Intermediates in the Decomposition of Aliphatic Diazo-compounds. Part 14.[1] Chemically Induced Dynamic Nuclear Polarisation during Benzylic Insertion of Diphenylmethylene into Diastereoisomeric Esters of α-Fluorophenylacetic Acid. Evidence for a Dual Mechanism of C–H Insertion

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Diazodiphenylmethane and a number of its substituted analogues have been decomposed thermally in esters of α-fluorophenylacetic acid as solvent, and the ^{1}H and ^{19}F CIDNP effects recorded. The pattern of the principal polarisation in the case of the methyl ester is consistent with benzylic C–H insertion by triplet diphenylmethylene. A minor ^{19}F polarisation showing no corresponding depolarised product is attributed to a metastable product formed by bonding of $PhĊFCO_2Me$ at the *para*-position of the diarylmethyl radical.

CIDNP has been observed during benzylic insertion into diastereoisomeric esters formed by esterification of racemic and resolved α-fluorophenylacetic acid with chiral alcohols (1 methylheptanol, bornan-2-*endo*-ol, *p*-menthan-3-ol). In the case of single diastereoisomers, the polarised ^{19}F signals of the insertion product indicate that geminate radical pair recombination occurs with complete loss of stereochemistry at the reaction centre. However, depolarised n.m.r. spectra indicate a 55 : 45 preference for retention of configuration. The species responsible for insertion with retention but without the generation of polarisation is considered to be singlet diphenylmethylene.

DIARYLMETHYLENES are carbenes whose formation and reactions are well documented.[2] Spectroscopic evidence, notably from electron paramagnetic resonance, establishes that diphenylmethylene is a ground state triplet molecule, and several reactions, for example non-stereospecific addition to olefins and reaction with ground state molecular oxygen, suggest that the carbene reacts through its ground state. The diarylmethylenes are not particularly reactive in insertion into carbon–hydrogen bonds, but such reactions do occur in benzylic systems where the C–H bond strength is particularly low. This type of observation too has been interpreted as evidence that the triplet carbene is the state responsible, generating by hydrogen atom abstraction a radical pair which can collapse to produce the product of formal insertion.

On the other hand, diarylmethylenes insert readily into O–H,[3] N–H,[4] and S–H[5] bonds and these reactions have been interpreted as involving the singlet electronic state of the carbene. Thus water, for example, sup-presses the production of radical products when diphenylmethylene is generated in acetonitrile solution. Diphenylmethanol becomes a major product, and, by comparison of deuterium and tritium isotope effects on its formation, it has been established that the O–H insertion process takes place by a two-step mechanism with intermediate formation of an oxygen ylide.[3] When diphenylmethylene is generated in the presence of isopropyl alcohol, O–H insertion competes with hydrogen atom abstraction from C-2.[6] Detailed examination of this competition suggests that singlet and triplet states of the carbene undergo equilibration rapidly in comparison with the carbene-consuming processes in acetonitrile at 85 °C. This result supported earlier suggestions[3] and Closs's analysis[7] of the competition between insertion and cyclopropanation with and without retention of stereochemistry in the reactions of diphenylmethylene with *cis*- and *trans*-but-2-enes.

[1] Part 13, D. Bethell and R. McKeivor, *J.C.S. Perkin II*, 1977, 327.

[2] For reviews, see W. Kirmse, ' Carbene Chemistry,' Academic Press, New York, 2nd edn., 1971; D. Bethell in ' Organic Reactive Intermediates,' ed. S. P. McManus, Academic Press, New York, 1973, ch. 2; W. J. Baron, M. R. DeCamp, M. E. Hendrick, M. Jones, jun., R. H. Levin, and M. B. Sohn, ' Carbenes,' vol. 1, eds. M. Jones, jun., and R. A. Moss, Wiley, New York, 1973, p. 1.

[3] (*a*) D. Bethell, J. D. Callister, and D. Whittaker, *J. Chem. Soc.*, 1965, 2466; (*b*) D. Bethell and R. D. Howard, *J. Chem. Soc. (B)*, 1969, 745; (*c*) D. Bethell, A. R. Newall, G. Stevens, and D. Whittaker, *ibid.*, 1969, 749; (*d*) D. Bethell, A. R. Newall, and D. Whittaker, *ibid.*, 1971, 23.

[4] D. Bethell, J. Hayes, and A. R. Newall, *J.C.S. Perkin II*, 1974, 1307.

[5] A. R. Newall, Ph.D. Thesis, Liverpool, 1969.

[6] D. Bethell, G. Stevens, and P. Tickle, *Chem. Comm.*, 1970, 792.

[7] G. L. Closs, *Topics Stereochem.*, 1968, **3**, 193.

In this paper we describe studies on chemically induced dynamic nuclear polarisation (CIDNP),[8] the generation of enhanced absorption and emission signals in the n.m.r. spectra of the products formed from radical pair precursors in high magnetic fields, during benzylic C–H insertion of diarylmethylenes at a chiral centre. The aim of the work was to examine the stereochemistry of the polarised product so as to provide direct experimental evidence on the spatial relationship between the components of the radical pair responsible for the nuclear polarisation. Moreover, we reasoned that comparison of the stereochemistry of the polarised product with that of the total, unpolarised product at the end of the reaction should provide important mechanistic information about the existence of multiple reaction pathways. Such a technique should be applicable beyond the confines of carbene chemistry to any system showing CIDNP, and might provide an alternative to the estimation of enhancement factors in assessing the importance of radical pair pathways.[9]

The observation of ^{19}F n.m.r. has a number of advantages for studies of CIDNP, not least the fact that diastereoisomeric fluorides can be readily distinguished.[10] The systems chosen for study were therefore chiral benzyl fluorides, namely esters of α-fluorophenylacetic acid. By resolving the acid and esterifying the enantiomers separately with an optically pure alcohol, two diastereoisomeric esters were obtained. Insertion into the benzylic C–H bond with retention would thus yield a single diastereoisomer, whereas any loss of stereochemistry at the reaction centre would be revealed by the appearance in the n.m.r. spectrum of the products of additional, separate ^{19}F signals for the other diastereoisomer.

RESULTS

Insertion into Methyl α-Fluorophenylacetate.—Thermal decomposition of diazodiphenylmethane (1M) in methyl α-fluorophenylacetate solution at 120 °C leads to a product mixture in which the compound resulting from benzylic C–H insertion by diphenylmethylene accounts for *ca.* 15% of the diazoalkane initially present. The identity of this product was confirmed by n.m.r. and g.l.c. comparison with an authentic specimen of methyl 2-fluoro-2,3,3-triphenylpropionate, obtained by treatment of the sodio-derivative of methyl α-fluorophenylacetate with diphenylmethyl bromide in hexamethylphosphoramide–benzene.

When the diazoalkane decomposition was conducted in the n.m.r. probe and the ^{19}F spectrum (56.4 MHz) scanned, two sets of polarised signals were observed (Figure 1). The more intense group, 466 Hz downfield from the solvent doublet at 120 °C, corresponded in

[8] For reviews, see 'Chemically Induced Magnetic Polarization,' eds. A. R. Lepley and G. L. Closs, Wiley, New York, 1973; D. Bethell and M. R. Brinkman, *Adv. Phys. Org. Chem.*, 1973, **10**, 53; C. Richard and P. Granger, 'Chemically Induced Dynamic Nuclear and Electron Polarization—CIDNP and CIDEP,' Springer Verlag, Berlin, 1974; R. Kaptein, *Adv. Free Radical Chem.*, 1975, **5**, 319.

chemical shift (both in the polarised state at 120 °C and in the depolarised state at *ca.* 40 °C) and coupling constant ($^3J_{HF}$ 32 Hz) with methyl 2-fluoro-2,3,3-triphenylpropionate. The pattern of polarisation of the insertion product is A + E/A, corresponding to a combination product of the radical pair (Ph$_2$CH· ·CFPhCO$_2$Me) resulting from hydrogen atom abstraction by triplet diphenylmethylene or from random encounter by free diphenylmethyl and α-fluoro-α-methoxycarbonylbenzyl
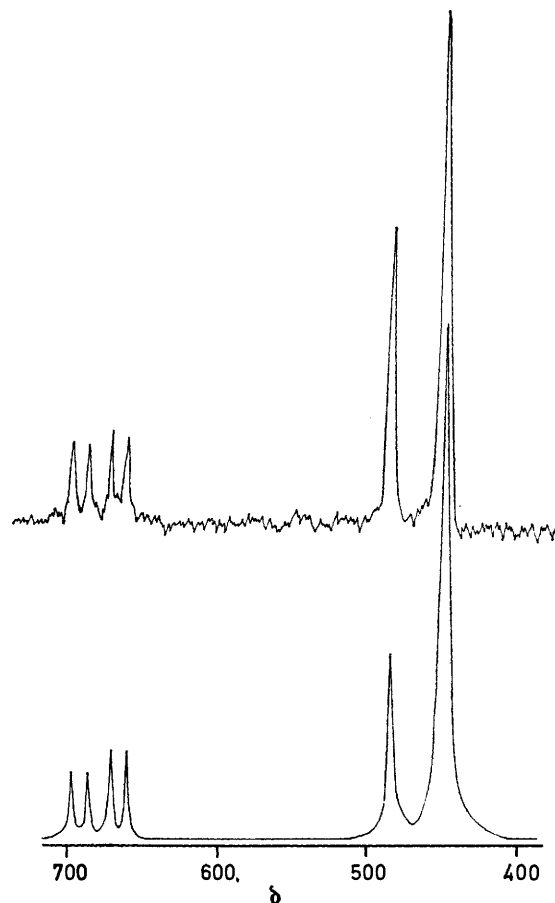

FIGURE 1   Polarised signals observed in the 56.4 MHz ^{19}F n.m.r. spectrum during thermal decomposition of diazodiphenylmethane (1M) in methyl α-fluorophenylacetate at 120 °C; simulated spectrum shown below; shifts in Hz downfield from the solvent doublet at 120 °C

radicals. The Kaptein analysis in both cases yields

$$\Gamma_{net} = \mu\varepsilon a_F \qquad \Delta g = + + + + = + = A, \qquad \text{and}$$

$$\Gamma_{multiplet} = \mu\varepsilon a_F a_H{}^3J_{HF}\sigma = + + + - + - = + =$$

E/A. That the insertion product arises almost entirely from the geminate triplet pair rather than the diffusive pair is shown by the small (though significant) reduction in the intensity of the polarised signals when the reaction was carried out in the presence of the free radical scavenger phenyl t-butyl nitrone[11] (0.2M; 0.4M scavenger caused no further reduction in intensity). This contrasts with the marked reduction of the polarised signals due

[9] U.-H. Dolling, G. L. Closs, A. H. Cohen, and W. D. Ollis, *J.C.S. Chem. Comm.*, 1975, 545.

to 1,2,2-triphenylethyl fluoride in the reaction of diphenylmethylene with benzyl fluoride.[10] Examination of reaction mixtures containing phenyl t-butyl nitrone by electron paramagnetic resonance spectroscopy showed intense signals attributable to nitroxide radicals (Figure 2). The pattern of splitting of the main lines indicates
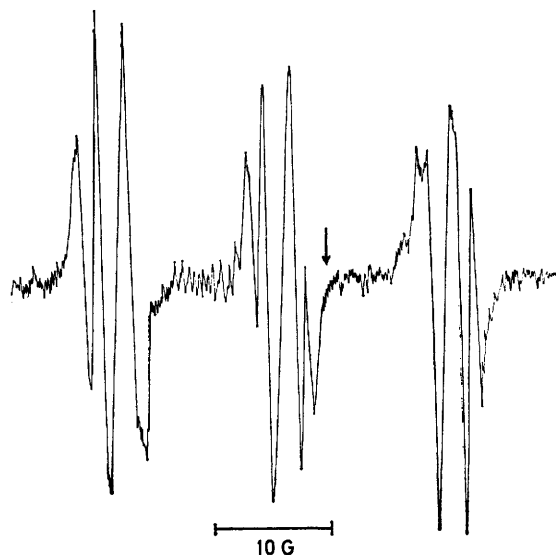

FIGURE 2 Electron paramagnetic resonance spectrum (microwave frequency 9.030 GHz; modulation frequency 100 kHz) of adduct radicals obtained on decomposition at 130 °C of diazodiphenylmethane (1M) in methyl α-fluorophenylacetate containing phenyl t-butyl nitrone (0.2M); arrow indicates 3 230 G

the presence of two radicals of virtually identical g value, one having a_N 14.9 and a_H 4.8 G and the other a_N 14.4 and a_H 2.4 G. These are attributable to the radicals (1) and (2) respectively.
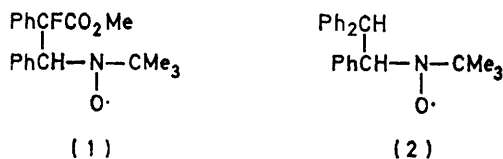
Introduction of *para*-substituents into diphenylmethylene by the use of substituted diazoalkanes modifies the observed polarisation in a manner analogous to that observed in studies of insertion into benzyl fluoride. Thus progression down the halogen series, by increasing the g factor of the diarylmethyl component of the radical pair, led to a change in polarisation from $A + E/A$ to $E + E/A$ as indicated by the results in Table 1. Simulation (by using den Hollander's program) of the polarised spectra of the insertion products from diphenylmethylene, bis-(4-chlorophenyl)methylene, and bis-(4-bromophenyl)methylene, by using the known g values for the diarylmethyl radicals,[12] gave a value of

[10] D. Bethell, M. R. Brinkman, J. Hayes, and K. McDonald, *J.C.S. Perkin II*, 1976, 966.

[11] E. G. Janzen, *Accounts Chem. Res.*, 1971, **4**, 31.

2.003 70 for the g factor of the α-fluoro-α-methoxycarbonylbenzyl radical.

In four cases (see Table 1) the proton polarisation of the insertion product was also recorded. Despite a

TABLE 1

Patterns of polarisation of methyl 3,3-diaryl-2-fluoro-2-phenylpropionates $(XC_6H_4)(YC_6H_4)CH\cdot CFPh\cdot CO_2Me$ at 120 °C

		Pattern of polarisation *a*			
X	Y	F *b*	Δδ_F/Hz	H *c*	Δδ_H/Hz
H	H	A A		EA	
H	2-F	A A/AA *d*	24	*e*	
H	4-F	A A/AA	9	*e*	
H	2-Cl	A A/AA	14	EA/EA	15
4-Cl	4-Cl	A A		EA	
H	2-Br	EA/EA	10	EA/EA	17
H	4-Br	EA/EA	6	*e*	
4-Br	4-Br	EE		*e*	

a The more intense line is shown in bold type. *b* 56.4 MHz. *c* 60 MHz. *d* Each line shows an additional 2 Hz splitting. *e* Not recorded.

substantial variation of Δg, almost perfect multiplet polarisation (E/A) was found. This differential behaviour is exactly analogous to that found in insertions into benzyl fluoride, and its origin has been discussed previously.

The minor group of polarised signals consisted of four lines centred 678 Hz downfield from the solvent doublet at 120° (Figure 1). The lines were of unequal intensity, the two lines at lowest field being less intense than the two high-field lines. We interpret these signals as due to two overlapping doublets with vicinal HF splitting ($^3J_{HF}$ 25 Hz) showing identical $A + E/A$ polarisation. Because of the close similarity of chemical shift, it seems probable that the two doublets arise from a pair of diastereoisomers. Spectral accumulation on the mixture at the end of the reaction showed no depolarised signals corresponding to these two doublets. We conclude that the species responsible for the less intense polarised signals is a metastable product which decomposes under the reaction conditions.[13] G.l.c. analysis of the mixture at the end of the reaction showed no products other than that from benzylic insertion, benzophenone and its azine, tetraphenylethane, and tetraphenylethylene.
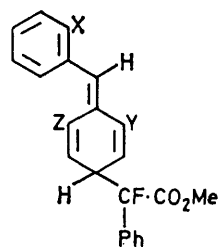
The introduction of substituents into the diphenylmethylene causes significant changes (Figure 3) in the minor group of polarised signals which are suggestive of the structure of the metastable product. A single *para*-fluoro-substituent does not affect the pattern except that the maximum intensity of the polarised signals is much lower than in the unsubstituted case. Two *p*-chloro-substituents, however, eliminate the minor polarisation completely. Introduction of an *ortho*-halogeno-substituent gives signals of the intensity observed in the

[12] G. L. Closs, ' Special Lectures Presented at the XXIIIrd International Congress of Pure and Applied Chemistry,' Boston, 1971, vol. 4, Butterworths, London, p. 19.

[13] *Cf.* D. Bethell, M. R. Brinkman, and J. Hayes, *J.C.S. Chem. Comm.*, 1972, 1324.

unsubstituted case but now some eight lines are detectable. From these observations we conclude that the minor polarisation arises from the same radical pair that is responsible for the polarised benzylic C–H insertion product, but combined by bonding between the benzylic carbon of the fluorine-bearing radical and the *para*-carbon atom of one of the aromatic rings of the diarylmethyl radical as shown in (3). Such a product would consist of an equal mixture of two diastereoisomers since it contains two chiral centres. If we assume that any *ipso*-attack is not detected, then one *para*-substituent should reduce the intensity of polarised signals since the number of sites for *para*-recombination is halved, and two

FIGURE 3 Patterns observed in the minor group of polarised ^{19}F signals (56.4 MHz) when substituted diazodiphenylmethanes were decomposed in methyl α-fluorophenylacetate at 120 °C: (a) diazodiphenylmethane; (b) diazo-(4-fluorophenyl)-phenylmethane; (c) diazo-(2-fluorophenyl)phenylmethane; (d) 2-chlorophenyl(diazo)phenylmethane; spectra recorded under identical conditions; shifts in Hz downfield from the solvent doublet at 120 °C

para-substituents should eliminate the polarisation. An *ortho*-substituent leaves both *para*-positions free for reaction, but three different products could result, viz.

(3b—d), each a diastereoisomeric pair. Of these, (3d) seems least likely to be formed appreciably on steric grounds, and we suggest that the eight lines observed are due to the products (3b and 3c).

(3) a; X = Y = Z = H
b; X = Cl or F, Y = Z = H
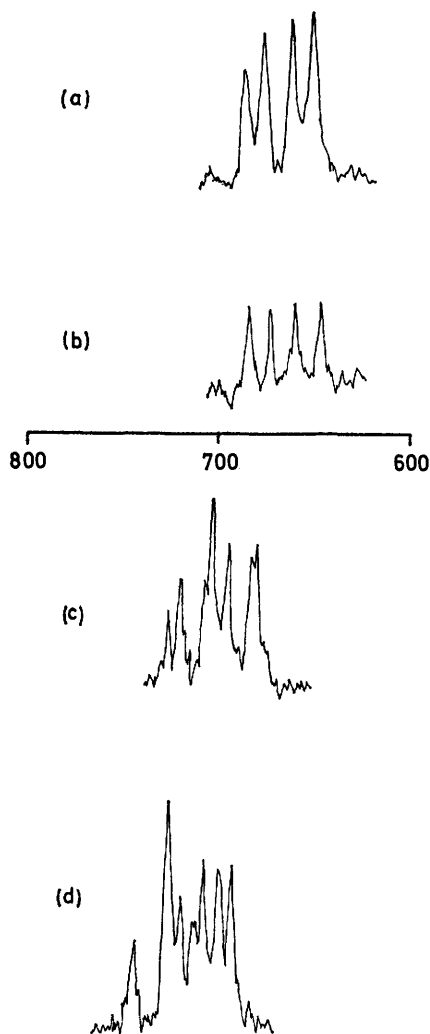c; X = Z = H, Y = Cl or F
d; X = Y = H, Z = Cl or F

Kaptein's rules again predict A + E/A polarisation and further support for this interpretation comes from computer simulation of the polarised signals. By using the parameters which permit the simulation of the polarised benzylic insertion product but substituting a_H —3.0 G for the *para*-hydrogen atom in the diphenylmethyl radical [14] for a_H —8.3 G, the value of the α-hydrogen atom, and with $^2J_{HF}$ 25 instead of 32 Hz, the minor polarisation was accurately reproduced.

Insertion into 1-*Methylheptyl,* *Bornan*-2-endo-*yl,* and p-*Menthan*-3-yl α-*Fluorophenylacetates.*—Esterification of α-fluorophenylacetic acid with the chiral alcohols 1-methylheptanol, bornan-2-*endo*-ol, and *p*-menthan-3-ol gives in each case a mixture of equal amounts of two diastereoisomeric esters having different ^{19}F chemical shifts.

Decomposition of diazodiphenylmethane in such mixtures at 135 °C gave again two sets of polarised signals in the ^{19}F spectrum. The set of lower intensity approximated in chemical shift to the less intense polarised signals in the reaction of diazodiphenylmethane with methyl α-fluorophenylacetate, but consisted of eight lines. This is as expected on the basis of a structure of type (3), since a third chiral centre is now present. The major polarisation had a chemical shift corresponding to the benzylic C–H insertion product. In the case of the diastereoisomeric *p*-menthan-3-yl esters, two clearly resolved doublets, one for each diastereoisomer were observed, and these were formed and polarised to the same extent. In the case of the diastereoisomeric 1-methylheptyl and bornan-2-*endo*-yl esters, there was accidental coincidence of the low-field line of one doublet and the high-field line of the other at the temperature which maximised the polarised signals (135 °C). The intensities of polarisation in the two diastereoisomeric insertion products were thus difficult to compare, but the relative intensity of the resolved lines (the low-field line of one diastereoisomer and the high-field line of the other) was the same as for the two polarised lines of methyl 2-fluoro-2,3,3-triphenylpropionate, indicating equal intensities for the isomeric products. At probe temperature (ca. 40 °C) the overlapping lines of the diastereoisomeric

[14] D. R. Dalton and S. A. Liebman, *J. Amer. Chem. Soc.*, 1969, **91**, 1194.

products are resolved and the two compounds could be seen to be formed in equal amounts. The diastereo-isomers from insertion into the *p*-menthan-3-yl ester have ¹⁹F n.m.r. signals which overlap at 40 °C.

α-Fluorophenylacetic acid was resolved through its (—)-ephedrine salt. Esterification of the enantiomers with optically pure alcohols gave single diastereoisomers, and these were used as solvents for the decomposition of diazodiphenylmethane at 135 °C. Patterns of ¹⁹F polarisation are shown in Figure 4, together with the spectrum of the depolarised insertion products recorded by accumulation at the end of the reaction. In each case the pattern of polarised signals for insertion into a single diastereoisomer is the same as that for the mixture of diastereoisomers, indicating that in all cases the polarised signals came from the product of insertion with equal amounts of retention and inversion at the reaction centre. However, the depolarised n.m.r. spectrum of the products from the 1-methylheptyl esters when the reaction was complete indicated that the diastereoisomeric insertion products are formed in unequal amounts; we estimate the product ratio to be
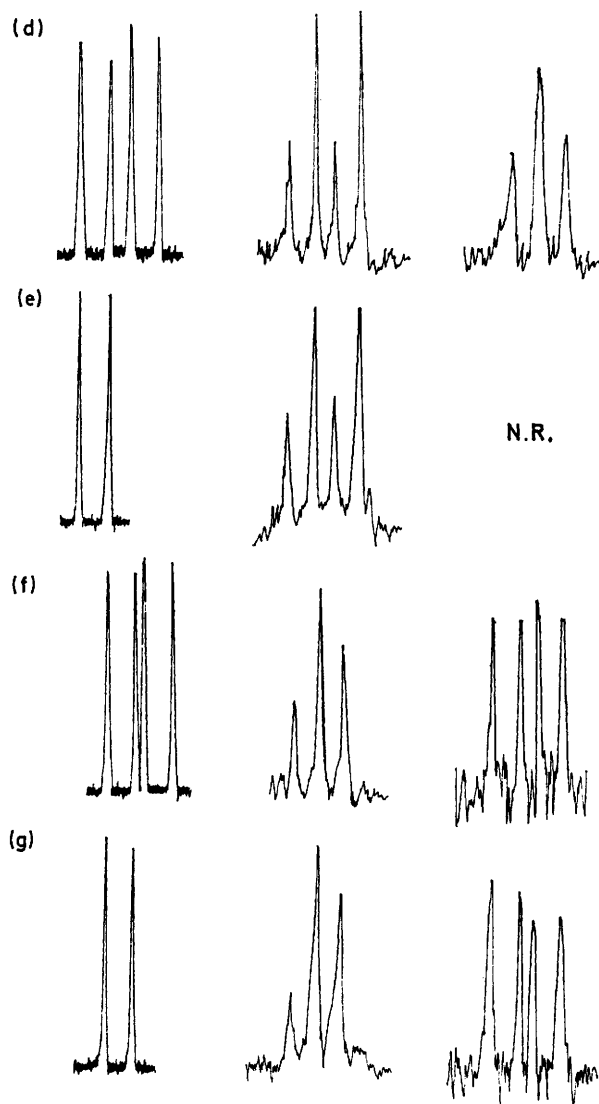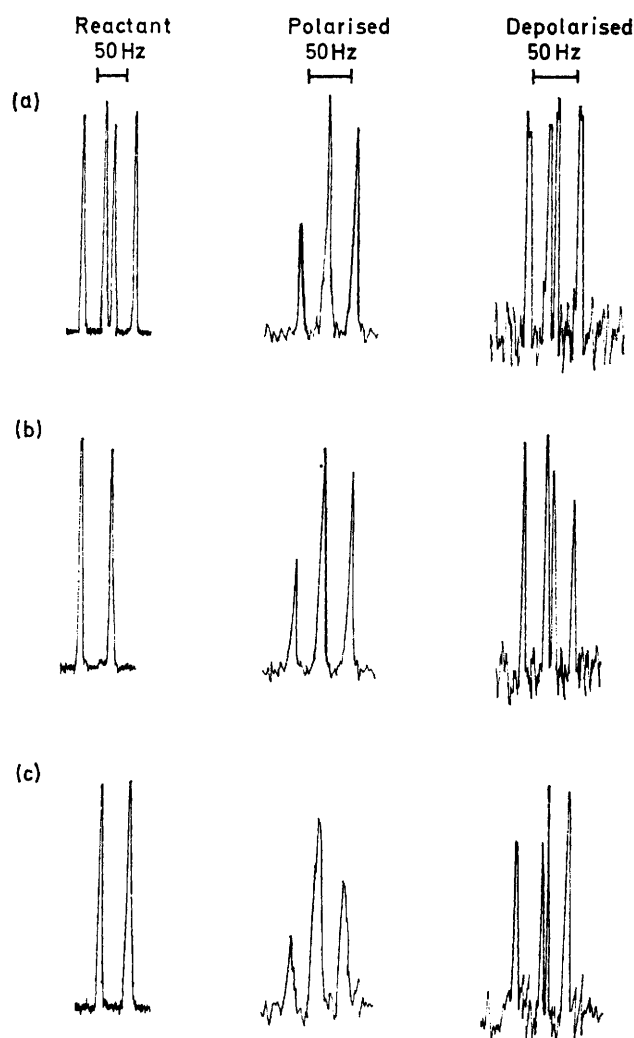

Figure 4   ¹⁹F N.m.r. signals (56.4 MHz) of reactant esters (probe temperature), polarised insertion product (135 °C), and depolarised insertion products (accumulation of 200—250 scans at probe temperature) in the thermal decomposition of diazodiphenylmethane at 135 °C in α-fluorophenylacetates of chiral alcohols: (a) (±)-1-methylheptyl (±)-α-fluorophenyl-acetate;   (b) (—)-1-methylheptyl (—)-α-fluorophenylacetate;   (c) (—)-1-methylheptyl (+)-α-fluorophenylacetate;   (d) (—)-*p*-menthan-3-yl (±)-α-fluorophenylacetate; (e) (—)-*p*-menthan-3-yl (—)-α-fluorophenylacetate;   (f) (—) bornan-2-*endo*-yl (±)-α-fluorophenylacetate;   (g) (—)-bornan-2-*endo*-yl (—)-α-fluorophenylacetate;   N.R. = not recorded

55 : 45. Moreover, the major insertion product is different for diastereoisomerically different reactant esters. This rules out the possibility that asymmetric induction is responsible. Since the reactant ester having ¹⁹F signals at lower field gives more of the insertion product having its ¹⁹F signals at lower field and *vice versa*, we presume that in the overall reaction the ratio of retention to inversion at the reaction centre is 55 : 45. We are confident that we would have detected such a preference in the polarised signals had it existed.

For purposes of comparison, diazodiphenylmethane

was decomposed photochemically at 311 nm (interference filter) by using benzophenone sensitisation at room temperature in one diastereoisomeric 1-methylheptyl ester as solvent. The product showed much less preference for insertion with retention than that from the thermal decompositions, being close to a 50:50 mixture.

In another experiment, diazophenylmethane was decomposed in the methyl ester. No polarisation was observed.

DISCUSSION

Stereochemistry of the Polarised Product.—The present evidence shows unequivocally that the combination of the components of the polarising radical pair in the present reactions takes place without any stereochemical preference. The polarised signals in each case correspond to complete loss of stereochemistry at the reaction centre. In these experiments the radical pairs are almost all geminate rather than pairs formed by diffusive encounter of free radicals in which the stereochemistry of the reactant would necessarily have been lost. It is clear then that even in the geminate pair the components separate sufficiently so that their re-encounter and combination is without stereochemical preference. This result provides support for Gerhart and Wilde's similar conclusion from studies of the rearrangement of diastereoisomeric 2-alkoxyquinoline N-oxides.[15] Unlike their experiments, ours demonstrate that the enhancement factors for the two diastereoisomers are indistinguishable. Moreover, the relative line intensities of our polarised spectra are not distorted by the admixture of appreciable intensity from depolarised products.

This finding provides direct justification of the diffusive model of the radical pair [16] in which the components are believed to undergo *ca.* 10^2 displacements during the lifetime of the pair. On the random walk model, the maximum separation of the components would thus be of *ca.* ten molecular diameters of the solvent, and this is consistent with our stereochemical finding.

Mechanistic Considerations.—The intense CIDNP signals observed in both the ^{19}F and ^{1}H n.m.r. spectra and the predominant loss of stereochemistry at the benzylic carbon atom indicate that the major route for insertion of diarylmethylenes into the benzylic C–H bond of α-fluorophenylacetates is by hydrogen atom abstraction by the carbene in its triplet electronic state. The experiments with phenyl t-butyl nitrone demonstrate further that a small proportion of the radicals generated by this pathway become free and later combine, yielding insertion product polarised in the same sense as the combination product from the geminate pairs and again showing complete loss of stereochemistry.

It remains to explain the small excess of insertion with retention of configuration, but without generation of polarised signals. There seem to us to be two possible interpretations of this, the second of which we prefer.

The less probable interpretation of this part of the reaction is that *ca.* 10% of the triplet pairs generated as discussed above remain trapped for their whole lifetime within a solvent cage.[17] Singlet–triplet mixing would have to occur within the solvent cage while the two odd electrons are strongly coupled, an unlikely process but one not wholly without precedent.[18] It would be necessary that the singlet–triplet mixing process under these circumstances should not give rise to nuclear polarisation, and this seems reasonable if the electron–nucleus coupling is much less strong than the electron–electron coupling in the radical pair.

An altogether simpler and more satisfying interpretation of the retention is that it occurs by way of the singlet carbene. This electronic state has available to it a concerted pathway for insertion, *via* a three-centre transition state, which of necessity would lead to retention of configuration without nuclear polarisation.[2] Since singlet and triplet electronic states of diphenylmethylenes are known to undergo equilibration rapidly in comparison with intermolecular reactions of either state, it is evident that the balance between insertion with retention and inversion at the reaction centre is determined by the position of equilibrium between the two states and by the activation energies for concerted insertion and hydrogen abstraction. Consistently, diazophenylmethane, which would yield phenylmethylene, a carbene which adds to olefins with a high degree of *cis*-stereospecificity,[19] although singlet and triplet states are again believed to undergo equilibration,[20] shows no polarisation when decomposed thermally under our conditions.

The results of the photochemical experiment can be tentatively interpreted in terms of our theory. Benzophenone sensitisation should lead to the generation of diphenylmethylene in its triplet electronic state initially. If there were no intersystem crossing of diphenylmethylene, we would anticipate complete loss of stereochemistry in the insertion product. That little or no retention of configuration at the benzylic centre is observed is consistent with this, but could merely indicate a change in the balance between singlet and triplet diphenylmethylene reactions at the photochemical reaction temperature which is *ca.* 100 °C lower than that of the thermal decompositions. These considerations point the way to further experiments.

EXPERIMENTAL

Methyl α-*Fluorophenylacetate.*[21]—Methyl phenylacetate was brominated with N-bromosuccinimide and the bromine

[15] F. Gerhart and L. Wilde, *Tetrahedron Letters*, 1974, 475.
[16] F. J. Adrian, *J. Chem. Phys.*, 1970, **53**, 3374; 1971, **54**, 3912.
[17] J. P. Lorand, *Progr. Inorg. Chem.*, 1972, **17**, 207.
[18] S. A. Weiner, *J. Amer. Chem. Soc.*, 1971, **93**, 425.

[19] C. D. Gutsche, G. L. Bachman, and R. S. Coffee, *Tetrahedron*, 1962, **18**, 617; G. L. Closs and R. A. Moss, *J. Amer. Chem. Soc.*, 1964, **86**, 4042; P. Scheiner, *J. Org. Chem.*, 1969, **34**, 199.
[20] R. A. Moss and U.-H. Dolling, *J. Amer. Chem. Soc.*, 1971, **93**, 954.
[21] B. Cavalleri, E. Bellasio, G. G. Gallo, and E. Testa, *Il Farmaco, Ed. Sci.*, 1968, **23**, 1127.

displaced by heating the α-bromo-ester with potassium fluoride in acetamide at 120 °C; the product had b.p. 139° at 46 mmHg (lit.,[21] 125—128° at 24 mmHg). The ^{19}F spectrum (56.4 MHz) of the neat ester showed a doublet ([2]J_{HF} 48 Hz) 5 544 Hz upfield from $CF_3 \cdot CCl_3$.

α-*Fluorophenylacetic Acid*.—The methyl ester was hydrolysed with potassium hydroxide in methanol, and the potassium salt (m.p. 217—219°) acidified with hydrochloric acid; the product had m.p. 85—86° (lit.,[21] 85—87°). The racemic acid was resolved through its (—)-ephedrine salt, one diastereoisomer of which was much less soluble in absolute ethanol than the other. After three recrystallisations the salts had $[\alpha]_D^{23}$ −84.3° (c 2.48 in MeOH) and

and the mixture stirred overnight. The *ester* was obtained as crystals from light petroleum–chloroform; m.p. 165—167°; *M* 334 (mass spec.) (Found: C, 78.6; H, 5.7. $C_{22}H_{19}FO_2$ requires C, 79.0; H, 5.7%).

Product Analyses.—Analyses were carried out by g.l.c. (Pye-Unicam 104 dual-head gas chromatograph with flame ionisation detector, fitted with a 2 m × 5 mm glass column packed with 5% OV1 on GasChrom Q). Triphenylmethane was used as calibration standard.

CIDNP.—The techniques used were as previously described.[10] Reaction temperatures were chosen so as to maximise the polarised signals, and the esters were used both as solvent and reactant. Depolarised spectra of

TABLE 2

Physical and analytical data for α-fluorophenylacetates of chiral alcohols

	Stereochemistry				Found (%)		Required (%)	
Alkyl group	Acid	Alcohol	B.p. (°C) [mmHg]	$[\alpha]_D^{25}$(°) [c] [a]	C	H	C	H
CHMeC$_6$H$_{13}$	±	±	120—122 [0.5]		71.9	8.6	72.2	8.7
	−	−	99—101 [0.2]	−69.6 [2.12]	72.1	8.5	72.2	8.7
	+	−	127—128 [0.6]	+27.7 [2.57]	71.9	8.7	72.2	8.7
p-Menthan-3-yl	±	−	154—156 [2]	−68.7 [2.11]	74.0	8.7	73.9	8.6
	−	−	132—133 [b] [0.5]	−113.6 [2.07]	73.8	8.7	73.9	8.6
Bornan-2-endo-yl	±	−	153—154 [2]	−17.4 [2.30]	74.6	8.2	74.5	8.0
	−	−	130—132 [0.5]	−59.7 [2.12]	74.2	8.1	74.5	8.0

[a] In acetone.   [b] M.p. 37—38°.

+26.7° (c 5.06 in MeOH), and on acidification with hydrochloric acid (1M) afforded, respectively, (−)-α-*fluorophenylacetic acid*, m.p. 103—105°, $[\alpha]_D^{23}$ −153.5° (c 1.52 in Me$_2$CO) (Found: C, 62.6; H, 4.6. $C_8H_7FO_2$ requires C, 62.3; H, 4.6%), and (+)-α-*fluorophenylacetic acid*, m.p. 99—101°, $[\alpha]_D^{23}$ 136.5° (c 1.45 in Me$_2$CO) (Found: C, 62.4; H, 4.6%).

Esters of α-Fluorophenylacetic Acid with Chiral Alcohols.—α-Fluorophenylacetyl chloride was prepared from the acid (racemic or resolved) by refluxing with thionyl chloride in benzene. The racemic acid chloride had b.p. 47—49° at 0.8 mmHg, but was normally used without distillation. Esterification was carried out in carbon tetrachloride solution in the presence of dry pyridine (1 equiv.), and the product was fractionated. Physical and analytical data for the esters prepared are in Table 2.

Methyl 2-Fluoro-2,3,3-triphenylpropionate.[22]—The sodio-derivative of methyl α-fluorophenylacetate was prepared under nitrogen by using sodium hydride in hexamethyl-phosphoramide–benzene (50 : 50 v/v). Diphenylmethyl bromide (1 equiv.) in the same solvent was added at 0 °C,

reaction mixtures were obtained by accumulation of ca. 200 scans.

Spin Trapping Experiments.—Phenyl t-butyl nitrone was used as the spin trap. In separate kinetic experiments it was established that the nitrone did not significantly alter the rate of decomposition of diazodiphenylmethane. The intensity of polarised signals was monitored in the presence of 0.2M- and 0.4M-nitrone; the intensity was the same in both experiments but was slightly less than in the absence of the spin trap. The electron paramagnetic resonance spectrum was recorded on reaction mixtures identical with those from the CIDNP experiments (Varian E4 spectrometer).

[22] R. Fraisse-Jullien and N. Thoi-Lai, *Bull. Soc. chim. France*, 1967, 3904.