

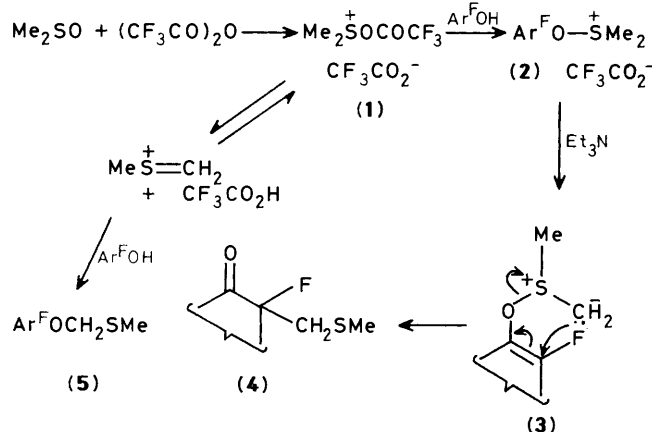
An Investigation of Potential [2,3]-Sigmatropic Rearrangements of Pentafluorophenyl-aza-, -thio-, and -methylene-sulphonium Ylides

Gerald M. Brooke* and J. A. K. Jamie Ferguson

Department of Chemistry, Science Laboratories, South Road, Durham DH1 3LE

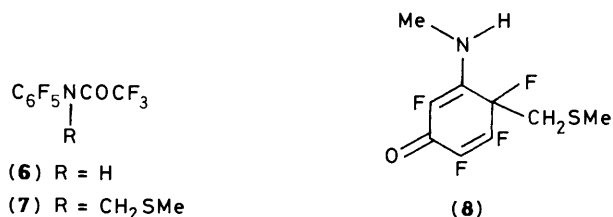
The reactions of pentafluoroaniline and pentafluorothiophenol with dimethyl sulphoxide-trifluoroacetic anhydride at low temperatures followed by triethylamine give the *N*-trifluoroacetyl compound (6) along with the *N*-trifluoroacetyl-*N*-methylthiomethyl compound (7) and decafluorodiphenyl disulphide, respectively; no molecular rearrangements occur. Under similar conditions 2,3,4,5,6-pentafluoro-*N*-methylaniline gives the cyclohexa-2,5-dienone derivative (8) via hydrolysis of the [2,3]-sigmatropic rearrangement intermediate (9). 2,3,4,5,6-Pentafluorobenzyl bromide and dimethyl sulphide give the sulphonium compound (10) which with butyl-lithium in tetrahydrofuran gives four products derived from the highly reactive [2,3]-rearrangement intermediate (17): (11) (32%), (12) (2.5%), (13) (5%), and (14) (11%). One product only (21) (6%) derived from (17), could be isolated from the reaction in ether. Dimethylsulphonium methylide reacts with hexafluorobenzene to give a much simpler product consisting of (13) (5%) and (14) (45%).

In a recent paper¹ we described the reactions of polyfluoroarenes and -heteroarenes with the complex (1) formed with dimethyl sulphoxide (DMSO)-trifluoroacetic anhydride (TFAA), followed by reaction with triethylamine (TEA); dearomatised materials (4) were the main products, resulting from deprotonation of the oxysulphonium salt (2) followed by a [2,3]-sigmatropic rearrangement of the resulting ylide (3) but in one case a small amount of an ether (5) was formed by the reaction of the starting material with $\text{MeS}^+=\text{CH}_2$ (Scheme 1). We



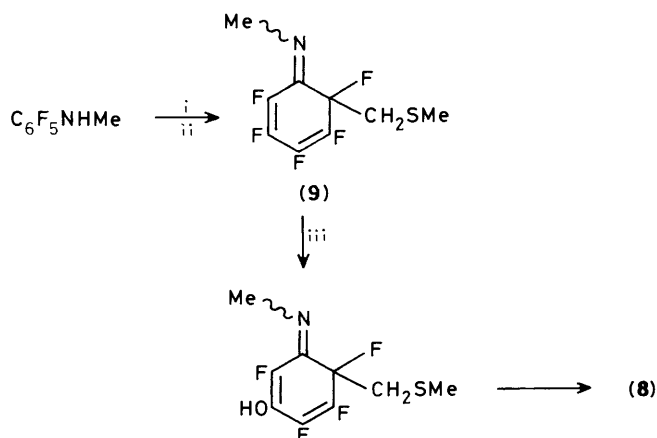
now report the results of attempted base-promoted rearrangements in which the oxygen in (2) is replaced by NH, NMe, and S. Using different synthetic routes, the system in which a CH_2 group replaces O in (2) has also been investigated.

The reaction of pentafluoroaniline with the DMSO-TFAA complex (1) in methylene dichloride at $\leq -50^\circ\text{C}$ followed by the addition of triethylamine gave a mixture of two products: 2,3,4,5,6-pentafluoro-*N*-trifluoroacetanilide² (6) (37%) and its *N*-methylthiomethyl derivative (7) (54%) formed by the trapping of $\text{MeS}^+=\text{CH}_2$ by the aniline before or after trifluoroacetylation; no product resulting from a [2,3]-sigmatropic rearrangement was isolated, unlike the *ortho*-methylthiomethyl aniline derivatives which were formed from a variety of mono-*ortho* and -*para* substituted anilines.³ In these successful rearrangements sodium methoxide in methanol had been



used to generate the ylide, but when this base was added to a mixture of the complex (1) and pentafluoroaniline, only (6) (91%) and (7) (8%) were obtained.

The reaction of 2,3,4,5,6-pentafluoro-*N*-methylaniline with complex (1) followed by treatment with TEA was shown by ^{19}F n.m.r. spectroscopy to give a mixture of products, the major component of which was isolated and identified as the cyclohexa-2,5-dienone derivative (8) (23%). The formation of (8) can be rationalised by invoking the initial formation of the [2,3]-sigmatropic rearrangement material (9), followed by hydrolysis at the 3-position of the imine and tautomerism (Scheme 2). The



Reagents: i, DMSO-TFAA; ii, Et_3N ; iii, water

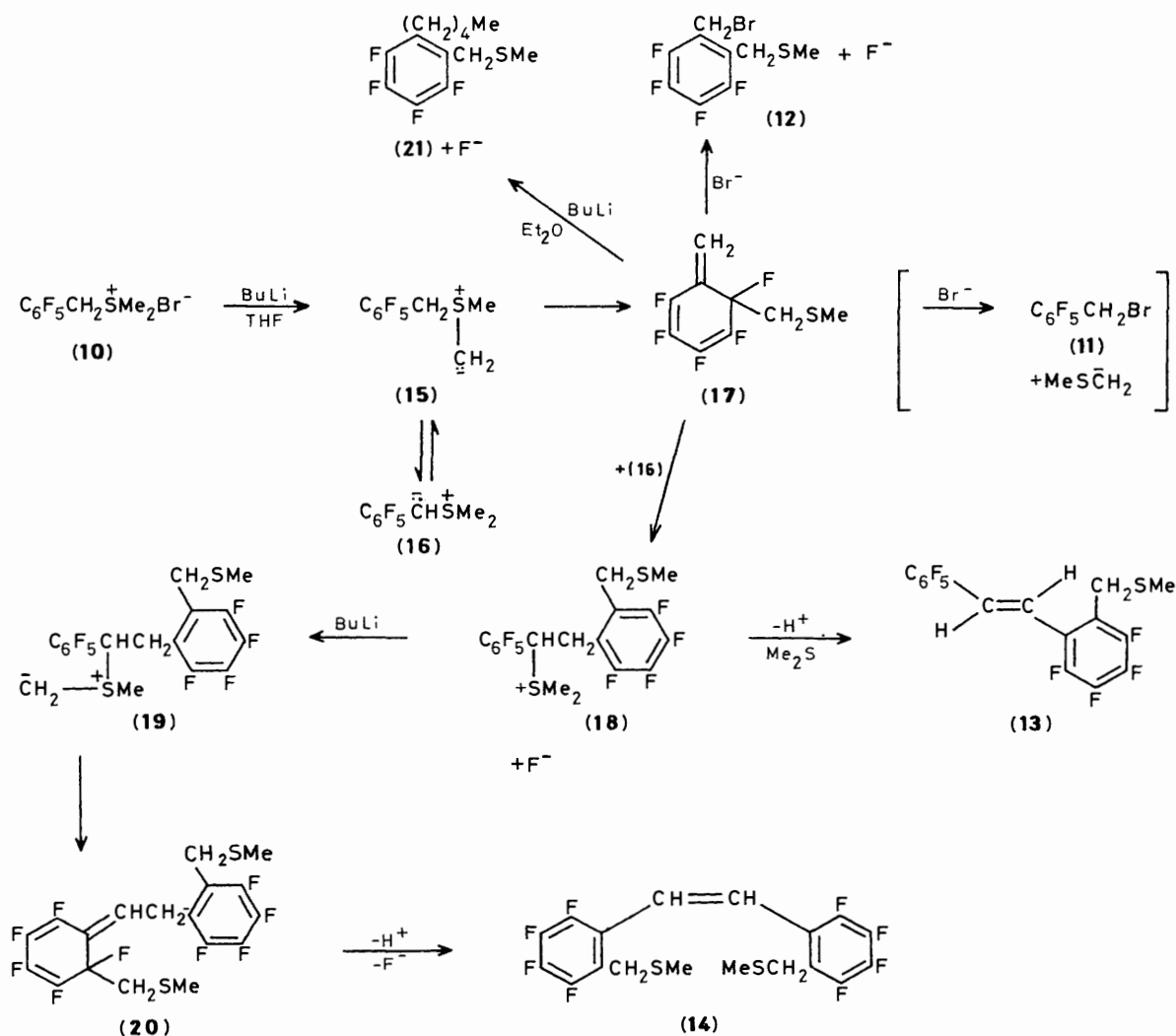
susceptibility of fluorine at C-3 to nucleophilic substitution is well established in highly fluorinated cyclohexadienones,^{1,4} so that a similar reaction with (9) is not unexpected.

Treatment of the DMSO-TFAA complex (1) with pentafluorothiophenol followed by the addition of triethylamine gave decafluorodiphenyl disulphide⁵ (94%). Previously, thiophenol had been treated with complex (1) at $\leq -50^\circ\text{C}$ without subsequent addition of base to give diphenyl disulphide³ and it was presumed the expected dimethylphenylthiosulphonium cation ($\text{C}_6\text{H}_5\text{S}^+\text{Me}_2$) had been immediately attacked by unchanged thiophenol to displace dimethyl sulphide. When TFAA followed by thiophenols were added to DMSO in acetonitrile at room temperature, methylthiomethylation of the sulphur occurred, and these yields decreased when triethylamine was added.³ In all these reactions no ylides are formed. Gassman, however, has described an alternative synthesis of phenylthiosulphonium ylides, which do undergo [2,3]-rearrangements.⁶

The formation of 2,3,4,5,6-pentafluorobenzyl(dimethyl)sulphonium salts, in which the oxygen in (2) is replaced by CH_2 , and the subsequent deprotonation reactions required different synthetic procedures to those given in Scheme 1. 2,3,4,5,6-Pentafluorobenzyl bromide⁷ and dimethyl sulphide readily formed the sulphonium bromide (10) (94%) which on treatment with one equivalent of butyl-lithium gave a complex mixture of products, four of which were isolated and identified: 2,3,4,5,6-pentafluorobenzyl bromide (11) (32%); 3,4,5,6-tetrafluoro-2-methylthiomethylbenzyl bromide (12) (2.5%); the unsymmetrical ethene (13) (5%), and the symmetrical ethene (14) (11%) (Scheme 3). The formation of all these products can be

accounted for on the basis of the initial formation of two ylides (15) and (16), only one of which, (15), can undergo a [2,3]-sigmatropic rearrangement to give (17). Nucleophilic attack by bromide ion on the exocyclic methylene group of (17) with loss of F^- gives the aromatic compound (12), while the formation of (11) would require the surprising loss of $\text{MeS}\bar{\text{C}}\text{H}_2$ in a reaction far more efficient than the loss of F^- . An alternative route to (11) would be the self-decomposition of (10) with loss of Me_2S , though we have no experimental evidence to confirm this. Attack on the exocyclic methylene group of (17) by the ylide (16) with loss of F^- gives the sulphonium salt (18) which either undergoes a simple elimination to form (13) or is deprotonated to a third ylide (19). A [2,3]-rearrangement of (19) to (20) followed by a 1,4-elimination of HF with aromatisation gives (14).

When diethyl ether was used as the solvent for the reaction of the sulphonium salt (10) with butyl-lithium, a complex product was again obtained which did not contain (11), (12) (13) or (14); the only product identified was the aromatic compound (21) (6%) (see Scheme 3), resulting from the nucleophilic attack of butyl-lithium on the exocyclic methylene group of (17) with loss of F^- . Other workers have brought about a similar reaction using CN^- on the base-induced rearrangement product from 2,6-dichlorobenzyl(dimethyl)sulphonium salts.⁸ The halogen in the *ortho* positions in these systems allows aromatisation of the initially formed rearrangement product, but this is prevented when both *ortho* positions are blocked with the Me group.⁹



Scheme 3.

In an attempt to simplify the product of the rearrangement of the ylide derived from a 2,3,4,5,6-pentafluorobenzyl(dimethyl)sulphonium salt, we decided to employ a counter ion less nucleophilic than bromide, namely fluoride, and chose to prepare it directly by reactions of hexafluorobenzene with Corey's reagent dimethylsulphonium methylide,¹⁰ $\text{Me}_2\text{S}^+\text{CH}_2 \longleftrightarrow \text{Me}_2\text{S}=\text{CH}_2$ derived from $\text{Me}_3\text{SBF}_4^-$ and MeSOCH_2Na ; an excess of $\text{Me}_2\text{S}=\text{CH}_2$ was used to generate the ylide from the $\text{C}_6\text{F}_5\text{CH}_2\text{S}^+\text{Me}_2\text{F}^-$ in the same reaction pot. The two ethenes (**13**) (5%) and (**14**) (45%) were the only products isolated.

Finally, hexafluorobenzene in tetrahydrofuran at -70°C was treated with two equivalents of $\text{Me}_2\text{S}=\text{CH}_2$ (i.e. inverse addition) and the mixture quenched with water at -25°C in an attempt to isolate the first [2,3]-rearrangement product (**17**). The symmetrical ethene (**14**) (23%) was the only product formed in the experiment, which demonstrated the extreme reactivity of (**17**) towards nucleophilic attack.

Experimental

N.m.r. spectra were obtained with a Varian EM360L spectrometer [^1H (60 MHz) and ^{19}F (56.4 MHz)] or with a Bruker AC250 [^1H (250 MHz) and ^{19}F (235 MHz)]. Chemical shifts are downfield from internal SiMe_4 (δ_{H}), or upfield from internal CFCl_3 (δ_{F}). Mass spectroscopy data were obtained with a VG 7070E instrument. Molecular ions M^+ are quoted for electron ionisation except where stated: c.i. represents chemical ionisation using isobutane.

Reactions of Polyfluoroaromatic Compounds with DMSO, Trifluoroacetic Anhydride (TFAA), and Triethylamine (TEA). (a) *With pentafluoroaniline.* A mixture of DMSO (1.6 ml) and dry methylene dichloride (25 ml) was cooled to -60°C in solid CO_2 -acetone, and TFAA (1.6 ml, 11 mmol) was added dropwise to the stirred solution whereupon a white solid precipitated. Pentafluoroaniline (1.079 g, 5.9 mmol) in dry methylene dichloride (25 ml) was added dropwise to the mixture, the temperature being maintained at $\leq -50^\circ\text{C}$. After 2 h, TEA (2.5 ml, 18 mmol) was added and the solution was allowed to warm to room temperature over 18 h. The mixture was diluted with ether, washed with water and with hydrochloric acid (2M), and the organic phase was dried (MgSO_4). The solvents were evaporated at $25^\circ\text{C}/0.05\text{ mmHg}$ and the residue, separated by chromatography on silica using CHCl_3 , gave two components: (i) a liquid 2,3,4,5,6-pentafluoro-*N*-methylthiomethyl-*N*-trifluoroacetanilide (**7**) (1.074 g, 54%) [Found: C, 35.2; H, 1.1; N, 4.5%; M^+ , 339 (c.i.). $\text{C}_{10}\text{H}_5\text{F}_8\text{NOS}$ requires C, 35.41; H, 1.49; N, 4.13%; M , 339]; $\delta_{\text{F}}(\text{CDCl}_3)$ 71.7 (s, CF_3), 143.1 (2-F, 6-F), 150.0 (4-F), and 161.1 p.p.m. (3-F, 5-F); $\delta_{\text{H}}(\text{CDCl}_3)$ 2.25 (s, Me) and 4.89 (s, CH_2); and (ii) 2,3,4,5,6-pentafluoro-*N*-trifluoroacetanilide (**6**) (0.612 g, 37%), identical with an authentic sample.²

When the experiment was repeated, but using sodium methoxide in methanol in place of TEA compounds (**7**) (8%) and (**6**) (91%) were again obtained.

(b) *With 2,3,4,5,6-pentafluoro-*N*-methylaniline.* The *N*-methylaniline (7.585 g, 41 mmol) in dry CH_2Cl_2 (100 ml) was added dropwise to a mixture of DMSO (12 ml), dry CH_2Cl_2 (100 ml), and TFAA (12 ml, 85 mmol) at $\leq -50^\circ\text{C}$ followed after 2 h by the addition of TEA (17 ml, 122 mmol). The subsequent procedure reported in (a) was repeated and the major component was separated by chromatography on silica using initially CHCl_3 followed by CH_2Cl_2 to give 2,4,5,6-tetrafluoro-3-(*N*-methylamino)-4-methylthiomethylcyclohexa-2,5-dienone (**8**) (2.243 g, 23%), m.p. $134\text{--}135^\circ\text{C}$ (from benzene) [Found: C, 42.6; H, 3.7; N, 5.8%; M^+ , 255 (c.i.). $\text{C}_9\text{H}_9\text{F}_4\text{NOS}$ requires C, 42.34; H, 3.55; N, 5.49%; M , 255]; $\delta_{\text{F}}([\text{C}_2\text{H}_6]$ acetone) (145.8

(dm, 5-F), 150.1 (dm, 4-F), 155.5 (nm, 6-F), and 171.6 p.p.m. (nm, 2-F); $J_{4-\text{F},5-\text{F}}$ 30.5 Hz; $\delta_{\text{H}}([\text{C}_2\text{H}_6]$ acetone) 2.16 (s, SMe), 3.17 (m, NMe), 3.42 (m, CH_2), and 6.55 (br s, NH); ν_{max} 3 320 cm^{-1} (NH).

(c) *With pentafluorothiophenol.* The thiophenol (1.104 g, 5.5 mmol) in dry CH_2Cl_2 (25 ml) was added dropwise to a mixture of DMSO (1.5 ml), dry CH_2Cl_2 (25 ml), and TFAA (1.5 ml, 10.6 mmol) at $\leq -50^\circ\text{C}$ followed after 2 h by TEA (2.4 ml, 17 mmol). The subsequent procedure reported in (a) was repeated to give decafluorophenyl disulphide (1.029 g, 94%) identical with an authentic sample.⁵

Reaction of 2,3,4,5,6-Pentafluorobenzyl Bromide⁷ with Dimethyl Sulphide.—The bromo compound (18.632 g) and dimethyl sulphide (19.4 g) were allowed to stand at room temperature for 7 days. The white solid which precipitated was filtered off and washed with light petroleum (b.p. $40\text{--}60^\circ\text{C}$) to give 2,3,4,5,6-pentafluorobenzyl(dimethyl)sulphonium bromide (**10**) (21.775 g, 94%), m.p. $110.5\text{--}112.5^\circ\text{C}$ (Found: C, 33.45; H, 2.55. $\text{C}_9\text{H}_8\text{BrF}_5\text{S}$ requires C, 33.45; H, 2.50%).

Reaction of 2,3,4,5,6-Pentafluorobenzyl(dimethyl)sulphonium Bromide (10) with Butyl-lithium.—(a) *In tetrahydrofuran (THF).* The sulphonium bromide (**10**) (5.596 g, 17.3 mmol) was suspended in dry THF (100 ml) at -70°C and treated over 10 min with butyl-lithium in hexane (1.61M; 11.0 ml, 17.7 mmol) and the temperature was maintained at $\leq -67^\circ\text{C}$ for a further 60 min. The mixture was allowed to warm to 4°C , during which time the colour turned from indigo to yellow-brown at ca. 0°C . After 18 h at room temperature, the mixture was evaporated under reduced pressure at room temperature to a small bulk, diluted with water, acidified (4M H_2SO_4), and extracted with ether. The dried (MgSO_4) extracts were evaporated to give the crude reaction product (4.736 g), which was evaporated further at room temperature 0.05 mmHg, the vapour being collected in a trap cooled in liquid air. The residue (3.654 g) was separated by flash chromatography on silica (6 in \times 2 in) using CCl_4 as the eluant to give four components: (i) the fastest moving component, combined with the material collected in the liquid air traps was 2,3,4,5,6-pentafluorobenzyl bromide (**11**) (1.429 g, 32%); (ii) the second component, having the same R_{F} value as the third component was partially separated by selective microdistillation at room temperature/0.05 mmHg followed by thick layer chromatography on silica using light petroleum (b.p. $40\text{--}60^\circ\text{C}$) as the eluant and gave a liquid, 3,4,5,6-tetrafluoro-2-methylthiomethylbenzyl bromide (**12**) (0.130 g, 2.5%) (Found: C, 36.0; H, 2.2%; M^+ 302, 304; $\text{C}_9\text{H}_7\text{BrF}_4\text{S}$ requires C, 35.66; H, 2.33%; M , 302, 304); $\delta_{\text{F}}(\text{CDCl}_3)$ 141.2, 142.5, 154.9, and 156.7 p.p.m. with intensities in the ratio 1:1:1:1; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.12 (CH_3), 3.85 (CH_2S), and 4.64 (CH_2Br); (iii) the third component, remaining after the removal of more volatile compound (**12**) was (E)-1-pentafluorophenyl-2-(3,4,5,6-tetrafluoro-2-methylthiomethyl)phenylethene (**13**) (0.163 g, 5%), m.p. $65.5\text{--}66.5^\circ\text{C}$ [from light petroleum (b.p. $40\text{--}60^\circ\text{C}$)] (Found: C, 47.7; H, 1.55%; M^+ , 402. $\text{C}_{16}\text{H}_6\text{F}_9\text{S}$ requires C, 47.77; H, 1.75%; M , 402); $\delta_{\text{F}}(\text{CDCl}_3)$ 140.4, 142.6, 154.6, 155.6, 157.1, and 162.6 p.p.m. in the ratio 1:3:1:1:2, respectively; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.14 (Me), 3.78 (CH_2S), 7.14 ($-\text{CH}=\text{}$), and 7.38 ($-\text{CH}=\text{}$), J_{E} 17 Hz; and (iv) 1,2-bis(3,4,5,6-tetrafluoro-2-methylthiomethylphenyl)ethene (**14**) (0.427 g, 11%), m.p. $79.0\text{--}79.5^\circ\text{C}$ [from light petroleum (b.p. $40\text{--}60^\circ\text{C}$)] (Found: C, 48.65; H, 2.65%; M^+ , 444. $\text{C}_{18}\text{H}_{12}\text{F}_8\text{S}_2$ requires C, 48.65; H, 2.72%; M , 444); $\delta_{\text{F}}(\text{CDCl}_3)$ 140.6, 142.6, 156.1, and 157.3 p.p.m. with intensities in the ratio 1:1:1:1; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.15 (Me), 3.83 (CH_2S), and 7.18 ($-\text{CH}=\text{}$).

(b) *In diethyl ether.* The sulphonium bromide (**10**) (4.013 g, 12.4 mmol) was suspended in dry diethyl ether (50 ml) at -70°C and treated with butyl-lithium (1.58M; 8.6 ml, 13.6 mmol) at $\leq -55^\circ\text{C}$. The mixture was allowed to warm to

–24 °C over 3 h and then added rapidly to 5M H₂SO₄. The solution was extracted with ether, the extracts were dried (MgSO₄), and the solvent was evaporated to give an oil (1.310 g). The oil was evaporated at room temperature/0.05 mmHg and the condensed vapours [shown by ¹⁹F n.m.r. spectroscopy to contain no C₆F₅CH₂Br (**11**)] were partially separated by flash chromatography on silica using light petroleum (b.p. 40–60 °C) to give almost pure product (0.195 g, 6%). The last traces of impurities were removed by vapour phase chromatography on a 10% silicone elastomer column at 230 °C to give a liquid 1,2,3,4-tetrafluoro-5-methylthiomethyl-6-pentylbenzene (**21**) (Found: C, 55.95; H, 6.0%; M⁺, 280. C₁₃H₁₆F₄S requires C, 55.70; H, 5.75%; M, 280); δ_F (CDCl₃) 143.6, 158.6, and 160.4 p.p.m. with intensities in the ratio 2:1:1, respectively; δ_H (CDCl₃) 0.90 (Me), 1.36 [(CH₂)₂], 1.55 (CH₂), 2.10 (MeS), 2.70 (CH₂), and 3.70 (CH₂S).

The residue after compound (**21**) had been removed was further evaporated at 60–65 °C/0.05 mmHg overnight, but neither the volatile nor the non-volatile materials contained compounds (**12**), (**13**), or (**14**); the components in these mixtures were not identified.

Reaction of Hexafluorobenzene with Dimethylsulphonium Methylide, Me₂S=CH₂.¹⁰—Sodium hydride (3.712 g, 155 mmol) was treated with dry DMSO (75 ml) under nitrogen at 65–70 °C, cooled to room temperature, and diluted with dry tetrahydrofuran (150 ml). The suspension was cooled to –15 °C and trimethylsulphonium tetrafluoroborate (25.517 g, 156 mmol) in dry DMSO (100 ml) was added over 4 min, during which time the temperature rose to –4.5 °C. The solution was maintained at this temperature for 5 min and hexafluorobenzene (7.329 g, 39.4 mmol) in dry tetrahydrofuran (30 ml) was added over 3 min, the temperature rising to –2 °C. The mixture was warmed to 20 °C whereupon a mild exothermic reaction occurred reaching a maximum of 29 °C after 12 min. Water was added to the mixture 40 min after the addition of the C₆F₆ had been completed, followed by ether. The ether layer was separated and dried (MgSO₄), and the solvent was evaporated to give an oil (7.279 g) which was separated by flash chromatography on silica using CCl₄. Two components were

separated and identified: (i) the unsymmetrical ethene (**13**) (0.45 g, 5%) and (ii) the symmetrical ethene (**14**) (3.937 g, 45%).

When dimethylsulphonium methylide [prepared from NaH (1.629 g, 68 mmol) in DMSO (25 ml), diluted with dry THF (75 ml), and cooled to –10 °C to which was added Me₃S⁺BF₄[–] (11.3 g, 69 mmol)] at –5 °C was added to hexafluorobenzene (6.4 g, 34 mmol) in dry THF (100 ml) at –70 °C (inverse addition), the reaction temperature rose to –47.5 °C over 5 min. After 100 min the temperature had reached –25 °C and the mixture was quenched with water and the product isolated by extraction with ether. Removal of unchanged C₆F₆ under reduced pressure at room temperature left a solid (1.772 g) which was identified as the pure symmetrical ethene (**14**) (23%).

Acknowledgements

We thank the S.E.R.C. for a research studentship (to J. A. K. J. F.).

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Received 2nd November 1987; Paper 7/1937