



Fluorodecarboxylation, rearrangement and cyclisation: the influence of structure and environment on the reactions of carboxylic acids with xenon difluoride

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ABSTRACT

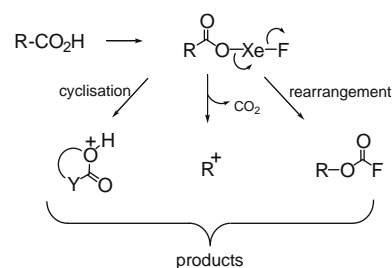
The reactions of structurally diverse carboxylic acids with XeF₂ in both CH₂Cl₂/Pyrex[®] and CH₂Cl₂/PTFE have been studied. Pyrex[®] appears to be a very effective heterogeneous catalyst for an electrophilic mode of reaction of polarised XeF₂, leading to rearrangement, cyclisation and cationic products. In CH₂Cl₂/PTFE, fluorodecarboxylation is the main mode of reaction, in accordance with previous studies, and may occur via a SET reaction of unpolarised XeF₂.

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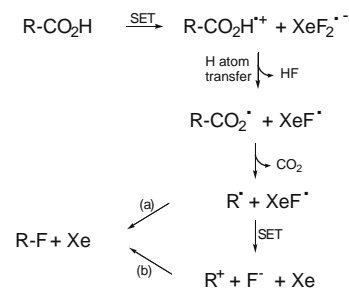
In earlier studies we have shown that the products of reaction of xenon difluoride with aryltrimethylsilanes,¹ trimethylsilyl benzoates² and trimethylsilyl enol ethers³ depend on the reaction environment (solvent and flask material).⁴ Reactions carried out in CH₂Cl₂/Pyrex[®] appear to proceed via an electrophilic mechanism, whereas reactions carried out in CH₂Cl₂/PTFE can be interpreted in terms of a single electron transfer (SET) mechanism. In Pyrex[®] the borosilicate wall can act as a very effective heterogeneous catalyst, presumably as a result of XeF₂ binding to Lewis acid (or possibly to Brønsted acid) sites [FXe^{δ+}–F→Pyrex^{δ-}]. The polarised reagent may then react via an electrophilic mechanism in which the electrophile can be formally regarded as an [FXe⁺] equivalent. These observations are consistent with borosilicate glass, such as Pyrex[®], containing 13% B₂O₃ and 2% Al₂O₃. Quartz flasks, which contain no additives, do not catalyse these reactions. We now report on studies of the reactions of six structurally diverse carboxylic acids with XeF₂, which provide further evidence that Pyrex[®] profoundly influences the mechanism of reaction and the products.

In CH₂Cl₂/Pyrex[®] we have found that the major products of reaction of carboxylic acids with XeF₂ can be rationalised by one of the initial pathways shown in Scheme 1. In particular, we propose that the vessel wall catalyses formation of the fluoroxenon ester,⁵ which cyclises, decarboxylates or rearranges depending upon the nature of the substituent R. In a detailed study of 21 carboxylic acids, Patrick and co-workers^{6–8} have previously shown that in CH₂Cl₂/polyethylene the major mode of reaction is fluorodecarboxylation giving the fluoride R–F. In accordance with these results, when we repeated our reactions in CH₂Cl₂/PTFE we found that the major products were the fluorides. We propose that in CH₂Cl₂/PTFE

the unpolarised XeF₂ initially reacts by SET leading to radical formation (Scheme 2). The radical may then either directly form the fluoride (pathway a) or undergo oxidation giving the fluoride via a carbenium ion (pathway b). This is a variation of the mechanisms proposed by Patrick and co-workers.^{6–8}



Scheme 1.



Scheme 2.

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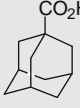
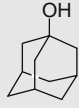
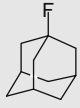
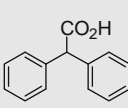
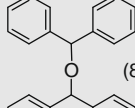
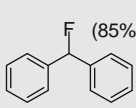
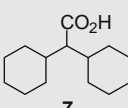
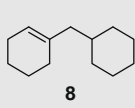
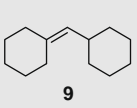
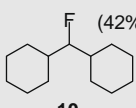
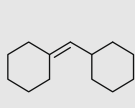
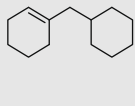
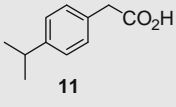
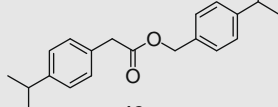
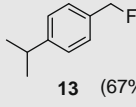
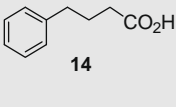
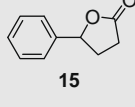
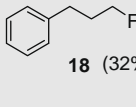
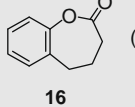
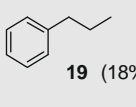
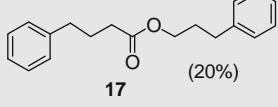
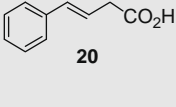
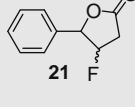
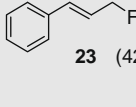
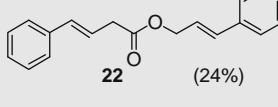
E-mail address: c.a.ramsden@chem.keele.ac.uk (C.A. Ramsden).

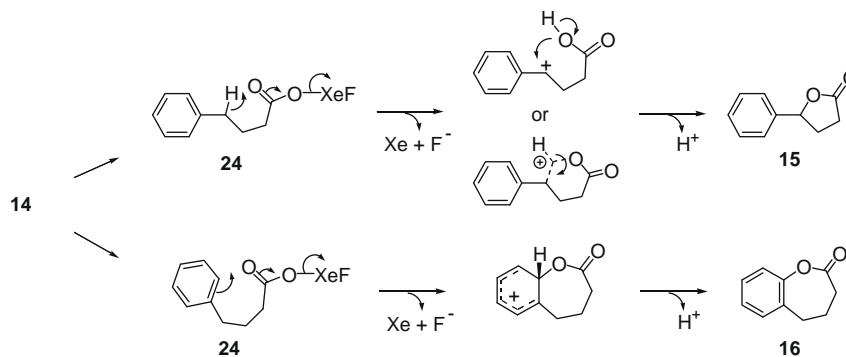
The results of our investigations of the structurally diverse carboxylic acids **1–6** are shown in Table 1. Major products were fully characterised, or pure material was shown to be identical to an authentic sample. In addition, we have monitored reaction mixtures using GC-MS and ^1H NMR, and have identified minor products that may have mechanistic significance. Reactions were repeated several times, and gave consistent yields.

Reaction of 1-adamantanecarboxylic acid **1** (entry 1) with XeF_2 in $\text{CH}_2\text{Cl}_2/\text{Pyrex}^\text{®}$ gave 1-adamantanol **2** in 77% yield. Under these

anhydrous conditions, the alcohol must form by an initial rearrangement of the fluoroxenon ester giving a fluorooxenon (Scheme 1), which is then cleaved by HF.⁹ We have previously isolated aryl fluorooxenonates from the reactions of trimethylsilyl benzoates with XeF_2 .² Under these conditions, the fluorooxenonates are stable since Me_3SiF is formed rather than HF. These observations are consistent with both aryl and tertiary alkyl substituents having high migratory aptitudes.^{10–12} A small amount of diadamantyl can be attributed to reaction with some unpolarised XeF_2 . In contrast,

Table 1
Products of reactions of xenon difluoride with carboxylic acids²¹

Entry	Substrate	Pyrex [®] / CH_2Cl_2 products		PTFE/ CH_2Cl_2 products	
		Major	Minor	Major	Minor
1		 (77%)	• diadamantyl (14%)	 (76%)	• 1-chloroadamantane (14%) • 1-adamantanol (10%)
2		 (82%)		 (85%)	• benzophenone (11%)
3		 (19%)	 (3%)	 (42%)	 (19%)  (10%)
4		 (56%)	• di(4-isopropyl)benzyl ether (12%)	 (67%)	• 4-isopropyl-benzaldehyde (10%)
5		 (18%)	• 1,3-difluoro-1-phenylpropane (12%)	 (32%)	• 1,3-difluoro-1-phenylpropane (12%) • 1-fluoro-1-phenylpropane (6%) • 1,6-diphenylhexane (11%) • 1,1,2,2-tetrachloroethane (14%)
		 (24%)		 (18%)	
		 (20%)			
6		 (45%)		 (42%)	• cinnamaldehyde (11%)
		 (24%)			



Scheme 3.

reaction in $\text{CH}_2\text{Cl}_2/\text{PTFE}$ gives a high yield of 1-fluoroadamantane **3** (76%), together with 1-chloroadamantane (14%) and a trace of diadamantyl. When increasing amounts of carbon tetrachloride (5–20%) were added to the solvent, the yield of the chloroalkane increased proportionally with a corresponding decrease in 1-fluoroadamantane and no trace of diadamantyl. These observations are consistent with product formation via an adamantyl radical (Scheme 2). The small amount of 1-adamantanol formed under these conditions probably arises from a rearrangement sequence initially catalysed by HF.

Reaction of diphenylacetic acid **4** (entry 2) with XeF_2 in $\text{CH}_2\text{Cl}_2/\text{Pyrex}^\circledast$ gave an 82% yield of di(diphenylmethyl) ether **5**. The formation of this product can be rationalised by rearrangement, leading to diphenylmethanol, together with formation of the relatively stable cation. This combination of the rearrangement and decarboxylation pathways (Scheme 1) leads to the ether product. The protonated alcohol may also be a source of the cation. Diphenylfluoromethane **6** was obtained in 85% yield when the reaction was carried out in $\text{CH}_2\text{Cl}_2/\text{PTFE}$, again emphasising the profound influence of the vessel.

In Pyrex^\circledast , the reaction of the dicyclohexylacetic acid **7** (entry 3) gave alkenes as the only identifiable products. The major product was cyclohex-1-enylcyclohexylmethane **8** (19%) together with a small amount of the cyclohexylmethylene isomer **9** (3%). These E_1 elimination products probably arise from initial formation of the secondary carbenium ion (Scheme 1), which deprotonates to give the minor product **9**. Reprotonation, or rearrangement of the initial cation, may then give a tertiary carbenium ion leading to the isomeric alkene **8**.^{13,14} There was no evidence of fluoroformate or alcohol formation, but these may also be precursors of elimination products, which cannot be formed from substrates **1** and **4**. As expected, in PTFE the fluoro derivative **10** was the major product (42%), but the alkenes **8** and **9** were also present in significant amounts, supporting the view that carbocations can form under these conditions (Scheme 2).

The benzylic carboxylic acid **11** (entry 4) reacted in Pyrex^\circledast to give a 56% yield of the ester **12**. A low yield (12%) of di(4-isopropyl)benzyl ether was also detected, indicating that some C–O rearrangement occurred to form the benzyl alcohol. The formation of the ester **12** and the dibenzyl ether implies that a benzyl cation intermediate probably formed via a decarboxylation mechanism (Scheme 1), followed by rapid reaction with the precursor acid **11**, or to a lesser extent with the benzyl alcohol. In Pyrex^\circledast there was no evidence of fluoro-products, but in a PTFE flask a good yield of the benzyl fluoride **13** was obtained.

An interesting variation in behaviour was observed when 4-phenylbutanoic acid **14** (entry 5) was reacted with XeF_2 in $\text{CH}_2\text{Cl}_2/\text{Pyrex}^\circledast$. The ester **17** was formed in 20% yield presumably

via the primary carbenium ion. Two other products that formed in comparable yields were identified as γ -phenyl- γ -butyrolactam **15** (18%) and 4,5-dihydro-1-benzoxepin-2(3H)-one **16** (24%). The formation of these cyclic products can be rationalised in terms of alternative modes of reaction of the fluoroxenone ester **24** (Scheme 3), which avoid formation of the unstable primary carbenium ion. Thus, elimination of xenon and fluoride, transfer of the γ -hydrogen (either by formation of a benzyl cation or via a three-centre bonded species formed by direct C–H bond insertion of the electrophilic oxygen^{15,16}) and subsequent loss of a proton give product **15**. Alternatively, electrophilic attack of the phenyl group (C=C bond insertion by the oxygen electrophile), accompanied by loss of xenon and fluoride, gives an arenium ion that can deprotonate to give product **16**. There was no evidence of rearrangement products, which is consistent with primary alkyl groups having poor migratory aptitude.

Reaction of the acid **14** in PTFE gave a relatively poor yield of 3-fluoro-1-phenylpropane **18** (32%) together with 1-phenylpropane **19** (18%). The hydrocarbon **19** is almost certainly formed via the alkyl radical, and this is supported by the observation of 1,6-diphenylhexane (11%). Since 1,1,2,2-tetrachloroethane (14%) was also detected, the alkyl radical is presumed to abstract hydrogen from the solvent; no 3-chloro-1-phenylpropane was detected. Secondary products resulting from fluorination of the benzylic position of products **18** and **19** were also detected. The primary alkyl substituent in the acid **14** probably disfavours pathway (b) shown in Scheme 2, and this leads to mainly radical products. This is in accordance with observations of Patrick and co-workers,⁸ and may account for the low yield relative to the acids **1**, **4**, **7** and **11**.

Finally, we investigated styrylacetic acid **20** (entry 6). As with the other primary acids (entries 4 and 5), in a Pyrex^\circledast flask this gave a moderate yield of the corresponding ester **22** (24%) suggesting some participation of the primary carbenium ion. The major product (45%) was the β -fluoro- γ -butyrolactone **21**, which was obtained as a diastereomeric mixture. This probably arises from XeF_2 reacting with the double bond to give a benzyl cation that cyclises leading to the product **21**. Using XeF_2 in PTFE the only significant product was the fluoride **23** (42%) with no evidence of radical derived products.

In conclusion, we have found that whereas reaction of carboxylic acids with XeF_2 in CH_2Cl_2 and a PTFE flask consistently results in fluorodecarboxylation ($\text{RCO}_2\text{H} \rightarrow \text{RF}$), use of a Pyrex^\circledast flask catalyses alternative modes of reaction, including rearrangement and cyclisation, which are consistent with the formation of intermediate fluoroxenone esters (Scheme 1). This behaviour is analogous to that of other hypervalent intermediates including those formed by (diacetoxyiodo)benzene.¹⁷ It is well known that Lewis acids can catalyse reactions of XeF_2 .¹⁸ Using CH_2Cl_2 as solvent, a Pyrex^\circledast

surface appears to be a superior catalyst for achieving rapid electrophilic reactions of XeF_2 . For example, we have found that reaction of 4-fluoro-1-trimethylsilylbenzene with XeF_2 in CH_2Cl_2 /Pyrex[®] rapidly gives an almost quantitative yield of 1,4-difluorobenzene and trimethylsilyl fluoride,^{1,19} whereas the same reaction in PTFE using catalytic $\text{BF}_3 \cdot \text{OEt}_2$ is reported to give only 34% of 1,4-difluorobenzene in a complex mixture containing six other products.²⁰

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- In a typical procedure, XeF_2 (1.5 mmol) was added to a solution of the carboxylic acid (1.0 mmol) in dry CH_2Cl_2 (15 mL) in a Pyrex[®] or PTFE flask. The solution was stirred under argon at ambient temperature (14–18 h), and the reaction mixture was analysed by GC–MS prior to work-up.