Intramolecular Alkylation of Phenols. Part III.[1] Asymmetric Induction by a Chiral Leaving Group [2]

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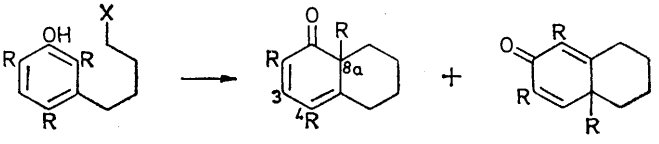
Intramolecular alkylation of 4-(3-hydroxy-2,4,6-trimethylphenyl)butyl (+)-camphor-10-sulphonate occurred under basic conditions. Both cyclic products were optically active. Optical purities were determined by n.m.r. and absolute configurations by c.d. The nature of the two transition states is compared and used to account for the observed effect. Asymmetric induction was also observed during the intermolecular alkylation of 2,4,6-trimethylphenol with allyl (+)-camphor-10-sulphonate under basic conditions.

RECENTLY we noted [3] that the phenol (1; R = H, X = *p*-Me·C_6H_4·SO_3) cyclised under basic conditions by an Ar_2^--6 mechanism. Since the leaving group is involved in the transition state, it occurred to us that asymmetric induction might be observed if a chiral leaving group were used in an appropriate system. The phenol [1; R = Me, X = (+)-camphor-10-sulphonyloxy] was chosen to test this hypothesis because the ring positions 2 and 4 exhibit planar prochirality [4] and the leaving group is both efficient and readily available in optically pure form.

Synthesis and Results.—The synthesis (see Scheme) of the phenol [1; R = Me; X = (+)-camphor-10-sulphonyloxy] requires comment. Aluminium chloride-catalysed introduction of a C_4 side chain [(4) ⟶ (5)] was not achieved with either α-butyrolactone or succinic anhydride, but use of the more reactive β-methoxycarbonylpropionyl chloride [5] was successful. The carbonyl

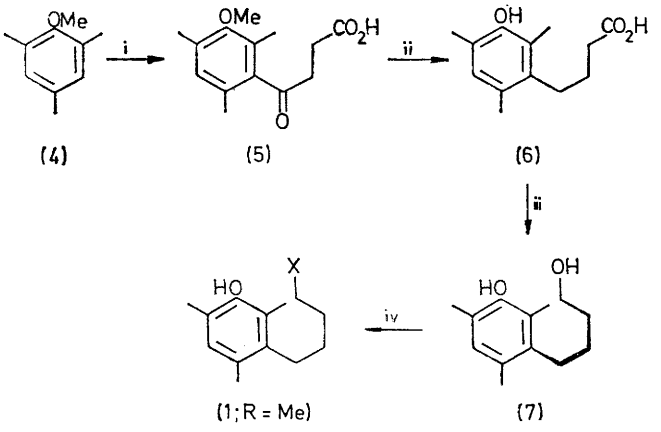


(1) (2) (3)

group of the acid (5) proved resistant to the Wolff–Kishner reaction but was readily reduced by the Clemmensen method.[6] Reduction of the acid (6) proceeded

[1] Part II, P. G. Duggan and W. S. Murphy, *J.C.S. Perkin II*, 1975, 1291.
[2] Preliminary communication, P. G. Duggan and W. S. Murphy, *J.C.S. Chem. Comm.*, 1974, 263.
[3] P. G. Duggan and W. S. Murphy, *J.C.S. Perkin II*, 1975, 1054.
[4] K. R. Hanson, *J. Amer. Chem. Soc.*, 1966, **88**, 2733.
[5] J. Carson, *Org. Synth.*, Coll. Vol. III, 1955, p. 169.
[6] E. L. Martin, *J. Amer. Chem. Soc.*, 1936, **58**, 1438.

smoothly with lithium aluminium hydride in pyridine.[7] In contrast with the synthesis of the phenol (1; R = H, X = p-MeC_6H_4·SO_3), which suffered predominant cyclisation (75%).[1] Very little asymmetric induction was observed in the cyclised products.



X = (+)-camphor-10-sulphonyloxy

SCHEME Reagents: i, $MeO_2C·CH_2·CH_2·COCl$–$AlCl_3$; NaOH–MeOH; ii, Zn–$HgCl_2$–HCl; HBr–HI–HOAc; iii, $LiAlH_4$–C_5H_5N; iv, (+)-camphor-10-sulphonyl chloride–C_5H_5N

Determination of Optical Purity.—The chiral shift reagent [8] tris-[3-(2,2,2-trifluoro-1-hydroxyethylidene)-(+)-camphorato]europium(III) [Eu(fdc)$_3$] was used successfully for the determination of the optical purities

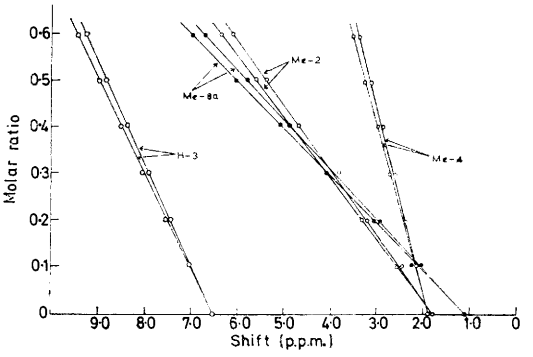


FIGURE 1 Eu(fdc)$_3$-induced shift and splitting response of n.m.r. signals of the decalone (2)

X = p-MeC_6H_4·SO_3),[3] the phenolic hydroxy-group in (7) did not require protection during the final acylation step [(7) ⟶ (1)].

The results (Table) of the reactions of the phenol [1; R = Me, X = (+)-camphor-10-sulphonyloxy] agree with our previous results.[1] Thus, the *ortho* : *para* ratio was dependent on the metal cation, the solvent polarity, and the reaction temperature. *ortho*-Alkylation was favoured by conditions conducive to ion pair or ion aggregate formation;[1] these conditions also lead to higher optical yields. No reaction was observed either when lithium hydride was the base used or when zinc chloride was added to the sodium salt of [1; R = Me, X = (+)-camphor-10-sulphonyloxy] in refluxing tetrahydrofuran. The optical yield (19% excess of one enantiomer) could probably be improved. In methanol, the behaviour of the sodium salt of [1; R = Me, X = (+)-camphor-10-sulphonyloxy], which underwent almost exclusive solvolysis (84%) contrasts with that of the substrate of compounds (2; R = Me) and (3; R = Me). Only the product (2; R = Me) will be considered in detail. Measured amounts of Eu(fdc)$_3$ were added to a solution in carbon tetrachloride of (2; R = Me), and the n.m.r. spectrum was recorded after each addition. Peak assignment was facilitated by plotting the induced shift ($\Delta\delta$) against the ratio of shift reagent to substrate. At low ratio values, this plot should be,[9] and is, linear (Figure 1). As expected, the pseudo-contact shifts ($\Delta\delta$) [10] were greatest for the protons closest to the metal,[11] which must reside near the oxygen atom.[12] Absorptions due to the α-methyl protons were clearly resolved into two sets of doublets at molar ratios above 0.4 (Figures 1 and 2). The shift difference $\Delta\Delta\delta$ for enantiomers was observed for all absorptions and was again dependent on the proximity to the metal. For each of these absorptions $\Delta\delta$ was greatest in all cases for protons of the major enantiomer. This is in agreement with the proposal [8a,b,13] that chiral splitting results from

Base-catalysed cyclisation of 4-(3-hydroxy-2,4,6-trimethylphenyl)butyl (+)-camphor-10-sulphonate [a]

Metal cation [b]	Solvent	Temp.	Yield[k] (%)	% Ratio [*ortho* (2) to *para* (3)] [c]	$[\alpha]_D^{15}$ (°) ($CHCl_3$)		
					Crude	*ortho* (2) [d]	*para* (3) [d]
Na	Bu^tOH	Reflux	85	80	+2.18	+4.55	−4.85
Na	$PhCH_3$	Reflux	51	83	+5.77		
Na	$[CH_2]_4O$	Reflux	90	82	+8.50	+6.00	−7.34
Na	Bu^tOH	35 °C	82	84	+3.89	+8.63	−8.93
Li [e]	Bu^tOH	Reflux	79	89	+13.36	+13.34[f]	−12.28 [g]
Na	C_6H_6 [h]	17 °C	12 [i]	91	+5.71		
Na	MeOH	Reflux	16 [j]	59		+1.97	

[a] Reactions at 1 × 10^{-2}M. [b] Metal phenoxide formed by addition of metal hydride. [c] By g.l.c. (SE30). [d] By preparative t.l.c. [e] No reaction at 17 °C. [f] Optical purity 19.0% (n.m.r.). [g] Optical purity 12.8% (n.m.r.). [h] Mixture stirred for 3 days. [i] Remainder mainly starting material. [j] Remainder mainly solvolysis product. [k] Claisen alkali-insoluble fraction.

[7] P. T. Lansbury and R. Thedford, *J. Org. Chem.*, 1962, **27**, 2383.

[8] G. M. Whitesides and D. W. Lewis, *J. Amer. Chem. Soc.*, (*a*) 1970, **92**, 6979; (*b*) 1971, **93**, 5914; (*c*) H. L. Goering, J. N. Eikenberry, and G. S. Koermer, *ibid.*, 1971, **93**, 5913.

[9] A. F. Cockerill and D. M. Rackhaun, *Tetrahedron Letters*, 1970, **59**, 5149.

[10] C. C. Hinchley, *J. Amer. Chem. Soc.*, 1969, **91**, 5160.

[11] D. R. Eaton and W. R. Phillips, *Adv. Magn. Resonance*, 1965, **1**, 103.

[12] B. C. Mayo, *Chem. Soc. Rev.*, 1973, **2**, 49.

[13] R. von Ammon and R. D. Fischer, *Angew. Chem. Internat. Edn.*, 1972, **11**, 675.

the differing formation constants of the diastereoisomeric complexes. Integration of these peaks for the sample with $[\alpha]_D$ +13.34° showed that there was a 19% excess

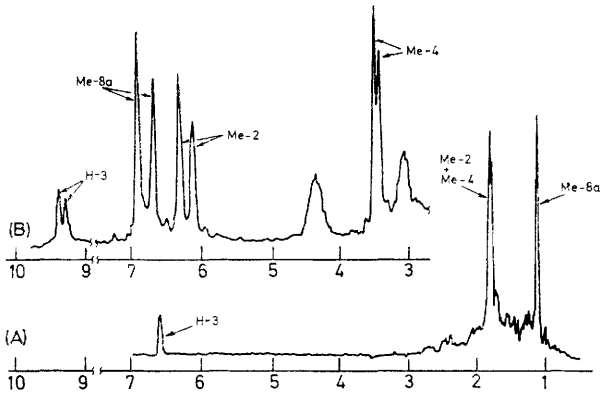


FIGURE 2 (A) N.m.r. spectrum of (+)-(2); (B) chiral splitting induced in the n.m.r. spectrum of (+)-(2) by $Eu(fdc)_3$ (0.6 equiv.)

of one enantiomer, which corresponds to $[\alpha]_D$ +70.28° for 100% optical purity.

In like manner, the optical purity of (3; R = Me) was determined. Again, both $\Delta\delta$ and $\Delta\Delta\delta$ were dependent on the distance factor r_i.[11] The methyl group protons at positions 1 and 3 were equivalent, and only enantiomeric splitting was observed. With a molar ratio of $Eu(fdc)_3$ to (3; R = Me) of 0.9 : 1 a value of 0.23 p.p.m. for $\Delta\Delta\delta$ was observed for Me-1 and -3, 0.03 p.p.m. for Me-4a, and, surprisingly, no splitting for the vinylic proton, H-4. Integration of the spectrum of a sample with $[\alpha]_D$ −12.28° showed a 12.8% excess of one enantiomer. This corresponds to $[\alpha]_D$ −95.92° for 100% optical purity.

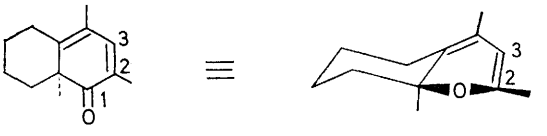
To remove any ambiguity concerning the possibility of simple shift differentiation of Me-1 and -3 in (3; R = Me), the effect of the non-chiral shift reagent tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato)europium(III) [$Eu(fod)_3$] on the spectrum of (3; R = Me) was studied. No differentiation of Me-1 and -3 was observed; neither was the Me-4a signal split. $Eu(fod)_3$ was the superior shift reagent.

Determination of Absolute Configuration.—Absolute configurations were determined by c.d. The alkylation product (2; R = Me) had $\Delta\varepsilon_{max.}$ † (methanol) +3.75 (368 nm, $n \longrightarrow \pi^*$), −1.40 (334 nm), and −4.33 (317 nm, $\pi \longrightarrow \pi^*$). A Dreiding model of (2; R = Me) shows that the dienone system is non-planar, with a C=C–C=O torsion angle of *ca.* 29° (Figure 3). It has been proposed[14] that αβ-enones with helicity in this sense exhibit negative c.d. in the $\pi \longrightarrow \pi^*$ region and positive c.d. in the $n \longrightarrow \pi^*$ region. Accordingly, we assigned the *S*-configuration to the predominant (dextrorotatory) enantiomer of (2). However, Djerassi has pointed out[15] that the Cotton effect of αβ-unsaturated systems is sensitive to subtle intramolecular interactions. Our assignment must remain tentative.

Cross-conjugated dienones are inherently symmetric in the immediate region of the carbonyl group and, accordingly, the normal octant rule is found[16] to apply to these systems in the $n \longrightarrow \pi^*$ region. The laevorotatory dienone (3; R = Me) had c.d. $\Delta\varepsilon_{max.}$ † (methanol) −0.91 (320 nm, $n \longrightarrow \pi^*$), −0.78 (288 nm), and −4.31 (268 nm). Accordingly, by applying the octant rule, the predominant laevorotatory enantiomer of (3; R = Me) is also assigned the *S*-configuration (Figure 4).

Relationship between the Absolute Configurations of the Substrate and the Products.—The ring positions involved in the reaction are prochiral and so intramolecular attack from above and below the phenoxide ring will lead to a racemic product mixture. When the leaving group is chiral, as in [1; R = Me, X = (+)-camphor-10-sulphonyloxy] the transition states will be diastereoisomeric. As these transition states will now involve different activation energies, one enantiomer will be formed preferentially and in proportion to this energy difference.

To explain the observed asymmetric induction, drawings, based on molecular models, for the transition states



(*S*) - (2)

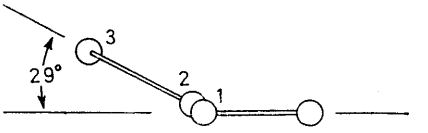
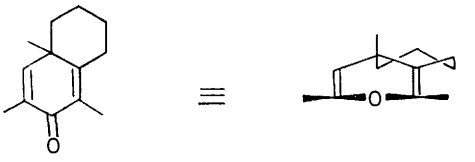


FIGURE 3



(*S*) - (3)

FIGURE 4

leading to (*R*)-(2) and (*S*)-(2) are shown (Figure 5). In constructing these models, we assumed that the sodium ion became co-ordinated to the carbonyl group of the (+)-camphor unit, the phenoxide oxygen atom, and an oxygen attached to sulphur. The normal sp^2 hybridisation of C-α of the side chain, that is the carbon atom undergoing nucleophilic attack, was also assumed.

In the transition state leading to (*S*)-(2) the methyl protons on C-8′ and C-9′ [in the (+)-camphor unit] are

† Corrected to 100% optical purity.

[14] G. Snatzke, *Tetrahedron*, 1965, **21**, 413, 439.

[15] C. Djerassi and J. E. Gurst, *J. Amer. Chem. Soc.*, 1964, **86**, 1755.

[16] G. Snatzke in 'Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry,' ed. G. Snatzke, Heydon, London, 1967, p. 208; C. Djerassi, R. Rimiker, and B. Rimiker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362; L. Velluz and M. Legrand, *Angew. Chem.*, 1961, **73**, 603.

oriented away from the site of reaction and are unlikely to interfere. Steric interaction occurs mainly through the *endo*-hydrogen atom on C-6′ with both the sulphonate and the α-methyl group (Me-6) of the phenoxide ring.

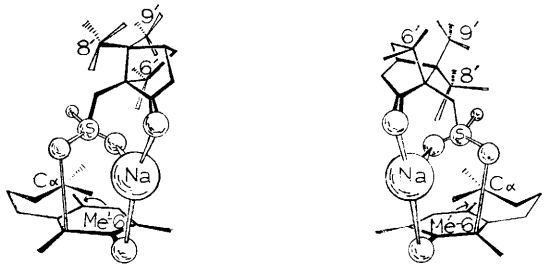


FIGURE 5 (A) (*S*)-(2) Transition state; (B), (*R*)-(2) transition state

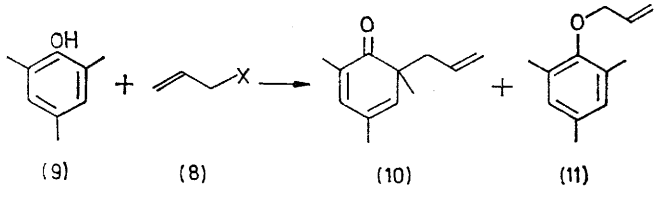
In the (*R*)-(2) transition state, the camphor group is inverted relative to the other transition state. Because of this, the methyl protons on C-8′ and C-9′ are oriented towards the reaction centre, so that one of these methyl groups gives rise to strong steric interactions with the sulphonate group and Me-6 of the phenoxide ring. There is also restricted rotation around the 7′,8′-bond.

For these reasons, the transition state of the *S*(*S*)-(2) isomer should be of lower energy and the (*S*)-isomer the predominant enantiomer.

Similar arguments can be used to explain the faster formation of (*S*)-(3; R = Me) during *para*-alkylation. However, co-ordination of the sulphonate group with the sodium ion is less important than in the *ortho*-alkylation, owing to the greater distance between these species. For this reason steric interactions will be smaller and asymmetric induction less efficient.

The predominant enantiomer from both *ortho*- and *para*-alkylation reactions has the *S*-configuration. This means that attack on the *ortho*- and *para*-positions occurs predominantly on one face of the phenoxide ring.

Intermolecular Asymmetric Induction.—The reaction was extended to an intermolecular example. Allyl



X = (+)-camphor-10-sulphonyloxy

(+)-camphor-10-sulphonate (8) was treated with the sodium salt of 2,4,6-trimethylphenol (9) under the conditions reported by Curtin and Crawford.[17] After 54 h at 15 °C in dry benzene the expected products, 6-allyl-2,4,6-trimethylcyclohexa-2,4-dienone (10) (22%) and allyl 2,4,6-trimethylphenyl ether (11) (49%) were obtained. The dienone (10) was optically active, $[\alpha]_D$ −7.26°. Optical purity was determined by addition of $Eu(fdc)_3$. The Me-4 and-6 singlets at τ 8.1 and 8.2, respectively, were each split into two singlets. Integration showed an 8.4% excess of one enantiomer. Interestingly the dienone (10) showed no c.d. However, compound (10) can undergo ring inversion readily (Figure 6). The chirality of the dienone system, on which the magnitude of Δε is largely dependent,[18] is 'enantiomerically' related in (10a) to the dienone system of (10b). Thus if these conformations are of equal importance no contribution to the c.d. can be expected from the dienone system. While it is expected that conformation (10a) will be favoured, the magnitude of the c.d. exhibited by (10b) would probably be larger owing to the relative sizes of the allyl and methyl substituents. Thus a small or even zero c.d. is not surprising. The configuration of (10), however, remains to be determined.

Optical Purity of the Leaving Group.—(+)-Camphor-10-sulphonic acid, $[\alpha]_D$ +26.7° (*c* 3.0 in AcOH), was used in the synthesis of the sulphonate esters [1; R = Me,

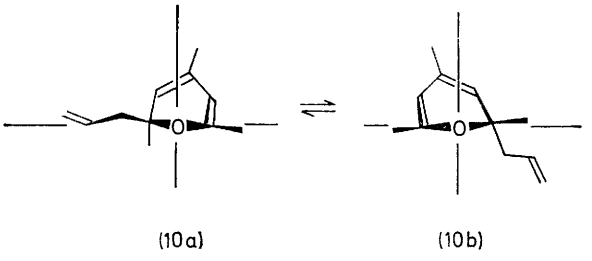


FIGURE 6

X = (+)-camphor-10-sulphonyloxy] and (8). The rotation corresponds to 81.4% optical purity.[19] This low rotation could be due to chemical or optical impurities. Repeated recrystallisation lowered $[\alpha]_D$ to +24.3°, which suggested that the impurity was optical. In search of more positive evidence, $Eu(fdc)_3$ was added to (+)-camphor-10-sulphonyl chloride. Although pseudo-contact shifts were observed, enantiomeric splitting was not. However, no traces of chemical impurities were detected.

EXPERIMENTAL

General procedures were as detailed previously.[3] Optical rotations were measured for solutions in chloroform with a Perkin-Elmer 141 polarimeter at 15 °C, unless stated otherwise.

Synthesis of 4-(3-*Hydroxy*-2,4,6-*trimethylphenyl*)*butyl* (+)-*Camphor*-10-*sulphonate* [1; R = Me, X = (+)-*camphor*-10-*sulphonyloxy*].— β-(3-*Methoxy*-2,4,6-*trimethylbenzoyl*)*propionic acid* (5). 2,4,6-Trimethylanisole (57 g, 0.38 mol) and β-methoxycarbonylpropionyl chloride [5] (87 g, 0.58 mol) were dissolved in benzene (200 ml) and maintained at 0—6.5 °C while aluminium chloride (102 g, 0.78 mol) was added slowly with stirring. After stirring for 16 h the mixture was decomposed with ice and dilute hydrochloric acid and extracted with ether. The oil isolated was immediately saponified by refluxing for 3 h with sodium hydroxide (56 g, 1.4 mol) in methanol (600 ml). A yellow solid (74.4 g) was

[17] D. Y. Curtin and R. J. Crawford, *J. Amer. Chem. Soc.*, 1957, **79**, 3156.

[18] G. Snatzke in ' Fundamental Aspects and Recent Developments in ORD and CD,' Heydon, London, 1973, p. 118.

[19] ' Handbook of Chemistry and Physics,' The Chemical Rubber Co., Cleveland, Ohio 44128, 51st edn., 1970, p. C-230.

isolated which was recrystallised from methylene chloride–hexane to give the *acid* (5) (65 g, 73%), m.p. 79—81° (Found: C, 66.95; H, 7.4. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.25%); $\nu_{max.}$ 1 700br cm^{-1}; τ 3.13 (s, ArH), 6.3 (s, CH_3O), 6.7—7.4 (m, $CH_2{\cdot}CH_2$), 7.74 (s, $ArCH_3$), and 7.84 (s, 2 × $ArCH_3$).

4-(3-*Hydroxy*-2,4,6-*trimethylphenyl*)*butanoic acid* (6). Clemmensen reduction [6] of the acid (5) (63 g) afforded a dark red oil (64 g). This was demethylated immediately in acetic acid with hydrobromic and hydriodic acids.[20] The resulting red oily solid (59 g) was recrystallised (charcoal) from methylene chloride–hexane to afford the *acid* (6) (30.8 g, 55%) as a white solid, m.p. 130—131° (Found: C, 69.9; H, 8.5. $C_{13}H_{18}O_3$ requires C, 70.25; H, 8.15%); $\nu_{max.}$ 1 700 cm^{-1}; τ 3.23 (s, ArH), 7.0—8.5 (m, $CH_2{\cdot}CH_2{\cdot}CH_2$), and 7.8 (s, 3 × $ArCH_3$).

4-(3-*Hydroxy*-2,4,6-*trimethylphenyl*)*butan*-1-*ol* (7). To a solution of lithium aluminium hydride (6 g, 0.16 mol) in dry pyridine (150 ml) at 0 °C was added a solution of the acid (6) (17.5 g, 0.08 mol) in dry pyridine (100 ml).[7] After stirring at room temperature for 2 days the mixture was decomposed by adding to dilute hydrochloric acid (3 l) at 0 °C. The product isolated was the *alcohol* (7) (15.7 g, 96%), m.p. 89—91° (Found: C, 75.0; H, 9.9. $C_{13}H_{20}O_2$ requires C, 74.95; H, 9.7%); $\nu_{max.}$ 3 360 cm^{-1}; τ 3.23 (s, ArH), 6.44 (t, *J* 8.0 Hz, $CH_2{\cdot}O$), 7.27 (t, *J* 8.0 Hz, $ArCH_2$), 7.77 (s, 3 × $ArCH_3$), and 7.9—8.5 (m, $CH_2{\cdot}CH_2$).

The (+)-*camphor*-10-*sulphonate*. The alcohol (7) (5 g, 28 mmol) was dissolved in dry pyridine (30 ml) and cooled to 0 °C. (+)-Camphor-10-sulphonyl chloride [21] (8.7 g, 36 mmol) was added rapidly and the mixture was kept in a sealed flask for 48 h at 0 °C. A yellow oil (10.67 g) was isolated and purified by recrystallisation from ether–hexane at −78 °C and dry column chromatography (3 : 2 ether–light petroleum) to afford the (+)-*camphor*-10-*sulphonate* (6.4 g, 63%) as a glass (at room temperature) (Found: C, 65.55; H, 8.55; S, 7.3. $C_{23}H_{34}SO_5$ requires C, 65.35; H, 8.1; S, 7.6%); $\nu_{max.}$ 3 515, 1 742, 1 350, and 1 161 cm^{-1}; τ 3.22 (s, ArH), 5.68 (t, *J* 6.0 Hz, $CH_2{\cdot}OS$), 6.70 (dd, J_{gem} 15 Hz, $CH_2{\cdot}S$), 7.80 (s, 3 × $ArCH_3$), 8.88 (s, CH_3), and 9.13 (s, CH_3); $[\alpha]_D$ +25.62°.

Reactions of the Camphor-10-*sulphonate* [1; R = Me, X = (+)-*camphor*-10-*sulphonyloxy*].—Reactions were carried out in a number of solvents and the results are summarised in the Table. The method was essentially unchanged throughout the study and is exemplified by the reaction in t-butyl alcohol.

The camphor-10-sulphonate (422 mg, 1 mmol) was dissolved in dry t-butyl alcohol (100 ml) under nitrogen and heated to reflux. To the solution was added sodium hydride (34 mg, 1.4 mmol). The solution was heated under reflux in nitrogen for 12 h and the solvent was removed under vacuum. The residue was dissolved in ether (50 ml) and 5% sulphuric acid (20 ml). The organic layer was washed with 3 portions of Claisen alkali [22] (20 ml) and water, dried (Na_2SO_4), and evaporated to afford a yellow liquid (162 mg), $[\alpha]_D$ +2.18°, shown by g.l.c. and t.l.c. to consist of two compounds (A and B) in the ratio 4 : 1, which were separated by preparative t.l.c. Compound A, a yellow liquid, was 6,7,8,8a-*tetrahydro*-2,3,8a-*trimethylnaphthalen*-1(5H)-*one* (2; R = Me) (79 mg) (Found: C, 82.0; H, 9.15. $C_{13}H_{18}O$ requires C, 82.05; H, 9.55%); $\nu_{max.}$ 1 659, 1 638, and 1 584 cm^{-1}; $\lambda_{max.}$ 335 nm (ε 5 400); τ 3.39 (s, ArH), 8.18 (s) and 8.2 (s, Me-2 and -4), 8.86 (s, Me-8a), and 7.0—9.0 (m, 4 × CH_2); $[\alpha]_D$ +4.55°.

Compound B, a colourless liquid, was 5,6,7,8-*tetrahydro*-1,3,4a-*trimethylnaphthalen*-2(4aH)-*one* (3; R = Me) (20 mg) (Found: C, 81.95; H, 9.45. $C_{13}H_{18}O$ requires C, 82.05; H, 9.55%); $\nu_{max.}$ 1 730, 1 665, and 1 625 cm^{-1}; $\lambda_{max.}$ 249 nm (ε 11 613); τ 3.65 (s, ArH), 8.18 (s, 2 × CH_3), 8.82 (s, Me-4a), and 7.0—9.2 (m, 4 × CH_2); $[\alpha]_D$ −4.85°.

When this reaction was undertaken in methanol, t.l.c. and g.l.c. indicated that the liquid product consisted of three components: the dienones (2; R = Me) (9.5%) and (3; R = Me) (6.5%), and another compound (84%), detected by g.l.c. only when the sample was first silylated. A sample (180 mg) separated by preparative t.l.c. afforded the dienones (2; R = Me) (15.2 mg), $[\alpha]_D$ +1.97°, and (3; R = Me) (10.3 mg) (no observable rotation), and 4-(3-*hydroxy*-2,4,6-*trimethylphenyl*)*butyl methyl ether* (98 mg), a colourless oil (Found: C, 75.3; H, 9.5. $C_{14}H_{22}O_2$ requires C, 75.8; H, 9.9%); $\nu_{max.}$ 3 410 cm^{-1}; τ 3.35 (s, ArH), 6.77 (s, OCH_3), 7.9 (s, 3 × CH_3), and 7.2—9.0 (m, 4 × CH_2).

Alkylation of 2,4,6-*Trimethylphenol* (9).—*Allyl* (+)-*camphor*-10-*sulphonate* (8). Redistilled allyl alcohol (3 g, 0.05 mol) was dissolved in dry benzene (500 ml) with (+)-camphor-10-sulphonyl chloride (10 g, 0.04 mol), and sodium hydroxide (2.8 g, 0.07 mol) was added.[23] The heterogeneous mixture was refluxed under a Dean–Stark head. After 48 h allyl alcohol (1 g) was added and refluxing was continued for 24 h. A yellow oil was isolated which was distilled (b.p. 148° at 0.15 mmHg) to afford *allyl* (+)-*camphor*-10-*sulphonate* (8) (3.8 g, 34.8%) (Found: C, 57.3; H, 7.4; S, 10.8. $C_{13}H_{20}SO_4$ requires C, 57.35; H, 7.4; S, 11.75%); $\nu_{max.}$ 1 745 (C=O), 1 355 (S=O), and 1 165 cm^{-1} (S=O); τ 3.7—5.3 (m, $CH{=}CH_2$), 6.7 (dd, *J* 16 Hz, $CH_2{\cdot}S$), 8.88 (s, CH_3), and 9.12 (s, CH_3).

Reaction of 2,4,6-*trimethylphenol with allyl* (+)-*camphor*-10-*sulphonate*. 2,4,6-Trimethylphenol (0.86 g, 6.3 mmol) was dissolved in dry benzene (20 ml) and sodium hydride (0.185 g, 7.7 mmol) was added with stirring under nitrogen. Allyl (+)-camphor-10-sulphonate (8) (2.12 g, 7.65 mmol) was added and the mixture was stirred at room temperature for 4 days, after which t.l.c. showed that the phenol had completely reacted. The mixture was diluted with dry ether and filtered. The filtrate was washed with Claisen alkali and water, dried (Na_2SO_4), and evaporated to give a yellow liquid (1.26 g), $[\alpha]_D$ +5.58°. A sample (253 mg) separated by preparative t.l.c. (ether–light petroleum, 1 : 9) yielded 6-allyl-2,4,6-trimethylcyclohexa-2,4-dienone [24] (10) (52.4 g, 21.7%); $\nu_{max.}$ 1 668sh and 1 652 cm^{-1}; $\lambda_{max.}$ 321 nm (ε 3 955); τ 3.42 (s, 2 × ring H), 4.1—5.3 (m, $CH{=}CH_2$), 8.12 (s, CH_3), 8.19 (s, CH_3), and 8.92 (s, CH_3); $[\alpha]_D^{25}$ −7.26°. Preparative t.l.c. also yielded allyl 2,4,6-trimethylphenyl ether [24] (11) (118.2 mg, 46.5%), $\nu_{max.}$ 1 650, 1 220, 1 150, 927, and 856 cm^{-1}.

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