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Reactivity of perfluorohexyl iodide with N,N-disubstituted amides and esters in the presence of a metal couple and radical initiator

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Abstract

The reactivity of perfluorohexyl iodide with N,N-disubstituted amides or ethyl formate as solvents and reactants, in the presence of a zinc-copper metal couple and radical initiator, has been investigated. In each case, the corresponding perfluorinated carbonyl compounds, such as aldehydes, amides, ketones and esters, were obtained in good yield, thus proving the efficacy of this reaction. The influence of the radical initiator on the reaction mechanisms has been studied and is discussed.

Keywords: Reactivity; Perfluorohexyl iodide; Disubstituted amines; Zinc-copper metal couple; Radical initiator; NMR spectroscopy; IR spectroscopy; Mass spectrometry

1. Introduction

Perfluorinated carbonyl compounds are of potential interest as suitable precursors for chemical products containing a linear perfluorinated chain, for use, for example, as surface-active agents.

In previous work, a new high-yield process for the synthesis of perfluoroalkylaldehydes, involving the reaction of perfluoroalkyl iodides R_FI ($R_F = C_n F_{2n+1}$) in the presence of a zinc-copper metal couple and a radical initiator in DMF (DMF being used as a reactant and solvent throughout) was described [1].

In order to extend the reactivity of perfluorohexyl iodide, reactions have been carried out under the same conditions but in the presence of different reactants and solvents, such as N,N-disubstituted amides: examples of such amides are N,N-diethylformamide to obtain pure perfluorohexylaldehyde, N,N-dimethylacetamide to allow the synthesis of a perfluorohexyl methyl ketone and N,N,N,N-tetramethylurea to optimize the formation of N,N-dimethylperfluorohexyl amide, as well as ethyl formate to obtain pure perfluorohexyl ethyl ether.

In each case, the expected fluorinated carbonyl compounds, involving C-alkylation of the solvent, was obtained in good yield.

2. Reactivity of n-perfluorohexyl iodide with various N,N-disubstituted amides

The reactivity of amides has been well investigated with hydrogenated Grignard reagents [2] but not with fluorinated compounds. A few examples of the Calkylation of amides are reported in the literature, for example the reaction of perfluorophenyl-lithium with *N*-methylformamide [3] and of perfluorophenylmagnesium chloride with *N*-methylformanilide [4], leading to the preparation of perfluorobenzaldehyde.

Some reactions involving the O-alkylation of amides via radical processes are also known, such as the reactions of perfluoroalkyl iodides with DMF [5] to give perfluorocarboxylic acids and of 1-iodo-2-(perfluoroalkyl)ethanes, $R_FC_2H_4I$, on *N*-methylformamide [6] or DMF [7] leading to the formation of the corresponding primary alcohols, $R_FC_2H_4OH$.

The addition of perfluorohexyl iodide, $C_6F_{13}I$ (I), in the presence of a zinc-copper metal couple and azobisisobutyronitrile as a radical initiator at a concen-

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tration of about 0.03 mol, to N,N-diethylformamide (Reaction 1), to N,N-dimethylacetamide (Reaction 2) or to N, N, N, N-tetramethylurea (Reaction 3) leads to the formation of both C-alkylation products of the corresponding solvents in good yield and to the formation of perfluoro-1-hydrohexane (V) as a by-product. No reaction occurred unless a stoichiometric amount of zinc and the radical initiator were both present in the medium. The results obtained depending on the solvent used are reported in Table 1.

Reaction 1 occurred as expected, and as shown in a previous work [1] the results obtained demonstrate the reactivity of the perfluorohexyl iodide towards the carbonyl carbon atom of N,N-diethylformamide, leading to the formation of perfluoroheptanal (III) and N,Ndiethylperfluorohexylamide (IV). However, in comparison with the reaction with N,N-dimethylformamide carried out under the same conditions it is necessary to point out, that: (i) it was not possible to increase the yield of perfluoroheptanal and still avoid the formation of N,N-dimethylperfluorohexylamide by using different molar ratio of II to I; and (ii) the perfluoroheptanal, C₆F₁₃CHO, thus obtained was free from N,N-diethylformamide.

With Reaction 2, the reactivity of perfluorohexyl iodide in the presence of the zinc-copper metal couple and azobisisobutyronitrile as the radical initiator was investigated in N,N-dimethylacetamide, in order to achieve the synthesis of perfluorohexyl methyl ketone.

Normally, fluorinated ketones are prepared from reactions of Grignard reagents, at a temperature of -60 °C in ethyl ether as solvent, on fluorinated esters [8], perfluorinated acid chlorides [9], fluorinated tertiary alkohols [10] or acyl anhydrides [11], or via a new method involving the hydrolysis of fluorinated β -ketophosphonium salts [12].

Reaction 2 which leads to the formation of perfluorohexyl methyl ketone in 70% yield at room temperature is indeed a good method of synthesizing this kind of fluorinated ketone.

Reaction 3 required the presence of zinc in stoichiometric amount and a radical initiator in the medium. In the absence of the radical initiator, the addition of

 $C_6F_{13}I + RCONR'_2 + Zn/Cu \xrightarrow{AIBN} C_6F_{13}COR + C_6F_{13}CONR'_2 + C_6F_{13}H$

Table 1

Results obtained depending on the nature of the N,N-disubstituted amides

(I) (I	I) (III)	(IV) (V)		
Reaction No.	Reactant (II)	Products obtained		
		ш	IV	v
1	2HCON(Et) ₂	C ₆ F ₁₃ CHO (70%)	$C_6F_{13}CON(CH_2CH_3)_2$ (20%)	C ₆ F ₁₃ H (10%)
2	2CH ₃ CON(CH ₃) ₂	C ₆ F ₁₃ COCH ₃ (70%)	$C_6F_{13}CON(CH_3)_2$ (20%)	C ₆ F ₁₃ H (10%)
3	$4(CH_3)_2CON(CH_3)_2$		C ₆ F ₁₃ CON(CH ₃) ₂ (87%)	C ₆ F ₁₃ H (13%)

perfluorohexyl iodide to tetramethylurea led to the formation of perfluoro-1-hydrohexane (IV) only.

3. Reactivity of n-perfluorohexyl iodide with ethyl formate

The addition of perfluorohexyl iodide, $C_6F_{13}I$ (I), in the presence of a zinc-copper metal couple and azobisisobutyronitrile as the radical initiator, to ethyl formate (II) (Reaction 4) leads to the formation of perfluorohexyl ethyl carboxylate C₆F₁₃COOEt (III) and perfluoroheptanal C_6F_{13} CHO (IV) in 45% and 40% yield, respectively. This reaction required the presence of zinc in stoichiometric amount and a radical initiator in the medium. In the absence of the radical initiator and/or zinc the addition of perfluorohexyl iodide to ethyl formate led to the formation of perfluorohydrohexane only.

$$C_{6}F_{13}I + 4HCO_{2}CH_{2}CH_{3} + Zn/Cu \xrightarrow{AIBN}_{25^{\circ}C}$$
(I) (II)
$$C_{6}F_{13}CO_{2}CH_{2}CH_{3} + C_{6}F_{13}CHO$$
(III) (IV)
(45%) (40%)

Reaction 4.

Normally reactions of fluorinated compounds with esters give ketones and not the corresponding fluorinated esters. However, fluorinated esters can be obtained from perfluoroalkyl iodides R_FI via reactions with ethyl carbonate [13], or reactions involving freeradical addition to 3-buten-1-ol, followed by zinc reduction of the adduct to give $R_{\rm F}(\rm CH_2)_{10}\rm COOR$ [14].

4. Discussion

All the reactions studied were performed under heterogeneous conditions and hence it was difficult to investigate their mechanisms. However, before discussing the reaction processes, it is important to point

out some experimental observations. Thus it was found that (i) no C-alkylation reaction occurred unless zinc in a stoichiometric amount together with a radical initiator are both present, and (ii) in some cases the reaction became exothermic after 5-min induction period and then required cooling to ca. 0 °C (particularly in the case of the reaction with N,N-diethylformamide).

It is therefore suggested that a two-step process occurs, involving firstly the formation of a perfluoroorganozinc iodide/solvent complex, $R_FZnI(R''COR')_2$, as an intermediate. Lang has described a similar complex $R_FZnCl(DMF)_2$ ($R_F = CF_3(CF_2)_nCCl_2$) [15]. This would entail an organized structure for the medium, as reported with many organometallic compounds [16] and therefore complexation by solvent molecules, leading to the formation of a four-membered transition state, stabilized by electrostatic interactions.

It is important to note that the observed induction period could be explained by the time necessary for complex formation. Moreover, the exothermicity of complex formation could be sufficient to initiate decomposition of the radical initiator and hence the subsequent radical process.

Electron transfer, either from the radical thus formed to the carbonyl bond of the solvent (Scheme 1, route A) or from the carbonyl bond to the radical (Scheme 1, route B) (initiated by the introduction of the radical initiator into the medium), subsequently induces homolytic cleavage of the C-Zn bond. The perfluoroalkyl radical would then react exclusively with the nearest atom of the solvent, i.e. the carbonyl carbon atom¹, leading to the formation of the intermediate $R_FCR''R'O-ZnI^+$, which by a classical elimination process would give either the perfluorohexylaldehyde (reactions 1 and 4) or the perfluorohexyl methyl ketone (reaction 2) or N,N-dimethylperfluorohexylamide (reaction 3) and the corresponding N,N-disubstituted perfluorohexylamide or ethyl perfluoroheptanoate (reaction 4) in each case. The radical initiator would be regenerated leading to a further radical process.

In this discussion, a reaction mechanism has been put forward involving the formation of an intermediary perfluoro-organozinc/solvent complex. This would explain the formation of C-alkylated products from the solvents, based on the usual reactivity of the intermediate and the nature of the leaving group R'. Moreover, the formation of the C-alkylation compounds of the solvents is favoured by a molar ratio of solvent to $R_{\rm F}I$ of two in the case of reactions performed with N,N-diethylformamide and N,N-dimethylacetamide, and of four in the case of N,N,N,N-tetramethylurea and ethyl formate, as required by complex formation in this proposal. This observation could be related to the existence of the perfluoro-organozinc DMF complex.

Hence, this proposed mechanism is adequate to explain the formation of C-alkylation compounds of the solvents.

5. Experimental details

Reagent quality DMF was used without further purification. The starting materials, R_FI and the radical initiators were supplied by Atochem Co. All reactions were carried out under atmospheric pressure. Yields refer to isolated compounds.

Microanalyses were obtained using a Dionex 2001 element analyser. Mass spectra were recorded on a JEOL JMS D 100 spectrometer. All reactions were obtained using a Varian EM 390 spectrometer (¹H at 90 MHz, internal standard Me₄Si; ¹⁹F at 84.7 MHz, internal standard CFCl₃). IR spectra were recorded on a Perkin-Elmer 1420 spectrometer.

5.1. Preparation of the Zn-Cu couple

The Zn–Cu couple was prepared by the addition of Zn powder (6.5 g, 0.1 mol) in small portions to a vigorously stirred solution of $(AcO)_2Cu$ (0.2 g, 0.001 mol) in hot AcOH. After a rapid exothermic reaction, the mixture was cooled and the AcOH evaporated in vacuo. The freshly prepared couple was dispersed in the solvent and azobisisobutyronitrile (0.5 g, 3 mmol) was then added.

5.2. Reaction of n-perfluorohexyl iodide with N, Ndiethylformamide

To a stirred and cooled (alcohol bath) solution of the Zn–Cu couple and azobisisobutyronitrile in N,Ndiethylformamide (23 ml, 0.2 mol) was added perfluorohexyl iodide, C₆F₁₃I, (44.6 g, 0.1 mol) dropwise. After ca. 20 min, the addition was complete. The mixture was then hydrolyzed with 30% HCl, the organic layer separated, dried (MgSO₄) and distilled under reduced pressure (133 Pa) to give 25.6 g of hydrated perfluoroheptanal, C₆F₁₃CH(OH)₂ (i.e. 70 mol%) and 8.4 g of N,N-diethylperfluoroheptylamide as a gummy residue (i.e. 20 mol%).

Hydrated perfluoroheptanal was compared to an authentic sample. Distillation of the white powder thus obtained from fresh P_2O_5 under reduced pressure gave $C_6F_{13}CHO$ (23.4 g).

To a suspension of 2-4-dinitrophenylhydrazine (0.25 g) in MeOH (5 ml) was added conc. H_2SO_4 (0.4–0.5

¹Perfluoroalkyl radicals R_F usually react exclusively with the oxygen atom of DMF, as shown in previous work [5,7]. Moreover, Kobrina has demonstrated the electrophilicity of perfluoroalkyl radicals and thus their reactivity with the carbonyl oxygens [17]. The formation of an organized structure in the medium could explain the reactivity of the perfluoroalkyl radical R_F with the carbon atom of DMF, rather than the oxygen atom, in this particular case.





ml). The warm solution was filtered, a solution of the aldehyde (0.5 g) in a small volume of chloroform was added and, after 10 min, the corresponding solid hydrazone was collected, washed with a little aq. MeOH and recrystallized from EtOH.

C₆F₁₃CHO: b.p. 132 °C. ¹H NMR δ: 9.57 (t, 1H, $J_{CH-CF_2}=1$ Hz, CHO) ppm. ¹⁹F NMR δ: 81.9 (t, 3F, CF₃); 122.6 (t, 2F, CF₂CHO) ppm. IR ν(cm⁻¹): 1730 (C=O); 1100–1300 (CF). MS m/z: 348 (0.9, M⁺); 347 [0.4, (M-H)]; 329 [0.5, (M-F)]; 319 (0.6, C₆F₁₃); 219 (0.4, C₄F₉); 169 (0.6, C₃F₇); 100 (0.9, C₂F₄); 69 (0.2, CF₃). Analysis: C₁₃H₅F₁₃N₄O₄ requires: C, 29.56; F, 46.76; H, 0.95%. Found: C, 29.62; F, 46.69; H, 0.98%. C₆F₁₃CON(CH₂CH₃)₂: b.p. 191 °C. ¹H NMR δ: 1.19 [tt, 6H, J_{H-H}=6 Hz, N(CH₂CH₃)₂]; 3.35 [dq, 4H, J_{H-H}=4 Hz, N(CH₂CH₃)₂] ppm. ¹⁹F NMR δ: 81.5 (t, 3F, CF₃); 120.2 (t, 2F, CF₂CO) ppm. MS m/z: 419 (0.8, M⁺); 355 [0.4, M–(FOCH₃CH₂)]; 305 [0.6, M–(CF₃OCH₃CH₂)]; 319 (0.8, C₆F₁₃); 219 (0.6, C₄F₉); 169 (0.5, C₃F₇); 100 [0.6, CON(CH₃CH₂)₂]; 82 [0.6, N(CH₃CH₂)₂]; 69 (0.4, CF₃). Analysis: C₁₁H₁₀F₁₃NO requires: C, 31.52; F, 58.93; H, 2.38%. Found: C, 31.56; F, 58.98; H, 2.47%.

5.3. Reaction of n-perfluorohexyliodide with N, Ndimethylacetamide

To a stirred solution of the Zn–Cu couple and azobisisobutyronitrile in N,N-dimethylacetamide (19 ml, 0.2 mol) was added perfluorohexyl iodide, $C_6F_{13}I$, (44.6 g, 0.1 mol) dropwise at room temperature. After ca. 20 min, the addition was complete. The mixture was

then hydrolyzed with 30% HCl, the organic layer separated, dried (MgSO₄) and distilled under reduced pressure (133 Pa) to give 25.3 g of perfluorohexyl methyl ketone, C₆F₁₃COCH₃ (i.e. 70 mol%) as a colorless liquid, and 7.8 g of *N*,*N*-dimethylperfluoroheptylamide, C₆F₁₃CON(CH₃)₂, as a gummy residue (i.e. 20 mol%). C₆F₁₃COCH₃: b.p. 90 °C. ¹H NMR δ : 2.42 (s, 3H, CH₃) ppm. ¹⁹F NMR δ : 81.6 (t, 3F, CF₃); 120.6 (t, 2F, CF₂CO) ppm. IR ν (cm⁻¹): 1760 (C=O); 1100–1300 (CF). MS *m*/*z*: 362 (0.8, M⁺); 328 [0.4, M–(FCH₃)]; 262 [0.6, M–(CF₃OCH₃)]; 319 (0.8, C₆F₁₃); 219 (0.6, C₄F₉); 169 (0.5, C₃F₇); 69 (0.4, CF₃). Analysis: C₈H₃F₁₃O requires: C, 26.53; F, 68.22%. Found: C, 26.59; F, 68.31%.

C₆F₁₃CON(CH₃)₂: b.p. 185 °C. ¹H NMR δ : 3.12 [d, 6H, $J_{H-H}=8$ Hz, N(CH₃)₂] ppm. ¹⁹F NMR δ : 81.5 (t, 3F, CF₃); 120.2 (t, 2F, CF₂CO) ppm. MS *m/z*: 391 (0.8, M⁺); 341 [0.4, M-(FOCH₃)]; 291 [0.6, M-(CF₃OCH₃)]; 319 (0.8, C₆F₁₃); 219 (0.6, C₄F₉); 169 (0.5, C₃F₇); 72 [0.6, CON(CH₃)₂]; 69 (0.4, CF₃); 44 [0.6, N(CH₃)₂]. Analysis: C₉H₆F₁₃NO requires: C, 27.63; F, 63.15%. Found: C, 27.67; F, 63.26%.

5.4. Reaction of n-perfluorohexyliodide with N, N-tetramethylurea

To a stirred solution of the Zn–Cu couple and azobisisobutyronitrile in N,N-tetramethylurea (48 ml, 0.4 mol) was added perfluorohexyl iodide, C₆F₁₃I, (44.6 g, 0.1 mol) dropwise at a temperature of 60 °C. After ca. 20 min, the addition was complete. The mixture was then hydrolyzed with 30% HCl, the organic layer separated, dried (MgSO₄) and distilled under reduced pressure (133 Pa) to give 34 g of N,N-dimethylperfluoroheptylamide, C₆F₁₃CON(CH₃)₂ (i.e. 87 mol%), described above.

5.5. Reaction of n-perfluorohexyl iodide with ethyl formate

To a stirred solution of the Zn–Cu couple and azobisisobutyronitrile in ethyl formate (33 ml, 0.4 mol) was added perfluorohexyl iodide, $C_6F_{13}I$, (44.6 g, 0.1 mol) dropwise at room temperature. After ca. 20 min, the addition was complete. The mixture was then hydrolyzed with 30% HCl, the organic layer separated, dried (MgSO₄) and distilled under reduced pressure (133 Pa) to give 13.9 g of perfluoroheptanal, $C_6F_{13}COH$, (i.e. 40 mol%), described and treated as above, and 17.6 g of perfluorohexyl ethyl carboxylate, $C_6F_{13}COOEt$ (i.e. 45 mol%).

C₆F₁₃COOEt: b.p. 87 °C/20 mmHg. ¹H NMR δ: 3.12 [d, 6H, J_{H-H} =8 Hz, N(CH₃)₂] ppm. ¹⁹F NMR δ: 83 (t, 3F, CF₃); 119 (t, 2F, CF₂CO) ppm. IR ν (cm⁻¹): 1715 (C=O); 1150–1300 (CF); 1050 (C=O). MS *m*/*z*: 392 (0.6, M⁺); 363 [0.8, M – (CH₂CH₃)]; 319 (0.8, C₆F₁₃); 219 (0.6, C₄F₉); 169 (0.5, C₃F₇). Analysis: C₉H₅F₁₃O₂ requires: C, 27.57; F, 62.99%. Found: C, 27.61; F, 63.05%.

6. Conclusions

In this paper, a new method for the functionalization of perfluorohexyl iodide, $C_6F_{13}I$, requiring the presence of a zinc-copper metal couple and a radical initiator in *N*,*N*-disubstituted amides or ethyl formate as solvent, is reported.

This process allows the formation of both C-alkylation products of the solvents which are not formed under other conditions. Fluorinated compounds of great interest such as perfluorohexylaldehyde, *N*,*N*-disubstituted perfluorohexylamides, perfluorohexyl methyl ketone and ethyl perfluorohexylcarboxylate were obtained in good yield.

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