Chemically Induced Dynamic Polarisation of ^{19}F Nuclei in the Dimerisation of α-Fluorobenzyl Radicals

By **Donald Bethell,*** **Max R. Brinkman, John Hayes, R. Angus Hearmon, Kenneth McDonald,** and **K. Sundarraja Rao,** The Robert Robinson Laboratories, The University, P.O. Box 147, Liverpool L69 3BX

Generation of α-fluorobenzyl radicals during thermal decomposition of diazodiphenylmethanes or benzoyl peroxide in benzyl fluoride as solvent or in the decomposition of t-butyl α-fluorophenylperacetate gives rise *inter alia* to *meso* and (±)-difluorobibenzyl. However, CIDNP observed in ^{19}F-spectra does not appear to match the pattern of signals of these products. The inference, in a preliminary report, that the dimerisation takes place in two stages, a head-to-tail co-ordination giving a semibenzene followed by rearrangement, is shown to be incorrect. Examination of the effect on the pattern of ^{19}F-polarisation of introducing deuterium into the phenyl ring and into the side-chain of α-fluorobenzyl radicals indicates that the predominant mode of dimerisation must be head-to-head giving directly *meso*- and (±)-1,2-difluoro-1,2-diphenylethanes. This conclusion is confirmed by computer simulation of the polarised spectrum.

IN the course of studies[1] of ^{19}F polarisation during benzylic insertion of substituted diphenylmethylenes into solvent benzyl fluoride we observed that, accompanying the polarised signals of the insertion product, there appeared a second group of polarised signals some 1 280 Hz downfield from the triplet due to the solvent. The pattern of signals was quite independent of the substituents present in the carbene and was ascribed to the product of dimerisation of fluorobenzyl radicals generated during the reaction. In our preliminary report of this observation[2] it was pointed out that the polarised signals showed a pattern which appeared significantly different from that of the head-to-head dimers, the 1,2-difluoro-1,2-diphenylethanes, formed by α,α-coupling, and a two-stage mechanism was proposed. In this mechanism, it was thought that the benzylic carbon of one radical attacked the aromatic ring of a second radical to give a polarised semibenzene (methylenecyclohexadiene) and that this product subsequently rearranged to give the normal dimer. There is ample precedent for both the head-to-tail combination of arylmethyl radicals[3] and the rearrangement of semibenzenes[4] and indeed ^{1}H CIDNP evidence has recently been reported[5] which showed that head-to-tail dimerisation (α,*o*- and α,*p*-coupling) of simple benzyl radicals generated by photolysis of dibenzyl ketone occurs in competition with α,α-coupling. We have also previously presented ^{19}F CIDNP evidence for α,*p*-coupling between α-alkoxycarbonyl-α-fluoro-benzyl radicals and diphenylmethyl radicals.[6]

We now report our observations on the dimerisation of α-fluorobenzyl radicals in detail and with the aid of results from reactions with deuterium-labelled radicals and computer simulation show that, despite appearances, the polarised signals observed when α-fluorobenzyl radicals dimerise are due only to the normal head-to-head dimers.

RESULTS AND DISCUSSION

Thermal decomposition of diazodiarylmethanes (*ca.* 1M) in solvent benzyl fluoride in the temperature range 120—135 °C gives considerable amounts of benzophenone azine, the product of insertion of the intermediate diarylmethylene into the benzylic C–H bond of the solvent, 1-phenyl-2,2-diarylethyl fluoride, and a small amount, typically 2% by g.l.c. analysis, of 1,2-difluoro-1,2-diphenylethane (difluorobibenzyl).[1] ^{19}F N.m.r. spectroscopy of the reaction products and g.l.c. analysis with comparison with authentic material prepared either by catalytic hydrogenation of *trans*-1,2-difluorostilbene or by treatment of 2-fluoro-1,2-diphenylethanol with fluoramine reagent identified the product as a 1 : 1 mixture of *meso*- and (±)-diastereoisomers. Figure 1(a) shows the spectrum of an authentic mixture of the two diastereoisomers in benzyl fluoride as solvent, and Figure 1(b) shows the spectrum in (−)-bornyl acetate which indicates by the additional splitting that the multiplet at lower field is due to the (±)-diastereoisomer. The spectrum of the reaction products obtained by accumulation is in Figure 2(a). The ^{19}F-spectrum of each diastereoisomer presents the expected pattern of AA′XX′ systems of nuclei.[7]

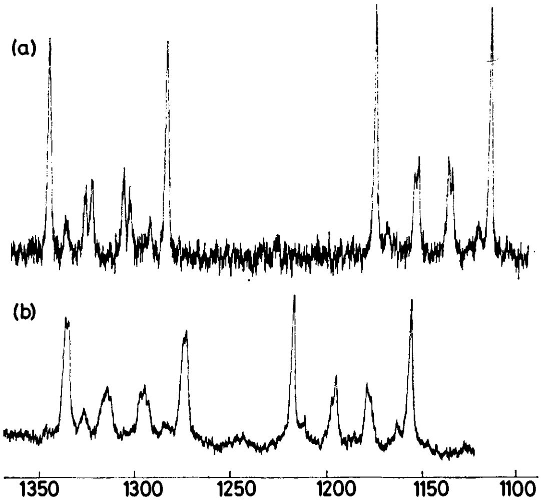

FIGURE 1 ^{19}F N.m.r. spectrum of a mixture of authentic specimens of *meso*- and (±)-1,2-difluoro-1,2-diphenylethanes in (a) benzyl fluoride and (b) (−)-bornyl acetate at normal probe temperature. The scale is in Hz downfield from benzyl fluoride

The same mixture of diastereoisomers was also obtained when benzoyl peroxide (0.1M) was thermally decomposed in solvent benzyl fluoride at 110 °C or when t-butyl α-fluorophenylperacetate decomposed in chlorobenzene at the same temperature. The difluorobibenzyls were the major constituent of the product mixture in these reactions.

When the diazodiphenylmethane decomposition in solvent benzyl fluoride was conducted in the probe of an n.m.r. spectrometer operating at 56.4 MHz and the ^{19}F-spectrum was observed during the course of the decomposition, polarised signals (CIDNP) were observed.[1] In the ^{19}F-spectral region where the difluorobenzyls are observed, *ca.* 1 280 Hz downfield from the benzyl fluoride triplet, the pattern of polarised signals shown in Figure 2(b) was recorded. No corresponding ^{1}H- or ^{13}C-polarisation could be detected. The pattern of ^{19}F-polarisation, a pure E/A multiplet, was unchanged when substituted diazodiphenylmethanes were used, and when the peroxides mentioned above were decomposed. It is concluded that the polarisation arises from the dimerisation of fluorobenzyl radicals. Since, when reactions are carried out in the presence of the diamagnetic free-radical scavenger phenyl t-butyl nitrone,[1,6] this group of polarised signals is suppressed, it is further inferred that the polarised product comes from a symmetrical pair formed by diffusive encounter of free fluorobenzyl radicals.

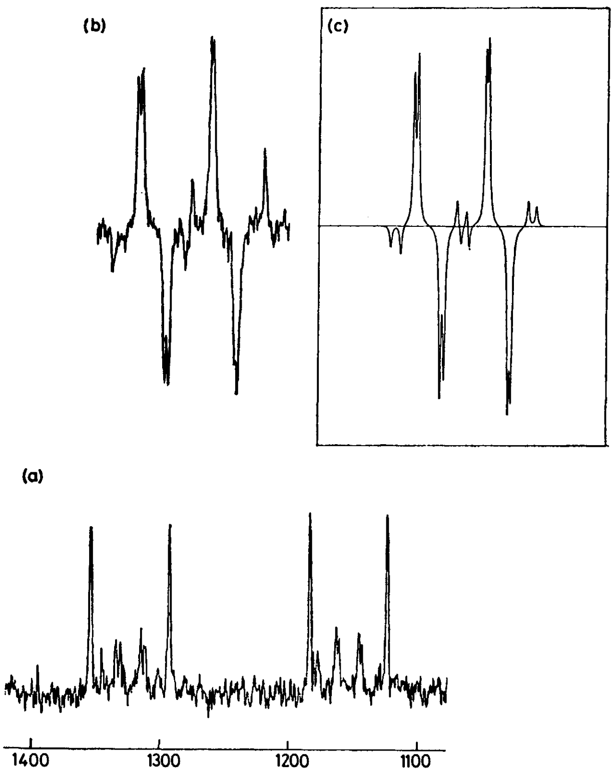

FIGURE 2 (a) Typical ^{19}F n.m.r. spectrum of difluorobibenzyls obtained from decomposition of diazodiarylmethanes in benzyl fluoride solvent at 120 °C. The spectrum is the computer average of 100 scans at normal probe temperature of the product from decomposition of diazo-2-fluorodiphenylmethane. The scale markings are in Hz downfield from the solvent triplet. (b) ^{19}F-CIDNP observed in the decomposition of diazodiphenylmethane in benzyl fluoride at 120 °C on the same scale as (a). (c) Simulated ^{19}F-CIDNP for a 1 : 1 mixture of *meso-* and (±)-1,2-difluoro-1,2-diphenylethanes using hyperfine splitting constants from Figure 3 and nuclear–nuclear coupling constants from the Table

The symmetrical appearance of the polarised signals led us to believe that they were due to two closely similar compounds, probably a pair of diastereoisomers, and this was confirmed in two ways. An experiment conducted in a ^{19}F n.m.r. spectrometer at 94.1 MHz led to a polarised spectrum similar to that in Figure 2 but, though less intense, clearly resolved into two similar but now well separated E/A multiplets. Then, in the perester decomposition in 1,2,4-trichlorobenzene solvent, the group of polarised signals became much more compressed than in chlorobenzene. However, the quite different appearance of the polarised spectrum from the two AA'XX' systems of *meso-* and (±)-difluorobibenzyl led us to believe that the polarisation was due to an intermediate dimer formed by coupling of the α-carbon atom of one fluorobenzyl radical with a ring carbon atom (*o*- or *p*-) of another. This intermediate was thought to rearrange to the head-to-head (αα) dimer 1,2-difluoro-1,2-diphenylethane under the reaction conditions. Both α*o*- and α*p*-coupling would give diastereoisomeric products although in the case of α*o*-coupling additional geometrical isomerism would be possible about the exocyclic double bond. Such head-to-tail products should give rise to polarised fluorine signals from the benzylic fluorine and the olefinic fluorine of which we believed the signals in Figure 2 to be due to the former. In the olefinic region we were unable to detect with certainty polarised fluorine signals which could be ascribed to the dimer. However, the polarisation in the benzylic region could be assigned to head-to-tail dimerisation since this would give rise to an ABX system of nuclei of which the X-part (^{19}F) would be expected to consist of four (or six) lines. The 2—3 Hz splitting observed in the most intense lines might be ascribed to the long-range fluorine–fluorine coupling in the head-to-tail dimer since a similar effect had been observed in the polarised ^{19}F-spectrum of 2-(*o*-fluorophenyl)-1,2-diphenylethyl fluoride;[1] consequently α*o*-coupling was the preferred interpretation of the polarisation of the fluorobenzyl dimer since such a dimer could also have a 5-bond F–F coupling.

Two lines of evidence make it clear that our preliminary suggestion is incorrect. Firstly, attempts to simulate the polarised spectrum of the α*o*-dimer using den Hollander's CIDNP simulation program with hyperfine splitting constants for the fluorobenzyl radical obtained by INDO calculation (see Figure 3) failed to reproduce the observed pattern of polarised signals. In all cases, whether a 5-bond F–F nuclear–nuclear coupling was included or not, the predicted pattern was A/E multiplet polarisation, the reverse of observation. We were, however, able to reproduce satisfactorily the polarisation observed when the triplet 2-fluorodiphenylmethyl-α-fluorobenzyl radical pair collapses to give the

2-(*o*-fluorophenyl(1,2-diphenylmethyl fluorides, as shown in Figure 4, using ${}^5J_{FF} = 3$ and 1.2 Hz.

The second line of evidence comes from the ${}^{19}F$-polarisation observed when benzoyl peroxide was decomposed in benzyl fluoride deuteriated either in the α-position ($C_6H_5CD_2F$ and $C_6H_5 \cdot CHDF$) or in the aromatic ring ($C_6D_5 \cdot CH_2F$). In the former case no appreciable polarisation was detectable; use of diazodiphenylmethane (1M) in place of benzoyl peroxide gave weak polarisation in the dimer region with C_6H_5CHDF as solvent, but the intensity was so low that the pattern of polarised signals could not be made out with certainty. Experiments using $C_6D_5 \cdot CH_2F$ as solvent and benzoyl peroxide gave polarised ${}^{19}F$-signals of satisfactory intensity and these were in every respect identical with those observed using $C_6H_5 \cdot CH_2F$. This observation clearly excludes α-ring coupling since the vicinal H–F and H–H couplings would have been replaced by smaller D–F and D–H couplings with a consequent drastic change in signal pattern. It is unreasonable to attribute the signals observed with $C_6D_5 \cdot CH_2F$ to reaction at the small number (*ca.* 2%) of undeuteriated ring positions present in the solvent; this would require an impossibly large secondary deuterium isotope effect. We conclude therefore that the dimerisation of α-fluorobenzyl radicals is a single step αα-coupling.

Simulation of the CIDNP spectrum for αα-coupling of fluorobenzyl radicals confirms that, despite appearances, the polarised signals are due to two AA'XX' multiplets. The simulation, shown in Figure 2(c), used the hyperfine splitting constants from Figure 3 together with the nuclear–nuclear coupling constants listed in the Table. An essential feature in the simulation is the use of negative values for ${}^3J_{FF}$. It is to be noted that the two most intense lines in the normal spectrum of the AA'XX' system of nuclei show zero intensity in the polarised spectrum since each arises from two transitions polarised equally but in opposite senses. The polarised spectrum which is observed therefore arises from the less intense lines of the normal spectrum. Moreover, the outer polarised lines in the group for each diastereoisomer are ones which are normally hidden under the two intense lines in the normal spectrum. Finally, we note that the chemical shift difference between the *meso*- and (±)-forms of 1,2-difluoro-1,2-diphenylethane in the CIDNP spectra (120—130 °C) is approximately one third that observed at normal probe temperature (*ca.* 40 °C). This is largely because of the temperature sensitivity of the shift of the *meso*-diastereoisomer which moves 130 Hz downfield (relative to benzyl fluoride) on raising the temperature from 40 to 120 °C; by contrast the (±)-diastereoisomer is shifted only *ca.* 20 Hz in the same direction over this temperature range.

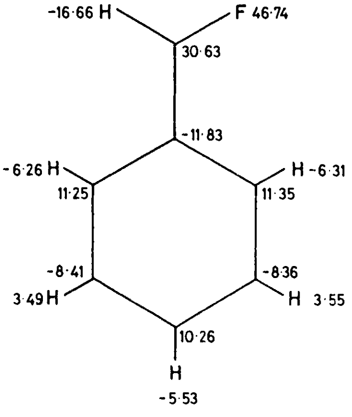

FIGURE 3 Hyperfine splitting constants (G) for the α-fluorobenzyl radical obtained by INDO calculation

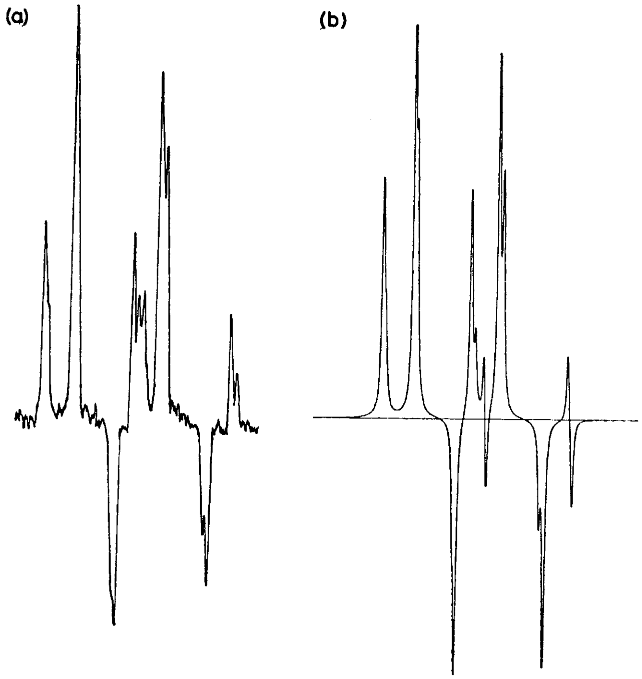

FIGURE 4 Observed (a) and simulated (b) ${}^{19}F$-CIDNP spectra for 2-(*o*-fluorophenyl)-1,2-diphenylethyl fluoride obtained by benzylic insertion of triplet 2-fluorodiphenylmethylene into benzyl fluoride at 120 °C

Coupling constants/Hz in *meso*- and (±)-1,2-difluoro-1,2-diphenylethanes from CIDNP at 120 °C in benzyl fluoride [a]

	meso	(±)
${}^2J_{HF}$	44.9_5 (45.4)	47.2 (46.5_5)
${}^3J_{HF}$	14.5 (14.9)	14.9 (14.5_5)
${}^3J_{HH}$	4.17 (3.98)	5.34 (6.40)
${}^3J_{FF}$	−17.0 (−17.7)	−15.1 (-16.9_5)

[a] Figures in parentheses refer to spectra recorded at normal probe temperature.

EXPERIMENTAL

Diazodiphenylmethane, its ring-substituted analogues, and benzyl fluoride were the samples described previously,[1] and the technique used for recording ${}^{19}F$ CIDNP has also been published.[1] Benzoyl peroxide was a commercial sample used without further purification.

t-Butyl α-Fluorophenylperacetate.—This was prepared by treatment of the racemic fluorinated acid chloride [6,8] with t-butyl hydroperoxide in the presence of pyridine.[9] The oily perester could be freed from di-t-butyl peroxide (which contaminates the t-butyl hydroperoxide) by careful chromatography on Florisil (200 mesh) and elution with benzene (Found: C, 63.8; H, 6.75. $C_{12}H_{15}FO_3$ requires

C, 63.7; H, 6.7%); ^{1}H n.m.r.: δ 5.85 (d, $^{2}J_{HF}$ 49 Hz); ^{19}F n.m.r.: doublet 23.49 p.p.m. downfield from benzyl fluoride (solvent), $^{2}J_{HF}$ 49 Hz.

α,α-Dideuteriobenzyl Fluoride.—α,α-Dideuteriobenzyl alcohol, prepared by the reduction of ethyl benzoate with a three-fold excess of lithium aluminium deuteride, was brominated ($SOBr_2$) according to the method of Frazer *et al.*[10] The bromide (4.5 g) was stirred for 36 h at 90—100 with potassium fluoride (4 g) and 18-crown-6-polyether (0.3 g).[11] After cooling, all the volatile components of the reaction mixture were removed at room temperature/0.1 mmHg, and the α,α-dideuteriobenzyl fluoride was redistilled, b.p. 40 °C/13 mmHg; yield 1.84 g (69%). The ^{19}F n.m.r. spectrum showed a quintet ($^{2}J_{DF}$, 7.4 Hz) isochronous with benzyl fluoride.

α-Deuteriobenzyl Fluoride.[12]—This was prepared in an analogous fashion from α-deuteriobenzyl alcohol obtained by reduction of benzaldehyde with lithium aluminium deuteride; ^{1}H n.m.r.: δ 4.6 (d of t, $^{2}J_{HF}$, 49 Hz; $^{2}J_{HD}$, 1.62 Hz); ^{19}F n.m.r.: doublet of triplets; $^{2}J_{HF}$, 49 Hz; $^{2}J_{DF}$, 7.4 Hz.

2,3,4,5,6-*Pentadeuteriobenzyl Fluoride.*—Perdeuteriobromobenzene, converted into the Grignard reagent and carbonated, gave the corresponding carboxylic acid. Reduction with lithium aluminium hydride gave pentadeuteriobenzyl alcohol which was fluorinated as described above; ^{1}H n.m.r.: δ 4.8 (d, $^{2}J_{HF}$, 49 Hz); ^{19}F n.m.r.: triplet (J_{HF}, 49 Hz) isochronous with benzyl fluoride.

1,2-*Difluoro*-1,2-*diphenylethanes.* Two methods were used, one giving a mixture of *meso*- and (±)-diastereoisomers and the other giving only (±)-difluorobibenzyl.

(i) (±)-1,2-Difluoro-1,2-diphenylethane was prepared in 95% yield by hydrogenation in cyclohexane over 5% palladium–charcoal of 1,2-difluorostilbene, obtained by reaction of tetrafluoroethylene with phenyl-lithium.[13] After recrystallisation from light petroieum (b.p. 40—60 °C) the compound had m.p. 78—78 °C (Found: C, 77.15; H, 5.6. $C_{14}H_{12}F_2$ requires C, 77.05; H, 5.54%), the ^{19}F n.m.r. spectrum in benzyl fluoride showed an AA′XX′ pattern centred 23.32 p.p.m. downfield from the solvent triplet. The spectrum in (−)-bornyl acetate as solvent confirms that this is the (±)-diastereoisomer.

(ii) 2-Fluoro-1,2-diphenylethanol (0.5 g), a mixture of diastereoisomers prepared by sodium borohydride reduction of α-fluorodeoxybenzoin,[14] in dichloromethane (20 ml) was set aside for 48 h at 0 °C with fluoramine reagent Et_2NCF_2-CHFCl. The reaction mixture was poured into ice-cold 10% aqueous potassium carbonate and the organic layer was separated, washed, and dried ($MgSO_4$) and the solvent was removed under reduced prssure. Removal of *NN*-diethylchlorofluoroacetamide at 60 °C/0.5 mmHg left a yellow residue (350 mg) which on crystallisation from light petroleum (40—60 °C) gave a colourless solid, which by ^{19}F-n.m.r. analysis consisted of a roughly 2 : 1 mixture of *meso*- and (±)-1,2-difluoro-1,2-diphenylethanes. The ^{19}F n.m.r. spectrum in solvent benzyl fluoride showed two AA′XX′ multiplets centred at 20.30 (*meso*) and 23.32 p.p.m. (±) downfield from benzyl fluoride at 40 °C; coupling constants are given in the Table. Further crystallisation yielded the pure *meso*-compound, m.p. 79—81 °C.

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