

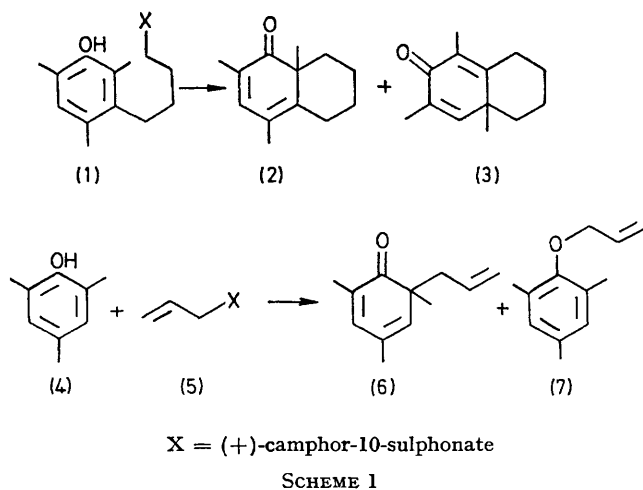
Displacement Reactions: Asymmetric Induction by a Chiral Leaving Group

By PATRICK G. DUGGAN and WILLIAM S. MURPHY*

(Chemistry Department, University College, Cork, Ireland)

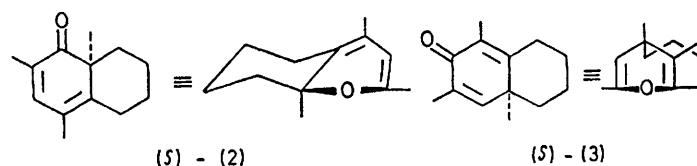
Summary The chiral (+)-camphor-10-sulphonate leaving group effected asymmetric induction in the products of the intra- and inter-molecular alkylation of 2,4,6-trimethylphenoxide; optical purity was readily determined by n.m.r. spectroscopy.

THERE has recently been considerable interest in asymmetric induction.¹ We report a new example. Further to our investigations² of the Ar_2^6 mechanism, we have now tested the effect of a chiral leaving group. The phenol† (1) (Scheme 1) was chosen as a model for the base-induced cyclisation because (a) C-2 and C-4 exhibit planar prochirality³ and (b) the leaving group is both efficient and readily available in optically pure form.‡ The results summarised



in the Table emphasise that not only the *ortho-para* ratio, but also the optical purity of the product, is dependent on both the metal cation and solvent polarity. The highest optical yield (19% excess of one enantiomer) has probably

not been optimised. The dienone (2)† (λ_{\max} 335, ϵ 5400) had c.d. (MeOH) $\Delta\epsilon_{\text{§}}$ +3.75 (368 nm, $n \rightarrow \pi^*$), -1.40 (334 nm), and -4.33 (317 nm, $\pi \rightarrow \pi^*$). The (*S*)-configuration is, thereby, tentatively assigned to (+)-(2), since the helicity of the dienone chromophore in (*S*)-(2) (Scheme 2) is the same as that of the corresponding chromophore in $\alpha\beta$ -enones, which exhibit a positive c.d. in the $n \rightarrow \pi^*$ region and a negative c.d. in the $\pi \rightarrow \pi^*$ region.⁴ This system has added interest in that the $\pi \rightarrow \pi^*$ region is



SCHEME 2

readily accessible. The ketone (3)† (λ_{\max} 249, ϵ 11,613) had c.d. (MeOH) $\Delta\epsilon_{\text{§}}$ -0.91 (320 nm, $n \rightarrow \pi^*$), -0.78 (288 nm), and -4.31 (268 nm). The (*S*)-configuration is, thereby, assigned to (-)-(3) (Scheme 2) by analogy with closely related systems.⁵ The relationship of the absolute configurations of (+)-(2) and (-)-(3) to each other and to the leaving group will be discussed elsewhere.

The optical purity of (2) was determined by integration of the 60 MHz n.m.r. spectrum after the addition of a 0.6 molar ratio of tris-[3-(trifluoro-methylhydroxymethylene)-(+)-camphorato]europium(III).⁶ Among other signals, the singlet at τ 3.4 corresponding to the vinylic proton was shifted downfield and split into two singlets at τ 0.62 and 0.72; their ratio was used as a direct measure of optical purity. The optical purity of (3) was determined similarly.

We found that asymmetric induction also occurs in the analogous intermolecular reaction. Thus, (4) reacted with (5)† in benzene at 15° after 54 h with the formation of the

TABLE. The base-catalysed cyclisation of (1)^a

Metal cation ^b	Solvent	Temp.	Proportion of <i>ortho</i> -(2) ^c (%)	[α] _D ¹⁵ (CHCl ₃)		
				Crude	<i>ortho</i> -(2) ^d	<i>para</i> -(3) ^d
Na	Bu ^t OH	Reflux	80	+2.18°	+4.55°	-4.85°
Na	PhMe	"	83	+5.77°		
Na	THF	"	82	+8.50°	+6.00°	-7.34°
Na	Bu ^t OH	35 °C	84	+3.89°		
Li ^e	Bu ^t OH	Reflux	89	+13.36°	+13.34° ^f	-12.28° ^g

^a Reactions investigated at 1×10^{-2} M. ^b Metal phenoxide formed by addition of metal hydride. ^c By g.l.c. (SE 30). ^d By p.t.l.c. ^e Li metal used: reaction of LiH with Bu^tOH is extremely slow. ^f Optical purity is 19.0% (n.m.r.), corresponding to [α]_D¹⁵ +70.28° for 100% optical purity. ^g Optical purity is 12.8% (n.m.r.), corresponding to [α]_D¹⁵ -95.93° for 100% optical purity.

† This compound had satisfactory elemental analysis and spectral data.

‡ (+)-Camphor-10-sulphonic acid [α]_D²⁰ +26.7° (EtOAc, $c = 3$) was used.

§ Corrected to 100% optical purity.

expected products? (Scheme 1). The dienone (6) isolated (22% yield) by preparative t.l.c. had $[\alpha]_D^{25} -7.26^\circ$. The optical purity (8.4%) was determined by n.m.r. spectroscopy as for (2) and (3). Interestingly, dienone (6) had no observable c.d.

One of us (P.G.D.) thanks the Irish Government for a State Maintenance Grant. We are very grateful to Dr. P. M. Scopes (Westfield College) for the c.d. spectra.

(Received, 21st January 1974; Com. 081.)

¹ M. F. Grundon, D. Stewart, and W. E. Watts, *J.C.S. Chem. Comm.*, 1973, 573; Y. Yamamoto, J. Ada, and Y. Inouye, *ibid.*, p. 848; C. R. Johnson and C. W. Schroeck, *J. Amer. Chem. Soc.*, 1973, **95**, 7418, 7424; N. T. Anh, O. Eisenstein, J.-M. Lefour, and M.-E. T. H. Dau, *ibid.*, p. 6146; B. Trost and W. G. Biddlecom, *J. Org. Chem.*, 1973, **38**, 3538.

² P. G. Duggan and W. S. Murphy, *J.C.S. Chem. Comm.*, 1972, 770.

³ K. R. Hanson, *J. Amer. Chem. Soc.*, 1966, **88**, 2733.

⁴ (a) G. Snatzke in 'Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry', ed. G. Snatzke, Heyden, London 1967, p. 208; (b) G. Snatzke, *Angew. Chem. Internat. Edn.*, 1968, **7**, 18.

⁵ Cf. ref. 4a, p. 219; L. Velluz and M. Legrand, *Angew. Chem.*, 1961, **73**, 603; C. Djerassi, R. Riniker, and B. Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362.

⁶ H. L. Goering, J. N. Eikenberry, and G. S. Koermer, *J. Amer. Chem. Soc.*, 1971, **93**, 5913.

⁷ D. Y. Curtin and R. J. Crawford, *J. Amer. Chem. Soc.*, 1957, **79**, 3156.