

Rearrangement of 2-iodo-3-perfluoroalkyl-1-propyl acetates to 1-iodo-3-perfluoroalkyl-2-propyl acetates

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Abstract

2-Iodo-3-perfluoroalkylpropyl acetates, $R_FCH_2CHICH_2OAc$ (**1**) ($R_F = i-C_3F_7, C_4F_9, C_6F_{13}, C_8F_{17}$), have been rearranged thermally to 1-iodo-3-perfluoroalkyl-2-propyl acetates, $R_FCH_2CH(OAc)CH_2I$ (**2**), in 89% yield over the temperature range 120–200 °C. The results indicate that the rearrangement is a reversible process which is shifted towards the formation of **2**. The equilibrium regio isomer ratio (**1/2** = 1:8) was independent of the temperature and of the nature of the R_F substituent. It is proposed that the rearrangement proceeds through a free-radical mechanism including 1,2-migration of the acetoxy group after thermal scission of the C–I bond.

Introduction

The addition of perfluoroalkyl iodides (R_FI) to C–C double bonds is a well-recognised and synthetically useful reaction for the preparation of perfluoroalkyl iodo compounds. A number of methods for the initiation or induction of this reaction have been reported. The addition has been initiated thermally [1, 2], photochemically [3], biochemically [4], electrochemically [5], by organic peroxides and by diazo compounds [6–9], by sodium dithionite and related reagents [10], by hydrogen peroxide [11] and even by such compounds as triethylborane [12] or by alkyl phosphines [13]. The addition has also been induced by various metals and metal salts [14–19], by metal complexes [14, 20–23] and by metal salt–amine systems [24–26]. In all cases, the expected non-rearranged adduct R_FCH_2CHIR was obtained as the sole product. However, it has been reported that in addition of perfluoro-t-

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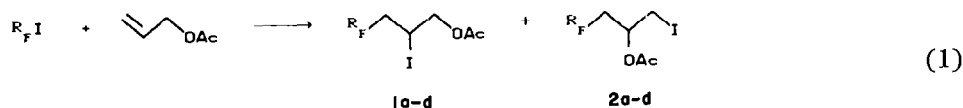
alkyl iodides to allyl acetate, a certain degree of rearrangement of the final product is observed [27]. The authors did not comment in detail on this unexpected result. In general, it is believed that the addition reactions of perfluoroalkyl iodides proceed by a free-radical chain mechanism [1–27].

This present work is focused on a more detailed study of the rearrangement of 2-iodo-3-perfluoroalkylpropyl acetates and its mechanism.

Results and discussion

Addition of perfluoroalkyl iodides to allyl acetate

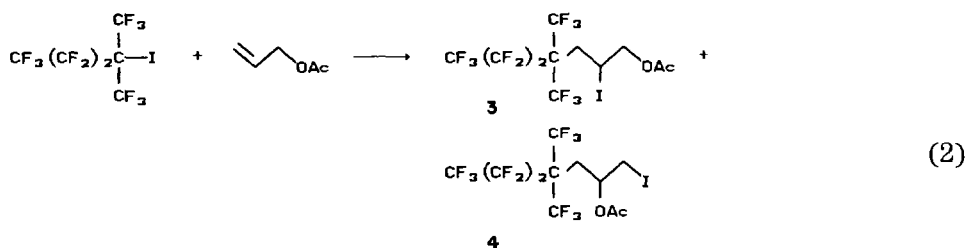
During investigations of the addition reaction of perfluoroalkyl iodides $R_F I$ ($R_F = i-C_3F_7$, C_4F_9 , C_6F_{13} , C_8F_{17}) with allyl acetate initiated by dibenzoyl peroxide or related free-radical initiators, the formation of a mixture of two regio isomers of **1a–d** and **2a–d** [eqn. (1)] was observed, especially at longer reaction times (12 h).



$R_F = i-C_3F_7$ (a), C_4F_9 (b), C_6F_{13} (c), C_8F_{17} (d)

In order to examine the course of the rearrangement, the pure compounds **1a–d** were prepared by the addition of perfluoroalkyl iodides to allyl acetate at 120 °C in the presence of dibenzoyl peroxide. This method allowed the complete conversion of the starting compounds within a short reaction period (10 min) without rearrangement of the products. The addition reaction afforded compounds **1a–d** as the sole products in 80–85% yield after isolation. Their ^1H NMR spectra were in good agreement with published data [9]. The absence of rearranged products in the reaction mixture indicated that the rearrangement of **1a–d** did not occur under these reaction conditions. No rearrangement products were observed by Brace [9] during the addition of perfluoroalkyl iodides to allyl acetate at 96 °C (3 h) in the presence of dibenzoyl peroxide. Accordingly, these results indicate that the formation of the products **2a–d** was not as a consequence of a free-radical mechanism for the addition reaction.

The formation of the regio isomers **2a–d** was only observed after prolonged reaction times, which indicates that their formation is probably caused by thermal rearrangement of addition products **1a–d**. This assumption is supported by the results obtained by Probst *et al.* [27], who observed the formation of a mixture of regio isomers **3** (72%) and **4** (28%) during the thermal addition of perfluoro-1,1-dimethylbutyl iodide to allyl acetate at 130 °C after 15 h [eqn. (2)]. The authors explained the formation of regio isomer **4** by thermal rearrangement of addition product **3**, but without any further details.



In contrast, no rearrangement was mentioned as being observed in the addition reaction of perfluoropropyl iodide with allyl acetate at 190 °C [28]. It is obvious from this that the reaction temperature is a determining factor in the thermal rearrangement.

Rearrangement of 2-iodo-3-perfluoroalkyl-1-propyl acetates

In order to estimate the effect of temperature on the rearrangement process, compound **1c** was heated over the temperature range 120–200 °C. The results presented in Fig. 1 show that the rearrangement of **1c** into **2c** took place even at temperature as low as 120 °C, though the reaction rate was rather small and only 30% of **2c** was formed after 12 h. At higher temperatures (140–200 °C), the same final ratio of both regio isomers **1c**/**2c**=1:8 was achieved (in 12 to 1 h) and remained unchanged even on prolonged heating (24 h). This result indicated that the final **1c**/**2c** ratio is

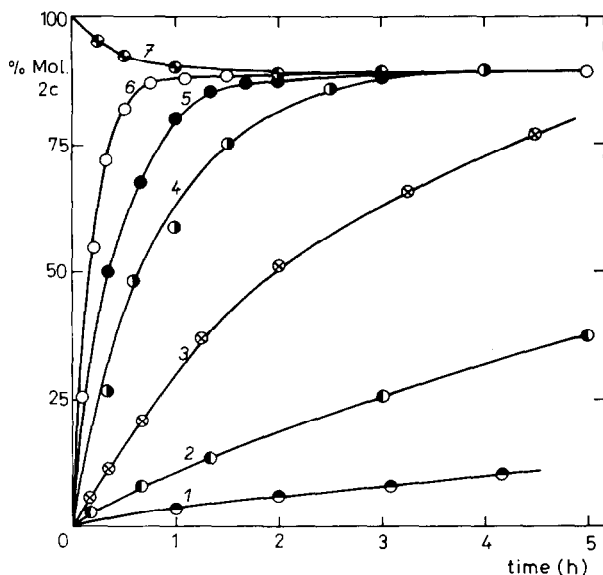
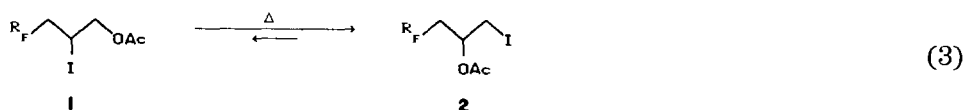


Fig. 1. Rearrangement of iodoperfluoroalkylpropyl acetates **1c** and **2c** at different temperatures. 1, **1c** at 120 °C; 2, **1c** at 140 °C; 3, **1c** at 160 °C; 4, **1c** at 180 °C; 5, **1c** at 190 °C; 6, **1c** at 200 °C; 7, **2c** at 182 °C.

independent of the reaction temperature and that the regio isomer **2c** probably undergoes reverse rearrangement to **1c** affording the final equilibrium mixture ($1c/2c = 1:8$).

This assumption was confirmed in the following manner. Regio isomer **2c** was prepared in three steps starting from **1c**. In the first step, **1c** was transformed by sodium hydroxide to the epoxide **5** [6], then the oxirane ring was cleaved regioselectively by lithium iodide affording the iodohydrin **6** [29], which was acetylated in the final step by means of acetyl chloride to yield compound **2c** (Scheme 1). Analysis of compound **2c** revealed no traces of **1c**. On heating regio isomer **2c** at 182 °C for 3 h, the final **2c/1c** ratio of 8.1:1 was obtained (Fig. 1).

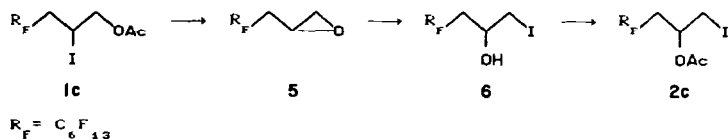
These results show that both regio isomer **1c** and **2c** undergo thermal rearrangement affording a mixture of both regio isomers in the same ratio, thus supporting the equilibrium nature of this rearrangement [eqn. (3)].



In additional experiments, the effect of the perfluoroalkyl substituent on the thermal rearrangement of $R_FCH_2CHICH_2OAc$ (**1a–1d**) was examined at 190 °C. The results presented in Fig. 2 show that the same equilibrium ratio (1:8) for each pair of regio isomers (**1a–d/2a–d**) was achieved in approximately 3 h, with the product ratio remaining constant on prolonged heating. The size of the R_F substituent had no significant influence on the rate of the rearrangement reaction and on the equilibrium isomer ratio of iodoperfluoroalkylpropyl acetates.

As far as a reaction mechanism for the rearrangement of iodoperfluoroalkylpropyl acetates is concerned, we have assumed that the rearrangement includes the following steps (Scheme 2). The first step involves the thermal scission of the C–I bond forming the 3-perfluoroalkyl-1-acetoxy-2-propyl radical **7**. This radical undergoes 1,2-rearrangement of the acetoxy group via a cyclic five-membered intermediate, which may be represented by the 1,3-dioxolan-2-yl radical **8'** or by a charge-separated structure **8''**. The resulting rearranged radical **9** abstracts iodine from **1** to yield regio isomer **2**.

This proposed mechanism is based on the fact that a similar rearrangement, with migration of the acetoxy group, has already been observed in radical reductions of non-fluorinated halogenoacetoxy compounds and explained in



Scheme 1.

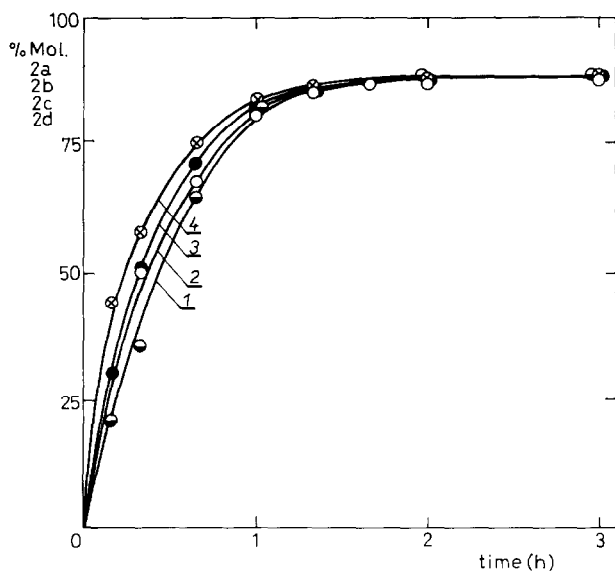
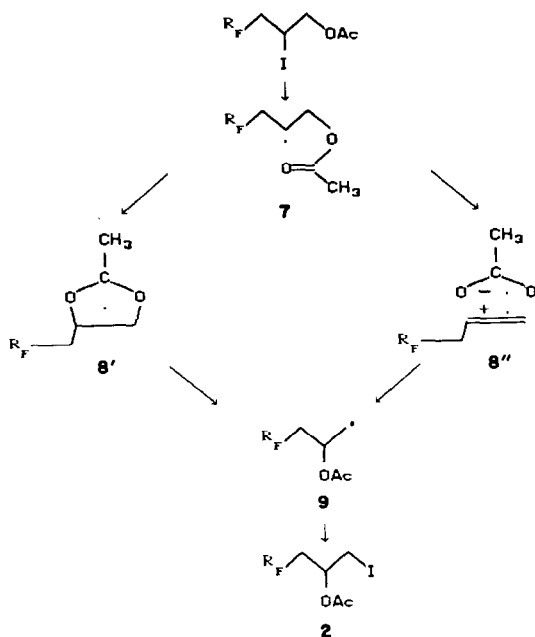


Fig. 2. Rearrangement of 2-iodo-3-perfluoroalkyl-1-propyl acetates **1a-d** at 190 °C. 1, **1a**; 2, **1c**; 3, **1d**; 4, **1b**.



Scheme 2.

terms of cyclic five-membered intermediates [30–36]. However, the true reaction mechanism is still not absolutely clear despite the use of theoretical calculations [34].

The results presented explain why both regio isomers are found in the reaction mixture after lengthy experiments even at relatively low reaction temperatures (120 °C) [27]. However, it is surprising, that Brace did not observe any rearrangement during the addition of perfluoropropyl iodide to allyl acetate at 190 °C [28].

Experimental

GC analysis of the products was performed on a HP-5890A instrument equipped with packed column containing 3% SE-30. The corresponding ^1H NMR spectra were recorded on 60 MHz Bruker spectrometer.

In order to determine the ratio of regio isomers, GC analysis was found to be more convenient and more precise than ^1H NMR analysis. Because of difficulties in the GC separation of iodoperfluoroalkylpropyl acetates **1a–d** and **2a–d**, however, their mixtures were reduced prior to each analysis to the corresponding perfluoroalkylpropyl acetates (**1'a–d**, **2'a–d**) by the use of tributylstannane.

Materials

Perfluoroalkyl iodides (kindly provided by Atochem), allyl acetate, dibenzoyl peroxide and tributylstannane (all Aldrich) were used as supplied. Lithium iodide was prepared by a modification of the method of Taylor and Grant [37] and the oxirane **5** was prepared by a known procedure [6].

General procedure for the addition of perfluoroalkyl iodides to allyl acetate

A 100 ml round-bottom flask equipped with a water condenser and a magnetic stirred was charged under nitrogen with 0.1 mol of $\text{R}_n\text{F}_n\text{I}$, 10 g of allyl acetate (0.1 mol) and 0.5 g of dibenzoyl peroxide (2 mmol). The flask was then immersed in an oil bath preheated to 120 °C and then stirred. After disappearance of the violet colour (traces of free iodine), a vigorous reaction commenced. At the end of the reaction the colourless solution again became violet. The addition reaction was complete within 10 min with total conversion of the starting materials. Perfluoroalkyl iodoacetates were isolated by distillation under reduced pressure in 80–85% yield. Compound **1a**: $\text{i-C}_3\text{F}_7\text{CH}_2\text{CHICH}_2\text{OAc}$, b.p. 80–85 °C/30 Torr; compound **1b**: $\text{C}_4\text{F}_9\text{CH}_2\text{CHICH}_2\text{OAc}$, b.p. 107–113 °C/30 Torr; compound **1c**: $\text{C}_6\text{F}_{13}\text{CH}_2\text{CHICH}_2\text{OAc}$, b.p. 62–65 °C/ 5×10^{-2} Torr; and compound **1d**: $\text{C}_8\text{F}_{17}\text{CH}_2\text{CHICH}_2\text{OAc}$, b.p. 91–99 °C/ 7×10^{-2} Torr.

The ^1H NMR spectra of the products were in agreement with published data [9].

Rearrangement of compound 1c on a preparative scale

A 15 ml glass ampoule equipped with a septum and a magnetic stirrer was charged with 10 mmol of **1c** under nitrogen. The ampoule was placed in an oil bath and heated with stirring at a given temperature (190 °C) until an equilibrium mixture of **1c** and **2c** was attained. ¹H NMR δ: **2c**: 2.00 (3H, s, CH₃); 2.1–3.0 (2H, td, R_FCH₂, *J*(HH) = 5 Hz, *J*(HF) = 19 Hz); 3.38 and 3.47 (2H, d, CH₂I, *J*(HH) = 5 Hz); 4.9–5.4 (1H, qnt, CHOAc, *J*(HH) = 5 Hz) ppm.

Reduction of a mixture of compounds 1c and 2c with tributylstannane

To the reaction mixture from the previous experiment containing **2c** and **1c** (10 mmol), 3.2 g tributylstannane (11 mmol) was added dropwise with stirring at room temperature over 30 min. After separation of the two layers by means of a syringe, distillation under reduced pressure afforded 3 g (total yield 73%) of a mixture of **2'c** (89%) and **1'c** (11%) (b.p. 75–78 °C/ 14 Torr). ¹H NMR δ: **1'c**: 2.05 (3H, s, CH₃); 1.8–2.4 (4H, m, R_FCH₂CH₂); 4.0–4.3 (2H, t, CH₂O, *J*(HH) = 6 Hz) ppm. **2'c**: 1.27 and 1.37 (3H, d, CH₃, *J*(HH) = 6 Hz); 2.00 (3H, s, CH₃CO); 1.8–2.8 (2H, m, R_FCH₂); 5.0–5.6 (1H, sxt, CH(OAc), *J*(HH) = 6 Hz) ppm.

Preparation of the iodohydrin 6

A 500 ml glass flask equipped with a magnetic stirrer was charged with 180 ml of dry tetrahydrofuran, 9.8 g epoxide **5** (0.026 mol), 6.6 g anhydrous lithium iodide (0.05 mol) and 4.5 glacial acetic acid (0.075 mol). The reaction mixture was stirred at room temperature for 1 h, and after evaporation of tetrahydrofuran, 100 ml of water was added. The mixture was washed three times with 30 ml of 1,1,2-trichlorotrifluoroethane, the organic layers were collected and dried with magnesium sulphate. The solvent was evaporated and distillation of the residue under reduced pressure afforded 11.6 g iodohydrin **6** in 88.5% yield (b.p. 75–85 °C/2.5 Torr). ¹H NMR δ: **6**: 2.1–3.0 (2H, td, R_FCH₂, *J*(HH) = 5 Hz, *J*(HF) = 19 Hz); 2.84 (1H, s, OH); 3.38 and 3.47 (2H, d, CH₂I, *J*(HH) = 5 Hz); 3.9–4.3 (1H, qnt, CHOH, *J*(HH) = 5 Hz) ppm.

Preparation of compound 2c

A 100 ml three-necked flask equipped with a reflux condenser, a dropping funnel and a magnetic stirrer was charged with 50 ml of dry diethyl ether, 5 g iodohydrin **6** (0.01 mol) and 3.2 g acetyl chloride (0.02 mol). A solution consisting of 2 g triethylamine (0.02 mol) in 10 ml diethyl ether was added dropwise to the reaction mixture over 1 h. At the end of reaction, 50 ml of water and 30 ml of n-pentane were added. The organic layer was separated, washed three times with 30 ml of water and twice with 30 ml of sodium carbonate solution and thereafter dried with magnesium sulphate. The solvent was evaporated and distillation of the residue under reduced pressure afforded 2.7 g pure **2c** in 50% yield (b.p. 80–85 °C/2 Torr). Compound **2c** did not

contain any trace of **1c**. $^1\text{H NMR } \delta$: **2c**: 2.00 (3H, s, CH_3); 2.2–2.8 (2H, td, $\text{R}_\text{F}\text{CH}_2$, $J(\text{HH})=5$ Hz, $J(\text{HF})=19$ Hz); 3.38 and 3.47 (2H, d, CH_2I , $J(\text{HH})=5$ Hz); 4.9–5.4 (1H, qnt, CHOAc , $J(\text{HH})=5$ Hz) ppm.

Procedure for monitoring the rearrangement of iodoperfluoroheptyl-propyl acetates 1c and 2c at different temperatures

A 3 ml glass ampoule equipped with a septum and a magnetic stirrer was charged with 10 mmol of **1c** or **2c** under nitrogen. The ampoule was then placed in an oil bath and heated with stirring at a given temperature (120–200 °C). The samples of the reaction mixture (10 μl) removed via a syringe were mixed with 0.2 ml of a solution of tributylstannane in ether (0.29 g ml^{-1}). The mixture was shaken for 1 min and analyzed by GC methods. The results are presented in Fig. 1.

Procedure for monitoring the rearrangement of the iodoperfluoroalkyl-propyl acetates 1a–d

A 3 ml glass ampoule equipped with a septum and a magnetic stirrer was charged under nitrogen with 1 mmol of the perfluoroalkyl iodoacetate **1a–d**. The ampoule was then placed in a preheated oil bath (190 °C) and stirred. Samples of the reaction mixture (10 μl) were taken via a syringe and mixed with a 2.0 ml solution of tributylstannane in ether (0.29 g ml^{-1}). The mixture was shaken for 1 min and analyzed by GC methods. The results are presented in Fig. 2.

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