Reactions of Octafluoroacridone and Related Compounds

By **David M. Owen, Alan E. Pedler,** and **J. Colin Tatlow,** Department of Chemistry, The University of Birmingham, Birmingham

A new route to polyfluoroacridones is described and the substitution reactions of octafluoroacridone with methoxide ion are discussed, the position of substitution being confirmed by alternative synthesis from an amino-methoxy-octafluorobenzophenone. From octafluoroacridone was prepared 9-chloro-octafluoroacridine, but not nonafluoro-acridine, owing to its ready hydrolysis. Polyfluoroacridones give stable sodium salts, isolable in crystalline form.

Ready demethylation of methyl polyfluoroaryl ethers occurred with concentrated sulphuric acid when a carboxy-group or hydrogen atom was *para* to the methoxy-group; this is explained in terms of protonation of the *para* ring carbon atom.

WE recently described the synthesis [1] of octafluoro-acridone by electrochemical oxidation of 2-amino-nonafluorobenzophenone and by pyrolysis of perfluoro-3-phenylanthranil. An alternative synthesis has also been reported.[2] We now describe some reactions of octafluoroacridone, particularly nucleophilic substitution by methoxide ion.

During this work another method of cyclizing amino-polyfluorobenzophenones to polyfluoroacridones was devised. Previous attempts [3,4] to cyclize 2-substituted polyfluorobenzophenones by using aqueous potassium hydroxide and potassium carbonate–dimethylformamide were only partially successful since the nucleophilic character of the base caused halogenoform-type cleavage of the ketone. However the successful cyclization of 2-hydroxy-polyfluorobenzophenones to polyfluoroxan-thones by using potassium fluoride–acetone has been described,[3] although trial experiments with this system and 2-amino-nonafluorobenzophenone (I) gave only low yields of octafluoroacridone (II). We have found that good yields (60%) of octafluoroacridone (II) are obtained with anhydrous dimethylformamide and potassium fluoride at 100 °C. This reaction was extended to give 1,2,3,4-tetrafluoroacridone (IV) from 2′-amino-2,3,4,5,6-pentafluorobenzophenone (III) and 1,2,4,5,-6,7,8-heptafluoro-3-methoxyacridone (VI) from 2-amino-

octafluoro-4-methoxybenzophenone (V) (see later). The 1,2,4,5,6,7,8-heptafluoro-3-methoxyacridone prepared by this route had the same n.m.r. and i.r. spectra as the compound previously reported [2] but a higher m.p.

(I)	R^1 = R^2 = F	(II)
(III)	R^1 = R^2 = H	(IV)
(V)	R^1 = F, R^2 = MeO	(VI)
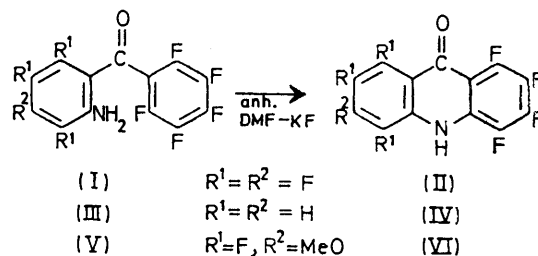
SCHEME 1

Our original intention was to study the position of nucleophilic substitution in octafluoroacridone by pre-paring a monomethoxy-derivative. The position of substitution was then to be confirmed by an unambi-guous synthesis following the route previously employed.[1] The first stage involved the reaction of tetrafluoro-4-methoxybenzaldehyde (VII) with a Grignard reagent prepared from 1-bromo-2,3,4,5-tetrafluorobenzene, to give the diphenylmethanol (VIII). Oxidation of this with chromium trioxide afforded the benzophenone (IX).

[1] C. M. Jenkins, A. E. Pedler, and J. C. Tatlow, *Tetrahedron,* 1971, **27**, 2557.

[2] S. Hayashi and N. Ishikawa, *Chem. Letters,* 1972, **2**, 99; *Nippon Kagaku Kaishi,* 1973, **7**, 1319.

[3] E. G. Lubenets, T. N. Gerasimova, and E. P. Fokin, *Zhur. org. Khim.,* 1971, **7**, 805.

[4] P. L. Coe, A. E. Jukes, and J. C. Tatlow, *J. Chem. Soc.,* 1966, 2020.

However, attempts to nitrate this ketone with boron trifluoride–tetramethylene sulphone–fuming nitric acid mixture [5] failed, starting material being recovered in indifferent yield. In view of the anomalous behaviour

diphenylmethanol (VIII). Reduction of the chloride over palladium–charcoal gave the diphenylmethane (XI). However, attempted nitration of each compound (HNO_3–H_2SO_4 at 90 °C) failed.

Scheme 2   All unmarked bonds to fluorine.   Reagents: i, 2,3,4,5-tetrafluorophenylmagnesium bromide; ii, CrO_3; iii, BF_3–HNO_3–$[CH_2]_4SO_2$; iv, conc. H_2SO_4; v, $SOCl_2$; vi, Pd–H_2; vii, HNO_3–H_2SO_4; viii, KF–DMF; ix, MeO^-; x, aq. KOH; xi, $POCl_3$

of the octafluoromethoxybenzophenone, the stability of the compound in concentrated sulphuric acid at 100 °C was investigated. From this reaction no starting material was recovered, the sole product found being 2,3,4,5-tetrafluorobenzoic acid.

Since scission of the ketone had occurred, the synthesis of compounds containing an alternative bridging group was considered. The diphenylmethyl chloride (X) was obtained in good yield from thionyl chloride and the

Finally, a suitable amino-methoxy-octafluorobenzophenone was obtained by the nucleophilic substitution of 2-amino-nonafluorobenzophenone (I) with methoxide ion. A compound was obtained with the appropriate chemical analysis and i.r. spectrum for a monosubstituted derivative. The mass spectrum showed that the

[5] P. L. Coe, A. E. Jukes, and J. C. Tatlow, *J. Chem. Soc. (C)*, 1966, 2323; P. L. Coe and A. E. Jukes, *Tetrahedron*, 1968, **24**, 5913.

methoxy- and amino-groups were in the same poly-fluorophenyl ring, and a comparison of experimental and calculated [6] chemical shifts for the fluorine n.m.r. spectrum showed the compound to be 2-amino-octa-fluoro-4-methoxybenzophenone (V).

This result is surprising since simple considerations lead to the expectation that substitution by the meth-oxide group would occur in the unsubstituted penta-fluorophenyl ring (because of the deactivating effect of the amino-group). However there is evidence [7] from u.v. spectra that in aromatic ketones containing a 2-amino-group there is an appreciable contribution to the electronic structure of the molecule from resonance forms of the type (A). Compounds for which this is

(A)
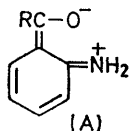
possible generally also absorb in the visible region of the spectrum, and 2-amino-nonafluorobenzophenone is yel-low. If, in fact, there is a significant contribution from a resonance form of this type then the anticipated enhanced reactivity of the unsubstituted ring (beyond that of hexafluorobenzene) in 2-aminononafluoro-benzophenone towards nucleophiles due to the carbonyl function will be absent, since delocalization of the negative charge on the incoming group by the carbonyl group will no longer be easy. In addition the presence of the $=N^+H_2$ group in the substituted ring will render that ring more electron-deficient, so increasing its reactivity towards methoxide. Substitution at the 4-position then means that in the Wheland intermediate the negative charge is not located on a carbon atom bearing fluorine, where I_π repulsion renders the inter-mediate unstable. In addition a canonical form of the intermediate may be written involving a p-quinonoid structure, regarded as important.[8,9]

The structure of the 2-amino-octafluoro-methoxy-benzophenone was confirmed by halogenoform-type cleavage with aqueous potassium hydroxide. From the product was isolated an amino-methoxy-trifluorobenzoic acid, confirming that the methoxy- and amino-groups were in the same ring. Since in the proton n.m.r. spectrum the methoxy-signal was a triplet, the acid is either 2-amino-4-methoxy- (XII) or 2-amino-5-methoxy-trifluorobenzoic acid (XIII). This is consistent with the [19]F n.m.r. spectrum, and a comparison of calculated [6] and experimental chemical shifts showed the acid to be (XII). Attempts were made, without success, to prepare the acid by nucleophilic substitution of methyl tetra-fluoro-4-methoxybenzoate, but from reactions with aqueous ammonia or lithium amide only starting material was recovered.

The nucleophilic reaction of octafluoroacridone with sodium methoxide in dimethyl sulphoxide–methanol gave a dimethoxy-derivative. The [19]F n.m.r. spectrum consisted of three signals only, indicating that sub-stitution had given a symmetrical derivative. The proton n.m.r. spectrum consisted of one signal only which was a triplet; the methoxy-group was again coupling with two adjacent fluorine atoms. A signal due to the acidic proton attached to the nitrogen atom was absent owing to exchange broadening at the high temperature at which the proton spectrum was taken. Thus the compound was either 2,7- or 3,6-dimethoxy-hexafluoro-acridone. The latter structure (XIV) was confirmed by nucleophilic substitution of 3-methoxyheptafluoro-acridone (VI) (obtained from the potassium fluoride cyclization) by methoxide ion, which gave an identical dimethoxy-derivative.

The position of substitution is in general accord with other results of nucleophilic substitution of polyfluoro-nitrogen heterocycles.[9,10] However, under the condi-tions of the reactions described here, in which excess of sodium methoxide was employed, octafluoroacridone would be present in the form of the anion. This would probably exist as a resonance hybrid of the two struc-tures (B) and (C), in which (B) is the dominant form, by

(B)   (C)
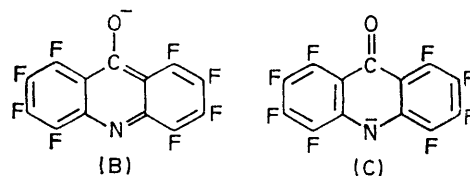
analogy with 4-hydroxy-tetrafluoropyridine, where the anion yields on methylation only an O-methyl product. In considering the most important contributors to the Wheland intermediate for nucleophilic substitution in fluoro-nitrogen heterocycles the favoured resonance structures are considered to be those where the ring nitrogen atom participates in delocalizing the negative charge (other structures being unfavourable for the reason outlined above), particularly where p-quinonoid forms can be drawn. All these factors favour nucleo-philic substitution of octafluoroacridone at the 3-position, for which an important resonance contributor to the stability of the intermediate is (D). This structure

(D)

is analogous to that postulated as important in the nucleophilic substitution of octafluorophenazine.[9]

[6] M. I. Bruce, *J. Chem. Soc.* (*A*), 1968, 1459.
[7] L. Deub and J. M. Vandenbelt, *J. Amer. Chem. Soc.*, 1949, **71**, 2414.
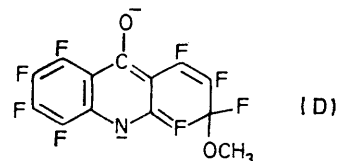[8] G. M. Brooke, E. J. Forbes, R. D. Richardson, M. Stacey, and J. C. Tatlow, *J. Chem. Soc.*, 1965, 2088; J. Burdon, *Tetra-hedron*, 1965, 3373 and references therein.
[9] A. G. Hudson, M. L. Jenkins, A. E. Pedler, and J. C. Tatlow, *Tetrahedron*, 1970, **26**, 5781.
[10] R. D. Chambers, M. Hole, W. K. R. Musgrave, R. A. Storey, and B. Iddon, *J. Chem. Soc.* (*C*), 1966, 233.

Other derivatives of octafluoroacridone were prepared. By reaction with phosphoryl chloride (standard procedure) was obtained 9-chloro-octafluoroacridine (XV): this was hydrolysed slowly in moist air back to octafluoroacridone. Attempted conversion of the chloroacridine into nonafluoroacridine by potassium fluoride in tetramethylene sulphone gave only octafluoroacridone, presumably because of hydrolysis of the product during the aqueous work-up.

The relatively high acidity of octafluoroacridone and its methoxy-derivatives was demonstrated by the formation of stable sodium salts. Although acridone may be dissolved in alcoholic potassium hydroxide the solution of the potassium salt is completely decomposed by water.[11] Tri- and tetra-nitro-acridones are considerably more acidic and are capable of liberating carbon dioxide from aqueous sodium carbonate.[11] Likewise, substitution of fluorine into the acridone system considerably increases the acidity of the NH group so that stable sodium salts may be prepared from octafluoroacridone (II) and 1,2,4,5,7,8-hexafluoro-3,6-dimethoxyacridone (XIV). These salts were sufficiently stable to withstand washing, although on prolonged contact with water slow hydrolysis occurred. The salts were identified by the absence of OH and NH stretching frequencies in the i.r. spectrum and by chemical analysis, although a correct fluorine analysis could not be obtained owing to interference by sodium.

Further experiments were performed to explain the failure to nitrate successfully 2,2′,3,3′,4′,5,5′,6-octafluoro-4-methoxybenzophenone (IX): the behaviour of model compounds in the presence of concentrated sulphuric acid was investigated. All the compounds studied were treated with the acid on a steam-bath for $3\frac{1}{2}$ h. As expected, from pentafluoroanisole and methyl pentafluorobenzoate only starting material and pentafluorobenzoic acid, respectively, were recovered. However, from methyl tetrafluoro-4-methoxybenzoate and 2,3,5,6-tetrafluoroanisole, 2,3,5,6-tetrafluorophenol was obtained in each case.

Two mechanisms have been proposed for the demethylation of aromatic ethers by strong acid, the first involving protonation of the oxygen atom of the methoxy-group, the second protonation of the carbon atom *para* to it, each followed by loss of the alkyl or aryl group from the ether. It is unlikely that the difference in stability of our anisoles can be ascribed to changes in the protonation of the oxygen atom since the inductive properties of the pentafluoro- and tetrafluoro-phenyl rings are unlikely to be materially different. However, back-conjugation of electrons from the oxygen atom may well be greater in 2,3,5,6-tetrafluoroanisole than in pentafluoroanisole (due to I_π repulsion in the latter case), thus increasing the probability of protonation and hence the rate of demethylation of the tetrafluoroanisole.

The decarboxylation of aromatic acids in acidic media has been explained [12] by protonation of the carbon atom bearing the carboxy-group, so that in terms of the arguments advanced above the rapid decarboxylation and demethylation of methyl tetrafluoro-4-methoxybenzoate to 2,3,5,6-tetrafluorophenol may be rationalized.

All these results offer a possible explanation of the difference towards nitration of 2*H*-nonafluorobenzophenone [1] and the methoxy-derivative (IX). Presumably the presence of the methoxy-group aids protonation and cleavage of the phenone to form 2,3,4,5-tetrafluorobenzoic acid and 2,3,5,6-tetrafluoroanisole, which is itself cleaved and degraded by extended heating in strong acid.

EXPERIMENTAL

Mass spectra were measured on an A.E.I. MS9 spectrometer; i.r. spectra on a Perkin-Elmer 257 instrument (all solids as Nujol mulls unless otherwise stated); and u.v. spectra for ethanolic solutions on a Unicam SP 800 spectrophotometer. N.m.r. spectra were measured with either a Perkin-Elmer R10 or R12B spectrometer at 38.5 °C unless otherwise stated. Proton chemical shifts (at 60 MHz) are quoted in δ values (Me$_4$Si internal standard) and ^{19}F chemical shifts (at 56.4 MHz) in ϕ values (trichlorofluoromethane internal standard) except where stated otherwise.

Octafluoroacridinone (II).—To a solution of 2-aminononafluorobenzophenone [1] (I) (1.68 g) in dry dimethylformamide (DMF) (15 cm³) was added dried potassium fluoride (1.0 g) and the mixture was heated for 5 h at 100 °C. The solution was then poured into water (150 cm³), and the yellow precipitate (1.15 g) filtered off and sublimed (200°; 0.02 mmHg) to give octafluoroacridone (II) (1.0 g), m.p. 282° (lit.,[1] 282—284°), with correct i.r. spectrum; ϕ [(CD$_3$)$_2$SO; 100 °C; CF$_3$·CO$_2$H internal standard] 67.5 (1F, ddd, $J_{1,2}$ 22, $J_{1,3}$ 8, $J_{1,4}$ 14.6 Hz, F-1), 73.2 (1F, dt, J 22 and 8 Hz, F-3), 78.0 (1F, ddd, $J_{2,4}$ 2.6, $J_{3,4}$ 22 Hz, F-4), and 90.5 (1F, dt, J 2.6 and 22 Hz, F-2).

The aqueous DMF phase was extracted with ether (3 × 50 cm³) and the combined ether layers were washed with water (3 × 100 cm³), dried (MgSO$_4$), and evaporated to give 2-aminononafluorobenzophenone (0.53 g), identified by i.r. spectroscopy.

1,2,3,4-*Tetrafluoroacridone* (IV).—Dried potassium fluoride (1.5 g) was added to a solution of 2′-amino-2,3,4,5,6-pentafluorobenzophenone [4] (III) (1.1 g) in DMF (10 cm³), and the mixture was heated on a steam-bath for 3 h. The solution was poured into water (150 cm³) and the precipitate filtered off and dried. This was shown by t.l.c. to contain starting material and a second component, and was heated with carbon tetrachloride (20 cm³). The suspension was filtered and the solid shown to be 1,2,3,4-tetrafluoroacridone (IV) (0.23 g), m.p. 360°, by i.r. spectroscopy.[4] The filtrate was evaporated and the residue (0.6 g) shown by t.l.c. to be a mixture of 2′-amino-2,3,4,5,6-pentafluorobenzophenone and 1,2,3,4-tetrafluoroacridone.

4-*Methoxytetrafluorophenyl*-(2,3,4,5-*tetrafluorophenyl*)-*methanol* (VIII).—To a stirred suspension of magnesium (0.66 g) in dry ether (30 cm³) was added 1-bromo-2,3,4,5-tetrafluorobenzene [13] (6.0 g) in ether (30 cm³). The mixture

[11] R. M. Acheson, 'Acridines,' Interscience, New York, 1956.
[12] H. Schenkel and M. Rudin-Schenkel, *Helv. Chim. Acta*, 1948, 31, 514; B. R. Brown, W. W. Elliott, and D. L. Hammick, *J. Chem. Soc.*, 1951, 1384; W. M. Schubert and R. Gardner, *J. Amer. Chem. Soc.*, 1953, 75, 1401.

[13] J. F. Tilney-Bassett, *Chem. and Ind.*, 1965, 693; J. Burdon, D. R. King, and J. C. Tatlow, *Tetrahedron*, 1966, 22, 2541.

was stirred and refluxed for 2 h, then cooled to 0 °C and tetrafluoro-*p*-methoxybenzaldehyde [14] (VII) (6.4 g) in ether (50 cm³) was added. After 16 h at 15 °C, 4N-hydrochloric acid (100 cm³) was added. The ether layer was separated and the aqueous phase extracted with ether (2 × 100 cm³). Drying (MgSO₄) and evaporation of the extracts left a residue (11.0 g) which was distilled (0.2 mmHg) to give a yellow oil (6.0 g). This was separated by column chromatography (silica gel; benzene) to give a product which was recrystallized from petroleum (b.p. 60—80°) to yield a solid (3.0 g), m.p. 56—59°. A sample (1.0 g) of the solid recrystallized from petroleum (b.p. 60—80°) gave the *diphenylmethanol* (VIII) (0.63 g), m.p. 59.5—60° (Found: C, 47.0; H, 1.9; F, 42.7. $C_{14}H_6F_8O_2$ requires C, 46.9; H, 1.7; F, 42.5%), $\nu_{max.}$ 3 520 (OH), 3 092 (aromatic CH), and 1 498 cm⁻¹ (fluoroaromatic rings), M^+ 358, δ [(CD₃)₂CO] 3.33 (1H, s, OH), 4.12 (3H, t, *J* 1.5 Hz, OMe), 6.4 (1H, s, aliphatic), and 7.68 (1H, m, ArH), φ [(CD₃)₂CO] 141.1, 145.0, 146.1, and 159.7 (1F, 1F, 2F, and 4F respectively, all m).

2,2′,3,3′,4′,5,5′,6-*Octafluoro-4-methoxybenzophenone* (IX). —A solution of the diphenylmethanol (VIII) (5.25 g) in glacial acetic acid (50 cm³) was oxidized with chromium trioxide (4.5 g) at room temperature for 2½ days. The mixture was poured into water (300 cm³) and extracted with ether; washing, drying, and evaporation gave a residue (4.98 g) which was recrystallized from perfluoro-1,4-dimethylcyclohexane and sublimed (140°; 12 mmHg). The sublimate was recrystallized from the solvent used initially to afford the *benzophenone* (IX) (2.0 g), m.p. 41.5—42° (Found: C, 36.9; H, 1.0; F, 42.3. $C_{14}H_4F_8O_2$ requires C, 47.2; H, 1.1; F, 42.7%), M^+ 356 (required), $\nu_{max.}$ (in hexachlorobutadiene) 3 062 (aromatic CH), 2 950 (aliphatic CH), 1 678 (C=O), and 1 640 and 1 477 cm⁻¹ (fluoroaromatic ring); δ (CDCl₃) 4.27 (3H, t, *J* 2.0 Hz, OMe) and 7.37 (1H, m, ArH), φ (CDCl₃) 137.4 (1F, dddd, $J_{2'5'}$ 12.5, $J_{4'5'}$ 19.7, $J_{3'5'}$ 3.2, $J_{5'6'}$ 9.3 Hz, F-5′), 139.2 (1F, m, F-2′), 143.5 (2F, m, F-2, -6), 146.3 (1F, m, F-4′), 154,1 (1F, t, *J* 19.7 Hz, F-3′), and 158.0 (2F, m, F-3, -5).

Attempted Nitration of the Methoxy-octafluorobenzophenone (IX).—A mixture of tetramethylene sulphone (7 cm³), fuming nitric acid (0.3 cm³) saturated with boron trifluoride at 0 °C, and the benzophenone (IX) (0.5 g) was heated at 65 °C for 3 h. The mixture was then poured onto ice (100 g) and the precipitate (0.26 g) identified by i.r. spectroscopy as starting material. The sulphone–water mixture was extracted with ether but afforded only the sulphone.

Reaction of the Methoxybenzophenone (IX) *with Sulphuric Acid.*—The benzophenone (0.37 g) was dissolved in concentrated sulphuric acid (10 cm³) and heated at 100 °C for 18 h. The mixture was poured into ice–water (70 cm³) and extracted with ether (3 × 40 cm³), and the combined extracts were dried (MgSO₄) and evaporated. The residue (0.36 g) was dissolved in aqueous sodium hydrogen carbonate (30 cm³; 10% w/v) and extracted with ether (3 × 20 cm³); evaporation of the dried (MgSO₄) extracts gave no product. The aqueous hydrogen carbonate solution was acidified and extracted with ether (3 × 50 cm³). The combined extracts were dried (MgSO₄) and evaporated and the residue (0.20 g) was sublimed (60°; 12 mmHg) and

recrystallized from petroleum (b.p. 60—80°) to yield 2,3,4,5-tetrafluorobenzoic acid (0.11 g), m.p. 84.5—87° (lit.,[15] 85.5—87°; lit.,[16] 92—92.5°), with correct i.r. spectrum.

4-*Methoxytetrafluorophenyl-(2,3,4,5-tetrafluorophenyl)-methyl Chloride* (X).—A solution of the diphenylmethanol (VIII) (4 g) in chloroform (18 cm³) and pyridine (1.5 cm³) was treated with thionyl chloride (5 cm³) in chloroform (15 cm³). The mixture was refluxed for 3 h, then cooled, and 4N-hydrochloric acid (30 cm³) was added. The chloroform layer was separated and the aqueous phase extracted with ether (2 × 50 cm³). The combined chloroform layer and ethereal extracts were dried (MgSO₄) and evaporated under reduced pressure. The residue (4.2 g) was purified by column chromatography (silica gel; ether) and the product recrystallized from petroleum (b.p. 60—80°) at −18 °C to afford the *chloride* (X) (3.5 g), m.p. 31.5—33° (Found: C, 45.0; H, 1.5; F, 40.1. $C_{14}H_5ClF_8O$ requires C, 44.6; H, 1.3; F, 40.4%), M^+ 398 (one Cl), $\nu_{max.}$ 3 080 (aromatic CH) and 1 649, 1 525, and 1 490 cm⁻¹ (fluoroaromatic ring), δ [(CD₃)₂CO] 7.56 (1H, m, ArH), 6.51 (1H, s, CHCl), and 4.1 (3H, t, *J* 1.6 Hz, OMe); φ [(CD₃)₂CO] 138.6 (1F, ddd, $J_{4'5'}$ 20.8, $J_{2'5'} = J_{5'6'} =$ 10.4 Hz, F-5′), 143.1 (1F, m, F-2′), 144.1 (2F, m, F-2, -6), 155.6 (1F, dt, $J_{4'6'}$ 6, *J* 20 Hz, F-4′), 156.7 (1F, t, *J* 20 Hz, F-3′), and 158.4 (2F, m, F-3, -5).

4-*Methoxytetrafluorophenyl-(2,3,4,5-tetrafluorophenyl)-methane* (XI).—The chloromethane (X) (1.0 g) in ethanol (40 cm³) containing palladium–charcoal (10%; 0.1 g) was treated with hydrogen. When absorption had ceased the solution was filtered and evaporated. The residue was separated by column chromatography (silica gel; carbon tetrachloride) and the product vacuum-distilled to give a solid (0.7 g) which was recrystallized from petroleum (b.p. 60—80°) at −18° C to afford the *diphenylmethane* (XI) (0.5 g), m.p. 39.5—40° (Found: C, 48.5; H, 1.9; F, 44.3. $C_{14}H_6F_8O$ requires C, 49.1; H, 1.8; F, 44.4%), M^+ 342, $\nu_{max.}$ 3 080 (aromatic CH), 1 525 and 1 492 cm⁻¹ (aromatic ring), δ (CCl₄; 100 MHz) 4.02br (2H, s, CH₂), 4.09 (3H, t, *J* 1.3 Hz, OCH₃), and 6.74 (1H, m, ArH), φ (CCl₄) 140.6 (1F, dddd, $J_{2'5'}$ 13.3, $J_{3'5'}$ 2.2, $J_{4'5'}$ 20.6, $J_{5'6'}$ 10.5 Hz, F-5′), 144.2 (1F, m, F-2′), 146.4 (2F, m, F-2, -6), 156.8 (1F, tt, $J_{3'6'}$ 2.0, $J_{3'4'} = J_{2'3'} =$ 20.1 Hz, F-3′), and 159.0 (3F, m, F-4′, -3, -5).

Attempted Nitrations of the Diphenylmethyl Chloride (X) *and the Diphenylmethane* (XI).—Attempts were made to nitrate the title compounds (0.26 g) in concentrated sulphuric acid (3 cm³) and fuming nitric acid (1.5 cm³) at 90 °C for 1½ h. The products were diluted with water (100 cm³) and the aqueous solution extracted with ether to give an acidic residue from which no identifiable products were isolated; starting materials were not recovered.

2-*Amino-octafluoro-4-methoxybenzophenone* (V).— 2-Aminononafluorobenzophenone [1] (I) (0.5 g) in dry methanol (7 cm³) was stirred with a solution of sodium methoxide in methanol (2 cm³; 0.558N) at room temperature for 12 h. The mixture was then poured into water (100 cm³) and the aqueous solution extracted with ether (3 × 40 cm³). Washing, drying, and evaporation left a residue (0.50 g), which was shown by t.l.c. (silica gel; carbon tetrachloride) to contain three components, one of which had the same R_F value as starting material. The major component was separated by column chromatography (silica gel; carbon tetrachloride) and recrystallized from perfluoro-1,4-dimethyl-

[14] E. V. Avoskar, P. J. N. Brown, R. G. Plevey, and R. Stephens, *J. Chem. Soc. (C)*, 1968, 1569.
[15] L. J. Belf, M. W. Buxton, and J. F. Tilney-Bassett, *Tetrahedron*, 1967, **23**, 4719.

[16] R. J. Harper, E. J. Soloski, and C. Tamborski, *J. Org. Chem.*, 1964, **29**, 2385.

cyclohexane to afford the *methoxy-derivative* (V) (0.49 g), m.p. 73—74° (Found: C, 45.6; H, 1.7; F, 40.6; N, 4.0. $C_{14}H_5F_8NO_2$ requires C, 45.3; H, 1.35; F, 41.0; N, 3.8%), *m/e* 371 (M^+), 204, 195, 176, and 167 (no peaks at 207, 192, 179, and 164), $v_{max.}$ 3 505, 3 360 (NH_2), 1 658 (C=O), 1 500, and 1 465 cm⁻¹ (fluoroaromatic ring), δ (CCl_4) 4.18 (3H, t, *J* 1 Hz, OMe) and 6.49br (2H, s, NH_2), φ (CCl_4) 142.4 (1F, dd, $J_{3,6}$ 11.3, $J_{5,6}$ 22.6 Hz, F-6), 144.3 (2F, m, F-2′, -6′), 153.2 (1F, t, *J* 20.3 Hz, F-4′), 160.6 (1F, dd, $J_{3,6}$ 11.3, $J_{3,5}$ 2.4 Hz, F-3), 161.8 (2F, m, F-3′, -5′), and 170.6 (1F, dd, F-5) (calc.[6] φ for 4-methoxy-substitution: F-3, 158.4; F-5, 171.3; F-6, 142.1; F-2′, -6′, 143.6; F-4′, 153.6; F-3′, -5′, 161.0; for 5-methoxy-substitution: F-3, 164.7; F-4, 142.1; F-6, 135.7; F-2′, -6′, 143.6; F-4′, 153.6; F-3′, -5′, 161.0).

Halogenoform-type Cleavage of 2-Amino-octafluoro-4-methoxybenzophenone (V).—The title compound (0.26 g), ethanol (5 cm³), water (10 cm³), and potassium hydroxide (6 g) were shaken for 4 h. The mixture was then poured into water (50 cm³): extraction with ether gave only ethanol. The aqueous phase was acidified (4N-HCl) and extracted with ether (3 × 50 cm³). The dried ($MgSO_4$) extracts were evaporated to afford a solid which was recrystallized twice from water to yield *2-aminotrifluoro-4-methoxybenzoic acid* (XII) (0.06 g), m.p. 181.5—182° (Found: C, 43.7; H, 2.7; F, 25.7; N, 6.5. $C_8H_6F_3NO_2$ requires C, 43.4; H, 2.7; F, 25.8; N, 6.3%), $v_{max.}$ 3 520 and 3 398 (NH_2), 3 300—2 000br (OH), 1 653 (C=O), and 1 460 cm⁻¹ (fluoroaromatic ring), δ [(CD_3)₂CO] 4.1 (1H, *J* 2.0 Hz, OMe) and 4.7br (1H, s, $^+NH_3$), φ [(CD_3)₂CO] 135.9 (1F, dd, $J_{3,6}$ 12, $J_{5,6}$ 21.5 Hz, F-6), 156.7 (1F, dd, $J_{3,5}$ 2.8 Hz, F-3), and 169.8 (1F, dd, F-5) (calc.[6] φ for 4-methoxy-substitution: F-3, 157.4; F-5, 168.4; F-6, 143.8; for 5-methoxy-substitution: F-3, 163.8; F-4, 149.7; F-6, 137.4).

Attempted Synthesis of 2-Aminotrifluoro-4-methoxybenzoic Acid.—(a) *With aqueous ammonia.* Methyl tetrafluoro-4-methoxybenzoate [14] (1.0 g), methanol (6 cm³), and aqueous ammonia (1 cm³; *d* 0.880) were heated in an autoclave at 132 °C for 24 h. Pouring into water, acidification, and extraction with ether afforded starting material (0.9 g), identified by i.r. spectroscopy.

(b) *With lithium amide.* To a stirred suspension of lithium amide (0.5 g) in ether (10 cm³) at —70 °C, was added methyl tetrafluoro-4-methoxybenzoate (1.0 g) in ether (10 cm³). The mixture was then allowed to warm to room temperature, stirred for 24 h, and cooled to 0 °C, and water (40 cm³) was added. Acidification and extraction afforded the tetrafluorobenzoate (1.0 g), identified by i.r. spectroscopy.

Nucleophilic Substitution of Octafluoroacridone.—The title compound (0.16 g) in freshly distilled dimethyl sulphoxide (7 cm³) at 110 °C was stirred with a solution of sodium methoxide in methanol (5 cm³; 1.13N) for 30 min. The mixture was cooled and acidified (4N-HCl; 5 cm³). The buff-coloured precipitate was filtered off, dried, and recrystallized from ethanol to give 1,2,4,5,7,8-*hexafluoro-3,6-dimethoxyacridone* (XIV) (0.07 g), m.p. 266—267° (Found: C, 49.8; H, 2.0; F, 31.6; N, 3.9. $C_{15}H_7F_6NO_3$ requires C, 49.6; H, 1.9; F, 31.4; N, 3.9%), $v_{max.}$ (hexachlorobutadiene) 3 395 (NH and OH), 3 005, 2 960, 2 900 (CH), and 1 640 cm⁻¹ (C=O), $λ_{max.}$ 222.5, 260, 277, and 375 nm (ε 17 000, 48 400, 23 000, and 5 750), δ [(CD_3)₂SO; 84 °C] 4.07 (t, *J* 2.0 Hz) (no NH signal owing to exchange broadening at high temperature), φ (CF_3·CO_2H internal standard) 70.5 (1F, dd, $J_{1,2}$ 21.4, $J_{1,4}$ 14.7 Hz, F-1), 76.5 (1F, dd, $J_{2,4}$ 2.7 Hz, F-4), and 87.0 (1F, dd, F-2).

Heptafluoro-3-methoxyacridone (VI).—To a solution of 2-amino-octafluoro-4-methoxybenzophenone (V) (0.6 g) in dry DMF (10 cm³) was added potassium fluoride (0.3 g), and the mixture was heated on a steam-bath for 8 h. The product was poured into water (150 cm³) and the yellow precipitate (0.46 g) filtered off and dried. The solid was separated by column chromatography [silica gel; carbon tetrachloride–ether (5%)] to give the polyfluorobenzophenone (0.18 g), identified by i.r. spectroscopy. The column packing was Soxhlet extracted with ethanol, the ethanolic solution was evaporated, and the solid residue (0.23 g) was recrystallized from ethanol to yield *heptafluoro-3-methoxyacridone* (VI) (0.19 g), m.p. 247.5—248.5° (Found: C, 47.6; H, 1.4; F, 38.2; N, 3.6. $C_{14}H_4F_7NO_2$ requires C, 47.9; H, 1.1; F, 37.9; N, 4.0%), $v_{max.}$ 3 180, 1 639 (C=O), 1 487, and 1 460 cm⁻¹ (fluoroaromatic rings), $λ_{max.}$ 221.5, 253.5, 277, 349, and 385 nm (ε 20 875, 41 076, 14 600, 6 400, and 5 900), δ [(CD_3)₂SO; 80 °C] 4.07 (t, *J* 2.0 Hz, OMe), φ [(CD_3)₂SO; CF_3·CO_2H internal standard] 70.5 (1F, ddd, $J_{5,8}$ 14.4, $J_{6,8}$ 8.5, $J_{7,8}$ 21.5 Hz, F-8), 72.0 (1F, dd, $J_{1,2}$ 20, $J_{1,4}$ 13.5 Hz, F-1), 76.5 (2F, m, F-4, -6), 80.5 (1F, ddd, $J_{5,7}$ 3.3, $J_{5,6}$ 22 Hz, F-5), 87.5 (1F, dd, $J_{2,4}$ 2 Hz, F-2), and 93.5 (1F, dt, *J* 3.3 and 22 Hz, F-7).

Nucleophilic Substitution of Heptafluoro-3-methoxyacridone (VI).—To a solution of the title compound (0.12 g) in dry dimethyl sulphoxide (5 cm³) at 80 °C was added sodium methoxide in methanol (5 cm³; 1.13N). The mixture was stirred for 20 min, then cooled and acidified (4N-HCl, 5 cm³). The precipitate was filtered off, dried, and recrystallized from ethanol to give hexafluoro-3,6-dimethoxyacridone (XIV) (0.04 g), shown by m.p., mixed m.p. (265—266°), and i.r. and n.m.r. spectroscopy to be identical with the compound obtained by the reaction of methoxide ion with octafluoroacridone.

9-Chloro-octafluoroacridine (XV).—A mixture of octafluoroacridone (0.4 g) and phosphoryl chloride (20 cm³) was heated at 125—130 °C for 3 h. Excess of the reagent was distilled off, the residue was dissolved in chloroform (40 cm³), and the solution was poured into a mixture of ice (50 g) and aqueous ammonia (80 cm³; *d* 0.880). The chloroform layer was separated and the aqueous layer extracted with chloroform (2 × 50 cm³). The combined chloroform solutions were dried ($CaCl_2$) and evaporated to leave a residue which was sublimed (130°; 12 mmHg). The sublimate was recrystallized from petroleum (b.p. 60—80°) to afford 9-*chloro-octafluoroacridine* (XV) (0.28 g), m.p. 164—165° (sealed tube) (Found: C, 43.6; F, 42.2; N, 4.3. $C_{13}ClF_8N$ requires C, 43.6; F, 42.5; N, 3.9%), M^+ 359 (one Cl), $v_{max.}$ 1 680, 1 480 (fluoroaromatic rings), 1 358, and 1 066 cm⁻¹, φ ($CDCl_3$) 140.9 (1F, t, *J* 16.9 Hz), 148.6 (1F, t, *J* 18.3 Hz), 149.3 (1F, t, *J* 16.9 Hz), and 152.8 (1F, t, *J* 16.9 Hz), $λ_{max.}$ 258.5, 367.0, 385.0, and 410 nm (ε 94 600, 3 750, 4 350, and 3 465).

Attempted Preparation of Nonafluoroacridine.—Potassium fluoride (1.0 g) in tetramethylene sulphone (15 cm³) was dried by azeotropic distillation with benzene, and 9-chloro-octafluoroacridine (0.37 g) was added. The mixture was stirred at 125 °C for 20 h, and acquired an intense red colour. The products were poured into ice–water (150 cm³), and the mixture was extracted with ether (3 × 50 cm³). The combined extracts were washed with water (3 × 100 cm³), dried ($MgSO_4$), and evaporated and the residue was separated by column chromatography on silica gel.

Impurities were removed by elution with 5% ether in carbon tetrachloride, the major product being then eluted with ether to afford octafluoroacridone (0.29 g), identified by m.p. and i.r. spectroscopy.

Sodium Octafluoroacridonate.—To a suspension of octa-fluoroacridone (0.1 g) in water (10 cm³) was added sodium hydroxide (0.75 g). The mixture was stirred to dissolve the sodium hydroxide, and the suspension filtered. The yellow residue was washed with water and dried to afford *sodium octafluoroacridonate* (0.09 g), m.p. 360° (Found: C, 43.5; F, 40.3; N, 3.8. $C_{13}F_8NNaO$ requires C, 43.2; F, 42.1; N, 3.9%), no i.r. peaks (in hexachlorobutadiene) character-istic of NH or OH, $\lambda_{max.}$ 248, 333, 347, 370, 388, 407, and 431 nm (ε 36 690, 5 564, 9 833, 4 110, 6 306, 7 037, and 4 550).

Sodium 1,2,4,5,7,8-Hexafluoro-3,6-dimethoxyacridonate.—To a suspension of 1,2,4,5,7,8-hexafluoro-3,6-dimethoxy-acridone (0.1 g) in water (10 cm³) was added sodium hydr-oxide (0.75 g) and the mixture was stirred. The yellow precipitate was filtered off and dried to afford the *acridonate* (0.09 g), m.p. 360° (Found: C, 46.7; H, 1.7; F, 27.2; N, 3.6. $C_{15}H_6F_6NNaO_3$ requires C, 46.8; H, 1.6; F, 29.6; N, 3.6%), no i.r. peaks (in hexachlorobutadiene) character-istic of OH or NH, $\lambda_{max.}$ (EtOH) 262, 282, 350, and 375 nm (ε 40 660, 18 860, 3 536, and 5 008).

Reactions with Sulphuric Acid.—(a) *Methyl tetrafluoro-4-methoxybenzoate.* The benzoate (1.0 g) in concentrated sulphuric acid (10 cm³) was heated at 100 °C for 4 h, then poured into water (100 cm³). The solution was extracted with ether (3 × 50 cm³), and the combined extracts dried MgSO₄) and evaporated. The residue was distilled in vacuum to afford 2,3,5,6-tetrafluorophenol (0.8 g), identi-fied by i.r. and n.m.r. spectroscopy, and by formation of the toluene-*p*-sulphonate, m.p. 79—80° (lit.,[8] 80—81°)

(b) *Methyl pentafluorobenzoate.* The methyl benzoate (0.5 g) was heated on a steam-bath with concentrated sulphuric acid (10 cm³) for 3½ h, and the products were poured into water (100 cm³). The aqueous solution was neutralized (aqueous NaHCO₃) and extracted with ether (3 × 50 cm³). The combined extracts were dried (MgSO₄) and evaporated and the residue (0.09 g) was identified by i.r. spectroscopy as starting material. The aqueous phase was acidified (4N-HCl) and extracted with ether (3 × 50 cm³). The combined ether layers were dried (MgSO₄) and evaporated to leave a residue shown to be pentafluoro-benzoic acid (0.39 g), m.p. 100° (lit.,[17] 101.5—102°) by i.r. spectroscopy.

(c) *2,3,5,6-Tetrafluoroanisole.* The title compound (1.0 g) in concentrated sulphuric acid (10 cm³) was heated at 100 °C for 3½ h. The mixture was poured into ice–water (100 cm³) and the solution extracted with ether (3 × 50 cm³). The ether layers were dried (MgSO₄) and evaporated and the residue was distilled from P_2O_5 under reduced pressure to give 2,3,5,6-tetrafluorophenol (0.72 g), identified by i.r. spectroscopy.

(d) *Pentafluoroanisole.* A mixture of pentafluoroanisole (1.6 g) and concentrated sulphuric acid (10 cm³) was treated as described above to afford, after evaporation of the ethereal extracts, a residue, which was vacuum-distilled from P_2O_5 to yield pentafluoroanisole (1.3 g) only.

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