Effects of Remote Unsaturated Bonds on Nucleophilic Aromatic Substitution in Polyfluoroaromatic Compounds. Profound Effect of a Remote Carbonyl Group

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Approximate values of the second-order rate constants for fluorine replacement by isopropoxide ion in a series of unsaturated and related saturated 5,6,7,8-tetrafluoro-1,4-bridged naphthalenes have been determined. For 5,6,7,8-tetrafluoro-1,4-dihydro-3,3-dimethyl-1,4-methanonaphthalen-2(3*H*)-one, the rate constant (extrapolated to 25 °C) is greater than that for 5,6,7,8-tetrafluoro-1,2,3,4-tetrahydro-*endo*-2-methoxy-3,3-dimethyl-1,4-methanonaphthalene by a factor of 100 with similar rates of reactions at C-6 and -7, rationalised in terms of the field effect of the carbonyl group and the exclusion of regiospecific homoconjugation in the transition state for reaction at C-6. All other systems examined reacted with similar rate constants, irrespective of remote unsaturated or saturated bonds.

SOLVOLYSIS reactions of 1,4-dihydro-1,4-methanonaphthyl compounds have been used extensively to study the effect of the aromatic π-system on developing cationic centres at the 2- and 9-positions, and there is now considerable evidence from kinetic investigations for homobenzylic participation in certain cases in both systems.[1,2] In superacid media, a series of secondary 1,4-dihydro-1,4-methano-2-naphthyl precursors (even from *exo*-2,*anti*-9-dihalogeno-derivatives) form long-lived tetracyclic cations.[3] Recently, the effects of a remote double bond and of a cyclopropane ring on electrophilic aromatic substitution reactions have been reported,[4] illustrating the continued interest in the positively charged entities.

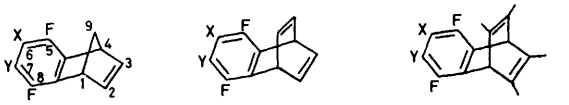
In contrast, the possible stabilisation of carbanions by homoconjugative interactions has a much smaller

[1] H. C. Brown and K.-T. Liu, *J. Amer. Chem. Soc.*, 1969, **91**, 5909.
[2] H. Tanida and H. Ishitobi, *J. Amer. Chem. Soc.*, 1966, **88**, 3663.
[3] G. A. Olah and G. Liang, *J. Amer. Chem. Soc.*, 1975, **97**, 2236.
[4] M. W. Galley and R. C. Hahn, *J. Org. Chem.*, 1976, **41**, 2006.

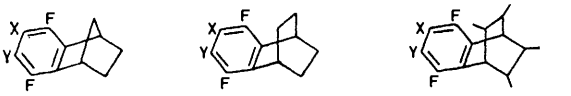
literature. Notable examples, however, include (i) the bicyclo[3.2.1]octa-2,6-dienide ion, a 6 π-electron bishomocyclopentadienide ion which has been proposed as the intermediate in some base-catalysed deuterium-exchange reactions;[5] and (ii) the formation of homoenolate ions.[6] Nickon has recently shown that homoenolates are formed from camphor and t-butoxide in t-butyl alcohol at 185—250 °C by proton abstraction at C-6, -8, and -10.[7]

Our work is concerned with the effect of remote unsaturated bonds upon nucleophilic aromatic substitution reactions. In a previous paper we reported the second-order rate constants for the reaction of potassium isopropoxide in propan-2-ol with 9-alkenyl-5,6,7,8-tetrafluoro-1,4-dihydro-1,4-methanonaphthalenes and compared these with the rate constants for related saturated 9-alkyl derivatives.[8] A factor of 6—7 separated the values for the most reactive [the 9-(4-trifluoromethyl)benzylidene derivatives] from those of the least reactive compounds [the *syn*-9-isopropyl derivatives] in both the tetrafluoro- and the difluoro-series, and it was concluded that homoallylic conjugation in the alkenyl compounds was not the reason for these small reactivity differences. We now report data for the nucleophilic replacement of a fluoro-substituent by isopropoxide ion in 5,6,7,8-tetrafluoro-1,4-dihydro-1,4-methanonaphthalene (1), 5,6,7,8-tetrafluoro-1,4-dihydro-1,4-ethenonaphthalene (2), 5,6,7,8-tetrafluoro-1,4-dihydro-2,3,9,10-tetramethyl-1,4-ethenonaphthalene (3), 5,6,7,8-tetrafluoro-1,4-dihydro-3,3-dimethyl-1,4-methanonaphthalen-2(3*H*)-one (4), 2-benzylidene-5,6,7,8-tetrafluoro-1,4-dihydro-3,3-dimethyl-1,4-methanonaphthalene (5), and some of their saturated derivatives. The conclusion to be drawn from Olah's work, that overlap of the 6 π-electron system of the aromatic ring with a *p* orbital at C-2 has a more favourable geometry than the corresponding overlap at C-9,[3] emphasises the relevance of the present study.

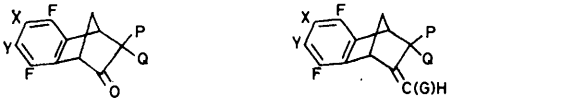
Syntheses.— 5,6,7,8-Tetrafluoro-1,4-dihydro-1,4-methanonaphthalene (1) was prepared by generation of tetrafluorobenzyne (from pentafluorophenyl-lithium, made from C_6F_5Br and Bu^nLi) in the presence of cyclopentadiene in ether; this synthesis is more convenient than that described previously.[9] Compounds (2) and (3), prepared as before,[9] and (1) were hydrogenated to give the 2,3-dihydro-derivatives (7), (8), and (6), respectively. Hydroboration–oxidation of compound (1) gave the *exo*- (9), and *endo*- (10) alcohols in the ratio 86 : 14, respectively, which could be separated. Oppenauer oxidation of the mixture of alcohols gave the ketone (11), reduction of which with borane–tetrahydrofuran gave a mixture of the *exo*- and *endo*-alcohols (9) and (10) in the ratio 15 : 85, respectively. The stereochemistry of the two alcohols was determined by observing the chemical shift changes to lower field in the ^1H n.m.r. spectra on addition of increasing amounts of tris-(1,1,1,2,2,3,3-heptafluoro-7,7-di[$^2H_3$]methyl[8-$^2H_3$]octane-4,6-dionato)europium(III) {Eu([$^2H_9$]fod)$_3$}. For a bicyclo[2.2.1]hept-5-en-*exo*-2-ol system, one proton in each of the two AB systems at C-3 and C-7 (the *exo*-H at C-3 and the *anti*-H at C-7) is expected to exhibit a much greater shift than the other; indeed two such protons in AB systems at C-3 and C-9 were found in the alcohol (9), the magnitudes of the H-3



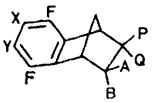
(1) X = Y = F
(37) X = OPr^i, Y = F
(2) X = Y = F
(39) X = OPr^i, Y = F
(3) X = Y = F
(41) X = OPr^i, Y = F



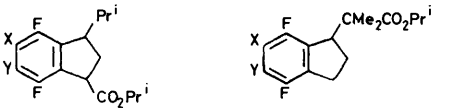
(6) X = Y = F
(38) X = OPr^i, Y = F
(7) X = Y = F
(40) X = OPr^i, Y = F
(8) X = Y = F
(42) X = OPr^i, Y = F



(4) P = Q = Me, X = Y = F
(11) P = Q = H, X = Y = F
(23) P = Q = Me, X = Pr^{i}O, Y = F
(24) P = Q = Me, X = F; Y = Pr^{i}O
(5) G = Ph, P = Q = Me, X = Y = F
(16) *E* - form; G = $C_6H_4NO_2$-4, P = Q = H
(17) *Z* - form; G = $C_6H_4NO_2$-4, P = Q = H
(35) G = Ph, P = Q = Me, X = Pr^{i}O, Y = F
(36) G = Ph, P = Q = Me, X = F, Y = Pr^{i}O



(9) A = OH, B = P = Q = H, X = Y = F
(10) A = H, B = OH, P = Q = H, X = Y = F
(12) A = CH_2Ph, B = OH, P = Q = H, X = Y = F
(13) A = CH_2Ph, B = OAc, P = Q = H, X = Y = F
(14) A = $CH_2C_6H_4NO_2$-4, B = OAc, P = Q = H, X = Y = F
(15) A = $CH_2C_6H_4NO_2$-2, B = OAc, P = Q = H, X = Y = F
(18) A = H, B = OH, P = Q = Me, X = Y = F
(19) A = H, B = OMe, P = Q = Me, X = Y = F
(20) A = H, B = OMe, P = Q = Me, X = Bu^n, X = F
(21) A = H, B = OMe, P = Q = Me, X = F, Y = Bu^n
(22) A = CH_2Ph, B = OH, P = Q = Me, X = Y = F
(31) A = H, B = OH, P = Q = Me, X = Pr^{i}O, Y = F
(32) A = H, B = OH, P = Q = Me, X = F, Y = Pr^{i}O
(33) A = H, B = OMe, P = Q = Me, X = F, Y = Pr^{i}O
(34) A = H, B = OMe, P = Q = Me, X = Pr^{i}O, Y = F
(43) A = CH_2Ph, B = OH, P = Q = Me, X = Pr^{i}O, Y = F



(25) X = Y = F
(27) X = Pr^{i}O, Y = F
(29) X = F, Y = Pr^{i}O
(26) X = Y = F
(28) X = Pr^{i}O, Y = F
(30) X = F, Y = Pr^{i}O

[5] J. M. Brown and J. L. Occolowitz, *Chem. Comm.*, 1965, 376.
[6] D. H. Hunter, A. L. Johnson, J. B. Stothers, A. Nickon, J. L. Lambert, and D. F. Covey, *J. Amer. Chem. Soc.*, 1972, **94**, 8582.
[7] A. Nickon, J. L. Lambert, J. E. Oliver, D. F. Covey, and J. Morgan, *J. Amer. Chem. Soc.*, 1976, **98**, 2593.
[8] G. M. Brooke and A. C. Young, *J. Fluorine Chem.*, 1976, **8**, 223.
[9] D. D. Callander, P. L. Coe, J. C. Tatlow, and A. J. Uff, *Tetrahedron*, 1969, **25**, 25.

shifts being similar to those of H-3 in bornan-*exo*-2-ol, which had shift changes of 35 and 72% of the H-2 shift for *endo*- and *exo*-H, respectively.[10] In a bicyclo[2.2.1]-hept-5-en-*endo*-2-ol, however, the *endo*-H component of the AB system at C-3 is expected to exhibit a rapid shift to low field as compared with the other component (the *exo*-H), whereas the two protons at C-7 are expected to exhibit shifts of approximately the same extent. Exactly this behaviour was found for the AB pairs of protons at C-3 and -9 in the alcohol (10), the magnitudes of the shifts being similar to those for the analogous protons in norborn-5-en-*endo*-2-ol (which showed shift changes of 67, 45, 25, and 21% of the H-2 shift for *endo*- and *exo*-H at C-3, and for *anti*- and *syn*-H at C-7, respectively).[11]

Benzylmagnesium chloride and the ketone (11) gave a tertiary alcohol (12) (almost certainly the *endo*-alcohol by analogy with other reactions of 2-oxo-compounds described in this paper). The acetate (13) was nitrated to give the 4-nitrobenzyl compound (14) and an isomer which was presumably the 2-nitrobenzyl compound (15). Pyrolysis of the nitro-compound (14) gave *E*- (16) and *Z*- (17) isomers of 5,6,7,8-tetrafluoro-1,4-dihydro-2-(4-nitrobenzylidene)-1,4-methanonaphthalene as a mixture of two crystalline forms, one containing a 50 : 50 mixture of isomers and the other the pure *Z*-isomer. The assignment of stereochemistry is based on the positions of the vinylic proton resonances: that in the *Z*-isomer is shielded by the tetrafluorobenzene ring.

Methylation of the ketone (11) gave the 3,3-dimethyl ketone (4), reduction of which gave the *endo*-alcohol (18).

Treatment of the alcohol (18) with n-butyl-lithium–methyl iodide gave the methyl ether (19) and a mixture of the n-butyl-trifluoro-methoxy-compounds (20) and (21) The stereochemistry of the alcohol and the methyl esters was deduced from lanthanide shift and interconversion experiments described later. The structures of the n-butyl-trifluoro-compounds were indicated by the differences in ^{19}F chemical shifts between these compounds and the parent molecule (19) (the n-butyl substituent effect). No data are available for n-butyl compounds, but the *ortho*-fluorine signals of $C_6F_5CH_3$ are shifted downfield by 18 p.p.m. relative to C_6F_6, whereas the *meta*-fluorine absorptions are shifted upfield by *ca.* 2 p.p.m.;[12] higher alkyl homologues are expected to behave similarly. In all our 5,6,7,8-tetrafluoro-compounds, the ^{19}F absorptions at lower field (143.0—147.5 p.p.m.) are assigned to the 5- and 8-fluorine atoms, whereas those at higher field (156.7—160.0 p.p.m.) are assigned to F-6 and -7. Both n-butyl-trifluoro-compounds showed absorptions at *ca.* 150, 143, and 130 p.p.m., consistent with the 6- and 7-n-butyl structures (20) and (21), though it was not possible to differentiate between them.

Treatment of the ketone (4) with benzylmagnesium chloride gave a tertiary alcohol (22) (almost certainly the *endo*-alcohol, by analogy with other alcohols described in this paper), which was converted into the 2-benzylidene compound (5).

The structures of the isopropoxy-trifluoro-compounds obtained by treatment of 5,6,7,8-tetrafluoro-compounds with potassium isopropoxide in propan-2-ol were determined from ^{19}F n.m.r. spectra by observing the isopropoxy-substituent effects as before.[8] Symmetrical substrates yielded racemic 6-isopropoxy-5,7,8-trifluoro-compounds (equimolar amounts of the 6- and 7-substitution products), but the unsymmetrical compounds (4), (19), and (5) gave unequal amounts of 6- and 7-isopropoxy-compounds. The structures of these compounds were determined in the following way.

Reaction of the ketone (4) with isopropoxide–propan-2-ol under conditions used for kinetics experiments gave two isopropoxy-trifluoro-ketones, (23) and (24), and two other tetrafluoro-compounds detected by additional F-6 and -7 resonances to high field in the ^{19}F n.m.r. spectrum. One of these compounds was identified from the ^{19}F absorptions as the alcohol (18), which must have been formed by Meerwein–Ponndorf reduction of the starting material with the nucleophilic system; the other is thought to be the ring-opened material (25) or (26), though it was not possible to distinguish between these possibilities unequivocally by ^{1}H n.m.r. because of overlapping absorptions. Confidence for the identification of the ring-opened material and the alcohol is based on the isolation from a reaction under more vigorous conditions of two inseparable ring-opened isopropoxy-trifluoro-compounds, (27) and (29) or (28) and (30), and the separable isopropoxy-trifluoro-alcohols (31) and (32). No distinction could be made between the two pairs of ring-opened compounds, but from their individual ^{19}F n.m.r. absorptions and the isopropoxy-substituent effect it was possible to infer the positions of the fluorine resonances in the parent ring-opened tetrafluoro-compound, and absorptions were found in these regions in the spectrum of the product from the mild reaction of (4) with isopropoxide. Possession of the alcohols (31) and (32), however, enabled the structures of all the substitution products to be determined ultimately. Lanthanide-induced ^{19}F shift experiments showed the triplet signal shifting the fastest in one isomer, *i.e.* that due to F-8 of the 6-isopropoxy-compound (31), whereas the other isomer had the lower field doublet shifting the fastest [F-8 of the 7-isopropoxy-compound (32)]. In the ^{1}H n.m.r. shift experiments, the *syn* and *anti* C-9 proton signals shifted about the same extent in both cases [(31) and (32)] and so the alcohols were *endo*-2-ols. Oppenauer oxidation of the individual alcohols (31) and (32) gave the isopropoxy-trifluoro-ketones (23) and (24), respectively.

The tetrafluoro-*endo*-methyl ether (19) and potassium isopropoxide gave two isopropoxy-compounds. Methylation of the alcohol (32) showed that one was the 7-isopropoxy-compound (33), and the isopropoxy-substituent

[10] P. V. Demarco, J. K. Elzey, R. B. Lewis, and E. Wenkert, *J. Amer. Chem. Soc.*, 1970, **92**, 5734.

[11] M. R. Willcott, III, R. E. Lenkinski, and R. E. Davis, *J. Amer. Chem. Soc.*, 1972, **94**, 1742.

[12] M. I. Bruce, *J. Chem. Soc.* (*A*), 1968, 1459.

shift effect in the ^{19}F n.m.r. spectrum showed the other was the 6-isomer (34).

Treatment of the tetrafluorobenzylidene compound (5) with isopropoxide gave two isopropoxy-compounds. The reaction of the ketone (23) with benzylmagnesium chloride gave an alcohol which was converted into the 6-isopropyl-benzylidene compound (35) and the isopropoxy-substituent shift effect in the ^{19}F n.m.r. spectrum showed that the other was the 7-isomer (36).

Finally, the mixture of 4-nitrobenzylidene derivatives (16) and (17) and isopropoxide gave a product containing at least four components which was not investigated further. A small amount of nucleophilic addition to the double bond had been found previously with the 9-(4-nitrobenzylidene) compound.[8]

RESULTS AND DISCUSSION

The kinetic data are summarised in the Table. The general reactivities of the simpler tricyclic compounds (1), (2), and (6)—(8), are very similar with the exception of the tetramethyl-diene (3), which is less reactive by a factor of 4 than its reduction product (8). This effect is small, and it is clear from comparison of the other unsaturated with the related saturated compounds that a remote C=C bond is having no effect on the nucleophilic replacement of fluorine. It is of interest that the overall rate of nitration of 1,4-dihydro-1,4-methanonaphthalene itself is only marginally greater (by a factor of 1.6) than the rate for the 1,2,3,4-tetrahydro-derivative, indicative of no special activating effect by the alkene group in electrophilic aromatic substitution.[4]

Second-order rate constants [a] for reactions with potassium isopropoxide in propan-2-ol ($dm^3\ mol^{-1}\ min^{-1}$)

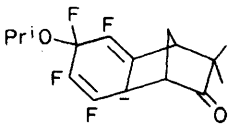
Compound	At 100 °C	At 75 °C	At 50 °C
(1)	0.008		
(6)	0.008		
(2)	0.007		
(7)	0.007		
(3)	0.002		
(8)	0.008		
(4)	0.25	0.04	0.003
(19)		0.000 6	0.000 04
(5)		0.002 5	

[a] Based on one determination of the percentage reaction at a given time.

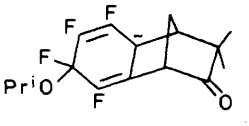
The ketone (4) was the most reactive compound studied and it was necessary to work at 75 and at 50 °C for convenient kinetic runs. Relative to the saturated *endo*-methyl ether (19), the ketone was more reactive towards fluorine replacement by factors of 70 at 75 °C, and 80 at 50 °C, giving an extrapolated value of over 100 : 1 at 25 °C for the ratio of the second-order rate constants; since some ketone could be in equilibrium with a hemiacetal form, these rate constant ratios are considered to be minimum values. For comparison, the benzylidene derivative (5) at 75 °C was more reactive than the ether by a factor of 4.

The most significant factor, however, in interpreting the kinetic data, is the fact that two products are formed from the ketone: 57% 6-isopropoxy (23) and 43% 7-isopropoxy (24). It is clear that the remote carbonyl group is affecting the transition states (44) and (45) (the *para*-Wheland structures being the most relevant) associated with attack at C-6 and -7, respectively, to similar extents, and no special homoconjugative interaction of the type (46) need be invoked, which of necessity would be highly selective for C-6 substitution. The field effect of the carbonyl group seems to offer the best explanation of these observations, activating the system towards nucleophilic displacement of fluorine. In contrast, the carbonyl groups in 5- and 6-oxo-2-norbornyl esters, which bear the same relationship to the developing charge as do the carbonyl groups in (45) and (44) respectively, exert a powerful deactivating effect in the solvolyses of these compounds.[13] In the benzylidene compound (5) the field effect of the double bond could be a contributor to the modest reactivity of this substrate to nucleophilic replacement of fluorine.

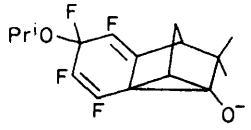
At 75 °C both the methyl ether (19) and the benzylidene compound (5) form 6- and 7-isopropoxy-compounds, in the proportions 35 : 65 and 31 : 69, respectively. The departure of these proportions from 50 : 50 indicates



(44)



(45)



(46)

that subtle effects are responsible for the reactivity differences.

It is known that the site of substitution in polyfluoroaromatic compounds is that which has the maximum number of fluorine atoms in *ortho*- and *meta*-positions,[14] and it was recognised in the case of 9-alkylidene-5,6,7,8-tetrafluoro-1,4-dihydro-1,4-methanonaphthalenes that the rate constants for fluorine replacement could be determined largely by contributions from the remaining three fluorine atoms and that any activation due to homoallylic conjugation might be overwhelmed.[8] Nevertheless, the pattern of reactivity for the 6,7-difluoro-compounds was similar to that found for the 5,6,7,8-tetrafluoro-compounds, which indicated that the remaining fluorine atom was controlling the overall pattern of reactivity even in the lightly fluorinated substrates.

[13] J. C. Greever and D. E. Gwynn, *Tetrahedron Letters*, 1969, **10**, 813.

[14] R. D. Chambers, W. K. R. Musgrave, J. S. Waterhouse, D. L. H. Williams, J. Burdon, W. B. Hollyhead, and J. C. Tatlow, *J.C.S. Chem. Comm.*, 1974, 239.

Work is in progress on the 6,7-difluoro-analogues of some of the compounds described in this paper in an attempt to find examples of homoconjugative activation: 6,7-difluoro-1,4-difluoro-3,3-dimethyl-1,4-methanonaphthalen-3(2*H*)-one seems the compound most likely to exhibit this effect.

EXPERIMENTAL

^{1}H N.m.r. (90 MHz) and ^{19}F n.m.r. (84.67 MHz) spectra were obtained with a Brücker HX-90E spectrometer; fluorine absorptions are quoted in p.p.m. upfield from internal $CFCl_3$. For chemically induced shift experiments tris-(1,1,1,2,2,3,3-heptafluoro-7,7-di[$^2H_3$]methyl[8-$^2H_3$]octane-4,6-dionato)europium(III) {Eu([$^2H_9$]fod)$_3$} was used, the extrapolated induced shifts at 1 : 1 molar ratio {Eu([$^2H_9$]-fod)$_2$: substrate} being expressed as percentages of the H-2 shift change.

5,6,7,8-*Tetrafluoro*-1,4-*dihydro*-1,4-*methanonaphthalene* * (1).—Bromopentafluorobenzene (51.0 g) in dry ether (400 ml) at −70 °C was treated under nitrogen with n-butyllithium in hexane (202 ml; 1.03M) with stirring over 80 min. The mixture was maintained at −70 °C for a further 4 h, then warmed rapidly (external water-bath); when the temperature reached 15 °C, freshly distilled and dried ($MgSO_4$) cyclopentadiene (30 ml) was added rapidly. The internal temperature of the mixture rose rapidly and at 30 °C external cooling was applied. The temperature reached *ca.* 42 °C and the mixture boiled vigorously and then quickly subsided. [WARNING: Pentafluorophenyl-lithium has been known to explode. Great care must be taken by performing this reaction behind a safety screen. All nitrogen leads were removed from the apparatus during the reaction, and three condensers were necessary to contain the solvent.] The cream-coloured heterogeneous mixture was heated under reflux for 2 h, then cooled, and water was added followed by an excess of dilute hydrochloric acid. The organic layer was separated, washed with the sodium carbonate solution, dried ($MgSO_4$), and evaporated. Distillation of the residue at 18 mmHg gave three fractions: (i) (0.45 g), b.p. <90°; (ii) (14.35 g), b.p. 90—101°; and (iii) (2.79 g), b.p. 101—130°. Redistillation of fraction (ii) gave the adduct (1), b.p. 93—94° at 18 mmHg, m.p. 44—44.5° [from light petroleum (b.p. 40—60 °C)] (lit., m.p. 43.5—44°), δ_F ($CDCl_3$) 146.2 (F-5, F-8) and 160.9 (F-6, F-7).

5,6,7,8-*Tetrafluoro*-1,4-*dihydro*-1,4-*ethenonaphthalene* (2).—This compound was prepared by the published method; [9] δ_F ($CDCl_3$) 150.9 (F-5, F-8) and 163.5 (F-6, F-7).

5,6,7,8-*Tetrafluoro*-1,4-*dihydro*-2,3,9,10-*tetramethyl*-1,4-*ethenonaphthalene* (3). This compound was prepared by the published method; [9] δ_F ($CDCl_3$) 152.2 (F-5, F-8) and 163.9 (F-6, F-7).

Catalytic Hydrogenations.—(a) Compound (1) in ethanol was hydrogenated at atmospheric pressure over 10% Pd–C at room temperature to give 5,6,7,8-*tetrafluoro*-1,2,3,4-*tetrahydro*-1,4-*methanonaphthalene* (6), m.p. 49—50° (from methanol), δ_F ($CDCl_3$) 147.3 (F-5, F-8) and 160.4 (F-6, F-7) (Found: C, 60.9; H, 3.5. $C_{11}H_8F_4$ requires C, 61.1; H, 3.7%).

(*b*) Compound (2) was hydrogenated in a similar manner to give 5,6,7,8-*tetrafluoro*-1,2,3,4-*tetrahydro*-1,4-*ethanonaphthalene* (7), m.p. 113—114° (from methanol), δ_F ($CDCl_3$) 150.9 (F-5, F-8) and 162.2 (F-6, F-7) (Found: C, 62.9; H, 4.6. $C_{12}H_{10}F_4$ requires C, 62.6; H, 4.5%).

(*c*) Compound (3) was hydrogenated in a similar manner to give a 5,6,7,8-*tetrafluoro*-1,2,3,4-*tetrahydro*-2,3,9,10-*tetramethyl*-1,4-*ethanonaphthalene* (8), m.p. 92—93° (from methanol); δ_F ($CDCl_3$) 151.8 (F-5, F-8) and 161.8 (F-6, F-7) (Found: C, 66.9; H, 6.6. $C_{16}H_{18}F_4$ requires C, 67.1; H, 6.3%).

5,6,7,8-*Tetrafluoro*-1,2,3,4-*tetrahydro*-1,4-*methanonaphthalen*-exo-2-*ol* * (9).—A mixture of compound (1) (14.0 g) and sodium borohydride (1.58 g) in dry tetrahydrofuran (120 ml) at 0 °C was treated with boron trifluoride–ether (4.5 ml) under nitrogen over 10 min. The mixture was stirred at room temperature for 9 h, and water (5 ml) was added to destroy the excess of diborane, followed by sodium hydroxide solution (20 ml; 3M), and hydrogen peroxide (25 ml; 30% w/w) at such a rate that the internal temperature did not rise above 30 °C (external ice-bath). After stirring vigorously overnight at room temperature, sodium chloride was added and the mixture was then extracted with methylene chloride. The extracts were dried ($MgSO_4$) and evaporated to give an oil (16.8 g), which was shown to contain *exo*- and *endo*-alcohols in the molar ratio of 86 : 14, respectively by g.l.c. (free fatty acid phase; at 150 °C). Repeated recrystallisation from benzene–n-hexane, or thick-layer chromatography on silica [chloroform–ethyl acetate (90 : 10 v/v)] gave the exo-*alcohol* (9), m.p. 60—60.5° (Found: C 57.2; H, 3.7. $C_{11}H_8F_4O$ requires C, 56.9; H, 3.5%). Two AB systems in the ^{1}H n.m.r. spectrum exhibited 38 and 78% and 31 and 62% of the H-2 lanthanide-induced shift (LIS).

5,6,7,8-*Tetrafluoro*-1,4-*dihydro*-1,4-*methanonaphthalen*-2-(3H)-*one* * (11).—A mixture of the *exo*- and *endo*-alcohols from the hydroboration–oxidation of compound (1) (23 g), aluminium tri-t-butoxide (100 g), and *p*-benzoquinone (35 g) in dry toluene (350 ml) was heated under reflux for 21 h. The black solution was cooled to room temperature and washed twice with sulphuric acid (250 ml; 4N) and then with sodium hydroxide solution (4N) until the organic phase was colourless. Evaporation of the dried ($MgSO_4$) solution and recrystallisation of the residue (15.4 g) from n-hexane, gave the *ketone* (11), m.p. 85.5—86° (Found: C, 57.5; H, 2.7. $C_{11}H_6F_4O$ requires C, 57.4; H, 2.6%).

5,6,7,8-*Tetrafluoro*-1,2,3,4-*tetrahydro*-1,4-*methanonaphthalen*-endo-2-*ol* * (10).—Compound (11) (2.28 g) in dry tetrahydrofuran (25 ml) was treated with borane–tetrahydrofuran (10 ml; 4.88M in BH_3) with cooling (external ice-bath). Sodium hydroxide solution (3M) was carefully added, and the mixture was then extracted with ether; the dried ($MgSO_4$) extracts were evaporated. The residue was shown to be a mixture of *exo*- and *endo*-alcohols in the molar ratio of 15 : 85, respectively, by g.l.c. (as before). Repeated crystallisation from n-hexane gave the endo-*alcohol* (10), m.p. 76.5—77° (Found: C, 57.0; H, 3.4%). The two AB systems in the ^{1}H n.m.r. spectrum exhibited 76 (H-2 *endo*) and 38% (H-2 *exo*) and 25% (9-H_2) of the H-2 LIS.

Treatment of the ketone (11) with benzylmagnesium chloride in ether gave a 2-*benzyl*-5,6,7,8-*tetrafluoro*-1,2,3,4-*tetrahydro*-1,4-*methanonaphthalen*-2-*ol* (12), m.p. 70.5—71.5° [from light petroleum (b.p. 40—60 °C)] (Found: C, 67.3; H, 4.4. $C_{18}H_{14}F_4O$ requires C, 67.1; H, 4.4%). This alcohol was acetylated (Bu^nLi–THF and AcCl); the *acetate* (13) had m.p. 130.5—131° [from benzene–light petroleum (b.p. 60—80 °C)] (Found: C, 65.9; H, 4.7. $C_{20}H_{16}F_4O_2$ requires C, 65.9; H, 4.4%).

* Carried out in the laboratories of Professor H. C. Brown, Purdue University, Lafayette, Indiana, U.S.A., during the tenure of a Fulbright Scholarship by G. M. B. in 1968—1969. We thank Professor Brown for permission to publish this work.

Nitration of the acetate (13) with nitric acid (95%) in acetic anhydride at 25—40 °C for 16 h gave two products which were separated by chromatography on silica (chloroform as eluant). The faster moving component was presumed to be a 5,6,7,8-*tetrafluoro*-1,2,3,4-*tetrahydro*-2-(2-*nitrobenzyl*)-1,4-*methano*-2-*naphthyl acetate* (15), m.p. 154—155° [from benzene–light petroleum (b.p. 60—80 °C)] (Found: C, 58.9; H, 3.7; N, 3.6. $C_{20}H_{15}F_4NO_4$ requires C, 58.7; H, 3.7; N, 3.4%). (The orientation of the NO_2 group was not proven.) The slower moving component was a 2-(4-*nitrobenzyl*) *isomer* (14), m.p. 127—127.5° (Found: C, 58.9; H, 3.6; N, 3.0%).

(E)- *and* (Z)-5,6,7,8-*Tetrafluoro*-1,2,3,4-*tetrahydro*-2-(4-*nitrobenzylidene*)-1,4-*methanonaphthalene* (16) *and* (17).—The ester (14) (5.70 g) was sublimed at 0.05 mmHg through a silica tube (20 cm × 1.5 cm diam.) packed with silica fibre, heated to 470—480 °C; the product was collected in a trap cooled in liquid air. Chromatography of the product on silica (chloroform as eluant) gave the main component (4.30 g), which was crystallised from benzene–light petroleum (b.p. 60—80 °C). Two sorts of crystal were obtained, which were separated manually and recrystallised. One crystal form was the Z-*isomer* (17), m.p. 138.5—139.5°; the ^{1}H n.m.r. spectrum showed a symmetrical A_2B_2 system in the aromatic region and a singlet at τ 3.38 (vinylic H) with relative intensities 2 : 2 : 1, respectively; $\lambda_{max.}$ (cyclohexane) 225 (ε 14 800) and 306 nm (17 200) (Found: C, 62.0; H, 3.0; N, 3.6. $C_{18}H_{11}F_4NO_2$ requires C, 61.9; H, 3.2; N, 4.0%; *M*, 349). The other was a 1 : 1 mixture of *E*- and *Z*-isomers (16) and (17), m.p. 121.5—122.5°; the ^{1}H n.m.r. spectrum showed two singlets at τ 3.25 and 3.60 in the ratio 1 : 1; $\lambda_{max.}$ (in cyclohexane) 224 (ε 15 600) and 305 nm (16 800) (Found: C, 61.7; H, 3.2; N, 4.3%; M^+, 349). (4-Nitrotoluene in cyclohexane has $\lambda_{max.}$ 265 nm.)

5,6,7,8-*Tetrafluoro*-1,4-*dihydro*-3,3-*dimethyl*-1,4-*methanonaphthalen*-2(3H)-*one* (4).—The ketone (11) (28.15 g) in dry tetrahydrofuran (50 ml) at −40 °C was treated with triphenylmethylsodium in ether (450 ml; 0.29M; from triphenylchloromethane and Na–Hg), the internal temperature being maintained below −20 °C. Methyl iodide (100 ml) was added, and the mixture heated under reflux for 1 min and left at room temperature for 3 days. The solvent was evaporated off, the residue distilled in steam, and the distillate extracted with ether. The dried ($MgSO_4$) extracts were evaporated. The product (13.84 g) in dry tetrahydrofuran (125 ml) was treated with triphenylmethylsodium in ether (450 ml; 0.29M), followed by methyl iodide (100 ml), as before, and the mixture was finally distilled in steam and extracted with ether. Concentration of the ethereal extracts caused a white solid to separate [suspected methylmercury(II) iodide], which was filtered off. The filtrate was evaporated and the residue (10.96 g) was separated by chromatography on silica (CCl_4 as eluant). The first component (1.58 g) was not identified; the second (0.43 g) was suspected methylmercury(II) iodide. The material remaining on the column was eluted with ether; the eluate was evaporated to give crude product (8.32 g). Recrystallisation from light petroleum (b.p. 30—40 °C) gave the *ketone* (4), m.p. 66.5—67.5°, δ_F ($CDCl_3$) 145.0 (F-5), 156.7 (F-6, F-7), and 143.0 (F-8) (Found: C, 60.7; H, 3.6. $C_{13}H_{10}F_4O$ requires C, 60.5; H, 3.9%).

5,6,7,8-*Tetrafluoro*-1,2,3,4-*tetrahydro*-3,3-*dimethyl*-1,4-*methanonaphthalen*-endo-2-*ol* (18).—The ketone (4) (1.289 g) was treated with borane–tetrahydrofuran (15 ml; 1M) at room temperature for 2.5 h. Water was added, the solution made alkaline with sodium hydroxide, and the mixture extracted with ether. Evaporation of the dried ($MgSO_4$) extracts, and purification of the product by preparative t.l.c. on silica ($CHCl_3$ as eluant) gave an oil (1.18 g), b.p. 95—103° at 0.05—0.1 mmHg, which solidified to give the *alcohol* (18), m.p. 72—73° [from light petroleum (b.p. 30—40 °C)], δ_F ($CDCl_3$) 147.0 (F-5), 159.3 (F-6, F-7), and 146.1 (F-8) (Found: C, 60.3; H, 5.0. $C_{13}H_{12}F_4O$ requires C, 60.0; H, 4.65%).

Treatment of the alcohol (18) (1.05 g) in dry tetrahydrofuran at 0 °C with n-butyl-lithium in n-hexane (5 ml; 1.5M) followed by methyl iodide (5 ml), and heating the mixture under reflux for 3 min, gave two products which were separated by preparative t.l.c. on silica. (i) Elution with carbon tetrachloride gave 5,6,7,8-*tetrafluoro*-1,2,3,4-*tetrahydro*-endo-2-*methoxy*-3,3-*dimethyl*-1,4-*methanonaphthalene* (19), b.p. 63—86° at 0.01—0.05 mmHg, δ_F ($CDCl_3$) 147.5 (F-5), 160.0 (F-6, F-7), and 146.1 (F-8) (Found: C, 61.1; H, 5.2; M^+, 274. $C_{14}H_{14}F_4O$ requires C, 61.3; H, 5.1%; *M*, 274). (ii) Carbon tetrachloride–chloroform (85 : 15 v/v) eluted a mixture of two components, 6-butyl-5,7,8-trifluoro-1,2,3,4-tetrahydro-*endo*-2-methoxy-3,3-dimethyl-1,4-methanonaphthalene (20), δ_F ($CDCl_4$) 151.5 (F-5), 143.1 (F-7), and 129.5 (F-8), and 5,6,8-trifluoro-7-n-butyl-isomer (21), δ_F 130.8 (F-5), 143.4 (F-6), and 150.1 (F-8), b.p. 90—103° at 0.01 mmHg (Found: C, 69.3; H, 7.7%; M^+, 312 Calc. for $C_{18}H_{23}F_3O$: C, 69.2; H, 7.4%; *M*, 312).

2-*Benzylidene*-5,6,7,8-*tetrafluoro*-1,2,3,4-*tetrahydro*-3,3-*dimethyl*-1,4-*methanonaphthalene* (5).—Benzylmagnesium chloride [from benzyl chloride (1.18 g) and magnesium (0.38 g) in dry ether (20 ml)] was treated with the ketone (4) (0.297 g) in dry ether (5 ml) at reflux temperature for 5 min. Preparative t.l.c. of the product on silica (chloroform as eluant) gave a 2-*benzyl*-5,6,7,8-*tetrafluoro*-1,2,3,4-*tetrahydro*-3,3-*dimethyl*-1,4-*methanonaphthalen*-2-*ol* (22), m.p. 69.5—70° [from light petroleum (b.p. 40—60 °C)] (Found: C, 68.9; H, 5.0%; M^+, 350. $C_{20}H_{18}F_4O$ requires C, 68.6; H, 5.2%; *M*, 350).

The alcohol (22) (0.132 g) in pyridine (0.5 ml) and carbon tetrachloride (5 ml) at 0 °C was treated with thionyl chloride (1 ml) in carbon tetrachloride (5 ml) to give the *benzylidene derivative* (5) (0.112 g), m.p. 84—84.5° [from light petroleum (b.p. 40—60 °C)], δ_F ($CDCl_3$) 146.3 (F-5), 159.5 (F-6), 158.5 (F-7), and 144.0 (F-8) (Found: C, 72.5; H, 5.0%; M^+, 332. $C_{20}H_{16}F_4$ requires C, 72.3; H, 4.9%; *M*, 332).

Reaction of the Ketone (4) *with Potassium Isopropoxide*.—(a) The ketone (4) (0.2545 g) and potassium isopropoxide in propan-2-ol (5.0 ml; 0.20M) were heated together in a sealed tube at 100 °C for 3 h. The mixture was extracted with ether, and the extracts were dried ($MgSO_4$) and evaporated. Preparative t.l.c. on silica (chloroform as eluant) gave a mixture of 5,7,8-trifluoro-1,4-dihydro-6-isopropoxy-3,3-dimethyl-1,4-methanonaphthalen-2(3*H*)-one (23), δ_F ($CDCl_3$) 138.3 (F-5, d), 150.6 (F-7, d), and 144.7 (F-8, t), and its 5,6,8-trifluoro-7-isopropoxy-isomer (24), δ_F ($CDCl_3$) 146.7 (F-5, t), 150.4 (F-6, d), and 136.2 (F-8, d), b.p. 100—140° at 0.2 mmHg (Found: C, 64.2; H, 5.9%; M^+, 298. Calc. for $C_{16}H_{17}F_3O$: C, 64.4; H, 5.7%; *M*, 298), in the ratio 57 : 43, respectively.

(*b*) A mixture of the ketone (4) and the isopropoxy-ketones (23) and (24) (1.31 g) and potassium isopropoxide in propan-2-ol (8 ml, 0.99M) was heated in a sealed tube at 100 °C for 3 h, and the product was worked up as before. Preliminary separation by preparative t.l.c. on silica ($CHCl_3$ as eluant) gave as the fastest moving component a mixture of ring-

opened isopropoxy-trifluoro-ketone [*i.e.* the isopropyl esters (27) and (29) or (28) and (30)], b.p. 125—140° at 0.01 mmHg; δ_F ($CDCl_3$) (i) 130.2 (d), 145.2 (d,d), and 151.9 (d); (ii) 136.4 (d), 139.7 (t), and 152.8 (d) (Found: C, 63.9; H, 6.3%; M^+, 358. $C_{19}H_{25}F_3O_3$ requires C, 63.7; H, 7.0%; *M*, 358).

Slower moving components were rechromatographed on silica [chloroform–ethyl acetate as eluant (95 : 5 v/v)] to give two alcohols (31) and (32). The faster moving component was 5,7,8-*trifluoro*-1,2,3,4-*tetrahydro*-6-*isopropoxy*-3,3-*dimethyl*-1,4-*methanonaphthalen*-endo-2-*ol* (31), b.p. 100—110° at 0.01 mmHg, δ_F ($CDCl_3$) 140.0 (F-5, d), 152.8 (F-7, d), and 147.6 (F-8, t); percentages of the H-2 LIS 24 (F-5), 21 (F-7), and 51 (F-8) (Found: C, 64.1; H, 6.5%; M^+, 300. $C_{16}H_{19}F_3O_2$ requires C, 64.0; H, 6.4%; *M*, 300).

The slower moving component (32) was the 5,6,8-*trifluoro*-7-*isopropoxy-isomer*, m.p. 100.5—101°, δ_F ($CDCl_3$) 148.6 (F-5, t), 153.0 (F-6, d), and 139.1 (F-8, d); percentages of the H-2 LIS 25 (F-5), 19 (F-6), 48 (F-8), and 26 and 21 (9-H_2) (Found: C, 63.9; H, 6.4%; M^+, 300).

Oppenauer Oxidation of the Alcohols (31) *and* (32).—The alcohol (31) (0.135 g), *p*-benzoquinone (2.79 g), and aluminium tri-t-butoxide (7.32 g) in dry toluene (40 ml) were heated under reflux for 65 h, and the product was worked up as before. Preparative t.l.c. on silica ($CHCl_3$ as eluant) gave the ketone (23) (0.104 g), identified by ^{19}F n.m.r.

In a similar manner, the alcohol (32) (0.052 g) gave the ketone (24) (0.0259 g), b.p. 100—160° at 0.01—0.05 mmHg, M^+ 298, identified by ^{19}F n.m.r.

Reactivity Data. Reactions of 5,6,7,8-*Tetrafluoro-compounds with Potassium Isopropoxide in Propan*-2-*ol.*—The approximate values of the second-order rate constants (Table) were determined as in the following typical experiment.

(*a*) The diene (1) (0.1491 g) and alkoxide solution (1 ml; 0.98M) were heated together for 180 min at 100 °C. The ^{19}F n.m.r. spectrum of the product in $CDCl_3$ showed the formation of the trifluoro-isopropoxy-compound to the extent of 65%, giving the calculated second-order rate constant 8×10^{-3} dm^3 mol^{-1} min^{-1}. Reaction of compound (1) (0.14 g) with potassium isopropoxide in propan-2-ol (1 ml; 0.8M) at 100 °C for 4 days and work-up in the usual way followed by distillation at *ca.* 150 °C and 0.05 mmHg gave (±)-5,7,8-*trifluoro*-1,4-*dihydro*-6-*isopropoxy*-1,4-*methanonaphthalene* (37) (0.12 g), δ_F ($CDCl_3$) 139.4 (F-5, d), 154.5 (F-7, d), and 147.6 (F-8, t) (Found: C, 66.2; H, 5.4. $C_{14}H_{13}F_3O$ requires C, 66.1; H, 5.2%).

(*b*) (±)-5,7,8-*Trifluoro*-1,2,3,4-*tetrahydro*-6-*isopropoxy*-1,4-*methanonaphthalene* (38) was prepared as in (*a*); δ_F ($CDCl_3$) 140.0 (F-5, d), 153.7 (F-7, d), and 148.6 (F-8, t) (Found: C, 65.4; H, 6.3. $C_{14}H_{15}F_3O$ requires C, 65.6; H, 5.9%).

(*c*) (±)-5,7,8-*Trifluoro*-1,4-*dihydro*-6-*isopropoxy*-1,4-*ethenonaphthalene* (39), m.p. 51—52°, was prepared as in (*a*); δ_F ($CDCl_3$) 143.9 (F-5, d), 157.0 (F-7, d), and 152.3 (F-8, t) (Found: C, 67.9; H, 4.7. $C_{15}H_{13}F_3O$ requires C, 67.7; H, 4.9%).

(*d*) (±)-5,7,8-Trifluoro-1,2,3,4-tetrahydro-6-isopropoxy-1,4-ethanonaphthalene (40) was not isolated; δ_F ($CDCl_3$) 143.9 (F-5, d), 155.7 (F-7, d) and 152.7 (F-8, t).

(*e*) (±)-5,7,8-*Trifluoro*-1,4-*dihydro*-6-*isopropoxy*-2,3,9,10-*tetramethyl*-1,4-*ethanonaphthalene* (41), m.p. 103—104°, was prepared as in (*a*); δ_F ($CDCl_3$) 145.1 (F-5, d), 157.1 (F-7, d), and 153.3 (F-8, t) (Found: C, 70.5; H, 6.2. $C_{19}H_{21}F_3O$ requires C, 70.8; H, 6.6%).

(*f*) (±)-5,7,8-*Trifluoro*-1,2,3,4-*tetrahydro*-6-*isopropoxy*-2,3,9,10-*tetramethyl*-1,4-*ethanonaphthalene* (42) was prepared as in (*a*); δ_F ($CDCl_3$) 144.6 (F-5, d), 155.2 (F-7, d), and 153.5 (F-8, t) (Found: C, 70.3; H, 7.4. $C_{19}H_{25}F_3O$ requires C, 69.6; H, 7.7%).

(*g*) A kinetic experiment with the ketone (4) was carried out at 75 °C. ^{19}F N.m.r. analysis of the product in $CDCl_3$ showed that in addition to starting material (26.0%) and the trifluoro-isopropoxy-ketones (23) and (24) (50.8%, in the ratio 57 : 43 respectively), there were two other, tetrafluoro-compounds. These were identified as the *endo*-alcohol (18) [7.1%, with δ_F 147.4 (F-5), 159.8 (F-6, F-7), and 146.1 (F-8)] and a ring-opened ester (25) or (26) (15.9% with δ_F 137.9, 143.4, 158.2, and 159.0 p.p.m.). [In a similar reaction with NaOMe–MeOH, an analogous reaction pattern was followed, with the exception that no alcohol (18) was produced.] Use of a mixture [8] of the two racemates from 6-isopropoxy-5,7,8-trifluoro- and 7-isopropoxy-5,6,8-trifluoro-1,2,3,4-tetrahydro-9-(4-trifluoromethylbenzylidene)-1,4-methanonaphthalene as an internal standard showed the same extent of reaction. At 50 °C the ratio of (23) to (24) formed was 52 : 48.

(*h*) A kinetic experiment with compound (19) at 75 °C gave two components, the trifluoro-methyl ethers (34) [δ_F ($CDCl_3$) 140.6 (F-5, d), 153.4 (F-7, d), and 147.8 (F-8, t)] and (33) [δ_F ($CDCl_3$) 149.2 (F-5, t), 153.8 (F-6, d), and 139.2 (F-8, d)], in the ratio 34 : 66 respectively.

At 50 °C, compounds (34) and (33) were formed in the ratio 31 : 69, respectively. These products were separated as a mixture from unchanged (19) by preparative t.l.c. on silica [$CHCl_3$–CCl_4 (50 : 50 v/v)] and had b.p. 90—140° at 0.01—0.05 mmHg (Found: C, 65.0; H, 6.8%; M^+, 314 Calc. for $C_{17}H_{21}F_3O_2$: C, 65.0; H, 6.7%; *M*, 314).

Methylation of the alcohol (32) (0.03 g) in dry THF by treatment with n-butyl-lithium (1.5 ml; 1.52M) at −78 °C, followed by methyl iodide (5 ml), and heating the mixture under reflux for 5 min, and separation of the crude product by preparative t.l.c. as before gave as a single isomer, compound (33) (0.034 g), b.p. 74—130° at 0.01 mmHg, M^+ 314.

(*i*) A kinetic experiment with compound (5) gave 2-benzylidene-5,7,8-trifluoro-1,2,3,4-tetrahydro-6-isopropoxy-3,3-dimethyl-1,4-methanonaphthalene (35) [δ_F ($CDCl_3$) 139.5 (F-5, d), 152.3 (F-7, d), and 145.4 (F-8, t)] and its 5,6,8-trifluoro-7-isopropoxy-isomer (36) [δ_F ($CDCl_3$) 148.0 (F-5, t), 153.1 (F-6, d), and 137.2 (F-8, d)] in the ratio 31 : 69, respectively. These products were separated as a mixture from unchanged (45) by preparative t.l.c. on silica (CCl_4 as eluant) and had b.p. 130—164° at 0.01 mmHg (Found: C, 74.0; H, 6.0. $C_{23}H_{23}F_3O$ requires C, 74.2; H, 6.2%).

Treatment of the ketone (23) (0.108 g) with benzylmagnesium chloride and separation of the product by preparative t.l.c. on silica (CCl_4 as eluant) gave 2-benzyl-5,7,8-trifluoro-1,2,3,4-tetrahydro-6-isopropoxy-3,3-dimethyl-1,4-methanonaphthalen-2-ol (43) (0.126 g), M^+ 390. Reaction of this material in carbon tetrachloride–pyridine, with thionyl chloride in carbon tetrachloride as before, and separation of the product by preparative t.l.c. on silica (CCl_4 as eluant) gave as a single isomer compound (35) (0.08 g), b.p. 140—170° at 0.01—0.05 mmHg (Found: C, 74.2; H, 6.1%), identified by ^{19}F n.m.r.

[6/2312 *Received*, 20*th December*, 1976]