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POLYFLUOROARYL ORGANOMETALLIC COMPOUNDS—VII[1, 2]

SYNTHESIS AND NUCLEOPHILIC SUBSTITUTION IN OCTAFLUORODIBENZOTHIOPHEN AND IN OCTAFLUOROTHIANTHREN

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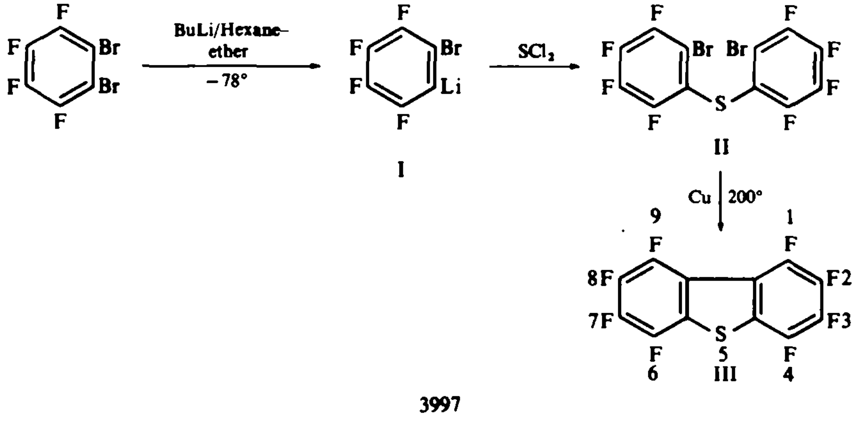
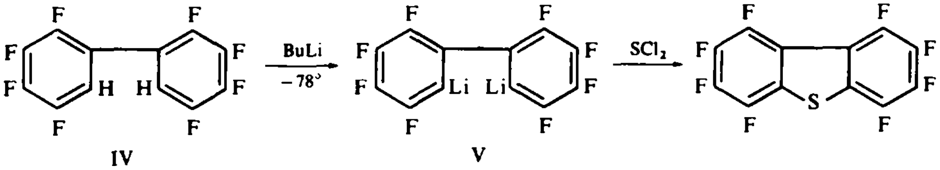
Abstract—Octafluorodibenzothiophen is synthesized by Ullmann coupling of bis(*o*-bromotetrafluorophenyl) sulphide and is shown to undergo nucleophilic substitution in the 2-position by methoxide ion. Similarly, substitution in octafluorothianthren occurs in the 2-position. The orientation of substitution in octafluorodibenzothiophen was deduced from the NMR spectra of the products and of the biphenyls which are produced by desulphurization of the dibenzothiophens with Raney nickel.

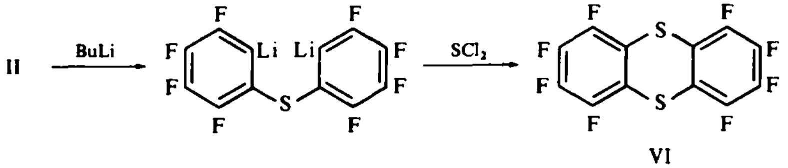
Previous papers in this series have been concerned with the general chemistry of polyfluoroaryl derivatives of some main group elements and we now begin to describe the application of polyfluoroaryllithiums in the synthesis of some polyfluoroaryl heterocyclic compounds of the dibenzo series. Apart from intrinsic interest in the latter as new compounds, they represent derivatives of the parent systems which will undergo easy nucleophilic aromatic substitution, a process which, e.g. for the dibenzothiophen or -furan series had not been investigated when this work began. It is of interest then to determine the effect of hetero-atoms on the carbanionic transition states involved in nucleophilic aromatic substitution since much work has been concerned with the effect of hetero-atoms on carbanion stabilities in other systems.[3]

Syntheses of tetrafluorothiophen[4] and, more recently, tetrafluorofuran[5] have been described but no corresponding compounds of the dibenzo series had been reported when this work began; octafluoro-[6] and tetrafluoro-dibenzofuran[7] have been reported recently. We describe here the synthesis of octafluorodibenzothiophen (III) according to the annexed scheme.

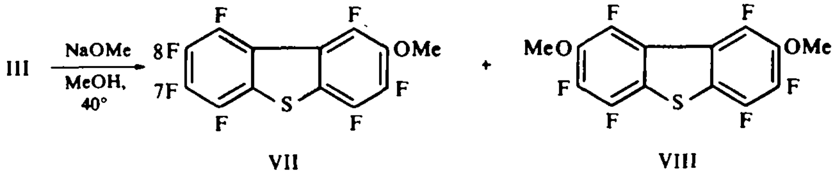


Bis(*o*-bromotetrafluorophenyl) sulphide (II) is obtained in high yield by reaction of *o*-bromotetrafluorophenyl-lithium (I) with sulphur dichloride and this reaction has been described elsewhere.[1] Coupling of the sulphide (II) to octafluorodibenzothiophen (III) was achieved, in high yield, by the classical Ullmann process, heating the sulphide (II) with copper powder in a sealed tube at 200°, although attempts to effect this coupling with copper powder in dimethylformamide[8] led to reaction with the solvent before the desired reaction occurred. The dibenzothiophen (III) was also synthesized by reaction of the di-lithio derivative (V), formed by reaction of 2,2'-dihydrooctafluorobiphenyl[9] (IV) with butyl-lithium, with sulphur dichloride but the yield was rather lower than in the method described above. In a related manner, synthesis of octafluorothianthren (VI) by reaction of the di-lithio derivative, obtained from the sulphide (II), with sulphur dichloride has been described.[1] However, an alternative synthesis of octafluorothianthen was also published recently.[10]

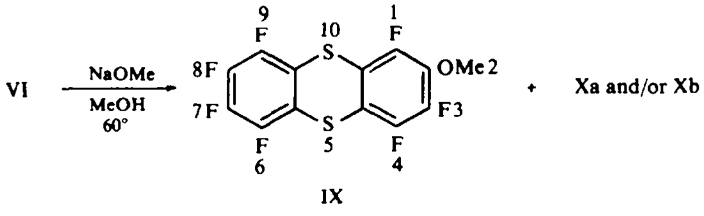




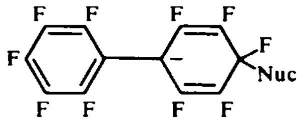
Reaction of octafluorodibenzothiophen (III) with an equivalent quantity of methoxide ion in anhydrous methanol occurred under mild conditions giving mainly the 2-methoxy derivative (VII) together with some of the 2,8-dimethoxy derivative (VIII).

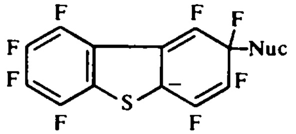


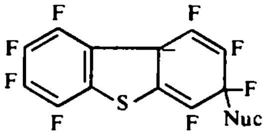
Similarly, octafluorothianthren reacted with methoxide ion under analogous conditions to give 2-methoxy-(IX) and 2,8-(Xa) and/or 2,7-(Xb) di-methoxy derivatives. The orientation of substitution in these systems was deduced from ^{1}H and ^{19}F-NMR data on these and model compounds and is outlined later.

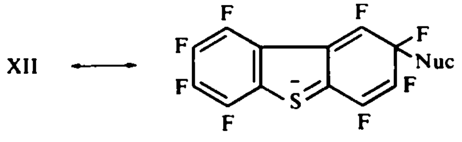


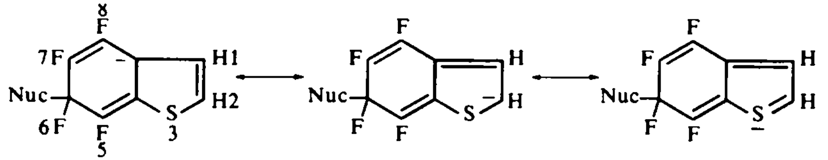
Nucleophilic substitution in decafluorobiphenyl occurs very readily and in the 4-position,[11] indicating that a polyfluoroaromatic ring para to the point of attack by the nucleophile stabilizes the transition state (XI).[12] However, such an effect is not the dominant one in substitution in octafluorodibenzothiophen (III) because 2-substitution indicates that transition state (XII) is preferred to (XIII), i.e. that sulphur stabilizes the former as in (XIIa). This is consistent with the known ability of sulphur to stabilize an adjacent carbanionic centre in other systems[13] and is usually attributed to d-orbital participation. Brooke and Quasem[14] have established, recently, that substitution in tetrafluorobenzo[b]thiophen (XIV) occurs in the 6-position and at first sight there is an apparent anomally between these orientation results. However, there is really a fundamental difference between these two systems (XII) and (XIV). Tetrafluorobenzo[b]thiophen is probably best regarded as an extended benzylic system where a maximum delocalization can occur in the transition state represented by (XIV, a, b) for 6-substitution, involving the double bond and sulphur. Substitution in the analogous 3-position in octafluorodibenzothiophen (XV, a, b), on the other hand, would lead to loss of resonance energy in the second ring in order to obtain maximum delocalization onto sulphur. Consequently, the dibenzothiophen is best compared with bis(pentafluorophenyl) sulphide (XVI).

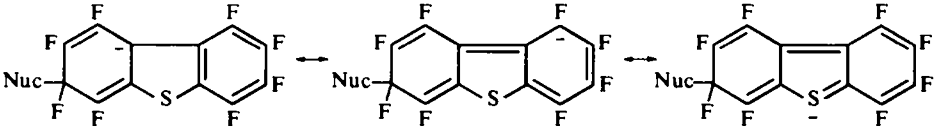

XI


XII

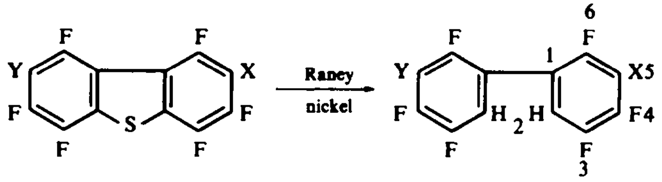

XIII


XIIa


XIV XIVa XIVb


XV XVa XVb

Sulphur is very conveniently removed from polyfluorodibenzothiophens using Raney nickel and the resulting biphenyls are useful in establishing the orientation of substitution.



XVII: X = Y = F
XVIII: X = OMe; Y = F
XIX: X = Y = OMe

Orientation of substitution

The ^{19}F NMR spectrum of octafluorodibenzothiophen showed four groups of peaks (Table 2) two to lower and two to higher field. It is well-known that ortho substituents in a polyfluoroaromatic system usually lead to a downfield shift of ^{19}F-resonance positions[15, 16] and so the two lower field resonances can be assigned to the 1- and 4-fluorine atoms and the lowest field peak is easily assigned to the fluorine atoms adjacent to sulphur because of the comparable low-field shift of this peak with the resonance of corresponding fluorines in bis(pentafluorophenyl) sulphide (XVI) and octafluorothianthren (VI). The ^{1}H spectrum of the methoxy derivative (VII) showed a doublet of doublets, arising from coupling of the protons with *two* adjacent fluorines[17] and so indicates entry of the methoxyl at positions 2, or 3. The data presented in Table 1 indicates that the effect on ^{19}F shifts, of introducing a methoxyl group into a polyfluoroaromatic system is that the resonances of ortho fluorine atoms are shifted ~ 4–6 ppm downfield and of meta- and para-fluorines shifted ~ 2 ppm upfield. It can be seen then that there is no resonance in the spectrum of the methoxy derivative (VII) which occurs to *lower* field than the value for the 4-fluorine in octafluorodibenzothiophen (III) showing that methoxyl did not enter at the 3-position and, indeed, only the calculated shifts for the 2-methoxy

Table 1. Effect of methoxyl on ^{19}F chemical shifts (position of the fluorine atom in parentheses)

Compound (solvent)	Chemical Shift (ppm)*	Effect on ^{19}F Shifts (*ortho*)	(*meta*)	(*para*)	Reference compound
A. C_6F_6[15]	162·9				
B. C_6F_5OMe[15]	158·5(2,6); 164·9(3,5); 164·6(4)	−4·4	+2·0	+1·7	A
C. $(C_6F_5)_2S$ (acetone)	133(2,6); 161(3,5); 151(4)				
($CHCl_3$)	132(2,6); 160(3,5); 150(4)				
D. $C_6F_5{\cdot}S{\cdot}C_6F_4OMe$ (para) (acetone)	135(2,6); 157(3,5)	−4	+2	—	C
E. Octafluorothianthren (VI) ($CHCl_3$)	134(1,4); 155(2,3)				
F. 2-Methoxyheptafluorothianthren (IX) ($CHCl_3$)	128(1); 149(3); 136(4)	−6	+2	—	E

* From $CFCl_3$

TABLE 2. ^{19}F CHEMICAL SHIFTS (PPM FROM CFCl$_3$)

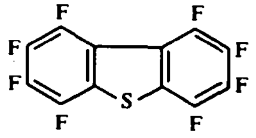
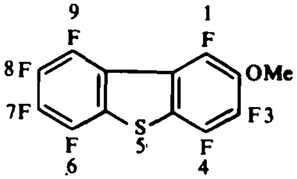
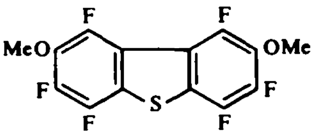
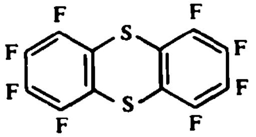
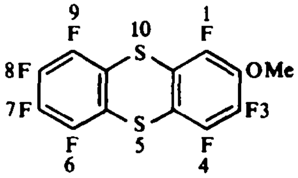
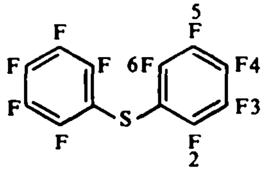
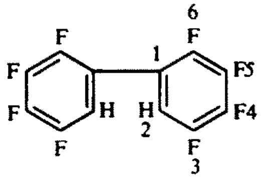
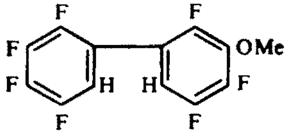
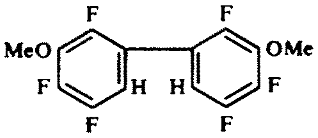
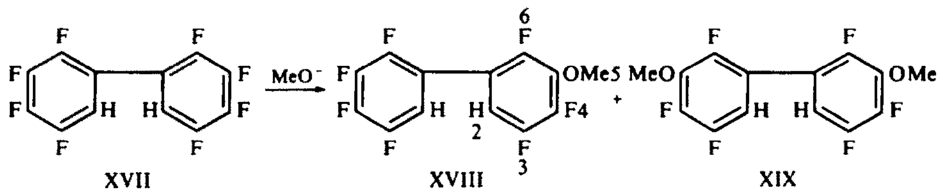
Compound	Solvent	Shifts (assignments and relative intensities in brackets)
	Me$_2$CO	134(4); 141(1); 156(2); 158(3).
	Me$_2$CO	134(x2) (1·6); 136(4); 141(9); 153(3); 156(8); 158(7).
	Me$_2$CO	134(1); 135(4); 153(3)
	Me$_2$CO	134(1,4); 155(2,3).
	CHCl$_3$	128(1); 136(4); 149(3); 134(6,9); 155(7,8)
	Me$_2$CO	133(x2) (2,6); 151(4); 161(x2) (3,5)

Table 2—*continued*

Compound	Solvent	Shifts (assignments and relative intensities in brackets)
	Me_2CO	140(3,6); 156(4,5)
	Me_2CO	142(3); 151(4); 134(6); 140(x2) (3′,6′); 156(x2) (4′,5′)
	Me_2CO	140(3); 149(4); 134(6).

derivative agree with the observed shifts. Further confirmation of structure came from the spectra of the biphenyls (XVIII and XIX) obtained by Raney nickel desulphurization of the mono- and di-methoxy derivatives (VII and VIII). The same biphenyls (XVIII and XIX) were also obtained by reaction of 2,2′-dihydro-octafluorobiphenyl with sodium methoxide.



XVII XVIII XIX

The ^{19}F spectrum of the biphenyl (XVII) showed only two resonances, at 140 and 156 ppm, the lower field resonance arising from the 3- and 6-fluorines, being shifted by *ortho* substituents.[15,16] Also, the shifts for the methoxy compound (XVIII) indicate that a low field resonance has been moved upfield by ~2 ppm (a meta or para MeO shift) and one downfield by ~6 ppm (*ortho* MeO shift) indicating a MeO at positions 4 or 5 in (XVIII). However, the resonance at 140 ppm, in the dimethoxy derivative (XIX) was clearly resolved into eight lines of equal intensity, from which coupling constants $J_1 = 19{\cdot}9$ c/s; $J_2 = 12{\cdot}4$ c/s; and $J_3 = 10$ c/s were obtained.

Burdon and co-workers[18] have obtained values J_{H-F} (*ortho*) ~10 c/s; J_{F-F} (*ortho*) ~20 c/s; J_{F-F} (*para*) ~12 c/s and Fenton and Massey[19] have obtained values of the same order as these, J_{F-F} (*ortho*) = 22·4 c/s; J_{F-F} (*para*) = 12·4 c/s; J_{F-F} (*meta*) = 2·7 c/s; J_{H-F} (*ortho*) = 10·3 c/s. Hence, J_1 arises from an *ortho* F–F coupling, J_2 from a *para* F–F coupling and J_3 from *ortho* H–F coupling. This can only arise from a 3-fluorine in structure (XIX). Recent data by Brown and Mooney[20] indicates that in some situations J_{F-F} (*para*) can be much higher than the values discussed above but, apparently, not greater than the corresponding J_{F-F} (*ortho*) value. The resonance at 149 ppm in XIX consisted of a doublet of triplets (ignoring the small splitting with the MeO group) from which coupling constants J_4 = 19·6 c/s and J_5 = 7·8 c/s were obtained; J_4 corresponds to an *ortho* F–F coupling, indicating that the absorption arises from the 4-fluorine in XIX, but the coupling J_5 appears to be unusual and arises from equal values for J_{F-F} (*meta*) and J_{H-F} (*meta*). The data presented above assigns, conclusively, the entry of the MeO group into octafluorodibenzothiophen into the 2-position.

EXPERIMENTAL

Octafluorodibenzothiophen. A mixture of bis(*o*-bromotetrafluorophenyl) sulphide[1] (3·0 g, 6 mmoles) and Cu powder (1·8, 29 mmoles) was heated to 200° for 120 hr in a sealed, evacuated Carius tube. On cooling, the contents of the tube were extracted with ether and excess Cu was removed by filtration before solvent was removed by vacuum transfer to leave a white solid which was sublimed (90°/10^{-3} mm) yielding *octafluorodibenzothiophen* (1·9 g ~ 100%), m.p. 99–100°. (Found: C, 43·8; F, 46·3. $C_{12}F_8S$ requires: C, 43·9; F, 46·3%).

Attempts to couple the dibromide using Cu in dimethylformamide at temps up to 150° lead to recovery of starting material but above this temp a complex product containing C—H was obtained, obviously arising from reaction with the solvent.

Octafluorodibenzothiophen from 2,2'-dihydro-octafluorobiphenyl. The biphenyl[9, 21] (0·25 g, 1·8 mmole) in ether hexane (10 ml, 1:1 vols) soln was slowly added to n-BuLi (1·7 ml hexane solution; 3·9 mmole) in ether–hexane (10 ml), cooled to −78°. After 2 hr at that temp, sulphur dichloride (0·19 g, 1·8 mmole) in ether (5 ml) was added. The mixture was stirred at −78° for a further one hr and then allowed to come to room temp before being hydrolyzed. When the organic layer had been separated and dried ($MgSO_4$), solvent was removed under vacuum to leave a white solid which was then sublimed. The sublimate (0·5 g) was shown by VPC to contain octafluorodibenzothiophen (66%) and starting material in ratio 4:1.

Reactions of octafluorodibenzothiophen

(a) *With sodium methoxide.* A soln of Na (0·033 g, 1·47 mmoles) in dry MeOH (20 ml) was added dropwise, during 1 hr to a stirred soln of octafluorodibenzothiophen (0·46 g, 1·4 mmoles) in MeOH (30 ml). After 24 hr at 40°, the mixture was allowed to cool and a ppt appeared; water (50 ml) was added and the soln was extracted with CH_2Cl_2, the combined extracts being dried ($MgSO_4$) before solvent was removed by vacuum transfer to yield a white solid (0·6 g) which was shown by VPC to consist of three components. Fractional sublimation yielded recovered octafluorodibenzothiophen; *heptafluoro-2-methoxydibenzothiophen* (0·4 g, 83%); and a residue which was shown by VPC and mass-spectrometry to be a mixture of mono- and di-methoxy derivatives. Heptafluoro-2-methoxydibenzothiophene gave (Found: C, 45·9; H, 1·00; F, 38·6. $C_{13}H_3F_7SO$ requires C, 45·9; H, 0·9; F, 39·1%), m.p. 105–107°.

(b) *With Raney nickel.* A mixture of octafluorodibenzothiophen (0·14 g, 0·43 moles) and Raney Ni (ca. 0·4 g) in EtOH (20 ml) was stirred at room temp for 4 hr under N_2. After filtration to remove the Ni, and washing the Ni with EtOH, solvent was removed by distillation to leave a white solid (0·1 g) which sublimed easily (80°/10^{-2}mm). Gas chromatography showed that the solid was a mixture of starting material and 2,2'-dihydro-octafluorobiphenyl which was then separated readily by fractional sublimation of the solid at room temp.

Reaction of heptafluoro-2-methoxydibenzothiophen with Raney nickel. Raney Ni which had been washed with benzene was added to heptafluoro-2-methoxydibenzothiophen (0·06 g, 0·18 mmole) in benzene (30 ml) and the mixture was heated under reflux for 24 hr. Ni was removed by filtration and washed several times with hot CH_2Cl_2 and then solvent was removed from the combined soln leaving a white solid. The mass-spectrum of the sublimed solid indicated a mol wt of 310 and the product was identical (IR, NMR, mass-spect) with 2,2'-dihydroheptafluoro-5-methoxybiphenyl, obtained from the reaction of 2,2'-dihydro-octafluorobiphenyl with NaOMe.

Reaction of 2,2' dihydro-octafluorobiphenyl with sodium methoxide. A soln of Na (0·04 g, 2·0 mmoles) in dry MeOH (15 ml) was added, dropwise, during 1 hr to a stirred, refluxing soln of 2,2' dihydro-octafluorobiphenyl (0·53 g, 1·8 mmoles) in MeOH (25 ml). After 21 hr at 80° (oil bath temp), the mixture was allowed to cool and a ppt appeared; water (50 ml) was added, and the soln was extracted several times with CH_2Cl_2, the combined extracts being dried ($MgSO_4$), before solvent was removed under vacuum to yield a white solid (0·53 g), which was shown by VPC to consist of 3 components. Fractional sublimation yielded 2,2' dihydro-octafluorobiphenyl, *2,2'-dihydroheptafluoro-5-methoxybiphenyl* (0·35 g, 63%); and *2,2'dihydro-5,5' dimethoxyhexafluorobiphenyl* (0·15 g, 26%). The mono and di-ethers were recrystallized from MeOH-water soln: 2,2' dihydro-5-methoxyheptafluorobiphenyl gave (Found: C, 50·4; H, 1·5; F, 43·1. $C_{13}H_5F_7O$ requires: C, 50·3; H, 1·6; F, 42·9%), m.p. 98–99°; and 2,2' dihydro-5,5'-dimethoxyhexafluorobiphenyl gave (Found: C, 52·1; H, 2·7; F, 35·4. $C_{14}H_8F_6O_2$ requires: C, 52·2; H, 2·5; F, 35·5%), m.p. 147°. The products had mol wts of 310 and 322 respectively (mass spectra) and the orientation of substitution was deduced by analysing their ^1H and ^{19}F NMR spectra.

Reaction between octafluorothianthren and sodium methoxide. Octafluorothianthren (0·41 g, 1·1 mmoles) was dissolved in dry MeOH (40 ml) in a 100 ml 2-neck flask, fitted with a dropping funnel and reflux condenser. The apparatus was purged with dry N_2 and the soln stirred. Na (0·028 g, 1·2 mmoles) in dry MeOH (10 ml) was added dropwise to the mixture under reflux and which was maintained at reflux for a further 96 hr. On cooling, and dilution with water, a white ppt appeared and was extracted into ether. After separation of the organic layer and drying ($MgSO_4$), solvent was removed by vacuum transfer, to yield a yellowish solid, which sublimed (100°/10^{-3} mm) to a cream coloured product, (0·42 g) which was shown to contain 3 components by VPC. The major product was separated by preparative-scale VPC and shown to be *2-methoxyheptafluorothianthren* (0·3 g, 75%). (Found: C, 41·7; $C_{13}F_7H_5S_2O$ requires: C, 41·9%). The mass spectrum gave the required mol wt of 372, and PMR confirmed that the substituent was in position 2 and the ^{19}F chemical shifts support this assignment (Table 2). The remaining components of the product were starting material and a very small amount of a dimethoxy derivative, as indicated by the mass-spectrum.

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[21] L. J. Belf, M. W. Buxton and T. F. Tilney-Bassett, *Ibid.* **23**, 4719 (1967).