaining them. However, the Pfitzner–Moffatt method is not generally effective, and we were not able to prepare compound (31) by its aid (see later). To return to the β-oxo-sulphone (9), its enol phosphate (11) (yield 98%) was obtained as before, and its reduction was completed in 1 h to give the dienyne (13) in 63% yield. Some of the β-oxo-sulphone (9) was recovered from the reduction product; if this is recycled, the yield of the dienyne (13) is raised to 79%. This dienyne has previously [12] been obtained by a different route, and has been converted by semihydrogenation into *cis*-1,2-di(cyclohex-1-enyl)ethylene.

It was of interest to determine whether the new elimination reaction is applicable to the synthesis of dialkylacetylenes. β-Oxo-sulphones of the required type are readily obtained by the phenylsulphenylation [13] of ketones, followed by peroxy-acid oxidation of the phenylthio-group, so that the sequence, if successful, would allow an acetylenic link to be introduced into a chain (or ring) containing a keto-group, a result not easily achieved in other ways. Accordingly, 1-cyclohexylheptan-1-one (14) was converted first into the thioether (15) and then into the β-oxo-sulphone (16). The enol phosphates (17), unlike all the others here described, could not be obtained from the lithium enolate, nor indeed from the sodium enolate, in tetrahydrofuran alone. However, addition of hexamethyl-



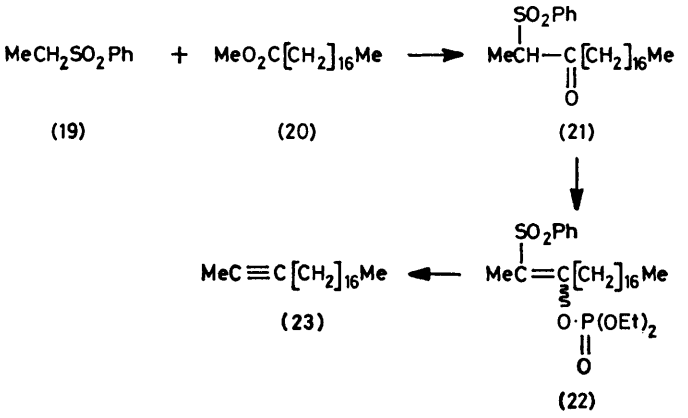
phosphoric triamide promoted the reaction of the sodium derivative with diethyl phosphorochloridate, and gave a mixture (*ca.* 1 : 1) of the two geometric forms of the enol phosphates (17). It should be noted that the other enol phosphates here described, obtained by the simple lithium enolate method, showed no evidence of geometric heterogeneity. Reduction of the unconjugated enolates (17) required *ca.* 8 h for completion, and gave 21% of the oxo-sulphone (16) and 64.5% of the acetylene (18), or 82% when adjustment is made for recycling the oxo-sulphone.



(24) (25) (26) (28) (27)

A third method of preparing β-oxo-sulphones lies in the reaction [14] of metallated sulphones with saturated esters. Since the product is more acidic than the starting sulphone it is desirable to use 2 mol of metallated sulphone to one of ester; the unused sulphone can be recovered at the end of the reaction. Thus, from 2 mol of ethyl phenyl sulphone (19) to 1 mol of methyl octadecanoate (20) we obtained the β-oxo-sulphone (21) in 70% yield; it was separated from the unused sulphone (19) by chromatography. The enol phosphate (22) was then obtained (yield 77%) by the lithium enolate method. Reduction of this enol phosphate, as of the analogue (17), was slow (4 h); it gave the β-oxo-sulphone (21) together with crystalline eicos-2-yne (23) (50%; adjusted yield 68%).

When allylic sulphones are treated with potassium t-butoxide in tetrahydrofuran and the product is treated with an αβ-unsaturated ester, only a low yield of conjugated β-oxo-sulphone is obtained, the main reaction being 1,4-addition to the conjugated ester.[15] However,

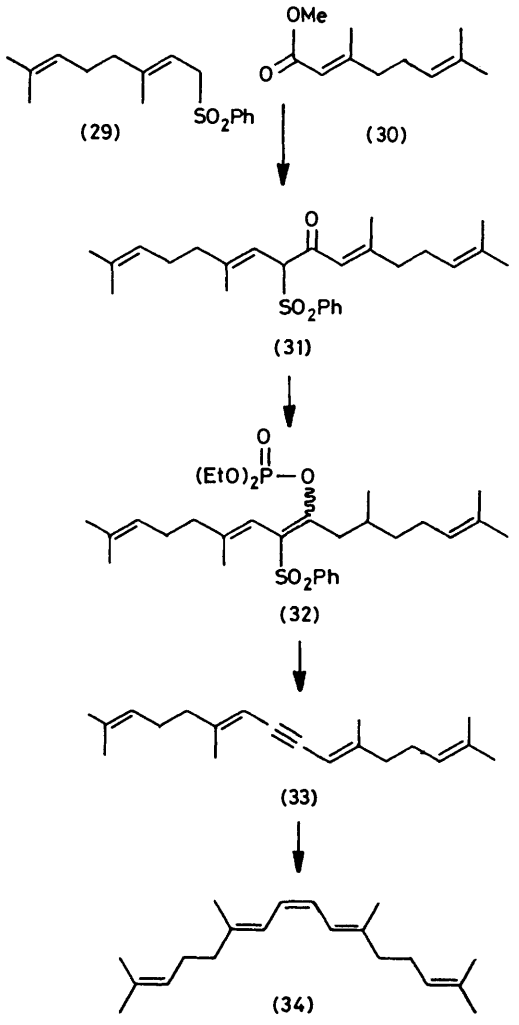


(19) (20) (21) (23) (22)

the magnesium bromide derivative of methyl *p*-tolyl sulphone is known [16] to react with ethyl cinnamate exclusively by 1,2-addition. We found that 1,2-addition took place exclusively in the reaction of the magnesium bromide derivatives of allylic sulphones with αβ-unsaturated esters. Thus the magnesium bromide derivative (2 mol. equiv.) of the allylic sulphone (24) reacted with methyl ββ-dimethylacrylate (25) to give the crystalline β-oxo-sulphone (26) [17] in 81% yield (based on the ester). Most of the unused sulphone was recovered also. The enol phosphate (27), prepared in the normal way, underwent reduction relatively rapidly, giving the conjugated dienyne (28) in 69% yield.

In order to show the full synthetic potential of the above methods we undertook the preparation of the conjugated enynene (33) in which the conjugated trisubstituted double bonds have the *E*-geometry. The starting materials, the sulphone (29) [17] and the methyl ester (30), can both be prepared, with retention of geometry, from (*E*)-geraniol. Oxidation of the latter with manganese dioxide affords (*E*)-citral, which on treatment with silver oxide gives (*E*)-geranic acid [18] containing a little *Z*-isomer. The latter can be removed by crystallisation, and esterification with diazomethane then furnishes the pure *E*-ester (30). Reaction of this ester with the magnesium bromide derivative of the sulphone (29) (2 mol. equiv.) gave a mixture of this sulphone and the β-oxo-sulphone (31). The β-oxo-sulphone can be separated by chromatography, but the process is difficult except on a small scale. The mixture was therefore treated with lithium di-isopropylamide (1 mol. equiv.) and diethyl phosphorochloridate, which converted the β-oxo-sulphone into the enol phosphate (32). After chromatographic separation from the sulphone (29) it was obtained in 83% yield [based on the ester (30)]. Reduction with sodium amalgam in the usual way gave the conjugated enynene (33) in 78.5% yield (85.5% allowing for recovered β-oxo-sulphone);

its structure was apparent from the spectral data. In order to confirm its stereochemistry it was converted by semihydrogenation over Lindlar catalyst into the conjugated *E,Z,E*-triene (34). This compound and its geometric isomers have previously [19] been obtained by applications of the Wittig method; for example, reaction between (*E*)-geranyltriphenylphosphonium bromide and (*E*)-citral gave a mixture (35 : 65) of the *E,Z,E*-compound (34) and its *E,E,E*-isomer, which were separated chromatographically. Examination of our sample of the compound (34) by i.r., g.l.c., and ^{13}C n.m.r.



showed that it contained only a small amount (<5%) of the *E,E,E*-isomer, and that it was essentially free from other isomers; in particular, none of the *Z,Z,E*-isomer could be detected, from which it was clear that the *E*-configuration of the double bonds in the starting materials (29) and (30) had been maintained throughout the synthesis. Such control of the geometry of all three double bonds in conjugated trienes has not previously been possible. The synthesis of (34) constitutes a model for a stereoselective synthesis of natural (15*Z*)-phytoene from (all-*E*)-geranylgeraniol, and experiments with this aim are now in hand; the existing synthesis,[20] using the Wittig reaction, gives (15*Z*)-phytoene only as the minor component (20%) in a mixture with other isomers, mainly the 15*E*-isomer.

After the publication of our preliminary communication [1] of the above work, a paper appeared in which P. A. Bartlett and his colleagues [21] described their independent development of a similar synthesis of unconjugated acetylenes from β-oxo-sulphones; it was applied [22] to the construction of an unconjugated *trans*-disubstituted double bond in an interesting synthesis of brefeldin A. The authors remarked that ' the synthesis of unsaturated β-ketosulphones . . . by an acylation procedure is foiled by the tendency of sulphonyl carbanions to add in a 1,4-manner to unsaturated esters,' and they therefore did not extend their experiments to the formation of conjugated enynes, compounds which were among the main objectives of our own work.

EXPERIMENTAL

N.m.r. spectra were measured for solutions in $CDCl_3$. Light petroleum, unless otherwise specified, refers to the fraction of b.p. 40—60 °C. T.l.c. and p.l.c. were performed with Kieselgel GF_{254}. Tetrahydrofuran was distilled from sodium, and dimethyl sulphoxide from calcium hydride. Reactions using lithium or magnesium derivatives were conducted under nitrogen.

2(*Cyclohex-1-enyl-1-oxo-1-phenyl-2-phenylsulphonylethane* (8).—The sulphone (5) (354 mg) and 1.5M-n-butyl-lithium in hexane (1.1 cm^3) were stirred together in dry tetrahydrofuran (6 cm^3) at −78 °C for 15 min; benzaldehyde (190 mg) in tetrahydrofuran (3 cm^3) was then added, discharging the orange colour. After 0.5 h saturated aqueous ammonium chloride (3 cm^3) was added; the mixture was allowed to warm to 20 °C, and was then poured into water. Isolation with ether gave the diastereoisomeric β-hydroxy-sulphones (6) (*ca.* 3 : 2) as a crystalline solid (578 mg), $\nu_{max.}$ (Nujol) 1 135s, 1 295s, and 3 495m cm^{-1}, τ(major isomer) 2.05—2.6 (5 H, m, SO_2Ph), 2.73 (5 H, s, Ph), 4.45 (1 H, m, CH=), 4.62 (1 H, d, *J* 10 Hz, CHO), and 6.25 (1 H, d, *J* 10 Hz, $CHSO_2$); (minor isomer) 2.05—2.6 (5 H, m, SO_2Ph), 2.73 (5 H, s, Ph), 4.08 (1 H, m, CH=), 4.32 (1 H, m, CHO), and 6.48 (1 H, d, *J* 4 Hz, $CHSO_2$).

To a stirred solution of the mixed hydroxy-sulphones (380 mg) in acetone (12 cm^3) at 0 °C, Jones' reagent (2.67M; 0.83 cm^3) was added; after 35 min the reaction was worked up in the usual way. The β-*oxo-sulphone* (8) separated from ether–light petroleum as prisms (272 mg, 81%), m.p. 124—126 °C, $\nu_{max.}$ (Nujol) 1 147s, 1 305s, 1 686s, and 3 060w cm^{-1}, τ 1.95—2.75 (10 H, m, ArH), 4.33 (1 H, m, CH=), and 4.57 (1 H, s, $CHSO_2$) (Found: C, 70.7; H, 6.05; S, 9.1. $C_{20}H_{20}O_3S$ requires C, 70.6; H, 5.9; S, 9.4%).

1-*Phenylethynylcyclohex-1-ene* (12).—A solution of the β-oxo-sulphone (8) (200 mg) in tetrahydrofuran (4 cm^3) was added dropwise with stirring to lithium di-isopropylamide (0.68 mmol) in tetrahydrofuran (2 cm^3) at −78 °C, and stirring was continued at the same temperature for 20 min, after which diethyl phosphorochloridate (131 mg) in tetrahydrofuran (3 cm^3) was added. The mixture was stirred and brought to 20 °C and kept at that temperature for 0.5 h; it was then diluted with ether (40 cm^3) and washed with water. Evaporation of the ether layer and p.l.c. of the product (ethyl acetate–benzene, 1 : 4) gave the *enol phosphate* (10) as an oil (251 mg, 90%), $\nu_{max.}$ (film) 1 025vs,

1 152s, 1 300s, and 1 617m cm^{-1}, τ 1.85—2.75 (10 H, m, ArH), 4.54 (1 H, m, CH=), 5.95 (4 H, m, 2 × CH_2O), 8.80 3 H, t, *J* 7 Hz, CH_3), and 8.82 (3 H, t, *J* 7 Hz, CH_3) (Found: M^+, 476.142 3. $C_{24}H_{29}O_6PS$ requires *M*, 476.142 2).

The enol phosphate (10), prepared as described above from the oxo-sulphone (8) (120 mg), but without chromatographic purification, and 5.65% sodium amalgam (500 mg) were stirred together at −5 °C in tetrahydrofuran (3 cm^3) and dimethyl sulphoxide (2 cm^3); after 1 h more amalgam (200 mg) was added. After 2 h the mixture was added to water, and the product was isolated with light petroleum and purified by p.l.c. (same solvent). Bulb-to-bulb distillation at 120 °C and 1 mmHg gave the acetylene [23] (12) (46 mg) as an oil, $\nu_{max.}$ (film) 688vs, 753vs, 1 435s, 1 488s, 1 594m, and 2 195w cm^{-1}, $\lambda_{max.}$ (hexane) 274 (ε 20 500) and 291 nm (17 600); τ 2.4—2.85 (5 H, m, ArH) and 3.80 (1 H, m, CH=); *m/e* 182 (100%), 181 (28), 167 (52), 166 (24), 165 (27), 154 (41), 153 (31), and 152 (27) (Found: M^+, 182.109 3. Calc. for $C_{14}H_{14}$: *M*, 182.109 5). G.l.c. (5 ft of 5% SE30 at 150 °C, retention time 13 min) showed a purity of 96%.

1,2-*Di*(*cyclohex*-1-*enyl*)-1-*oxo*-2-*phenylsulphonylethane* (9).—Interaction of the sulphone [9] (5) (1.42 g), 1.5M-n-butyl-lithium in hexane (4.5 cm^3), and cyclohex-1-enecarbaldehyde (790 mg) in tetrahydrofuran, in the way described for the epimers (6), gave the diastereoisomeric β-hydroxy-sulphones (7) (2.4 g) as a mixture of crystals and oil, $\nu_{max.}$ (Nujol) 1 140s, 1 300s, and 3 510s cm^{-1}; the crystalline isomer had τ 6.28 (1 H, d, *J* 10 Hz, $CHSO_2$) and the oily isomer τ 6.46 (1 H, d, *J* 5 Hz, $CHSO_2$).

The mixture (2.4 g), dicyclohexylcarbodi-imide (4.28 g) and dichloroacetic acid (453 mg) were stirred together at 21 °C in benzene (28 cm^3) and dimethyl sulphoxide (15 cm^3) for 1 h. After dilution with ether (100 cm^3) the mixture was washed with water, aqueous sodium hydrogen carbonate, and water, and then dried and evaporated. Chromatography of the residue on silica gel (benzene), and crystallisation from a mixture of chloroform, light petroleum, and ether, gave the β-*oxo-sulphone* (9) (1.74 g, 85% from the starting sulphone), m.p. 115—117 °C, $\nu_{max.}$ (Nujol) 1 140s, 1 305s, 1 632m, and 1 665s cm^{-1}, τ 2.0—2.6 (5 H, m, ArH), 3.19 (1 H, m, CH=), 4.39 (1 H, m, CH=), and 4.83 (1 H, s, $CHSO_2$) (Found: C, 69.85; H, 7.2; S, 9.1. $C_{20}H_{24}O_3S$ requires C, 69.75; H, 7.0; S, 9.3%).

Di(*cyclohex*-1-*enyl*)*acetylene* (13).—The β-oxo-sulphone (9) (666 mg) was converted into the *enol phosphate* (11) as described for the analogue (10). After passage through a short column of silica gel (ether–benzene, 1 : 1) it was obtained as an oil (907 mg, 98%), $\nu_{max.}$ (film) 1 020s, 1 148s, 1 285s, and 1 605s cm^{-1}, τ 1.9—2.5 (5 H, m, ArH), 4.04 (1 H, m, CH=), 4.47 (1 H, m, CH=), 5.74 (4 H, m, 2 × CH_2O), 8.63 (3 H, t, *J* 8 Hz, CH_3), and 8.71 (3 H, t, *J* 8 Hz, CH_3) (Found: M^+, 480.173 68. $C_{24}H_{33}O_6PS$ requires *M*, 480.173 54).

The enol phosphate (11) (907 mg) was stirred with sodium amalgam (2.9 g) in tetrahydrofuran (11 cm^3) and dimethyl sulphoxide (7 cm^3) at 0 °C under nitrogen for 1 h; the solution was then decanted into light petroleum and washed with water. The solution was dried and evaporated, and the product was first chromatographed on silica gel (benzene–light petroleum, 1 : 4) and then distilled (bulb-to-bulb) at 115 °C and 0.6 mmHg. The dienyne [12] (13) formed an oil (222 mg, 63%), $\nu_{max.}$ (film) 797m, 839m, 914m, and 3 020w cm^{-1}, $\lambda_{max.}$ (EtOH) 241sh (ε 9 700), 251sh (ε 13 300), 264 (ε 16 900), and 277 nm (ε 13 000), τ 3.93 (2 H, m, 2 × CH=), 7.85 (8 H, m, 4 × CH_2CH=), and 8.35 (8 H, m, 4 × CH_2) (Found: M^+, 186.140 65. Calc. for $C_{14}H_{18}$: *M*, 186.140 84). G.l.c. (5 ft of 5% SE30 at 150 °C, retention time 10.4 min) showed a purity of 95%.

From the chromatogram the crystalline β-oxo-sulphone (9) (132 mg) was recovered by elution with ether and purification by p.l.c.

1-*Cyclohexylheptan*-1-*one* (14).—Interaction of n-hexylmagnesium bromide and hexahydrobenzaldehyde afforded 1-cyclohexylheptan-1-ol as an oil (68%), b.p. 110—112 °C at 1 mmHg, τ 6.63 (1 H, m, CH·O). The alcohol (2.21 g), pyridinium chlorochromate (4.3 g), and Celite (5 g) were stirred together at 20 °C in dichloromethane (110 cm^3) for 1.5 h; the mixture was then filtered, and the filtrate was diluted with ether and washed with dilute hydrochloric acid, aqueous sodium carbonate, and water, and then dried and evaporated. Distillation (bulb-to-bulb) at 170—175 °C and 28 mmHg gave the ketone (14) (2.103 g, 96%), $\nu_{max.}$ (film) 1 710s cm^{-1}, τ 7.56 (2 H, t, *J* 7 Hz, CH_2CO) and 7.66 (1 H, m, CHO) (Found: M^+, 196.182. Calc. for $C_{13}H_{24}O$: *M*, 196.182 7); *m/e* 196 (11%), 126 (21), 113 (44), 111 (41), 85 (17), and 83 (100).

1-*Cyclohexyl*-2-*phenylsulphonylheptan*-1-*one* (16).—To a solution of lithium di-isopropylamide (2.2 mmol) in tetrahydrofuran (4 cm^3) at −78 °C a solution of the ketone (14) (392 mg) in tetrahydrofuran (5 cm^3) was added dropwise with stirring, and after 1 h at the same temperature a solution of phenyl benzenethiosulphonate (600 mg) in tetrahydrofuran was added. Stirring was continued for 0.5 h, and the mixture was then allowed to warm to 20 °C; 2N-hydrochloric acid (40 cm^3) was added, the mixture was extracted with ether, and the extract was washed with dilute aqueous sodium hydroxide, and with water, and was then dried and evaporated. Chromatography of the residue on silica gel (30 g) in benzene–light petroleum (1 : 1) gave the β-*oxo-sulphide* (15) as an oil (486 mg, 80%), $\nu_{max.}$ (film) 690s, 745s, 1 585w, and 1 703vs cm^{-1}, τ 2.5—2.8 (5 H, m, ArH), 6.29 (1 H, t, *J* 7 Hz, C*H*SPh), and 7.30br (1 H, m, CHCO) (Found: M^+, 304.185 77. $C_{19}H_{28}OS$ requires *M*, 304.186 08); *m/e* 304 (22%), 194 (19), 193 (100), 123 (26), and 83 (59).

Oxidation of the β-oxo-sulphide (15) (405 mg) with 80% *m*-chloroperbenzoic acid (575 mg) in dichloromethane (13 cm^3) at 20 °C for 1.5 h, followed by dilution with ether, and washing with aqueous solutions of sodium hydrogen sulphite and sodium carbonate, and water, gave on evaporation the β-*oxo-sulphone* (16) as an oil (443 mg, 99%), which was homogeneous to t.l.c. It separated from methanol at −20 °C as fine needles, m.p. 46—48°, $\nu_{max.}$ (film) 1 150s 1 315s, 1 586m, and 1 712s cm^{-1}, τ 2.15—2.60 (5 H, m, ArH), 5.70 (1 H, t, *J* 7 Hz, C*H*SO_2), and 7.26br (1 H, m, CHCO) (Found: M^+, 336.175 92. $C_{19}H_{28}O_3S$ requires *M*, 336.175 91).

1-*Cyclohexylhept*-1-*yne* (18).—Sodium hydride (130 mg of 50% dispersion in mineral oil) was added to a stirred mixture of the β-oxo-sulphone (16) (606 mg) in tetrahydrofuran (3 cm^3) and hexamethylphosphoric triamide (1 cm^3) at 20 °C; hydrogen was evolved. After 2 h the mixture was cooled to 0 °C and diethyl phosphorochloridate (862 mg) in tetrahydrofuran (1 cm^3) was added. The mixture was stirred at 20 °C for 20 h, and then diluted with ether (50 cm^3) and washed with water. The product was chromatographed on silica gel (35 g) with ether–benzene (1 : 3); elution with ether–benzene (1 : 1) gave the mixed enol phosphates (17) as an oil (640 mg, 75%). Its composite

nature (*E* : *Z* *ca.* 1 : 1) was shown by t.l.c. with ethyl acetate–benzene (1 : 4). The mixture had $\nu_{max.}$ (film) 1 025vs, 1 152s, 1 300s, and 1 622m cm^{-1}, τ 6.60 [m, >CH–C(OP)= of one isomer] and 7.3—7.75 [m, CH_2C= of both isomers and >CH–C(OP)= of second isomer].

The enol phosphate mixture (485 mg) and sodium amalgam (1.8 g) were stirred together in tetrahydrofuran (7 cm^3) and dimethyl sulphoxide (4 cm^3) at 0 °C; after 2 h more amalgam (0.5 g) was added. After 8 h the mixture was decanted into light petroleum, and the solution was washed with water, and dried and evaporated. Passage through a short column of silica gel (light petroleum) and bulb-to-bulb distillation at 140 °C and 40 mmHg gave the acetylene [24] (18) (118 mg, 64.5%). Further elution of the column gave the β-oxo-sulphone (16) (75 mg). G.l.c. (75 ft of 1.5% Carbowax P.L.O.T. at 118 °C; retention time 9.2 min) showed the acetylene (18) to be 96% pure; it showed $\nu_{max.}$ (film) 1 449m, 2 855s, and 2 925s cm^{-1}, τ 7.5—7.95 (3 H, m, >CH–C≡ and CH_2C≡). The [^{13}C n.m.r. resonances (p.p.m.) are tentatively assigned as follows: δ 84.65 and 80.16, acetylenic C; 29.06, C-1 of cyclohexyl; 33.28, C-2 and C-6 of cyclohexyl; 25.03, C-3 and C-5 of cyclohexyl; 18.79, C-3 of hept-1-ynyl chain; 22.30, C-6 of that chain; 14.1 C-7 of that chain; other resonances, 31.14, 29.25, and 26.07 (Found: M^+, 178.172 5. Calc. for $C_{13}H_{22}$: *M*, 178.172 1); *m/e* 178 (13%), 149 (22), 122 (31), 121 (23), 107 (49), 93 (55), 81 (85), 79 (82), and 67 (100).

2-*Phenylsulphonyleicosan*-3-*one* (21).—Ethereal 1.05M-ethylmagnesium bromide (2.9 cm^3) was added to a stirred solution of ethyl phenyl sulphone (561 mg) in benzene (8 cm^3); the mixture was heated under reflux for 1 h, and then cooled to 20 °C, and methyl stearate (448 mg) in benzene (4 cm^3) was added. The mixture was stirred at 20 °C for 24 h and then diluted with ether and washed successively with 2N-hydrochloric acid, aqueous sodium carbonate, and water; it was then dried and evaporated. Chromatography on silica gel (80 g) (ethyl acetate–benzene, 1 : 19) and crystallisation from ether (0 °C) gave the β-*oxo-sulphone* (21) (457 mg, 70%), m.p. 70—72 °C, $\nu_{max.}$ (Nujol) 1 150vs, 1 310s, 1 320s, and 1 723vs cm^{-1}, τ 2.1—2.7 (5 H, m, ArH), 5.82 (1 H, q, *J* 7 Hz, C*H*SO_2), 7.22 (2 H, m, CH_2CO), and 8.59 (3 H, d, *J* 7 Hz, CH_3) (Found: C, 71.7; H, 10.1; S, 7.6. $C_{26}H_{44}O_3S$ requires C, 71.5; H, 10.2; S, 7.3%).

Eicos-2-*yne* (23).—The oxo-sulphone (21) (355 mg) was converted into its lithium enolate as described in the preparation of the enol phosphate (10), and then, by similar reaction with diethyl phosphorochloridate (181 mg) in tetrahydrofuran (−78 °C; then 20 °C for 2 h) into the *enol phosphate* (22). It was purified by p.l.c. (ethyl acetate–benzene, 1 : 4) and then formed an oil (358 mg, 77%) which was homogeneous to t.l.c.; $\nu_{max.}$ (film) 1 025vs, 1 148vs, 1 300vs, and 1 638s cm^{-1}, τ 7.50 (2 H, t, *J* 7 Hz, CH_2C=) and 7.96 (3 H, d, *J* 2 Hz, =CCH_3) (Found: M^+, 572.328 86. $C_{30}H_{53}O_6PS$ requires *M*, 572.330 03).

Reduction of a portion (327 mg) with sodium amalgam (800 + 500 mg) in tetrahydrofuran (4 cm^3) and dimethyl sulphoxide (3 cm^3) (4 h at 0 °C) gave in the usual way *eicos*-2-*yne*, which after distillation at 140—145 °C (air-bath temp.) and 0.1 mmHg formed an oil (79 mg, 50%), $\nu_{max.}$ (film) 1 460m, 2 850s, and 2 920vs cm^{-1}. Crystallisation from ethanol (0 °C) gave crystals, m.p. 24—25 °C, τ 7.93 (2 H, m, CH_2C≡) and 8.23 (3 H, t, *J* 2 Hz, CH_3C≡) (Found: C, 86.55; H, 13.65. $C_{20}H_{38}$ requires C, 86.25; H, 13.75%); *m/e* 278 (1.2), 110 (27), 109 (44), 96 (76), 95 (100), 83 (26), 82 (39), 81 (83), 69 (31), 68 (65), 67 (56), 57 (42), and 55 (65).

Further elution of the chromatogram from which the eicos-2-yne was obtained yielded the β-oxo-sulphone (21) (68 mg).

2,7-*Dimethyl*-5-*phenylsulphonylocta*-2,6-*dien*-4-*one* (26).—The sulphone [15] (24) (1.47 g) in benzene (15 cm^3) was treated with ethereal 1.08M-ethylmagnesium bromide (6.5 cm^3) and then with methyl 3,3-dimethylacrylate (399 mg) in tetrahydrofuran (5 cm^3) in the way described for the preparation of (21); the crude product, an oil (1.79 g), slowly solidified. Crystallisation from a mixture of ether, chloroform, and light petroleum gave the β-oxo-sulphone (26) as prisms (829 mg, 81%), m.p. 104—106 °C (lit.,[17] 104—105 °C), τ 2.0—2.6 (5 H, m, ArH), 3.63 (1 H, m, CHC=O), 4.58br (1 H, d, *J* 10 Hz, CH=), 5.18 (1 H, d, *J* 10 Hz, $CHSO_2$), and 7.86, 8.05, 8.24, and 8.57 (all 3 H, s, CH_3).

The residues from the crystallisation were distilled at 150 °C and 0.1 mmHg, and the resulting solid (652 mg) was allowed to crystallise from a mixture of ether, chloroform, and light petroleum; this gave the starting sulphone (24) (498 mg, 68%).

2,7-*Dimethylocta*-2,6-*dien*-4-*yne* (28).—The β-oxo-sulphone (26) (784 mg) was converted in the usual way into the lithium enolate, and then into the *enol phosphate* (27), which was purified by chromatography on silica gel (ether–benzene, 1 : 1); it then formed an oil (785 mg, 68%), $\nu_{max.}$ (film) 1 015s, 1 140s, 1 275s, 1 605m, and 1 642w cm^{-1}, τ 4.32 (2 H, m, 2 × =CH), 8.25 (6 H, s, 2 × CH_3), 8.35 (3 H, s, CH_3), and 8.72 (3 H, s, CH_3) (Found: M^+, 428.143 06. $C_{20}H_{29}O_6PS$ requires *M*, 428.142 24).

The enol phosphate (760 mg) was reduced in the usual way, and the product was purified by chromatography on silica gel (ether–light petroleum, 1 : 19) followed by distillation (bulb-to-bulb) at 105 °C and 20 mmHg. The *dienyne* (28) was obtained as an oil (164 mg, 69%) which solidified at −20 °C, but melted below 20 °C; $\nu_{max.}$ (film) 822s, 1 220s, 1 335s, 1 377s, 1 455s, and 1 640w cm^{-1}; $\lambda_{max.}$ (hexane) 260 (ε 14 000), 272 (19 000), and 287 nm (16 200); τ 4.57 (2 H, s, $W_{\frac{1}{2}}$ 4 Hz, 2 × CH=), 8.09 (6 H, s, 2 × CH_3), and 8.18 (6H, s, 2 × CH_3) (Found: M^+, 134.109 22. $C_{10}H_{14}$ requires *M*, 134.109 54); *m/e* 134 (100%), 119 (34), 105 (31), 93 (24), 91 (56), 79 (22), and 77 (28). G.l.c. (38-m P.E.G.A. W.C.O.T. at 96 °C; retention time 7 min) showed a purity of 92%.

Further elution of the chromatogram from which the dienyne (28) was obtained gave (ether–light petroleum, 1 : 1) the oxo-sulphone (26) (40 mg).

The β-*Oxo-sulphone* (31).—(*E*)-Geraniol (Fluka) (≥98%) was converted [18] successively into (*E*)-citral, (*E*)-geranic acid, and methyl (*E*)-geranate, $\nu_{max.}$ (film) 1 148s, 1 225s, 1 650m, and 1 725s cm^{-1}, τ 4.32br (1 H, s, =$CHCO_2$), 4.92 (1 H, m, =CH), 6.30 (3 H, s, OMe), 7.74—7.90 (7 H, m, 2 × CH_2 + CMe=$CHCO_2Me$), 8.31 (3 H, s, CH_3), and 8.38 (3 H, s, CH_3). G.l.c. (50 ft of D.E.G.S. P.L.O.T. column at 95—110 °C; retention time, 12.2 min) showed the absence of the *Z*-isomer. (*E*)-Geraniol was also converted, by reaction with chloromethylenedimethylammonium chloride into the *E*-chloride, and then, by reaction with sodium benzenesulphinate in dimethylformamide, into (*E*)-geranyl phenyl sulphone (yield 84%), $\nu_{max.}$ (film) 1 147s, 1 305s, and 1 665m cm^{-1}; τ 2.02—2.60 (5 H, m, ArH), 4.80br (1 H, t, *J* 8 Hz, =C*H*CH_2SO_2), 4.95 (1 H, m, =CH), 6.17 (2 H, d, *J* 8 Hz, CH_2SO_2), 7.88—8.01 (4 H, m, 2 × CH_2), 8.30 (3 H, s,

CH_3), 8.38 (3 H, s, CH_3), and 8.65 (3 H, s, CH_3C=CH-CH_2SO_2). No *Z*-isomer (τ 8.5) was detected.

The magnesium bromide derivative of the sulphone (29) (1.11 g) was generated and treated with methyl (*E*)-geranate (364 mg) in the way used for the β-oxo-sulphone (26). The crude product, a viscous oil (1.459 g), contained the β-oxo-sulphone (31) together with the excess of the sulphone (29); this mixture was used for the preparation of the enol phosphate (32) (see below). On one occasion a similar mixture was separated by p.l.c. (benzene) to give the *β-oxo-sulphone* (31) as an oil, $\nu_{max.}$ (film) 690m, 1 152s, 1 310s, 1 320s, 1 450s, 1 614s, and 1 686s cm^{-1}, τ 2.03—2.60 (5 H, m, ArH), 3.65br (1 H, s, $W_{\frac{1}{2}}$ 4 Hz, =CHCO), 4.59 (1 H, d, *J* 10 Hz, =C*H*-CHSO$_2$), 4.93 (2 H, m, 2 × C*H*=CMe$_2$), and 5.16 (1 H, d, *J* 10 Hz, CHSO$_2$) (Found: M^+, 428.238 13. $C_{26}H_{36}O_3S$ requires *M*, 428.238 50).

The Enol Phosphate (32).—A mixture (438 mg) of the sulphones (29) and (31), prepared as described above, was dissolved in tetrahydrofuran (4 cm^3) and added to a stirred solution of lithium di-isopropylamide (0.61 mmol) in tetrahydrofuran (3 cm^3) at −78 °C. After 0.5 h, diethyl phosphorochloridate (155 mg) in tetrahydrofuran (3 cm^3) was added, and after 10 min at −78 °C the stirred solution was allowed to warm to 20 °C. After 2.5 h it was diluted with ether, washed with water, dried and evaporated. P.l.c. of the residue (ethyl acetate–benzene, 1 : 4) gave the *enol phosphate* (32) as an oil (282 mg, 83% from methyl geranate), $\nu_{max.}$ (film) 1 030vs, 1 154s, 1 290s, 1 308s, 1 321s, 1 448, 1 611m, and 1 645w cm^{-1}, τ 4.28 (2 H, m, 2 × CH), 8.32br (9 H, s, 3 × CH_3), 8.41br (6 H, s, 2 × CH_3), 8.66 and 8.67 (each 3 H, t, *J* 8 Hz, OCH$_2$*Me*), and 8.73 (3 H, s, CH_3) (Found: M^+, 564.267 18. $C_{30}H_{45}O_6PS$ requires *M*, 564.267 43).

(6*E*,10*E*)-2,6,12,15-*Tetramethylhexadeca*-2,6,10,14-*tetraen*-8-*yne* (33).—Reduction of the enol phosphate (31) (1.11 g) with sodium amalgam (3.8 g) in tetrahydrofuran (12 cm^3) and dimethyl sulphoxide (7 cm^3) at 0 °C under nitrogen for 1.75 h, followed by normal work-up, and rapid chromatography on silica gel (ether–light petroleum) under nitrogen gave the conjugated *enynene* (33) as an oil (416 mg, 78.5%) together with the β-oxo-sulphone (31) (71 mg). The enynene had $\nu_{max.}$ (film) 830m, 1 104m, 1 212m, 1 345m, 1 380s, 1 445s, and 1 632w cm^{-1}, $\lambda_{max.}$ (hexane) 268 (ε 18 900), 276 (24 000), and 292 nm (20 200), τ 4.56 (2 H, s, 2 × =CH-C≡), 4.91br (2 H, m, 2 × *H*C=CMe$_2$), 7.77—7.92 (8 H, m, 4 × CH$_2$C=), 8.09 (6 H, s, 2 × CH_3C=CC≡), 8.32 (6 H, s, 2 × CH_3), and 8.40 (6 H, s, 2 × CH_3) (Found: M^+, 270.234 53. $C_{20}H_{30}$ requires *M*, 270.234 74); *m/e* 272 (20%), 203 (22), 147 (17), 121 (19), 119 (29), 109 (25), 105 (20), 93 (20), 91 (24), 81 (23), and 69 (100). G.l.c. (5 ft of 5% Carbowax at 179 °C; retention time 22 min) showed a purity of 95%.

(6*E*,8*Z*,10*E*)-2,6,12,16-*Tetramethylhexadeca*-2,6,8,10,14-*pentaene* (34).—The conjugated dienyne (33) (102 mg) was hydrogenated at room temperature and pressure in ethyl acetate (10 cm^3) with Lindlar catalyst (20 mg), poisoned with 2% quinoline in light petroleum (4 drops). Uptake ceased after 3 h; further catalyst (8 mg) was then added. When uptake again ceased after a further 1 h, more catalyst (8 mg) was added. After a total of 5 h the catalyst was removed, the filtrate was evaporated, and the residue was chromatographed on silica gel (10 g) with light petroleum. There were eluted first small amounts of a compound containing no conjugated unsaturation, and of a second compound containing a conjugated diene system. Further development eluted first the desired triene, and then unchanged (33); mixed fractions were resolved by p.l.c. (light petroleum), giving compound (33) (12 mg) and the conjugated triene (34) (71 mg 69% or, adjusted for recovered starting material, 78%). The compound (34) had $\nu_{max.}$ (film) 766s, 1 102w, 1 375s, 1 448s, 1 637m, and 3 030m cm^{-1}; there was no absorption at 966 cm^{-1} (a position, characteristic of the *E*,*E*,*E*-isomer); $\lambda_{max.}$ (hexane) 263infl. 276 (ε 30 100), 286 (35 900), and 297 nm (26 200); τ 4.87 (2 H, m, 2 × C*H*=CMe$_2$), 7.75—7.93 (8 H, m, 4 × CH$_2$C=), 8.22 (6 H, s, 2 × CH_3C=CC=), 8.30 (6 H, s, 2 × CH_3), and 8.37 (6 H, s, 2 × CH_3) (Found: M^+, 272.249 74. Calc. for $C_{20}H_{32}$: *M*, 272.250 39). G.l.c. (5 ft of 5% Carbowax at 172 °C) showed ≥95% *E*,*Z*,*E*-isomer and <5% *E*,*E*,*E*-isomer. The ^{13}C n.m.r. spectrum showed δ 16.51, 17.75, 25.74, 26.78, 40.50, 120.34, 123.47, 124.18, 131.66, and 139.46, in reasonable agreement with Pattenden's [19] data. Resonances at δ 40.24, 125.61, 127.37, and 138.03, characteristic of the *E*,*E*,*E*-isomer, were absent, as also were those at 24.33, 27.02, 32.34, 122.86, and 139.76, characteristic of the *Z*,*Z*,*E*-isomer.

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