

Table 1. Trifluoromethylalcohols from CF₃Br.

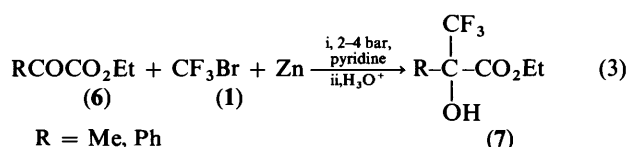
Product ^a	Starting material	Quantity (mol)	T (°C)	Yield (%)	B.p. or m.p. °C/mm Hg(lit.)	δ _F (J _{HF})
(3a)	Benzaldehyde	0.099	20	52	75/12 (64–65/5)	–77.7 (7.1)
(3b)	4-Methylbenzaldehyde	0.093	20	53	86–90/10 (102/15)	–78.3 (7.5)
(3c)	4-Methoxybenzaldehyde	0.099	20	47	122/13	–78 (7.1)
(3d)	4-Fluorobenzaldehyde	0.093	20	60	74–76/15	–77.8 (7.1)
(3e)	4-Chlorobenzaldehyde	0.093	40	46	90–95/12 (80/4)	–77.8 (6.6)
(3f)	4-Cyanobenzaldehyde	0.092	40	43	m.p. 89	–78.5 (7.5)
(3g)	Anthracene-9-carbaldehyde	0.049	20	37	m.p. 140–141 (142–143)	–74.7 (8.5)
(3h)	Pyridine-2-carbaldehyde	0.11	20	65	m.p. 46	–77.7 (6.6)
(3i)	2-Furaldehyde	0.12	20	26	60/12	–77.7 (7.1)
(3j)	Cyclohexanecarbaldehyde	0.083	20	30	60–64/12 (80–82/23)	–75.5 (7.7)
(3k)	Butanal	0.113	0–10	30	102–104 (107–108/736)	–79.5 (7.5)
(3l)	Cinnamaldehyde	0.096	20	55	98–102/0.5 (86–88/5)	–77.7 (6.6)
(3o)	Cyclohexanone	0.1	20	20	m.p. 61	–83 (s)
(3p)	Acetophenone	0.083	20	20		–80 (s)
(7a)	Ethyl pyruvate	0.091	20	35	60/65 (140–142/760)	–79.7 (s)
(7b)	Ethyl phenylglyoxylate	0.063	20	30		–75.3 (s)

(3a) 2,2,2-Trifluoro-1-phenylethanol; ⁷ identical with Aldrich product; δ_H 7.5 (Ph), 5 (q, CH), and 3.5 (OH); m/z 176 (M⁺), 140 (C₆H₅CHCF₂⁺), and 107 (C₆H₅CHOH⁺). (3b) 2,2,2-Trifluoro-1-(4-tolyl)ethanol.³² (3c) 2,2,2-Trifluoro-1-(4-methoxyphenyl)ethanol.¹ (3d) 2,2,2-Trifluoro-1-(4-fluorophenyl)ethanol.^b δ_F –107.2 (ArF). (3e) 1-(4-Chlorophenyl)-2,2,2-trifluoroethanol; ⁸ m/z 210, 212 (M⁺) and 141, 143 (p-ClC₆H₄CHOH⁺). (3f) 1-(4-Cyanophenyl)-2,2,2-trifluoroethanol; m/z 201 (M⁺) and 132 (p-NCC₆H₄CHOH⁺). (3g) 1-(9-anthryl)-2,2,2-trifluoroethanol; ⁹ δ_H 8.8–7.4 (ArH), 6.8 (q, CH), and 3 (OH). (3h) 2,2,2-Trifluoro-1-(2-pyridyl)ethanol; ^b δ_H 9–7.3 (ArH), 5.2 (q, CH), and 6.1 (OH). (3i) 2,2,2-trifluoro-1-(2-furyl)ethanol; ⁸ δ_H 7.4 (1 H, m), 6.5–6.32 (2 H, m), 4.6 (q, CH), and 3.5 (OH); m/z 166 (M⁺) and 97 (C₄H₃CHOH⁺). (3j) 1-Cyclohexyl-2,2,2-trifluoroethanol; ^c δ_H 4.1–3.4 (m, CH), 2.5 (OH) and 2.2–0.9 (m, 10 H). (3k) 1,1,1-trifluoropentane-2-ol; ³⁶ hydrolysis was performed with cold, stirred 20% sulphuric acid (15 ml) for 8 h. δ_H 3.9 (m, CH), 3.2 (OH), 2.7–1.3 (m, CH₂CH₂), and 1.2–0.8 (m, Me). (3l) 4-phenyl-1,1,1-trifluorobut-3-en-2-ol; ⁷ δ_H 7.4 (Ph), 6.9 (dd, J_{HH} 6 Hz, CH), 4.7 (quint, CH), and 3.6 (OH). (3o) 1-trifluoromethylcyclohexanol; ^d GLC on 10% dinonyl phthalate on Chromosorb WDMCS 60/80 mesh at 120 °C; δ_H 2.1–1.4 (m). (3p) 1,1,1-trifluoro-2-phenylpropan-2-ol; ^d GLC on 10% dinonyl phthalate on Chromosorb WDMCS 60/80 mesh at 145 °C; δ_H 6.8–6.3 (Ph), 1.9 (OH), and 0.9 (s, Me). (7a) Ethyl 3,3,3-trifluoro-2-hydroxy-2-methylpropanoate; ^e δ_H 4.8 (q, J_{HH} 7 Hz, CH₂), 4.2 (OH), 1.7 (s, Me), and 1.5 (t, Me). (7b) Ethyl 3,3,3-trifluoro-2-hydroxy-2-phenylpropanoate; GLC on 30% SE 30 on Chromosorb PAW 45/60 mesh at 180 °C; δ_H 8.1–7.1 (Ph), 4.4 (q, J_{HH} 7 Hz, CH₂), 4.2 (OH), and 1.37 (t, Me); ν_{max}(CCl₄) 3 470 and 1 735 cm⁻¹; m/z 248 (M⁺), 175 (C₆H₅COHCF₃⁺), and 105 (C₆H₅C⁺=O).

^a Compounds (3m) and (3n) are described in the text. ^b W. H. Pirkle and T. G. Burlingame, *Tetrahedron Lett.*, 1967, 4039. ^c M. Buccarelli, A. Formi, I. Moretti, and G. Torre, *Synthesis*, 1983, 867. ^d N. Ishikawa and T. Kitazume, *Chem. Lett.*, 1981, 1679. ^e M. W. Buxton, M. Stacey, and J. C. Tatlow, *J. Chem. Soc.*, 1954, 366.

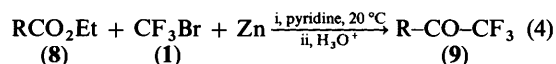
The formation of long-chain perfluoroalkylzinc compounds occurred in the absence of third component in the case of long-chain iodides.

In the case of an α-keto ester (6), the addition of the trifluoromethyl group occurred as expected to the keto group to afford the products (7) [equation (3)].



With simple esters like ethyl acetate, no reaction seemed to occur. However, ethyl benzoate, like acetone, initiated the

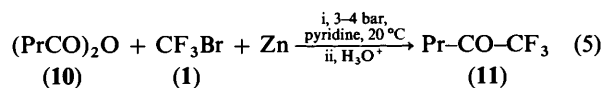
formation of the trifluoromethylzinc derivatives (4) and (5). The Barbier procedure was effective even at atmospheric pressure when the ester was activated by an electron-withdrawing group; ethyl trifluoropyruvate (9a) and hexafluoroacetone (9b) were respectively obtained from diethyl oxalate (8a) and ethyl trifluoroacetate (8b) [equation (4)]. Ethyl 2-oxotridecafluoro-octanoate was also prepared from perfluorohexyl iodide.



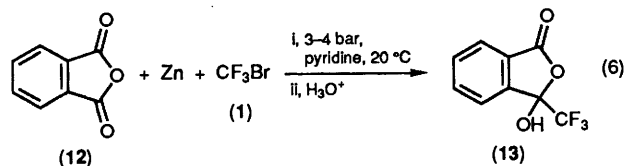
R = a, CO₂Et; b, CF₃

Attempts to condense aliphatic acid chlorides under similar

conditions failed because these substrates reacted first with pyridine and zinc. Nevertheless, some acid anhydrides were trifluoromethylated. Their reactivity was very dependent on the chain length. The condensation of acetic anhydride could not be controlled and led to a thick mixture. In contrast, heptanoic anhydride reacted very sluggishly. However, butyric anhydride (**10**) led to 1,1,1-trifluoropentan-2-one (**11**) but only in 20% yield [equation (5)].

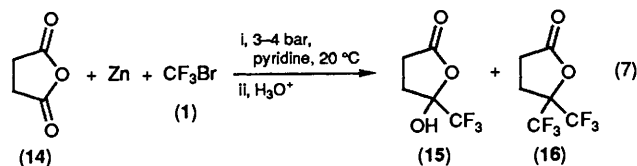


Yields were higher in the case of cyclic anhydrides. From phthalic anhydride (**12**), 3-hydroxy-3-trifluoromethylphthalide (**13**) was obtained in 61% yield [equation (6)]. This lactol had been previously prepared in several steps.^{14,15}



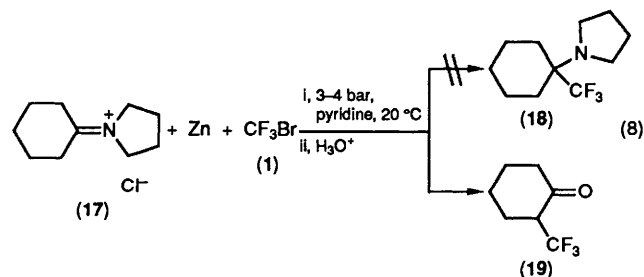
The corresponding 3-hydroxy-3-(tridecafluorohexyl)phthalide was also obtained similarly.

Besides a similar monotrifluoromethylated compound (**15**) (18%), a bis-trifluoromethylated product (**16**) (40%) was obtained from succinic anhydride (**14**) [equation (7)]. This lactol (**15**) is the cyclized form of 5,5,5-trifluorolaevalinic acid¹⁶



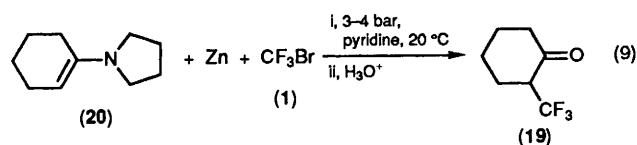
(see Experimental section). Compound (**16**) was probably produced by trifluoromethylation of the open form of this acid.

Iminium Salts and Enamines.—It is well known that iminium salts show a reactivity comparable to that of carbonyl compounds towards organometallics.¹⁷ Consequently, we tried to condense them with the bromide (**1**) in the presence of zinc following the Barbier procedure. The first example tried was the iminium ion (**17**) derived from cyclohexanone. The structure of the adduct should logically be the amine (**18**). Instead of this compound, we obtained 2-trifluoromethylcyclohexanone (**19**) in 25% yield [equation (8)] (only one fluorinated product was detected by ¹⁹F NMR analysis of the crude pyridine mixture).



Owing to the possibility that pyridine is able to transform the iminium ion into the enamine by elimination of HCl, we tried to condense this unsaturated amine itself. Indeed we obtained the

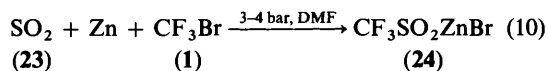
cyclic ketone (**19**) from the enamine (**20**) in similar yield [equation (9)]. This result is contradictory to the usual resistance of enamines to additions of organometallics.¹⁷



In order to avoid the possibility of enamine formation, we chose iminium salts (**21**) and (**22**) lacking removable α hydrogens. However, no condensation products were detected with these examples.



Sulphur Dioxide.—In contrast to the carbonyl condensations, where no reaction seemed to occur between the substrate and the metal, an initial attack on zinc by sulphur dioxide (**23**) in DMF was actually observed. Then, introduction of the bromide (**1**) under slight pressure led to the formation of zinc bromide trifluoromethanesulphinate (**24**) [equation (10)], as we described previously.¹³



When an electron-rich aromatic nucleus was present in this medium, trifluoromethylation of the ring occurred.^{18,19} Again, this trifluoromethylation is rather unusual for an organometallic condensation. Homologous zinc sulphinates have been obtained from the much more reactive long-chain perfluoroalkyl iodides when these halides were introduced at atmospheric pressure, before or after sulphur dioxide, in a suspension of zinc-copper couple in DMSO or DMF.²⁰ This condensation was interpreted as occurring at the metallic surface.²¹ In order to check this hypothesis, we performed the following experiment: in one flask, sulphur dioxide was bubbled into a stirred suspension of zinc in DMF. The mixture was allowed to settle, then was decanted during a few min. Then, approximately half of the supernatant liquid was transferred under nitrogen to a second flask containing perfluoroalkyl iodide. After the mixture had been stirred for 10 min, an aliquot was analysed by ¹⁹F NMR spectroscopy. Besides signals of the starting iodide, that of the corresponding sulphinate were also obtained. Consequently a reaction had occurred in this solution. Moreover, inhibition of sulphinate formation was noticed when nitrobenzene was mixed with the perfluoroalkyl iodide.

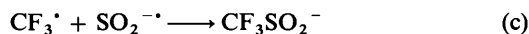
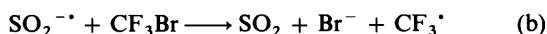
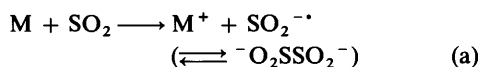
Discussion

Comparison of the condensation of carbonyl compounds and of sulphur dioxide showed striking differences. In the case of benzaldehyde, no reaction seemed to occur initially with zinc. In contrast, an initial attack of zinc occurred in the case of sulphur dioxide.²² When 1-methylpyrrole was introduced into the medium, trifluoromethylation of the ring occurred in the zinc-sulphur dioxide medium¹⁹ but not in that of benzaldehyde. It seemed that different intermediates were involved.

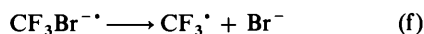
The intermediates could be solvated zinc derivatives which are known to be poorly reactive.^{12,23} The condensation of long-

chain perfluoroalkyl iodides with carbon dioxide or sulphur dioxide in DMSO or DMF in the presence of zinc was interpreted to occur by activation of the corresponding organometallic, owing to its adsorption at the metallic surface.^{20,21} However, our transfer experiment showed that an intermediate was present in solution in that particular case. Nevertheless, the possibility that the reaction with carbonyl compounds occurs in the solvation layer around the metal remains because a similar transfer experiment failed in the case of benzaldehyde.

Inhibition of sulphinate formation in our two-flask experiment by the electron scavenger nitrobenzene could be interpreted by a single-electron-transfer process^{1,13} (see the following reactions). Sulphur dioxide is known to be easily reducible (see step a).^{22,24} Its radical anion $\text{SO}_2^{\cdot-}$ (**25**) can react with the bromide (**1**), or with other perfluoroalkyl halides, to give a perfluoroalkyl radical (step b). Combination of this radical with (**25**) can explain the sulphinate formation (step c). Indeed, we have obtained a trifinate salt from other sources of radical anion (**25**), such as sodium dithionite or sodium hydroxymethanesulphinate.¹ Trifinate salts have also been prepared electrochemically from bromide (**1**) and the dioxide (**23**) using zinc²⁵ or carbon²⁶ anodes. Perfluoroalkylation of an electron-rich aromatic nucleus introduced in the zinc-sulphur dioxide mixture is also in agreement with the presence of a radical intermediate.^{18,19}



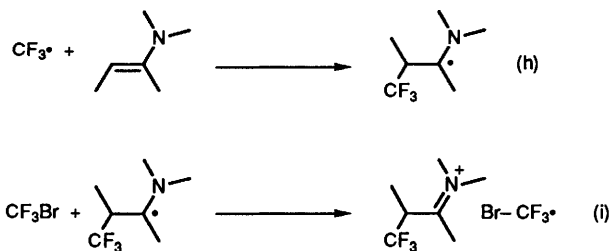
We have previously interpreted the initial step e of the reaction between trifluoromethyl bromide and sulphur dioxide radical anion (steps e and f) as an outer-sphere-electron transfer.^{1,14}



An alternative inner-sphere-electron transfer (step g) has been proposed recently.^{26,27}



The trifluoromethylation of enamine (**20**) seems to indicate the existence of the trifluoromethyl radical²⁸ in this Barbier condensation, even in the absence of sulphur dioxide (steps h and i).



The proposed mechanism for the formation of Grignard reagents, and probably for the zinc analogues, involves a radical and a carbanion as intermediates.²⁹

The absence of addition to various iminium salts seemed interesting. In contrast to the case of carbonyl compounds, iminium ions do not present a partial negative charge able to coordinate with the metal. On the other hand, carbonyl adsorption leaves the possibility for these compounds to play the part of a ligand around the nascent organometallic and to react in the co-ordination sphere. The peculiar behaviour of SO_2 could be due to the fact that it is the only substrate that we studied until now which is obviously more reducible than trifluoromethyl bromide; the major pathway can occur in solution owing to the easy formation of the corresponding sulphur dioxide radical anion. In the benzaldehyde condensation, no pinacol product, formed from a ketyl radical, was observed, as for a Barbier synthesis using lithium metal.³⁰ It seems that zinc in pyridine is a much milder reductant.³¹

Conclusions.—The Barbier procedure using zinc and trifluoromethyl bromide under slight pressure allowed the preparation of trifluoromethyl-containing molecules: alcohols, ketones, lactols, *etc.* These condensations seemed to occur generally in the neighbourhood of the metallic surface, where the electrophile can be adsorbed, and to involve nascent organozinc intermediates. However, sulphur dioxide behaved differently. The easy formation of sulphur dioxide radical anion could allow its condensation to occur with trifluoromethyl bromide, and related halides, in solution. The observation of enamine reactivity under these Barbier conditions could be the result of a chain process initiated by capture of an intermediate trifluoromethyl radical.

Experimental

¹H NMR spectra were recorded on a Bruker A 300 spectrometer with tetramethylsilane as internal reference. Fluorine NMR spectra were obtained on a Varian EM360L spectrometer (56.4 MHz) and were recorded in ppm (δ_F downfield from CFCl_3 (solvent: CDCl_3); ¹³C NMR spectra were recorded on a Varian CFT20 spectrometer with tetramethylsilane as internal reference. Trifluoromethyl bromide was purchased from Setic Labo, trifluoromethyl iodide from Fluorochem, DMF, pyridine, and organic reactants from Aldrich (and distilled before use), and zinc from Prolabo. Perfluoroalkyl iodides were generous gifts of Atochem. The enamine of cyclohexanone was prepared by azeotropic distillation of a mixture of cyclohexanone, pyrrolidine, benzene, and toluene-*p*-sulphonic acid. Microanalyses are recorded in Table 2.

Preparation of Alcohols (3).—*General method.* A pressure-safe bottle containing pyridine (25 ml), the aldehyde or the ketone, and zinc (1 mol equiv.) was placed under reduced pressure. The bottle was charged with trifluoromethyl bromide (3.7 bars) and shaken for 4 h or until the gas absorption ceased. The reaction began after a few min and was exothermic; the temperature was controlled and maintained by a water-bath. The pressure of CF_3Br was kept between 2.5–5 bar. In the case of benzaldehyde, CF_3Br (30 g, 0.2 mol) was absorbed. The flask was opened, and the non-reacting zinc was removed by filtration. The mixture was hydrolysed with cold 10% hydrochloric acid (50 ml) during 30 min. After extraction with diethyl ether, the extract was washed with water, and evaporated; the residual aldehyde was removed by crystallization with sodium hydrogen sulphite: the organic layer was shaken with 38% aq. hydrogen sulphite (120 ml) and methanol (30 ml); for ketones, crystallization with sodium hydrogen sulphite was not possible. After filtration to remove salt, extraction of the filtrate with diethyl ether, drying of the extract (MgSO_4), and removal of solvent, the alcohol was distilled or sublimed. Results are summarized in Table 1.

Table 2. Microanalyses.

Compound	Formula	Found (%)			Required (%)		
		C	H	N or F	C	H	N or F
(3a)	C ₈ H ₇ F ₃ O	54.5	4.2		54.55*	4.01*	
(3b)	C ₉ H ₉ F ₃ O	56.7	4.9		56.84*	4.77*	
(3c)	C ₉ H ₉ F ₃ O ₂	52.25	4.3		52.43	4.40	
(3d)	C ₈ H ₆ F ₄ O	49.6	3.0		49.49	3.11	
(3h)	C ₇ H ₆ F ₃ NO	47.7	3.3	N 8.2	47.46	3.41	N 7.91
(3j)	C ₈ H ₁₃ F ₃ O	53.0	7.3		52.74*	7.19*	
(3k)	C ₅ H ₉ F ₃ O	42.4	6.5		42.25*	6.38*	
(3l)	C ₁₀ H ₉ F ₃ O	59.6	4.6		59.40*	4.49*	
(3o)	C ₇ H ₁₁ F ₃ O	50.3	6.4		49.99	6.59	
(3p)	C ₉ H ₉ F ₃ O	56.8	5.0		56.84	4.77	
(7a)	C ₆ H ₉ F ₃ O ₃	38.9	5.0		38.71*	4.87*	
(11)	C ₅ H ₇ F ₃ O	42.85	5.4		42.83*	5.03*	
(15)	C ₃ H ₅ F ₃ O ₃	35.4	3.1	F 33.5	35.31*	2.96*	F 33.51*
(16)	C ₆ H ₄ F ₆ O ₂	32.8	2.0	F 51.3	32.45	1.82	F 51.33
(19)	C ₇ H ₉ F ₃ O	50.6	5.45	F 34.35	50.60*	5.46*	F 34.41*

* Calculated values for known compounds.

Reaction of Benzaldehyde with Perfluoroalkyl Iodides.—2,2,2-Trifluoro-1-phenylethanol (3a). A pressure-safe bottle containing pyridine (25 ml), the aldehyde (10 ml, 0.099 mol) and zinc (6.5 g) was placed under reduced pressure. The bottle was charged with CF₃I (24 g, 0.122 mol) and shaken for 4 h. The reaction began after a few min and was exothermic; the temperature was controlled and maintained by a water-bath at 20 °C. Then the flask was opened and the mixture was treated as above to give the alcohol (5.9 g, 34%), b.p. 75 °C/12 mmHg lit.,^{7,32} 84–87 °C/14 mmHg).

2,2,3,3,3-Pentafluoro-1-phenylpropan-1-ol (3m). The previous experiment was repeated with pentafluoroethyl iodide (32 g, 0.130 mol) to give the title compound (6.0 g, 27%), b.p. 72–75 °C/10 mmHg (lit.,⁷ 84–85 °C/10 mmHg); δ_F –81 (CF₃), –127.8 (dd, J_{HF} 15, J_{FF} 274.5 Hz, CF₂), and –121.7 (dd, J_{HF} 9.4 Hz, CF₂); δ_H 7.4 (ArH), 5.1 (dd, CH), and 3 (OH); m/z 226 (M⁺, 107 (C₆H₅CHOH⁺), and 119 (C₂F₅⁺).

Tridecafluoro-1-phenyl-1H-heptan-1-ol (3n). To a stirred mixture of pyridine (10 ml), benzaldehyde (2 ml, 0.02 mol), and zinc powder (2 g), under argon was added perfluorohexyl iodide (10 g). After 4 h, the mixture was treated as usual and sublimed to give the title alcohol (4.1 g, 48%), m.p. 47 °C (lit.,⁷ 49–51 °C); δ_F –79.7 (tt, CF₃), –115 and –125 (dd, J_{FF} 273 Hz), –118, –122, –124, –125 (m, 8F); δ_H 7.5 (ArH), 5.4–5.2 (dd, ³J_{HF} 17, ³J_{HF} 8 Hz, CH), and 3.8 (OH).

Reaction of Ketones.—**Reaction with acetone.** A pressure-safe bottle containing pyridine (25 ml), acetone (10 ml, 0.14 mol), and zinc (9 g, 0.14 mol) was placed under reduced pressure. The bottle was charged with trifluoromethyl bromide (3.7 bar) and shaken for 4 h or until the gas absorption ceased. The reaction began after a few min; temperature was controlled and maintained by a water-bath at 50 °C. The pressure of CF₃Br was kept between 2.5–5 bar. The gas absorption was slow. The flask was opened, the mixture was analysed by ¹⁹F NMR spectroscopy, and the rate of conversion was determined by integration after addition of α,α,α-trifluorotoluene. The transformation into trifluoromethylzinc compounds (4) and (5) was ca. 40% (based on zinc). However, the products were not reactive. They were only hydrolysed with water in trifluoromethane or destroyed to fluoride by being heated at 50 °C for 2 days; δ_F –39.5 and –40.3 (1:2) [(CF₃)₂Zn·2pyr; (δ_F –38)].³³

The same result was obtained when the acetone was replaced by ethyl benzoate (10 ml); δ_F –41.3 and –42.3 (1:1).

Reactions of Esters.—**Ethyl trifluoropyruvate (9a).** A pressure-

safe bottle containing pyridine, (50 ml), diethyl oxalate (20 ml, 0.147 mol), and zinc (10 g) was placed under reduced pressure. The same method was used as above. The temperature was maintained at 20 °C and the reaction took place within 2 h. After extraction, the pyruvate was obtained in a hydrated form and was distilled over 95% sulphuric acid (35 ml) at room temperature under 0.2 mmHg pressure and collected in a solid CO₂ condenser (9.5 g, 38%), δ_F –75.7 (s, CF₃); δ_H 4.5 (q, CH₂, J_{HH} 7 Hz) and 1.4 (t, Me); ν_{max} (CCl₄) 1 740 and 1 765 cm⁻¹.³⁴

Hexafluoroacetone (9b). A pressure-safe bottle containing pyridine (15 ml), ethyl trifluoroacetate (5 g, 0.035 mol), and zinc (2.5 g) was placed under reduced pressure. The same method was used as above. The temperature was maintained at 20 °C and the reaction took place within 2 h. After extraction, the ketone was obtained in a hydrated form and was distilled (3.5 g, 54%), b.p. 34–36 °C/20 mmHg (lit.,³⁵ 55–56 °C/80 mmHg; δ_F –83.3 (s, CF₃).

Ethyl tridecafluoro-2-oxo-octanoate. To a stirred mixture of pyridine (10 ml), diethyl oxalate (3 ml, 0.022 mol), and zinc powder (1.5 g, 0.023 mol) under argon, was added perfluorohexyl iodide (10 g, 0.022 mol). After 2 h, the mixture was treated as usual to give the keto ester (1.8 g, 20%), b.p. 52–58 °C/20 mmHg; δ_F –80.7 (tt, CF₃), –117 to –123 (m, 8 F) and –125 to –127 (m, 2 F); δ_H 4.5 (q, J_{HH} 7 Hz, CH₂) and 1.4 (t, Me); ν_{max} (CCl₄) 1 740 and 1 765 cm⁻¹; m/z 420 (M⁺), 349 (C₆F₁₃CHOH⁺) and 319 (C₆F₁₃⁺).

Reactions of Anhydrides.—1,1,1-Trifluoropentan-2-one (11). A pressure-safe bottle containing pyridine (25 ml), butyric anhydride (10 ml, 0.061 mol), and zinc (4 g, 0.06 mol) was placed under reduced pressure. The same method was used as before. The temperature was maintained at 20 °C and the reaction took place within 2.5 h. After extraction, the organic layer was washed successively with 10% aq. sodium carbonate and water, dried (MgSO₄), and distilled with a spinning band distillation apparatus to give 1,1,1-trifluoropentan-2-one, (1.7 g, 20%), b.p. 70–74 °C (lit.,³⁶ 67 °C/731 mmHg); δ_F –76 (s, CF₃); δ_H 2.3 (q, CH₂), 1.7 (sext, CH₂), and 1 (t, Me); ν_{max} (CCl₄) 1 765 cm⁻¹.

3-Hydroxy-3-(trifluoromethyl)phthalide (13). A pressure-safe bottle containing pyridine (40 ml), phthalic anhydride (5 g, 0.034 mol), and zinc (3 g, 0.046 mol) was placed under reduced pressure. The same method was used as before. The temperature was maintained at 20 °C and the reaction took place within 1.5 h. After extraction with chloroform, the organic layer was washed successively with 10% aq. sodium carbonate and water,

dried (MgSO₄), and distilled (b.p. 80–90 °C/7.6 mmHg) and 3-hydroxy-3-(trifluoromethyl)phthalide (13) crystallized (4.85 g, 61%), m.p. 98.2 °C (lit.,¹⁵ 98–100 °C); δ_F –82 (s, CF₃); δ_H 8–7.5 (m, ArH) and 4.4 (OH); δ_C 167.05 (C=O), 141.6, 135.5, 132.4, 126.7, 126.0, and 124.0 (C–Ar), 117.8 (q, *J* 280 Hz, CF₃), and 100.3 (q, *J* 35 Hz, CCF₃); ν_{max} (CCl₄) 1 815 and 1 775 cm⁻¹; ν_{max} (KBr) 3 350, 1 765, and 1 605 cm⁻¹; *m/z* 218 (M⁺), 201 (M⁺ – OH), 149 (M⁺ – CF₃), and 104 (C₆H₄CO⁺).

5-Hydroxy-5-trifluoromethyltetrahydrofuran-2-one (15) and 5,5-bis(trifluoromethyl)tetrahydrofuran-2-one (16). A pressure-safe bottle containing pyridine (50 ml), succinic anhydride (5 g, 0.05 mol), and zinc (4 g, 0.06 mol) was placed under reduced pressure. The same method was used as before. The temperature was maintained at 20 °C and the reaction took place within 1.5 h. After extraction with ether, the organic layer was washed successively with 10% aq. sodium carbonate and water, and dried (MgSO₄). The solvent was removed under reduced pressure and the two compounds were purified by GLC on 30% SE 30 on chromosorb PAW 45/60 mesh at 140 °C.

5-Hydroxy-5-trifluoromethyltetrahydrofuran-2-one (15)¹⁶ (1.5 g, 18%) showed δ_F –84.7 (s, CF₃); δ_H 6 (OH) and 3.2–2.1 (m, CH₂CH₂); δ_C 176.4 (C=O), 122.3 (q, *J* 287 Hz, CF₃), 102.3 (q, *J* 35 Hz, CCF₃), and 28.5 and 27.8 (CH₂CH₂); ν_{max} (CCl₄) 3 350 and 1 785 cm⁻¹.

5,5-Bis(trifluoromethyl)tetrahydrofuran-2-one (16) (4.45 g, 40%) showed δ_F –77.3 (s, CF₃); δ_H 3–2.4 (m, CH₂CH₂); δ_C 172.8 (C=O), 122.2 (q, *J* 285 Hz, CF₃), 80.8 [sept, *J* 32 Hz, C(CF₃)₂], and 26.2 and 23.2 (CH₂CH₂); ν_{max} (CCl₄) 1 825 cm⁻¹.

3-Hydroxy-3-(tridecafluorohexyl)phthalide. To a stirred mixture of pyridine (20 ml), phthalic anhydride (3 g, 0.021 mol), and zinc powder (1.5 g) under argon was added, perfluorohexyl iodide (10 g, 0.022 mol). The reaction was exothermic. After 2 h, the mixture was treated as usual (chloroform was used for extraction). The phthalide was first distilled (b.p. 94 °C/4 × 10⁻² mmHg), then sublimed (2.0 g, 20%), m.p. 107.3 °C; δ_F –81.3 (tt, CF₃) and –118.3 to –128.3 (m, 10 F); δ_H 8–7.5 (m, ArH) and 4.3 (OH); ν_{max} (CCl₄) 1 815 and 1 775 cm⁻¹; *m/z* 391 (M⁺ – C₆H₅), 363 (M⁺ – C₆H₅CO), 131 (OCC₆H₅CO⁺), and 104 (C₆H₄CO⁺).

2-Trifluoromethylcyclohexanone (19). Reaction with iminium chloride (17). The iminium salt was precipitated from the enamine [10 ml in pentane (20 ml) by a stream of hydrogen chloride]. It was isolated by filtration and was washed with pentane. Then a mixture of the salt (17) (4 g, 0.021 mol), pyridine (30 ml), and zinc (2 g, 0.031 mol) was placed under reduced pressure. The bottle was charged with trifluoromethyl bromide (3.7 bar) and shaken for 1.5 h. The reaction began immediately. The temperature was controlled and maintained by a water-bath at 20 °C. The pressure of CF₃Br was kept between 2.5–5 bar. The flask was opened; the non-reacting zinc was removed by filtration. The mixture was hydrolysed with cold 10% hydrochloric acid (50 ml). After extraction with diethyl ether, the extract was washed with water and worked up; the ketone was distilled (0.95 g, 30%), b.p. 80–82 °C/18 mmHg (lit.,²⁸ 90–92 °C/30 mmHg); δ_F –67.3 (d, *J* 8.5 Hz); δ_H 3.2–2.7 (m, 1 H) and 2.5–1.3 (m, 8 H); ν_{max} (CCl₄) 1 735 cm⁻¹.

Reaction with enamine (20). Enamine (20) (5 ml, 0.033 mol), pyridine (30 ml), and zinc (2.5 g) were mixed together and treated as above to give the trifluoromethylcyclohexanone (19) (1.6 g, 25%).

Attempts to Detect Perfluoroalkyl Intermediates.—Reaction with sulphur dioxide. Sulphur dioxide (4 g, 0.062 mol) was bubbled into DMF (25 ml). After addition of zinc powder (1.5 g, 0.023 mol), the mixture was stirred for 1 min. The mixture was allowed to settle and half of the upper liquid phase was quickly transferred under nitrogen pressure through a glass bridge into tridecafluorohexyl iodide (10 g, 0.022 mol). After

being stirred for 30 min, the mixture was analysed by ¹⁹F NMR spectroscopy. Besides signals of the starting iodide, perfluorobutanesulphinate (20% by integration) was detected. This experiment was repeated with nitrobenzene (2 ml, 0.021 mol) mixed with the iodide: no perfluoroalkanesulphinate was detected.

Reaction of benzaldehyde and diethyl oxalate. The same experiment was repeated with pyridine (30 ml) and zinc (6 g) in the first flask:

(1) First flask: stream of CF₃Br for 15 min; second flask: oxalate (3 ml): no product detected.

(2) First flask: stream of CF₃Br for 15 min; second flask: benzaldehyde (5 ml): no product detected.

(3) First flask: benzaldehyde (10 ml) or oxalate (10 ml); second flask: perfluorohexyl iodide (3 ml): no product detected.

(4) First flask: benzaldehyde (10 ml) and stream of CF₃Br for 15 min; second flask: oxalate (3 ml) and perfluorohexyl iodide (3 ml): product detected: 2,2,2-trifluoro-1-phenylethanol.

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References

- 1 Part 8: M. Tordeux, B. Langlois, and C. Wakselman, *J. Org. Chem.*, 1989, **54**, 2452.
- 2 C. Wakselman and C. Kaziz, *J. Fluorine Chem.*, 1986, **33**, 347.
- 3 S. T. Everett, *J. Chem. Educ.*, 1987, **64**, 143.
- 4 P. G. Gassman and N. J. O'Reilly, *J. Org. Chem.*, 1987, **52**, 2481.
- 5 J. A. Morrison, *Adv. Inorg. Chem. Radiochem.*, 1983, **27**, 293.
- 6 D. J. Burton and D. M. Wiemers, *J. Am. Chem. Soc.*, 1985, **107**, 5014.
- 7 T. Kitazume and N. Ishikawa, *J. Am. Chem. Soc.*, 1985, **107**, 5186.
- 8 S. Sibille, S. Mcharek, and J. Perichon, *Tetrahedron*, 1989, **45**, 1423.
- 9 F. Leroux and M. Jaccaud, *Eur. P. 0 203 851/1986 (Chem. Abstr., 1987, 107, 96 317k)*.
- 10 R. C. Hallcher and Z. V. Zeable, *US P. 4 647 350/1987 (Chem. Abstr., 1987, 106, 213 421 g)*.
- 11 C. Francese, M. Tordeux, and C. Wakselman, *J. Chem. Soc., Chem. Commun.*, 1987, 642.
- 12 C. Francese, M. Tordeux, and C. Wakselman, *Tetrahedron Lett.*, 1988, **29**, 1029.
- 13 C. Wakselman and M. Tordeux, *Bull. Soc. Chim. Fr.*, 1986, 868.
- 14 U. D. G. Prabhu, K. C. Eapen, and C. Tamborski, *J. Org. Chem.*, 1984, **49**, 2792.
- 15 D. A. Shaw and T. C. Tuominen, *Synth. Commun.*, 1985, **15**, 1291.
- 16 P. Brown, J. Burdon, T. Smith, and J. C. Tatlow, *Tetrahedron*, 1960, **10**, 164.
- 17 A. G. Cook, 'Enamines,' ed. M. Dekker, 447, New York, 1969.
- 18 C. Wakselman and M. Tordeux, *J. Chem. Soc., Chem. Commun.*, 1987, 1701.
- 19 M. Tordeux, B. Langlois, and C. Wakselman, following paper.
- 20 H. Blancou, P. Moreau, and A. Commeyras, *J. Chem. Soc., Chem. Commun.*, 1976, 885.
- 21 A. Commeyras, *Ann. Chim. (Paris)*, 1984, **9**, 673.
- 22 W. D. Harrison, J. B. Gill, and D. C. Goodall, *J. Chem. Soc., Dalton Trans.*, 1979, 847.
- 23 W. T. Miller Jr., E. Bergman, and A. H. Fainberg, *J. Am. Chem. Soc.*, 1957, **79**, 4159.
- 24 H. J. Wille, B. Kastening, and D. Knittel, *J. Electroanal. Chem.*, 1986, **214**, 221.
- 25 J. C. Folest, J. Y. Nedelec, and J. Perichon, *Synth. Commun.*, 1988, **18**, 1491.
- 26 C. P. Andrieux, L. Gelis, and J. M. Saveant, *J. Am. Chem. Soc.*, 1990, **112**, 786.
- 27 L. Gelis, Thesis, Paris VII University, September 23rd, 1988.
- 28 D. Cantacuzene, C. Wakselman, and R. Dorme, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1365.

- 29 E. C. Ashby and J. Oswald, *J. Org. Chem.*, 1988, **53**, 6068; K. S. Root, C. L. Hill, L. M. Lawrence, and G. M. Whitesides, *J. Am. Chem. Soc.*, 1989, **111**, 5405.
- 30 G. Molle and P. Bauer, *J. Am. Chem. Soc.*, 1982, **104**, 3481.
- 31 S. Kawai, H. Kato, T. Hatsushika, and Y. Hayakawa, *Denki Kagaku*, 1975, **43**, 127 (*Chem. Abstr.*, 1976, **84**, 64 093 z).
- 32 E. T. McBee, S. Resconich, L. R. Belohlav, and H. P. Braendlin, *J. Org. Chem.*, 1963, **28**, 3579.
- 33 E. S. Liu, *Inorg. Chem.*, 1980, **19**, 266.
- 34 I. L. Knunyants, V. V. Shokina, and V. V. Tyuleneva, *Dokl. Akad. Nauk. SSSR*, 1966, **169**, 594.
- 35 A. T. Morse, P. B. Ayschough, and L. C. Leitch, *Can. J. Chem.*, 1955, **33**, 453.
- 36 K. T. Dishart and R. Levine, *J. Am. Chem. Soc.*, 1956, **78**, 2268.

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