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POLYFLUOROARYL ORGANOMETALLIC COMPOUNDS—X[1,2]

NUCLEOPHILIC SUBSTITUTION IN OCTAFLUOROFLUOREN-9-ONE

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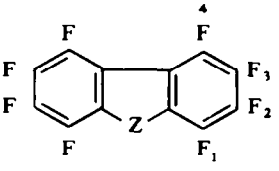
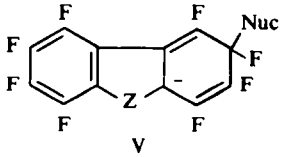
Abstract—The orientations of nucleophilic substitution are established as *meta-* to the carbonyl group in octafluorofluoren-9-one and *para-* to the carbonyl groups in decafluorobenzophenone and octafluoro-2,2'-dihydrobenzophenone. Hexafluoro-3,6-dimethoxyfluoren-9-one is prepared, for comparison, by an unambiguous cyclization reaction. Substitution in octafluorofluoren-9-one is discussed in relation to substitution in other similar fused ring systems and in benzophenones. It is concluded that there is an unusual feature of the fluorenone system that the carbonyl group conjugates more effectively with substituents in *meta* positions. This conclusion is supported by observation of the ^{19}F NMR spectra of solutions of the fluorenone in H_2SO_4 or FSO_3H, where fluorines at positions *meta* to the carbonyl are most de-shielded.

IN RECENT parts of this series we have described the synthesis of various polyfluoro derivatives of the fused ring systems I–IV, using lithio derivatives as precursors, and these compounds now allow the study of nucleophilic substitution in this type of system. The orientations of nucleophilic substitution have been established for compounds I–III, and can be rationalized by taking V and VI as simple models of the transition states for substitution. When Z is carbanion stabilizing (S, SO_2)[3,4] V is preferred, but when Z = O it is destabilizing[4] (by repulsion between the non-bonding electrons pairs on the oxygen and the carbanion) and VI is preferred. The

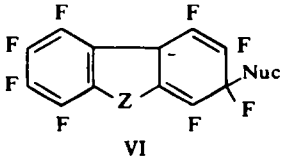


I: Z = S
II: Z = SO_2
III: Z = O
IV: Z = CO

same orientation of substitution has been found for 1,2,3,4-tetrafluorodibenzofuran.[5] We now describe nucleophilic substitution in octafluorofluoren-9-one (IV) and, since the carbonyl group is normally strongly carbanion stabilizing, we would expect type V orientation but it will be seen that the simple rationalization used above breaks down with this compound.

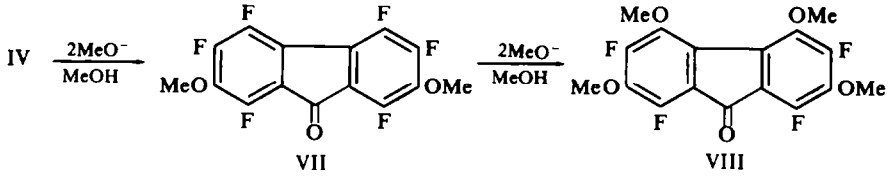


V

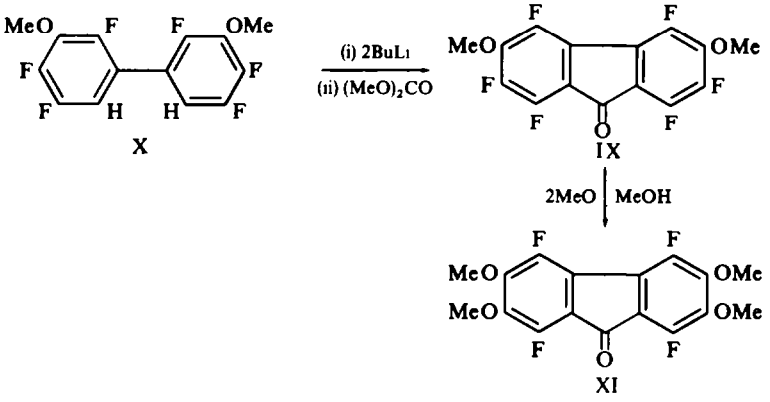


VI

The fluorenone (IV) reacted with sodium methoxide to give substitution first at the 2 (and 7) and then at the 4 (and 5) positions, the orientations being established by means of NMR spectroscopy (see later).

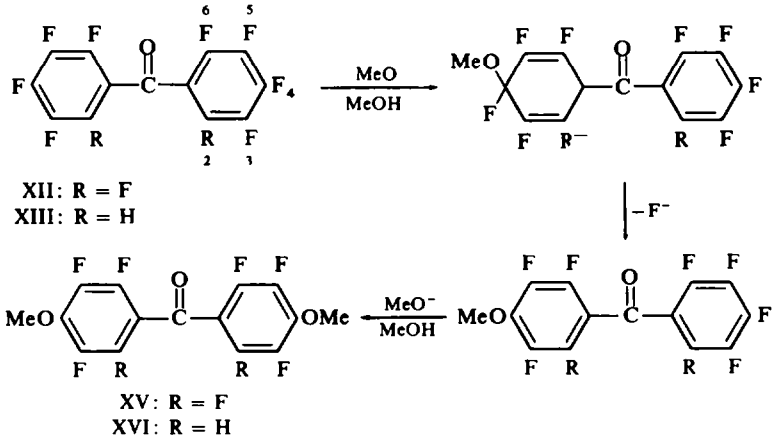


Chemical confirmation was obtained by synthesis of hexafluoro-3,6-dimethoxyfluoren-9-one (IX) by cyclization of the known[3] hexafluoro-2,2′-dihydro-5,5′-dimethoxybiphenyl (X). The cyclization step was accomplished using the same procedure as in the synthesis of IV from octafluoro-2,2′-dihydrobiphenyl.[1] This dimethoxy derivative (IX) has spectroscopic properties which are completely different from

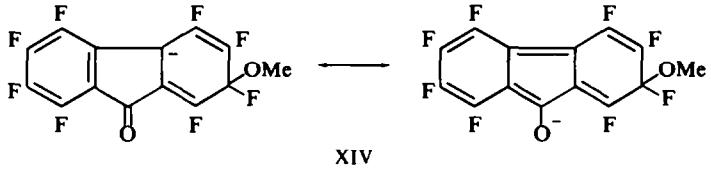


those of VII and further reaction of IX with two equivalents of methoxide yielded a tetramethoxy derivative (XI) whose spectroscopic properties differ from those of VIII.

This orientation, with the nucleophile entering *meta* to the carbonyl group, corresponds to type VI substitution rather than the type V observed with other carbanion stabilizing groups. Nevertheless decafluorobenzophenone (XII) and octafluoro-2,2′-dihydrobenzophenone (XIII) yield 4,4′-dimethoxy derivatives with



two equivalents of methoxide and are significantly activated by the carbonyl group, relative to the corresponding biphenyls.[6] It is possible that the anomalous orientation in the fluorenone (IV) arises from destabilization of the type V transition state by repulsion between the π electrons of the carbonyl group and the carbanionic centre and this opposes the more normal conjugative stabilization because of the fixed geometry compared to XII and XIII. This is unlikely because the rate of substitution in the fluorenone (IV) is of the same order as in decafluorobenzophenone.[6] As a result it appears that the dominant effect of the carbonyl group is conjugative stabilization of the carbanionic intermediate (XIV) and that, for reasons which are not yet understood, enhanced conjugation from the *meta* position to the carbonyl group occurs in this system. Indeed other workers, when investigating the effects of



XIV

substituents on the reduction of fluorenone with sodium borohydride, found that substituents in the 2 and 4 positions exerted extraordinary mesomeric effects, as if they were in direct conjugation with the carbonyl group.[7–9]

Further confirmation of this unusual electronic effect is shown by the results of protonation of IV and XII, carried out by recording the ^{19}F NMR spectra of solutions of the compounds in sulphuric or fluorosulphonic acid. The results are given in Table 1. For decafluorobenzophenone (XII) the spectra show that the *para* position is considerably more deshielded than the *ortho* or *meta* positions on protonation of the carbonyl group and this indicates more effective conjugation of the carbonyl group with the *para* position. However, for the fluorenone (IV) the 2 and 4 positions

are more deshielded than the 1 and 3 positions which again indicates this unusual conjugation effect.

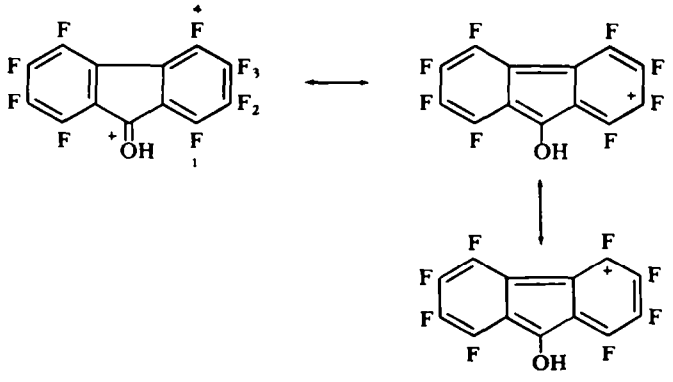
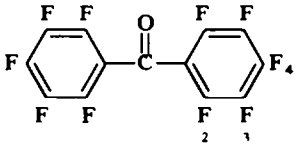
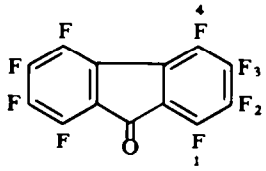


TABLE 1.[19] F NMR OF PROTONATED SPECIES

Compound	Solvent	Observed shifts (with assignment in brackets)	Changes in shift on protonation (with assignment in brackets)
	H_2SO_4[a]	−23·1 (2), −4·1 (3), −21·2 (4)	−1·9 (2), −2·5 (3) −5·1 (4)
	FSO_3H[b]	−27·4 (2), −6·8 (3) −25·2 (4)	−6·2 (2), −5·2 (3), −9·1 (4)
	H_2SO_4[a]	−32·2 (1), −25·0 (2), −12·8 (3), −28·9 (4)	−1·9 (1), −5·4 (2) −0·9 (3), −4·0 (4)
	FSO_3H[b]	−39·5, −38·3, −34·3 −17·3 (3)	−4 to −9 (1) −15 to −20 (2) −5·4 (3) −9 to −15 (4)

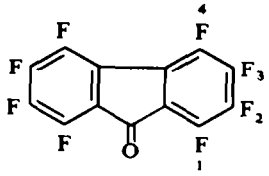
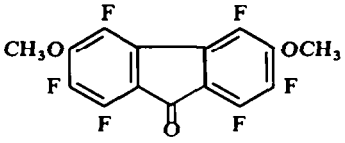
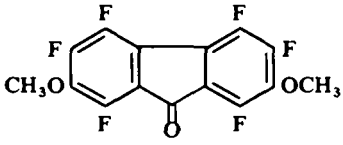
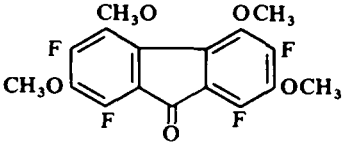
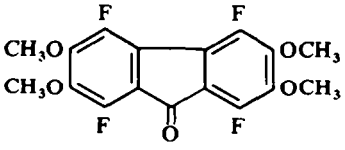
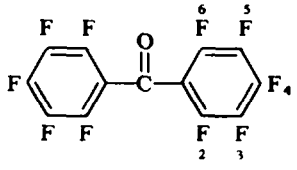
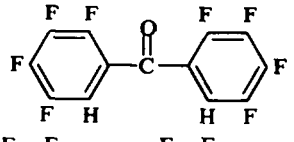
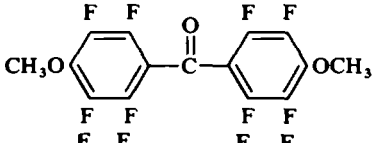
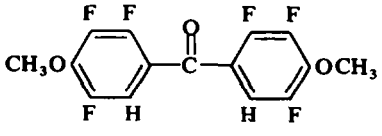
[a] Shifts relative to C_6F_6 internal reference.
[b] Shifts relative to C_6F_6 external capillary.

Therefore with regard to *both* the carbanionic transition state involved in nucleophilic substitution in IV and the positively charged species arising from protonation of IV, the results in each case indicate more effective conjugation of the carbonyl in the fluorenone system with the corresponding *meta* (2 and 4) positions. We await the results of sophisticated MO calculations on this system.[10]

Nuclear magnetic resonance spectra. When considering the orientation of substitution of fluorine in a polyfluoroaromatic system by methoxyl the most useful guide is the change in the chemical shift of the ring fluorines relative to the unsubstituted compound. For methoxyl these changes are very characteristic; *ortho* fluorines are invariably shifted *downfield*, while *meta* and *para* fluorines are shifted *upfield*.[3] Examination of coupling constants can also be a guide to orientation; the available evidence for various polyfluorobenzenes[11] and biphenyls[12] suggests that J_{FF}^{ortho} values lie in the range 18–22 c/s, J_{FF}^{meta} 0–8 c/s, and J_{FF}^{para} 9–12 c/s. Similarly, when aromatic protons are present, J_{HF}^{ortho} values lie in the range 9–12 c/s, J_{HF}^{meta} 5–8 c/s, and J_{HF}^{para} 2–3 c/s.[12–15] Coupling between methoxyl protons and the adjacent ortho fluorines usually (but not always) occurs.[15] Thus if methoxyl protons are split into a triplet or doublet of doublets, with a coupling constant in the range 0·5–3·5 c/s, then this is indicative of two *ortho* fluorine neighbours.

The ^{19}F NMR spectrum of octafluorofluoren-9-one showed four resonances at −30·3, −24·9, −19·6 and −11·9 ppm from C_6F_6 (Table 2). The two lowest field

TABLE 2. ^{19}F CHEMICAL SHIFTS (PPM FROM C_6F_6) IN CH_2Cl_2 OR $CHCl_3$

Compound		Shifts (assignments in brackets)
	IV	−30·3 (1), −24·9 (4), −19·6 (2), −11·9 (3)
	IX	−29·8 (4), −26·9 (1), −22·6 (2)
	VII	−35·4 (1), −22·1 (4), −13·3 (3)
	VIII	−32·8 (1), −18·4 (3)
	XI	−33·5 (1), −28·3 (4)
	XII	−21·4 (2), −16·5 (4), −2·7 (3)
	XIII	−25·3 (3), −24·5 (6), −15·2 (4), −8·7 (5)
	XV	−19·0 (2), −5·0 (3)
	XVI	−29·9 (3), −22·5 (6), −11·3 (5)

resonances may be assigned to the 1- and 4-fluorine atoms, since it is well known that *ortho* substituents in polyfluoroaromatic systems lead to downfield shifts;[11,16] also the resonance at −24·9 ppm may be assigned to the 4-fluorine since its shift is roughly the same as that observed for the corresponding fluorine in octafluorodibenzothiophen[3] (−22·9), octafluorodibenzothiophen-5,5-dioxide[4] (−22·9), and octafluorodibenzofuran[4] (−24·3). Hence the resonance at −30·3 ppm may be assigned to the 1-fluorine.

The ^{19}F spectrum of IX shows three resonances at −29·8, −26·9 and −22·6 ppm. Since, by unambiguous synthesis, the methoxyl is in the 3-position the 2- and 4-fluorines must have moved *downfield* with respect to IV and the 1-fluorine, which is *meta* to the methoxyl, must have moved upfield. Thus the resonances of IX can be assigned as in Table 1, and furthermore the resonances at −19·6 and −11·9 ppm of IV must correspond to the 2- and 3-fluorines respectively.

The ^{1}H spectrum of VII shows a doublet of doublets ($J \sim 0{\cdot}5$ and 1·5 c/s) at 5·8τ, which indicates that the methoxyl is in either the 2- or 3-position and the ^{19}F spectrum shows three resonances at −35·4 (unsplit), −22·1 (d, $J \sim 20$ c/s) and −13·3 ppm (d, $J \sim 20$ c/s). The lowest field peak of IV appears to have shifted *downfield* in VII which indicates that the methoxyl has entered at the 2-position. This is also supported by the fact that the 1-fluorine does not show an F—F ortho coupling.

The ^{19}F spectrum of VIII shows two unsplit resonances at −32·8 and −18·4 ppm. Comparison of these shifts with those observed for VII shows that they are only consistent with the methoxyl entering at the 4-position.

The ^{1}H NMR of XVI shows two resonances; one (relative intensity 1) at 3·4 τ (d.d.d., $J_1 = 11{\cdot}4$, $J_2 = 6{\cdot}1$, $J_3 = 2{\cdot}3$ c/s), and the other (relative intensity 3) at 6·5 τ (t. $J \sim 1{\cdot}5$ c/s). The latter suggests that the methoxyl is in the 4- or 5-positions. The coupling constants of the aromatic protons indicate that $J_1 = J_{HF}^{ortho}$, $J_2 = J_{HF}^{meta}$, and $J_3 = J_{HF}^{para}$, and that the methoxyl is in the 4- or 6-positions. Since the methoxyl splitting is not consistent with 6-substitution, the methoxyl must be in the 4-position.

The ^{19}F NMR spectra of solutions of XII and IV in sulphuric and fluorosulphonic acid were recorded and the results are given in Table 2. Since the solubility of these compounds in sulphuric acid was low, the signal to noise ratio was increased by using a Digico C.A.T. The assignment of the observed resonances for the benzophenone was made by consideration of relative intensities and the observable F–F *ortho* couplings. For the fluorrenone (IV) in fluorosulphonic acid not even the large F–F *ortho* couplings were observable and assignments could not be made. The resonance at −17·3 ppm can only correspond to the 3-fluorine since any other assignment would imply an *upfield* shift on protonation, which appears to be unlikely. For the remaining three fluorines in the molecule maximum and minimum values of the changes in chemical shift on protonation are given.

EXPERIMENTAL

Fluorine-19 and proton NMR spectra were recorded using a Perkin–Elmer R.10 spectrometer. Analyses were carried out under the supervision of Mr. T. F. Holmes.

Hexafluoro-2,7-dimethoxyfluoren-9-one. A soln of Na (0·042 g, 1·83 mmoles) in dry MeOH (10 ml) was added dropwise to a soln of octafluorofluoren-9-one (0·29 g, 0·90 mmoles) in dry MeOH (40 ml). After stirring for 16 hr at room temp the mixture was poured into water, and the yellow ppt extracted into ether. The extracts were dried ($CaCl_2$) and solvent removed. Sublimation of the residue (130°/10^{-2} mm) yielded

a yellow solid (0·3 g). The mass spectrum indicated that it was a mixture of a dimethoxy derivative (~85%, *m/e* 348) and a trimethoxy derivative (~15% *m/e* 360). Recrystallization from MeOH yielded *hexafluoro-2,7-dimethoxyfluoren-9-one*. (Found: C, 51·9; H, 1·9; F, 32·5. $C_{15}H_6F_6O_3$ requires: C, 51·7; H, 1·7; F, 32·8%), as yellow crystals, m.p. 115–117°.

The mass spectrum is not like that of the parent octafluorofluoren-9-one which fragments by CO loss, here the primary process appears to be Me loss. In this respect it is similar to heptafluoro-2-methoxydibenzothiophen-5,5-dioxide which also fragments primarily by Me loss, whereas with the parent compound SO loss is observed.[4] The principal peaks observed are those due to M-Me (*m/e* 333) and M-Me—CH (*m/e* 305) together with the corresponding metastable peaks.

Tetrafluoro-2,4,5,7-tetramethoxyfluoren-9-one. A soln of Na (0·089 g, 3·9 mmoles) in dry MeOH (10 ml) was added dropwise to a soln of octafluorofluoren-9-one (0·34 g, 1·1 mmoles) in dry MeOH (40 ml) heated under reflux. After 16 hr the mixture was poured into water, extracted with ether, the extracts dried ($CaCl_2$), and solvent removed. Sublimation (130°/10^{-2} mm) yielded a yellow solid (0·35 g). The mass spectrum indicated it to be a mixture of a tetramethoxy derivative (~90%, *m/e* 372) and a trimethoxy derivative (~10%, *m/e* 360). Recrystallization from MeOH/acetone yielded *tetrafluoro-2,4,5,7-tetramethoxyfluoren-9-one*. (Found: C, 54·6; H, 3·3; F, 20·1. $C_{17}H_{12}F_4O_5$ requires: C, 54·8; H, 3·2; F, 20·4%), m.p. 191–192°. Again the mass spectrum showed that the principal mode of fragmentation was by Me loss.

Hexafluoro-3,6-dimethoxyfluoren-9-one. Tetrahydrofuran (90 ml) which had been freshly distilled from LAH, and dry hexane (50 ml) were contained in a 500 ml flask which had previously been purged with dry N_2, and cooled to −78°. BuLi (8·6 ml of a 2·4 M soln, 20·6 mmoles) in hexane (20 ml) was added slowly, followed by a soln of hexafluoro-2,2'-dihydro-5,5'-dimethoxybiphenyl[3] (3·3 g, 10·3 mmoles) in THF (20 ml). The resulting mixture was left to stir for 4 hr at −78°, before dimethylcarbonate (1·0 g, 11·1 mmoles) was added rapidly and, after a further ½ hr at −78°, the mixture was allowed to warm to 0°. It was then hydrolysed with dilute acid, the organic layer separated, dried ($CaCl_2$), and solvent removed to yield an orange solid. Sublimation (120°/10^{-2} mm) yielded a pale yellow solid (1·5 g), leaving a black tar. Analytical scale GLC (silicone elastomer, 220°) indicated the solid to be a mixture of starting material (~80%) and another component of longer retention time (~20%). The latter component was separated by recrystallization from hexane to yield *hexafluoro-3,6-dimethoxyfluoren-9-one*. (Found: C, 51·8; H, 1·5; F, 32·8. $C_{15}H_6F_6O_3$ requires: C, 51·7; H, 1·7; F, 32·8%), m.p. 152–153°. The mass spectrum showed a parent ion at *m/e* 348 and a peak corresponding to Me loss at *m/e* 333.

Tetrafluoro-2,3,6,7-tetramethoxyfluoren-9-one. A soln of Na (0·032 g, 1·39 mmoles) in dry MeOH (10 ml) was added dropwise to a soln of hexafluoro-3,6-dimethoxyfluoren-9-one (0·20 g, 0·57 mmoles) in dry MeOH (40 ml) heated under reflux. After 26 hr the mixture was poured into water, extracted with ether, the extracts dried ($CaCl_2$) and solvent removed. Sublimation (170°/10^{-2} mm) yielded a yellow solid (0·2 g). The mass spectrum indicated it to be mainly a tetramethoxy derivative (*m/e* 372), with some pentamethoxy derivative (*m/e* 384). Recrystallization from aq.MeOH yielded *tetrafluoro-2,3,6,7-tetramethoxyfluoren-9-one*. (Found: C, 54·9; H, 3·8; F, 20·0. $C_{17}H_{12}F_4O_5$ requires: C, 54·8; H, 3·2; F, 20·4%), m.p. 184–185°. The mass spectrum showed a fragmentation peak (*m/e* 357) corresponding to Me loss.

Octafluoro-2,2'-dihydrobenzophenone. BuLi (28·0 ml of a 2·4 M soln, 66·7 mmoles) was added dropwise over 0·5 hr to a soln of 1,2,3,4-tetrafluorobenzene (10·0 g, 66·7 mmoles) in dry THF (100 ml, freshly distilled from LAH) and hexane (45 ml) contained in a 500 ml flask which had previously been purged with dry N_2 and cooled to −78°. After 2 hr dimethylcarbonate (3·0 g, 33·3 mmoles) was added rapidly and, after a further hr at −78°, the mixture was allowed to warm to −30°. It was then hydrolysed with dilute acid, the organic layer separated, dried ($CaCl_2$), and solvent removed by distillation. The residue was distilled (76–80°/10^{-2} mm) to yield *octafluoro-2,2'-dihydrobenzophenone* (6·0 g, 55%). (Found: C, 47·6; H, 1·0; F, 46·6. $C_{13}H_2F_8O$ requires: C, 47·8; H, 0·6; F, 46·6%) as a colourless liquid, which gave a *2,4-dinitrophenylhydrazone* m.p. 144–145°. (Found: C, 45·2; H, 1·3; F, 30·6. $C_{19}H_6F_8N_4O_4$ requires: C, 45·1; H, 1·2; F, 30·0%). The IR shows a C=O stretching frequency at ca. 1680 cm^{-1}. The mass spectrum shows a parent ion at *m/e* 326 and peaks corresponding to $C_6F_4HCO^+$ (*m/e* 177) and $C_6HF_4^+$ (*m/e* 149).

The ^1H NMR spectrum shows peaks (d.d.d.d.) at 3·3τ, with coupling constants 9·7, 8·2, 5·9 and 2·4 c/s, which correspond to J_{H3F}, J_{H4F}, J_{H6F}, and J_{H5F} respectively. The ^{19}F spectrum shows four resonances at −25·3 (3), −24·5 (6), −15·2 (4), and −8·7 (5) ppm (from C_6F_6) and the observed F–F coupling constants are J_{34} = 19·3, J_{35} = 3·1, J_{36} = 13·1, J_{45} = 18·8, J_{46} = 7·6, and J_{56} ~ 19 c/s, and these are consistent with the assigned structure.

Hexafluoro-2,2'-dihydro-4,4'-dimethoxybenzophenone. A soln of Na (0·13 g, 5·7 mmoles) in dry MeOH

(10 ml) was added dropwise to a soln of octafluoro-2,2'-dihydrobenzophenone (0·79 g, 2·4 mmoles) in dry MeOH (30 ml) heated under reflux. After 49 hr the mixture was poured into water, extracted with ether, the extracts dried ($CaCl_2$) and solvent removed. Sublimation (130°/10^{-2} mm) of the residue yielded a white solid (0·8 g), which was shown by analytical scale GLC (silicone elastomer, 220°) to be a mixture of a major component (~85%) and a minor component (~15%) of longer retention time. Recrystallization from MeOH aq yielded *hexafluoro-2,2'-dihydro,4,4'-dimethoxybenzophenone.* (Found: C, 51·6; H, 2·1; F, 32·3. $C_{15}H_8F_6O_3$ requires: C, 51·4; H, 2·3; F, 32·6%), m.p. 58–59°, as white needles. The mass spectrum showed a parent ion at *m/e* 350 and a base peak corresponding to $CH_3OC_6F_4H \cdot CO^+$ at *m/e* 189.

Octafluoro-4,4'-dimethoxybenzophenone. A soln of Na (0·065 g, 2·8 mmoles) in dry MeOH (10 ml) was added dropwise to a soln of decafluorobenzophenone (0·50 g, 1·4 mmoles) in dry MeOH (40 ml). After 15 hr the mixture was poured into water, extracted with ether, the extracts dried ($CaCl_2$), and solvent removed. Sublimation (110°/10^{-2} mm) of the residue yielded a white solid (0·5 g), and analytical scale GLC (silicone elastomer, 220°) showed it to consist of a major component (90%) and two minor components one of longer retention time and the other of shorter retention time than the principal peak. Recrystallization from b.p. 40–60° petroleum ether yielded *octafluoro-4,4'-dimethoxybenzophenone.* (Found: C, 46·5; H, 1·4; F, 39·0. $C_{15}H_6F_8O_3$ requires: C, 46·9; H, 1·6; F, 39·6%), m.p. 82–83°. The mass spectrum shows a parent ion at *m/e* 386 and a base peak at *m/e* 207 corresponding to $CH_3C_6F_4 \cdot CO^+$.

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