THE COLLEGE OF AERONAUTICS

CRANFIELD

SOME REACTIONS OF PERFLUOROGLUTARIC ACID

by

D.A. Smith

THE COLLEGE OF AERONAUTICS

DEPARTMENT OF MATERIALS

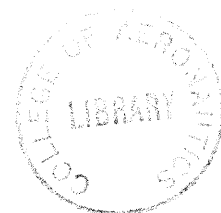Some reactions of perfluoroglutaric acid

- by -

D.A. Smith

SUMMARY

Perfluoroglutaric acid when reacted with methyl magnesium iodide affords 2,6 diol 2,6 dimethyl hexafluoro pyran[I] in high yield and 4-one, 1,2,3 hexofluoro caproic[II] acid in low yield. The former material appears to exist in a range-melting form (64-79°C) and a very labile form of melting point 96-98°C. The 2,6 diol 2,6 dimethyl hexafluoro pyran[I] yields a mono semi carbazone[III], and also a mono[IV] and a di 2:4 dinitro phenyl hydrazone. [V] The mono 2:4 dinitrophenyl hydrazone appears to be cyclic. Reduction both with lithium aluminium hydride and sodium borohydride yields 2,6 diol 3,4,5 hexafluoro n-heptane.[VI] There is evidence to suggest that reaction with dried calcium sulphate gives 2 ene, 2 methyl 3,4,5 hexafluor 6 one cyclo-hexane[VII] Reaction with benzoyl chloride affords 2,6 dibenzoate, 2,6 dimethyl hexafluoro pyran.[VIII]

4 one 1,2,3, hexafluorocaproic acid was characterised as a 2:4 dinitro phenyl hydrazone[IX] and also as an S benzyl thio-uronium salt.[X] Infra-red spectral evidence suggests the S benzyl thio uronium salt probably exists in the straight chain form.

Numbers in the above text refer to the Flow Sheet, Figure 1.

C O N T E N T S

Contents (Continued)

Introduction

In recent years there has been considerable interest in polymeric materials of increased thermal stability and one of the more successful commercial materials of this type is polytetrafluoroethylene. Also available are fluorinated rubbers of the Viton series. Nevertheless there are relatively few fluorinated polymers commercially available, this is not surprising, as far less is known about the reactions of fluorinated compounds than about organic compounds containing hydrogen, oxygen and nitrogen, etc.

The aim of the work described in this Note was to investigate the reactions of perfluoroglutaric acid,

$HOOC \cdot CF_2 \cdot CF_2 \cdot CF_2 \cdot COOH$, which has two functional groups, to see if other difunctional materials could be made from it that might be suitable starting points for new polymeric systems, of improved thermal stability.

Organo-magnesium compounds, (Grignard Reagents) are well-known intermediates of great use in synthetic organic chemistry and previous work had shown that trifluoracetic acid ($CF_3 \cdot COOH$) could be converted to 1,1,1, trifluoroacetone ($CF_3 \cdot CO \cdot CH_3$) in this way.[9] This reaction was taken as the base for further research, it was hoped that a diketone, a diol and a di-ene could be prepared, and possibly other di-functional materials. Any of these could conceivably form the basis of a polymeric system, though even so a good many polymers exist which do not have useful properties.

In the event a rather unexpected reaction took place, giving rise to a pyranose ring structure.

This compound appeared to have a normal or 'ground' state, with a melting range of 64-79°C, and also a very labile form of melting point 96-98°C. Even mechanical agitation could cause the labile form to return to the range-melting form. A full explanation of these phenomena is not apparent, undoubtedly this problem requires further research, as it is of an unusual nature.

An interesting diol, namely 2,6 diol, 3,4,5 hexafluoro n heptane,

$$(CH_3 \cdot \underset{H}{\overset{OH}{C}} \cdot CF_2 \cdot CF_2 \cdot CF_2 \cdot \underset{H}{\overset{OH}{C}} \cdot CH_3)$$
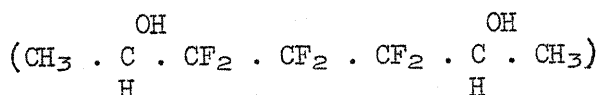
was also prepared. This may be a useful synthetic intermediate. It is interesting to note that theoretically this compound should show similar optical isomerism properties to tartaric acid, but this point was not investigated.

Historical Survey

The preparation of Perfluoroglutaric acid from hexafluoro dichlero cyclopentene is described by Henne and Zimmerschied.[1] This was done by oxidation using alkaline permangenate. They also describe the preparation of the dimethyl ester.

A preparation of the acid starting from hexa chloro cyclopentadiene, which was converted using antimony pentafluoride to hexafluordichlor cyclo pentene and subsequently oxidised to perfluoroglutaric acid using potassium permangenate is described by McBee, Wiseman and Bachman.[2] This paper describes the preparation of the diethyl ester, amides, nitriles and also several hydrogenations of these.

An alternative preparation from 3H nonafluoro cyclohexene, by oxidation using potassium permangenate is described by Evans and Tatlow[3]. They describe the di-anilinium salt (m.p. 219-220°C) and the di S-benzyl thio uronium salt (m.p. 188-190°C). They also describe the preparation of the di-amide.

Murray, Hauptschein and Groth, describe the use of the silver salts of perfluoroglutaric acid to prepare the corresponding perfluoroalkyl halides.[4]

The reaction of conventional non-fluorimated carboxylic acids with Grignard compounds is described in detail by Huston and Bailey[5]. The only previous descriptions of the reaction is a Bayer patent,[6] and by Grignard[7], where tertiary alcohols were obtained. Huston and Bailey made sixteen tertiary alcohols by adding one mole of the organic acid to 3.3 moles of the Grignard reagent, followed by 2 hrs reflux. Less than 15% yield of ketone was obtained from the reaction of butyric acid and s-butyl magnesium bromide, and less than 2% from the same acid and tert-butyl magnesium bromide. Attempts to prepare ketones by adding two moles of Grignard reagent to one mole of the acid gave, as the main product, the tertiary alcohol. Before the addition of water at the end of the reaction, the formation of a white complex, of uncertain composition, was noted.

The reaction of the sodium salts of the carboxylic acids with Grignard compounds was described by Salkind and Beburischwile[8]. Here ketones were obtained, but in yields below 25%.

The reaction of fluorinated carboxylic acids with Grignard compounds was described by Sykes, Tatlow and Thomas[9]. The authors had noted that highly fluorinated compounds can exist in which one carbon atom can be linked to two oxygen atoms, e.g. $R . CF_2 . CR'(OR'')_2$, because the stabilities of these materials are greatly enhanced by the presence of the electronegative fluorine atoms. It seemed therefore possible that when a carboxylic acid had first eliminated active hydrogen by the Zerewitinoff reaction, followed by addition to the carboxyl group, that the latter complex might resist further reaction with the Grignard reagent, particularly any replacement of oxygen containing groups such as O.Mg.X.

The authors describe the reaction of anhydrous trifluoracetic acid with a number of Grignard reagents R Mg X. Here R = methyl, ethyl, iso-propyl, n-butyl, tert-butoyl, phenyl. After decomposition of inter-mediates in the usual way the corresponding ketones (CF_3.CO.R) were obtained in 40-60% yields. Heptafluoro-butyric acid yielded heptafluoro propyl methyl ketone when reacted with methyl magnesium iodide. The best yields of ketone were found at a molar ratio of 2.5 moles of Grignard reagent to 1 mole of acid, no improvements were found by adding the Grignard reagent to the acid. In some cases dibutyl ether was used as a solvent to facilitate separations of ketones from the solvent.

The ketones were characterized as 2:4 dinitro phenyl hydrazones. On treatment of the ketones with aqueous alkali the usual haloform cleavage took place to give the corresponding carboxylic acid and fluoro-hydrocarbon. The acids were mainly identified as s-benzyl thio uronium salts.

The authors found that yields of the methyl and ethyl ketones from 0.1 mole of trifluoracelic acid were 25-30% with 0.18 moles Grignard compound, 35-40% with 0.2 moles Grignard compound, and 50-60% with 0.225 - .30 mole Grignard compound. In these reactions the acid was added to the Grignard compound. Thus after allowing 0.1 mole of Grignard compound for the Zerewitinoff reaction it appeared that more than 0.1 mole was required to complete the reaction.

Though it is known that fluoro-carbonyl compounds are liable to reduction to secondary alcohols if reacted with Grignard reagents having β hydrogen atoms the authors found that appreciable yields of ketones were obtained using branched-chain Grignard compounds. This shows that the groups adjacent to the fluoro-carbonyl function have profound influence on its behaviour with Grignard reagents. The authors believe that the known ability of fluoro-acids to form complexes with ethers is of some importance in this aspect of the reaction.

All the ketones described by the authors seemed to distil in the normal way and there was no evidence of stable hydrates being formed or isolated as such. In all cases the haloform reaction took a normal course.

Dishart and Levine[10] also found that perfluorinated monobasic acids could be converted to ketones using Grignard reagents.

Groth[11] describes the reactions of some perfluorinated dicarboxylic acids with Grignard compounds. The reaction of perfluorosuccinic acid with methyl magnesium bromide yielded the diketone, which was characterised as the 2:4 dinitro phenylhydrazone.

Methyl magnesium bromide was reacted with perfluoroglutaric acid in the ratio of 8 moles of Grignard compound to 1 mole of acid. This reaction was performed at 0°C. Fractionation of the ethereal layers and extracts gave a mixture, a liquid boiling at approximately 147°C and a material boiling

mostly at 177°C.   The higher boiling point fraction appeared to be a
cyclic hemi-ketal
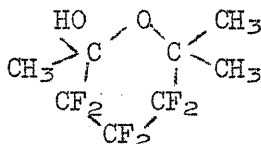
Presumably this would be formed by the cyclisation of $CH.C.CF_2.CF_2.CF_2.C(CH_3)_2$ (with O and OH labels above)
Infra-red analysis showed the absence of the carbonyl group and the presence
of the hydroxyl group.

It was claimed that the lower boiling point material was a mixture of
the diketone and one of two unsaturated mono ketones:

a) $CH_3.CO.CF_2.CF_2.CF_2.\overset{CH_3}{C} = CH_2$

b) $CH_3.CO.CF_2.CF_2.CF_2.CH = CH_2$

It was claimed that infra-red spectra showed the presence of a carbenyl and
olefin function, as did tests with bromine water, permangenate solution,
and 2:4 dinitro phenyl hydrazone.   The 2:4 dinitro phenyl hydrazone had
a m.p of 120°C, its nitrogen analysis (carbon or hydrogen were not reported)
supported the mono derivative of structure: a) Analysis of the mixture
itself however supported structure, b) Groth explained this by postulating
a mixture of the diketone and structure a).   The question of the material
of b.p. approx. 147°C thus appeared to be doubtful, but a reasonable analysis
is quoted for the hemi-ketal.   (Requires C38.09% H3.97% Found C37.75% H4.35%).

Because it was considered possible that we obtained 2,6 diol 2,6 dimethyl
hexafluoropyran in cis and trans forms, work on hydrocarbon analogues was
investigated.   W. Rigby[12]reports work on the separation of the cis and trans
forms of cyclo-hexane 1:3 diol.   (resorcitols).   Previous attempts by
fractional crystallisation were described by Sebatier and Mailke[13], Lindemann
and Baumann[14], Rothstein[15], Coops, Dienske and Aten[16]and Dimroth and Resin[17].
These workers had not achieved an efficient separation.   The attempts failed,
according to Rigby, because they attempted to separate first the less soluble
trans-compound.   The more soluble, but more easily crystallisable cis compound
was isolated first by Rigby, who describes an efficient separation.   Acetone
was used as a solvent and 97% of the total resorcitols present in the
original mixture were isolated as pure cis-compound (m.p. 85-85.7°C) and
pure trans resorcitol (m.p. 118-118.5°C).   The higher melting point form
was shown to be the transform by studies of alkaloidal salts.   There was
no suggestion that the cis and trans forms were unusually unstable in any
way.

Cope and Fournier describe a stereo specific synthesis of 2,6 dihydroxy-
methyl tetra hydro pyran from 2,6 pyran dicarboxylic acid[18].   The proof of
structure is accepted from the work of Czorndola[19]   This compound appeared
to have normal stability.

Some fluorinated ketones form stable hydrates. Hexafluoroacetone hydrate is reported by Henne, Shepherd and Young.[20] This material was dehydrated by distillation from phosphorus pentoxide and the resulting liquid was sufficiently stable to be distilled. However, on exposure to atmospheric moisture it reverted to the hydrated form.

Perfluoroheptane 4 one hydrate is described by Hauptschein and Braun.[21] The parent ketone was a fairly stable liquid of b.p. 83°C but on addition of water and evacuation a solid hydrate m.p. 35°C was obtained. This formed a triethylamine adduct which was recrystallised from benzene. No attempt at dehydration is described.

Reid and Calvin[22] describe the production of copper chelates from diketones of the type $CF_3.CO.CHR.CO.R'$. The ketones were not hydrates and could be regenerated from their copper chelates by reaction with hydrogen sulphide. Crystalline chelates are described prepared by reaction of an ethanolic solution of the ketone with aqueous, saturated cupric acetate solution. The chelates could be recrystallised from ethanol or xylene. The chelates gave definite analyses.

Discussion

After some slight exploratory work attempting a Claisen condensation of ethyl acetate with diethyl perfluoroglutarate it was decided to react perfluoroglutaric acid with methyl magnesium iodide. Following the work of Sykes, Tatlow and Thomas[9] we would have expected to get 2,6 dione, 3.4.5 hexafluoro heptane, but in fact we obtained initially very low yields of unidentified material. Azeotropic drying of the perfluoroglutaric acid produced some improvement, but at this stage the products of the reaction were contaminated with iodine. When it became clear that there were both acidic and neutral products it was decided to render the aqueous layer mildly alkaline, in order to fix the acids as their sodium salts, and perform a liquid-liquid continuous extraction to extract the neutral products, which could then be worked up from the ethereal solution. The aqueous layer had sodium thiosulphate dissolved in it in order to deal with iodine, and the ethereal solution of the neutral products was treated with precipitated silver and charcoal in order to deal with further iodine and decolourise the solution.

After removal of the neutral products the aqueous layer was rendered acid to litmus, by a small quantity of concentrated sulphuric acid, and another liquid-liquid extraction was performed to obtain an ethereal solution of the acid materials, which were freed from iodine using precipitated silver.

Attempts to distil the neutral products gave a material which distilled over a wide range, the liquid product solidified to a material whose analysis corresponded to the mono-hydrated form of the ketone

$$CH_3.\overset{O}{\overset{|}{C}}.(CF_2)_3.\overset{HO \quad OH}{\overset{|}{C}}.CH_3$$. The melting point of this material was over

a wide range (64-79°C), suggesting that it was a mixture of several forms. The inherent improbability of the existence of a monohydrate, in a symmetrical structure coupled with the absence of a ketone frequency in the infra-red spectrum, suggested that in fact the material was based on a pyranose ring structure
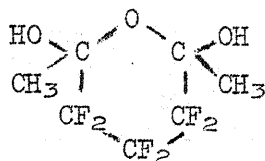
2,6 diol, 2,6 dimethyl hexafluoropyran.

Groth[11] had reported the occurence of a similar pyranose structure.

N.M.R. analysis shows two groups of peaks, one group based on 6.2p.p.m (OH?) and the other at about 1.5p.p.m. (CH_3) in approximately 1:3 ratio. In the CH_3 region there were two groups of peaks, each of which was further split inexplicably. All this can be roughly interpreted as a 4:1 mixture of cis and trans isomers.

The data cannot be interpreted in terms of a single structure. The data are consistent with the pyranose ring structure proposed.

It appears that the above structure can exist in cis and trans forms, presumably boat and chair forms as well. The existence of several stereo-isomers would explain the fact that the distillation and melting points were both over a range.

Working at a molar ratio of 8 moles of Grignard compound to 1 mole of acid the yield was 70.49%, at a molar ratio of 16 moles of Grignard reagent to 1 mole of acid the yield was 74.8%, and at a molar ratio of 4 moles of Grignard reagent to 1 mole of acid the yield was 30.12%. Distillation of the neutral products resulted in considerable losses, it was found satisfactory to evaporate off the ether in an evaporating dish and to purify the crude neutral products by recrystallisation procedures, to obtain analyses.

The acid materials gave a product b.p. 113-5°C at 12 mm in approx. 4% yield. This material appeared to be 1,2,3 hexafluoro 4-one caproic acid, in a non-hydrated form, this was supported by the presence of a pronounced ketone frequency in the infra red analysis. A 2:4 dinitro phenyl hydrazone was prepared, and characterised, also an S benzyl thio uronium salt. The presence of the carbonyl function frequency in the infra red spectrum of this latter compound, combined with its marked likeness to the spectrum of the S benzyl thiouronium derivative of penta fluoropropionic acid suggest that the material is linear. Also strange is the fact that the ketone group is not hydrated, as in the neutral products.

A similar case is recorded by Sayers, Stephens and Tatlow[25] who found that the S benzyl salt of 2,2,3,3,4,4,5,5 octa fluoro 6 one heptanoic acid showed the infra-red frequency of a free carbenyl group at about 1760cm^{-1}.

Here again the ketone group did appear to be hydrated.

It may be considered possible that the materials are cyclic, but the infra-red absorptions of the lactone carbonyl group that would result may be similar to that of the normal carbonyl group in any case. Otherwise it is difficult to see why a carbonyl group near to 3 or 4 CF_2 groups is hydrated in the neutral products, but not in the acid products.

The neutral product 2,6 diol 2,6 dimethyl hexafluoropyran formed two 2:4 dinitro phenyl hydrazones a mono compound of m.p. 140-1°C and a di-compound of m.p. 203-4°C. Infra-red evidence suggested that the mono material had a cyclic structure but the di-compound was linear, as might be expected.

A mono semi-carbazone was also prepared. This was not cyclic, and the ketone group was hydrated, according both to analysis and the infra-red spectrum. Why this is hydrated and the mono 2:4 DNPH cyclic, is not entirely clear, but may be connected with the fact that the NH group in 2:4 DNPH's is amine-like, whereas in the semi-carbazones it is amide-like.

Dehydration of the material proved difficult, most of the standard dehydrating reagents merely giving charring. Calcium sulphate gave a product which is believed to be 1:2 ene, 2 methyl 3,4,5 hexafluoro 6 one cyclo hexane. As this distils over in two layers, with water as the other layer, it may be doubtful if calcium sulphate is acting as a dehydrating agent. On the other hand, calcium sulphate is necessary for this reaction to occur, it seems to function as some sort of catalyst. N.M.R., and infra-red evidence was consistent with the proposed structure. (see Experimental Section).

Reduction of the material using sodium borohydride and lithium aluminium hydride yielded the same product, 2,6 diol 3,4,5 hexafluoro n-heptane. The infra-red spectra were in agreement with this structure. As might be expected, the m.p. of this compound is over a range 54-68°C. It may be supposed that this compound has D, L, meso and racemic forms analogous to tartaric acid, but this point was not investigated.

Reaction with benzoyl chloride yielded a dibenzoate, a material which crystallises with great difficulty and so was difficult to purify, its m.p. was 48-50°C. Theoretically this material could exist in cis and trans forms, but the relatively narrow melting range might be explained by the fact that the cis compound may be difficult to form due to steric hindrance.

The haloform reaction, which was examined under many different conditions, gave anomalous results, it certainly did not give acetic acid as might have been expected, fluoride ion was detected even using N caustic soda. Organic products were difficult to characterise, and varied according to the concentration of caustic soda. Hauptschein, Stokes and Grosse reported that even aqueous hydrolysis of perfluoro γ butyrolactone gave perfluoro-succimic acid.[23]

$$CF_2 \underset{\underset{CF_2}{|}}{\overset{}{\rule{0pt}{0pt}}} \hspace{-0.5em} \text{---} \hspace{-0.5em} CF_2 \xrightarrow{\ H_2O\ } CF_2 \text{---} CF_2$$
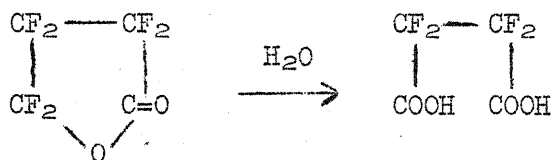
Two fluorine atoms are here removed as fluoride ion under mild conditions. The results of the haloform reaction, on the neutral material give support to the idea of a cyclic structure, rather than a simple linear diketone, where a normal haloform cleavage might have been expected.

Attempts to react the 2,6 diol 2,6 dimethyl perfluoropyran with both phosgene and malanoyl chloride gave no definite products. Attempts at condensing the material with acetone were unsuccessful.

Attempts at the formation of a copper chelate by the method of Reid and Calvin[22] did not yield any definite compound, but it is possible that a material of a polymeric nature, softening at 300°C was obtained. This material did not appear to be an oxide of copper.

As prepared, by removal of ether by evaporation, or even by distillation 2,6 diol 2,6 dimethyl hexafluoropyran has a melting range of 64-79°C. As theoretically a cis and a trans form of the above compound can exist it was supposed that the range-melting material was a mixture of the two forms. It was supposed that the sort of recrystallisation methods used by Rigby[12] on the resorcitols might conceivably effect a separation of the cis and trans forms, if these existed.

Preliminary exploration showed that hydroxylic solvents such as water and ethanol were not suitable, but good recrystallisations could be obtained from benzene, toluene, 80-100 petrol and chloroform. These particular solvents were examined in great detail. On some occasions it was found possible to obtain a form of the material m.p. 96-98°C. The preparation of this material was never certain, once it had started to form in the first instance high yields of the 96-98°C melting material could be obtained by evaporating down the mother liquors. If it were not formed in the first instance, it did not appear by further evaporations and crystallisations. Normally distillation yielded range-melting material, but there is one case at least where material melting above 90°C was also obtained by distillation. Apart from range-melting and 96-98°C melting materials, intermediate forms melting in the 80's were sometimes noted.

It was found possible to prepare large crystals of material, portions of which melted at 64-79°C, these crystals were birefringent and elongated.

The form of the material of melting-point 96-98°C appeared to be very labile, it returned to lower melting forms when merely left for two or three weeks. The return to range-melting material was hastened by increased temperature (45°C). Once range-melting material had been produced by this

thermal ageing process it did not appear to be possible to regenerate the 96-98°C form back again, using the accepted crystallisation procedures.

It was noted that shaking, as in a vehicle, or under controlled conditions in a laboratory shaker, also brought about a change in the 96-98°C form by lowering its melting-point. On one occasion agitation at the temperature of liquid air brought about the transformation. We have referred to this phenomenon as 'vibromutation' (L vilro, shake; mutare to change). Merely forcing the 96-98°C melting form through a sieve to prepare powders for X-ray work was found to change the 96-98°C melting form back into the range-melting form. It was also found that exposure to X-rays brought about the same transformation.

The 96-98°C form of the material is thus uncertain in its preparation and very labile when obtained.

X-ray crystallographic studies were undertaken, using the rotating crystal powder method and Cu K α radiation, to try to compare the range-melting form with the 96-98°C melting form. Subsidiary tests unfortunately suggested both X-rays and sieving procedures, necessary to get the powder into the small glass tubes of the X-ray machine, converted the 96-98°C form back into the melting range form. We cannot be sure that the photographs of the 96-98°C form represent that material. The melting range and 96-98°C forms showed a definite crystalline pattern, it was not possible to definitely distinguish between them. Both melting range and 96-98°C melting material showed pronounced asterism in the photographs. A careful check using powdered nickel showed that this effect was not due to the instrument. The usual interpretation of this phenomenon is that the materials are in a state of strain, thus causing lattice distortion.

Gas chromatography studies were undertaken on an ethereal solution of the neutral material. Using a silicone based column at 150°C, apart from the ether peak, a double peak was noted, suggestive of two materials in similar quantities. They are only just resolved and thus probably of a similar chemical character.

There is no evidence for hydration producing the 96-98°C melting form. The problem of the different forms of 2,6 diol 2,6 dimethyl hexafluoropyran is obscure, and undoubtedly further study will be required to elucidate it. The author would however like to put forward the following comments.

The pattern of events is not like the separation of two stable isomers, such as is reported by Rigby[12] in the separation of the resorcitols. Firstly, we do not obtain two definite forms as he did; as one form crystallises out, the mother liquors should become richer in the other form, this is not the case with the 2,6 diol 2,6 dimethyl hexafluoropyran.

This fact, coupled with the erratic nature of the process suggests the

96-98°C form is a particular lattice structure or polymorph, as a hypothesis we may say that the range-melting form may be a solid solution of cis and trans forms, but the 96-98°C form is a particular lattice structure into which both the cis and trans molecules can fit. For this form to crystallise certain exact conditions must be fulfilled, the nature of these are unknown, perhaps depending on crystal seeds or the exact proportion of cis and trans materials. Courtauld atomic models suggest the cis and trans forms are very similar and could fit into the same crystalline lattice. For reasons not at present clear, the 96-98°C melting material crystallises into crystals which contain internal strains, these at least partially ease themselves by the lattice changing into the solid solution lattice, or range-melting material. This would account for the various 'vibromutation' phenomena. The cis and trans materials are present and it has not proved possible to separate these because either:

a) they have very similar solubility properties in the solvents investigated

or b) they convert rapidly into each other and normally only exist in an equilibrium mixture, even in the solid state.

It was hoped to 'lock' the cis form by preparation of an internal carbonate or malonoate but this was unsuccessful. The dibenzoate may be the trans form due to steric hindrance. An attempt to prepare the di(phenyl urethane) was unsuccessful.

It is interesting to note a certain structural likeness between 2,6 diol, 2,6 dimethyl hexafluoropyran and glucose. Optical isomerism will not occur in the fluorine compound as it has a plane of symmetry.
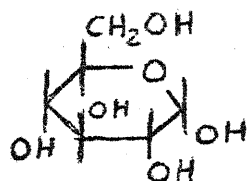
α-D glucose
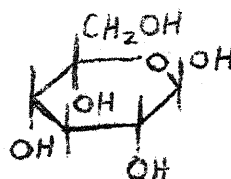
β-D glucose
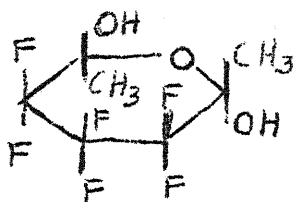
trans 2,6 diol
2,6 dimethyl hexafluoropyran
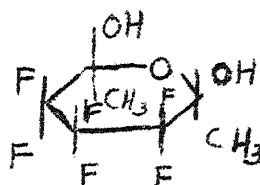
cis 2,6 diol 2,6 dimethyl
hexafluoropyran

α glucose is prepared by crystallisation of the ordinary D form (which contains mostly αD material, but some βD material) from acetic acid containing some water. Crystallisation from pyridise or at higher temperatures pure acetic acid, yields β glucose.[24]

No such simple separation can be effected using the analogous fluorine compound. Considering that there would be internal hydrogen bonding in the cis form and not in the trans, one might expect the behaviour of the two forms to differ in hydroxylic solvents, the two forms may differ in dipole moment which would possibly lead one to expect the two forms to differ from each other in a solvent such as chloroform. That this was not the case may support the idea that there is easy inter-conversion of one form into the other.

Models show that to change from the cis to the trans form a carbon-oxygen bond in the pyranose ring must be broken and reformed. If one or both of these bonds have a strongly ionic character, or even a totally ionic character under certain circumstances, this change might occur. It is possible that the strongly electronegative fluorine atoms, compared with the glucose structure, may bring this about. This would explain why it has not proved possible to separate the cis and trans forms by simple means, due to rapid inter-conversion.

The problem of the 96-98°C melting form, is in the author's opinion, an entirely separate problem to that of cis trans isomerism; its explanations would seem to be crystallographical in as far as it can be explained at all, at the present time.

EXPERIMENTAL SECTION

Claisen condensation of ethyl acetate and diethyl perfluoroglutarate

13g. of diethyl perfluoroglutarate (prepared by standard esterification procedures) were mixed with 18g of ethyl acetate and the mixture added, with caution, to 2.3g of sodium wire in a round-bottomed flask fitted for reflux.

The reaction was moderate and produced a dark syrupy liquid. To this 30 moles of sodium dried ether were added and the material refluxed overnight.

Ether was removed, the remaining brown solid was reacted with 150 moles of 10N sulphuric acid and the resultant solution extracted with ether (4 x 100 mls). The ethereal extracts were dried over anhydrous magnesium sulphate, ether stripped off and the remaining liquid distilled off under vacuum (10-14 mm). The distillation range was 62°C - 140°C. This material was redistilled under vacuum off phosphorous pentoxide and collected in three cuts. Once again the wide distillation range was noted.

Analysis of the central cut did not correspond to either the mono or di-Claisen esters of diethyl perfluoroglutarate.

Acid hydrolysis of this material was however attempted but a material distilling over the range 48°C - 120°C at 14 mm pressure was obtained.

The material had an acid reaction in water, but no positive sulphate reaction.

It proved impossible to prepare any definite crystalline 2:4 dinitro phenyl hydrazones from the material, which appeared to be a mixture.

Development of the Grignard system of preparation

Theory suggests that the molar ratio should be 6 moles Grignard reagent (methyl magnesium iodide) to 1 mole of perfluoroglutaric acid.

The initial experiment was at the above molar ratio.

7.2g of dried magnesium were reacted with 43g of methyl iodide dissolved in 75 c.c. of sodium - dried ether in the usual manner for Grignard reactions. After $\frac{1}{2}$ hr. reflux with stirring the material was decanted off the solid metal that remained. 12.00g of perfluoroglutaric acid in 30 c.c. of absolute ether were added, a violent reaction took place. The reactants were stirred for 1 hr. at room temperature after the addition of the acid. 30 c.c. of distilled water were then added followed by 75 c.c. of hydrochloric acid. (25 c.c. conc. acid in 100 c.c. water. Water and ethereal layers were separated and the water extracted with ether (3 x 50 c.c.) and the combined ether extracts were dried over anhydrous sodium sulphate overnight.

Ether was removed by distillation, the remaining liquid was then distilled initially at atmospheric pressure yielding a liquid boiling over a continuous range from 40-90°C, a further portion distilled at 180-200°C under vacuum, which solidified on cooling and was believed to be perfluoroglutaric acid.

The first fraction was again redistilled into two fractions, the higher boiling of which seemed to decompose. An attempt was made to redistill the first fraction using a 'pig', and semi-micro apparatus. All the fractions were brown or yellow and purple vapours were observed at about 104°C. It was assumed from this that the materials were polluted with iodine and this distillation was not persued. Exploratory attempts to make 2:4 dinitro phenyl hydrazones produced materials, but these did not have definite melting points, recrystallisation did not improve the melting points.

The following procedure was used for drying perfluoroglutaric acid.

12g of perfluoroglutaric acid were dissolved in 100 mls of benzene and refluxed for 3 hrs, approx. 2 mls of water were observed. Benzene was stripped off at atmospheric pressure, and sodium-dried ether (30 c.c.) was

run on to the perfluoroglutaric acid at the point when the first crystals
were seen forming on the surface of the molten perfluoroglutaric acid.
The ethereal solution of perfluoroglutaric acid was stored over anlydrous
sodium sulphate.   The above drying procedure has been used in all
subsequent work.

The previous preparation (molar ratio) was now repeated using dried
perfluoroglutaric acid and the following modifications:-

After drying over anhydrous sodium sulphate for 24 hours the ether
was removed using a Vigreux column, iodine vapour was observed, so anlydrous
ether was replaced.   The ethereal solution was washed by extraction with
aqueous sodium thio-sulphate solution (3 x 50 c.c.).   One extraction was
performed using acqueous sodium bicarbonate.   After the extractions the
ethereal solution was again dried for 24 hours over anlydrous sodium
sulphate.

Ether was then stripped off using a Vigreux column, the remaining
liquids were distilled under vacuum using a 'pig' and three cuts obtained

    1.   a liquid b.p. (Emich) 114°C yield .06g.
    2.   a liquid b.p.   117°C yield 0.29g.
    3.   a liquid b.p.   118°C yield 0.63g.

The material, especially of fraction 3 was yellow, probably due to traces
of iodine.

Attempts to prepare semi-carbazones resulted in solids, after recrystal-
lising from methanol, which had indeterminate melting-points.

Though some progress had been made in over-coming the problem of
contamination by iodine the yields were too low to make the process practical.

An attempt was made to use methyl bromide in place of methyl iodide,
but partly owing to the low boiling point of methyl bromide, this was not
successful.

A modified procedure was adopted, still using 60 moles Grignard reagent
to 1 mole of acid, but attempting to separate acidic from neutral products
in a more satsifactory way.   12g. of perfluoroglutaric acid were dried
azeotropically and dissolved in 40 c.c. sodium dried ether and dried over
anhydrous sodium sulphate.

Methyl magnesium iodide was prepared in the normal way, using stirring,
from 7.2g. oven dried magnesium, 43g. of methyl iodide in 75 c.c. of sodium-
dried ether.   The material was refluxed for 1 hour and the ethereal solution
of the Grignard reagent was added.   A pale yellow 'soap'-like substance was
observed, and a gas, presumed to be methane, was observed.   30 c.c. of
distilled water were cautiously added, followed by 75 mls of 25% hydrochloric
acid.

Sodium bicarbonate was added to the aqueous layer and the ethereal and aqueous layers shaken together for $1\frac{1}{2}$ hours, 2g. of thiosulphate of sodium were added and shaking continued. The aqueous layer was alkaline to litmus. It was hoped that the acidic substances would be fixed as their sodium salts, the aqueous layer was now extracted with ether continuously for 24 hours and the ethereal solution was worked up.

After removal of ether by distillation under atmospheric pressure, a liquid boiling at 92-94°C (1.16g) was obtained, small quantities of higher boiling materials were obtained which gave mushy solids on standing. All the products were a faint yellow colour, and presumably tainted with iodine.

The aqueous layer from the above experiment was now treated with conc sulphuric acid until it was acid to litmus. Sulphur was precipitated. The ethereal extract was distilled, but the presence of purple vapours, black crystals and brown distillates showed this material was contaminated with iodine. Attempts to prepare coppersalts of the acids failed. In spite of a revised procedure the preparation was still vitiated by the presence of iodine impurities and poor yields.

Preparation at a molar ratio of 8 moles Grignard reagent to 1 mole of perfluoroglutaric acid.

12g of perfluoroglutaric acid were dried in the usual way, and dissolved in 100 c.c. sodium dried ether.

57g of methyl iodide were redistilled, dissolved in 100 c.c. sodium dried ether and stored over anhydrous sodium sulphate.

9.7g of dried magnesium were reacted with 57g of methyl iodide, in the normal way, using 100 c.c. of ether. The reactants were refluxed for $1\frac{1}{2}$ hours. The perfluoroglutaric acid in sodium dried ether (100 c.c.) was then added, once again the cream 'soap-like' substance was noted. The ethereal slurry was stirred at room temperature for 3 hours. 30 mls of distilled water were added with caution, followed by 100 c.c. of a 25% hydrochloric acid solution. Sodium bicarbonate solid was added to the aqueous layer, until the aqueous layer was alkaline to litmus, the layers were then shaken together for $1\frac{1}{2}$ hours. The layers were separated, the alkaline aqueous layer was then extracted with ether for 16 hours and the combined ethereal portion dried over anhydrous sodium sulphate.

The aqueous layer was then acidified with concentrated sulphuric acid and again extracted with ether which was dried over anhydrous sodium sulphate.

Work up of neutral materials was by distilling off the ether, followed by distillation of the remaining products. At atmospheric pressure material was found that boiled over a continuous range of 94-130°C. Further material boiling from 40-82°C at 15 mm was obtained. No simple clear cut boiling point or points, were observed, the materials were brown or yellow, due to iodine contamination.

Total yield was 2.59g.   Iodine contamination prevented analysis.

The work up of the acidic materials was as follows:-

Ether was stripped off under reduced pressure, but the crude acids
(6.78g) were not distilled.   Attempts were made to prepare a semi-carbazone
from the crude material.   A material m.p. 238°C (decomp) yield .03g was
obtained after recrystallisation from methanol.   The yield suggested this
was not a significant material.   Attempts were made to prepare an s-benzyl
thio-uronium derivative from a portion of the crude acids.   A material m.p.
185°C yield 0.14g was obtained.   A separate S benzyl thio uronium salt was
prepared from 1g. perfluoroglutaric acid.   Yield 1.26g. m.p. 185-6°C.

Mixed m.p. of derivative from crude acids with material from perfluoro-
glutaric acid 185-6°C.

A few tests were performed on the crude acid materials:

1)   soluble in water, solution was acid to litmus, the brown colour of the
solution was discharged by sodium thio-sulphate solution.

2)   An aqueous solution gave a yellow precipitate with an aqueous, acidic
solution of 2:4 dinitro phenyl hydrazine, suggesting a carbenyl group.

3)   The hydroxylamine-feric chloride test for an ester was performed with
negative result.

It was decided to increase the molar ratio to 10 moles Grignard reagent
to 1 mole perfluoroglutaric acid.   It was decided to attempt to overcome
the iodine problem by washings with sodium thio-sulphate and treatment,
where necessary, with finely powdered silver.

The preparation was similar to the previous case except that the ethereal
layers of both neutrals and acids were washed with aqueous sodium thio-sulphate
solution, followed by water, and also treated with charcoal and precipitated
silver, prior to work up.

Work up of the neutral materials proceeded by evaporating off ether
under atmospheric pressure using a steam bath, followed by distillation under
atmospheric pressure and vacuum of the residual products.   Though the
materials appeared free of iodine contamination the total yield was very
small, being 0.78g in all, boiling over a continuous range of   90-125°C at
atmospheric pressure, and 45-75°C at 11-13 mm. pressure.

The work up of the acid materials was as follows:-

After filtering off charcoal, and sodium sulphate from the ethereal
solution, ether was removed by distillation using a steam-bath.   The crude
acid products were treated with precipitated silver overnight, filtered and
distilled in vacuo.   Yield of crude acids 8.4g.

	Boiling range	Pressure	Yield
1st cut	110 - 120°C	$14\frac{1}{2}$ mm.	1.13g. liquid
2nd cut	120 - 130°C	$14\frac{1}{2}$ mm.	1.27g. liquid
3rd cut	over 150°C	$14\frac{1}{2}$ mm.	1.55g. solid

Boiling point of 1st cut 160 - 162°C (Emich)
2nd cut ca. 193°C.

An S benzyl thio uronium salt was prepared from the entire 3rd cut.
Yield 0.49g. melting point 185°C.
Mixed m.p. with the salt from perfluoroglutaric acid 184°C.

The 3rd cut is largely unchanged perfluoroglutaric acid.

Attempts to prepare tosyl derivatives from the 1st and 2nd cuts proved unsuccessful.

An attempt was made to prepare a 2:4 dinitro phenyl hydrazone (see section on derivatives).

An attempt was made to separate monobasic from dibasic acids in mixtures of two, using aniline salts, but this proved unsuccessful with the above materials.

Though the iodine problem had been overcome to some extent, the objection of low yields still remained.

A preparation was now attempted using 10 moles of Grignard reagent to 1 mole of perfluoroglutaric acid. The above procedures were followed, except that the neutral materials were not processed. Using a portion of the ethereal extracts of the acid materials attempts were made again to separate monobasic from dibasic materials by means of their aniline salts. Again there was no significant precipitation, any aniline salts formed being presumably fairly soluble in ether.

The ethereal solution of the remaining acidic residues was worked-up in the following way:-

Ether was removed by distillation, the residues filtered to remove silver, and attempts were made to prepare the derivatives from the crude acid materials. (See section on derivatives).

12g. of perfluoroglutaric acid were dried by the usual procedure and dissolved in 100 mls sodium dried ether and stored over anhydrous sodium sulphate. Redistilled methyl iodide, stored over anhydrous sodium sulphate, was used in the preparation.

9.7g. of dried magnesium were reacted with 57g. of methyl iodide in 100 c.c.

of sodium-dried ether in the usual manner for Grignard reactions. Mechanical stirring was used. The reaction was concluded by $1\frac{1}{2}$ hours reflux.

Perfluoroglutaric acid in 100 mls sodium dried ether was carefully added, a cream 'soap' was obtained and more ether was added to make the materials into a slurry.

This was then refluxed for $2^1/_4$ hours. (This was not done in previous preparations).

After cooling 30 mls of distilled water were added, the reaction vessel being cooled by ice and great care being exercised. This was followed by 100 mls of a 25% solution of hydrochloric acid. Extra acid (50 mls of a 50% solution) were required to dissolve all solid materials. Sodium bicarbonate (solid) was added to the aqueous layer until the latter was mildly alkaline, sodium thio-sulphate was also added and the two layers shaken together for 1 hour, the brown colour of the ether layer was discharged. The aqueous layer was then continuously extracted for 24 hours with ether and the ether extract was dried over anhydrous sodium sulphate for 24 hours.

The acqueous layer was acidulated with concentrated sulphuric acid and extracted for 24 hours, the ether extracts were dried over anhydrous sodium sulphate for 24 hours. A yellow precipitate from the acids was filtered off and shown to be sulphur. (Lassaigne test).

Neutral materials were worked up as follows:-

Ether was removed by distillation using a steam-bath, the remaining oil was treated with precipitated silver and distilled, first under atmospheric and then under reduced pressure.

Material distilled continuously at atmospheric pressure between 70 and 115°C giving initially two liquid products, one of which seemed immiscible in the other.

Further distillation at 19 mm pressure gave an oil which distilled at approximately 80°C.

All these liquids, when left standing, turned into crystalline solids m.p. 64-79°C. Total yield 6.30g.

After washing with ether and drying a sample was analysed. Required for $CH_3 . \overset{O}{\overset{\|}{C}} . CF_2 . CF_2 . CF_2 . \overset{HO \quad OH}{\underset{}{C}} . CH_3$

C33.09% H 3.17% Found C32.80% H 3.11%.

Infra-red analysis showed an absence of the ketone frequency at ca. 1750 cm^{-1} and pronounced hydroxyl frequencies. Derivatives were prepared (see section on derivatives).

Acidic materials were worked up as follows:-

Ether was removed using a steam bath, the crude brown oil remaining was treated with precipitated silver by shaking for 6 hours and then storing overnight.

Little material could be distilled over under atmospheric pressure, the bulk of the material (1.22g) distilled at 13.5 mm. pressure at 112°C. 0.128g. were collected at 13.5 mm. pressure boiling at 115° - 125°C.

Analysis of material was b.p. 112°C/13.5 mm ND 1.3596. Required for 4 one 1,2,3 hexafluoro caproic acid C 30.27% H 1.69%, found C 29,32% H 2.05%.

The previous brew was repeated exactly, but the ethereal solution of neutral materials was used for gas chromatographical analysis. Using a propylene glycol column at 150°C one main substance, other than ether was observed. Using a silicone gel column at 150°C this one peak was partially resolved into two peaks. This suggests two very similar substances may be present.

Preparation at 10 moles Grignard compound to 1 mole acid

24g. of perfluoroglutaric acid were dried according to the conventional procedures. As usual, methyl iodide was redistilled.

12.1g of dried magnesium were reacted with 71g of methyl iodide (dissolved in 200 c.c. of absolute ether, in the usual manner for Grignard compounds and reflexed for $1\frac{1}{2}$ hours. Perfluoroglutaric acid in 200 c.c. (dried overnight over Na_2SO_4) absolute ether was added cautiously and the 'cream soap' obtained, further ether was added to give a slurry. This was refluxed for 2 hours.

40 mls of water were added, followed by 140 mls of 50% hydrochloric acid, the liquid then separated into 3 layers.

Work up of the middle layer (which was separated off using a separating funnel) showed that it largely consisted of water, ether, hydriodic acid, and iodine.

Work up, using the usual continuous extraction techniques on the aqueous layer, gave 4.07g. of a material m.p. 64-79°C after distillation. Work up of acid materials gave 0.614g. of a liquid b.p. 120-135°C at 27 mm. pressure. The effect of increasing the amount of Grignard compound and at the same time using more vigorous conditions is to increase the amount of iodine and hydrogen iodide impurity.

Preparation at 8 moles Grignard compound to 1 mole acid.

24g. of perfluoroglutaric acid were dried azeotropically in the usual way and dissolved in 200 c.c. of absolute ether, and stored over anhydrous

sodium sulphate.

Magnesium iodide was redistilled and dried over anhydrous sodium sulphate.

19.4g. of magnesium (dried at 100°C) were added to the flask and 114g. of methyl iodide in 200 c.c. of absolute ether were slowly added to maintain the reaction, the materials were then refluxed for 1½ hours.

The perfluoroglutaric acid in 200 c.c. of absolute ether was slowly added, the cream slurry so obtained was refluxed for 2 hours. 40 mls of distilled water were added with caution, followed by 140 mls of 50% hydrochloric acid.

The aqueous layer was rendered alkaline by sodium bicarbonate, sodium thio-sulphate was also added and the aqueous and ethereal layers shaken together for ½ hour. The alkaline aqueous layer was continuously extracted for 24 hours and the ether layer reduced in bulk and stored over anhydrous sodium sulphate.

After this the aqueous layer was acidulated with sulphuric acid, continuously extracted with ether for 24 hours, the ether extract was then dried over anhydrous sodium sulphate prior to work up.

The ethereal solution of the neutral products was treated with precipitated silver prior to work up, for several days. After removal of the ether, distillation was continued under atmospheric pressure. The liquid boiled continuously over a range of temperatures from 70-120°C when the distillation was continued under reduced pressure. Material boiling between 70-100°C initially formed two layers. Total yield of products distilled under atmospheric pressure was 6.55g.

Under a pressure of 19 mm. Hg liquid distilled continuously between 40-83°C, yield 1.44g.

Both layers, after separation, of liquid neutral products gave 2:4 DNPH's of m.p. 203-204°C (mixed m.p. with original 2:4 DNPH of the monohydrate). After exposure in Petri dishes all the liquid products crystallised to materials m.p. 63-79°C.

The acid residues were worked up as follows:-

The ethereal solution of the acid products was stood over precipitated silver for several days, filtered, the ether removed by distillation, followed by distillation of the remaining materials under vacuum. The bulk of the material distilled at 130-140°C under 27 mm. vacuum. Yield 0.183g.

The material was cloudy, but did not crystallise. A 2:4 DNPH was obtained m.p. 115°-120°C (impure).

A preparation was performed cutting out the procedure of distilling the neutral materials, this procedure was taken as standard for the preparation of the crude material, believed to be 2,6 diol, 2,6 dimethyl 3,4,5 hexafluoropyran.   The molar ratio is based on 8 moles methyl magnesium iodide to 1 mole perfluoroglutaric acid.   The following describes the standard preparative procedure.

1)   24g. of crude perfluoroglutaric acid were dried by azeotropic distillation in 200 mls benzene, using the Dean and Stark apparatus.   Benzene was removed by distillation, the material in the pot cooled, until the crystals first are seen forming, and then dissolved in absolute ether and dried over anhydrous sodium sulphate.

2)   Methyl iodide was redistilled and dried over anhydrous sodium sulphate.

3)   Using a three-necked reaction vessel with stirrer and double Liebig reflux condenser methyl magnesium iodide was prepared in the usual manner for Grignard compounds using 19.4g magnesium (previously dried at 100°C) and 114g. of methyl iodide dissolved in 200 c.c. sodium dried ether.   At the end of the reaction the materials were refluxed for 1½ hours.

The 24g. of perfluoroglutaric acid in 200 c.c. of absolute ether were added with caution, cooling the flask with ice-water.   More sodium-dried ether was added to obtain a more fluid slurry.   The cream coloured slurry was refluxed gently for $2^1/_4$ hours.

40 mls of distilled water were then added with great caution cooling the vessel with ice water.   This was followed by slow addition of 140 mls of 50% hydrochloric acid.

Sodium bicarbonate solid was added to the aqueous layer, until the aqueous layer was alkaline to litmus paper.   Sodium thio-sulphate was also added to the aqueous layer, the ethereal and aqueous layers were then shaken together for $^3/_4$ hour in a separating flask, the brown colour of the ethereal layer being discharged.

The alkaline acqueous layer was continuously extracted for 24 hours and the ethereal solution so obtained was treated with anlydrous sodium sulphate, charcoal, and precipitated silver overnight and then these materials were filtered off.   The solution was reduced in bulk by distillation and the ethereal solution placed in Petri dishes in a fume cupboard.   The crystalline material so obtained is the crude neutral product.

The alkaline aqueous layer, after this extraction was preformed was rendered acid to litmus-paper using a small quantity of sulphuric acid. Sulphur was precipitated and sulphur dioxide was observed.   The aqueous acid layer was continuously extracted with ether for 24 hours and the ethereal solution so obtained was treated with anhydrous sodium sulphate, charcoal and precipitated silver for 24 hours.   The acid material was normally worked up, after removal of ether by vacuum distillation.

The results of this procedure on several different preparations is set forth in table form below.

Molar Ratio	Type of Process	Yield of Acid Production	Boiling Point of Acid Products	Yield of neutral Products	Melting range of neutral Products	Page Reference
8 moles methyl magnesium iodide to 1 mole p.f.g. acid. 24g. acid.	2 stage	not worked up	not worked up	16.2g	55-65°C	2/67
8 moles methyl magnesium iodide to 1 mole p.f.g. acid. 24g. acid.	2 stage	stored for work-up combined with other preparations		16.7g	64-73°C	2/84
8 moles methyl magnesium iodide to 1 mole p.f.g. acid. 24g. acid	2 stage	stored for work up combined with other preparations		17.27g.	67-79°C	2/100
8 moles methyl magnesium iodide to 1 mole p.f.g. acid. 24g. acid.	2 stage	stored for work up combined with other preparations		18.03g	65-78°C	2/109
8 moles methyl magnesium iodide to 1 mole of acid. 24g. acid.	2 stage	stored for work up combined with other preparations		19.37g.	68-82°C	2/124
8 moles methyl magnesium iodide to 1 mole of acid. 24g. acid.	2 stage	stored for work up combined with other preparations		17.49g.	69-88°C	2/134
8 moles methyl magnesium iodide to 1 mole of acid. 24g. acid.	2 stage	stored for work up combined with other preparations		17.37g.	67-87°C	2/150
8 moles methyl magnesium iodide to 1 mole of acid. 24g. acid.	2 stage	stored for work up combined with other preparations		18.18g.	65-84°C	2/159

Molar Ratio	Type of Process	Yield of Acid Production	Boiling Point of Acid Products	Yield of Neutral Products	Melting Range of Neutral Products	Page Reference
8 moles methyl magnesium iodide to 1 mole of acid 24g. acid.	2 stage	stored for work up combined with other preparations		18.46g.	64-85°C	2/170
16 moles methyl magnesium iodide to 1 mole acid 12g. acid	2 stage	stored for work up combined with other preparations		9.52g.	66-80°C	2/186
4 moles methyl magnesium iodide to 1 mole acid. 24g. acid.	2 stage	0.8g	112-115°C at 12 mm.	7.65g.	64-83°C	3/10
8 moles methyl magnesium iodide to 1 mole acid 24g. acid.	2 stage	not worked up			Used in special recrystallising experiments at Birmingham University.	

Preliminary recrystallisation procedures and preliminary ageing experiments

Preliminary investigations revealed that the following materials are recrystallising solvents for the 2,6 diol 2,6 dimethyl hexafluoropyran.

1) carbon tetra-chloride 2) chloroform 3) benzene 4) toluene
5) 80-100 petroleum.

Trichloethylene is unsatisfactory as materials fail to recrystallise out from it.

3g. of crude 2,6 dimethyl 2,6 diol hexafluoropyran, (this will be referred to as DDHP in future accounts) were recrystallised from 80-100 petroleum, washed with this solvent, and dried for 16 hours in vacuo over phosphorus pentoxide. Solvent was removed under reduced pressure using a Claisen head. Four repeats of this experiment were performed, the effects of ageing the materials a) by leaving in the atmosphere under room temperature and pressure conditions (but inside desiccators). b) by thermal ageing, were investigated.

Room Temperature Ageing

Time	Melting range 1st expt.	Melting range 2nd expt.	Melting range 3rd expt.	Melting range 4th expt.
1 day	97-99°C	96-100°C	95-98°C	96-99°C
2 days	95-98°C	94-97°C	95-98°C	-
3 days	94-98°C	94-97°C	-	-
4 days	93-97°C	-	-	94-96°C
5 days	-	-	93-95°C	85-96°C
6 days	-	-	81-95°C	84-94°C
7 days	94-95°C	-	81-95°C	-
8 days	78-95°C	-	-	-
9 days	75-95°C	-	-	-
10 days	-	-	-	82-95°C
11 days	-	-	80-95°C	-
12 days	-	-	-	-
13 days	75-95°C	-	-	-

Material of m.p. 96-99°C was stored was aged at 45°C and at - 12°C. Material aged continuously at 100°C decomposed.

Ageing of DDHP (original m.p. 96 - 98°C)

Time	Aged at 45°C	Control Material at - 12°C
70 hours	83 - 89°C	95 - 97°C
94 hours	64 - 79°C	-
118 hours	63 - 75°C	-
214 hours	64 - 77°C	-

Material of m.p. 96 - 98°C sent to Birmingham University was found to have
a melting point in the range 64 - 79°C.

Preliminary attempts to crystallise crude DDHP from water were
unsuccessful.

Attempts to repeat the above recrystallisations, using 3g. of crude
DDPH, and similar techniques to the above yielded material of m.p. 90 - 93°C.

A portion of this was stored at - 12°C for 10 days and then recrystallised
from 80 - 100 petroleum.   m.p. 89 - 95°C.   A portion of material was aged
at 45°C for 10 days (m.p. 64 - 78°C) and then recrystallised from 80 - 100
petroleum.   m.p. 74 - 77°C.

Systematic crystallisation studies, using benzene, 80 - 100 petroleum,
toluene and chloroform.

The scheme is represented diagrammatically as follows:-

In all cases 4g. of material were dissolved in 100 mls of solvent, the
liquid raised to reflux temperature and then cooled overnight.   In all cases
materials filtered off were dried over phosphorus pentoxide in vacuo for
16 hours, before weighing and melting point measurements were taken.   Set
quantities of solvent were then removed by distillation at atmospheric
pressure, the liquid remaining was then cooled to - 12°C overnight and any
material obtained was collected by filtration and dried, as described above.

In several cases distillates were checked for crystalline residues and
it was established that materials distilled over with the solvents to some
extent.

In some cases precipitates were redissolved in set quantities of fresh
solvent and stated quantities removed.   Recrystallisation was then carried
out according to the procedures, as described below.

The key to the diagrams is as follows:-

20 moles off ————————	reduction of the initial quantity of solvent in moles.
20 moles on 10 off – – – – – – – – – – –	solid material was re-dissolved in 20 moles and then reduced by 10 moles to recrystallise.
⟵————————	a precipitate is formed. Melting ranges and yields are quoted.

Systematic Recrystallisation of DDHP from chloroform
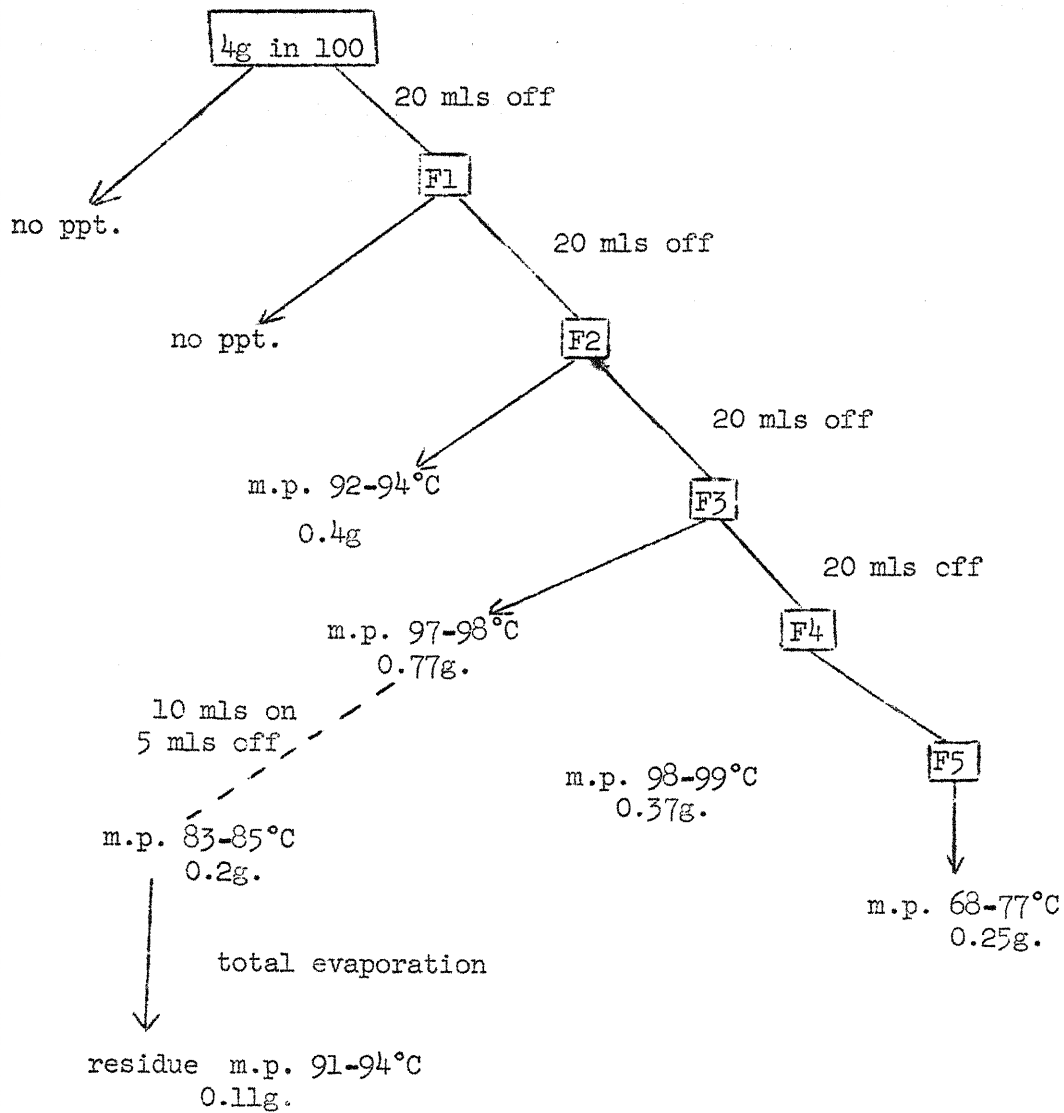
Systematic recrystallisation of DDHP from benzene

4g 100 mls

no ppt.

20 mls off

F1

m.p. 95-97°C
0.35g.

20 mls off

F2

m.p. 94-95°C
1.62g.

20 mls off

F3

m.p. 95-96°C
0.1g.

20 mls on
10 mls off

m.p. 94-96°C
0.77g.

20 off

F4

5 mls off

90-93°C
0.21g.

10 mls on
5 mls off

95-96.5°C
0.12g.

10 mls off

m.p. 94-96°C
0.53g.

F5

m.p. 96-97°C
0.15g.

5 mls
off

total
evaporation

residue
m.p. 88-90°C
0.03g.

total
evaporation

residue
m.p. 95-98°C
0.04g.

10 mls on
5 mls off

m.p. 95-97°C
0.16g.

F6

m.p. 95-97°C
0.19g.
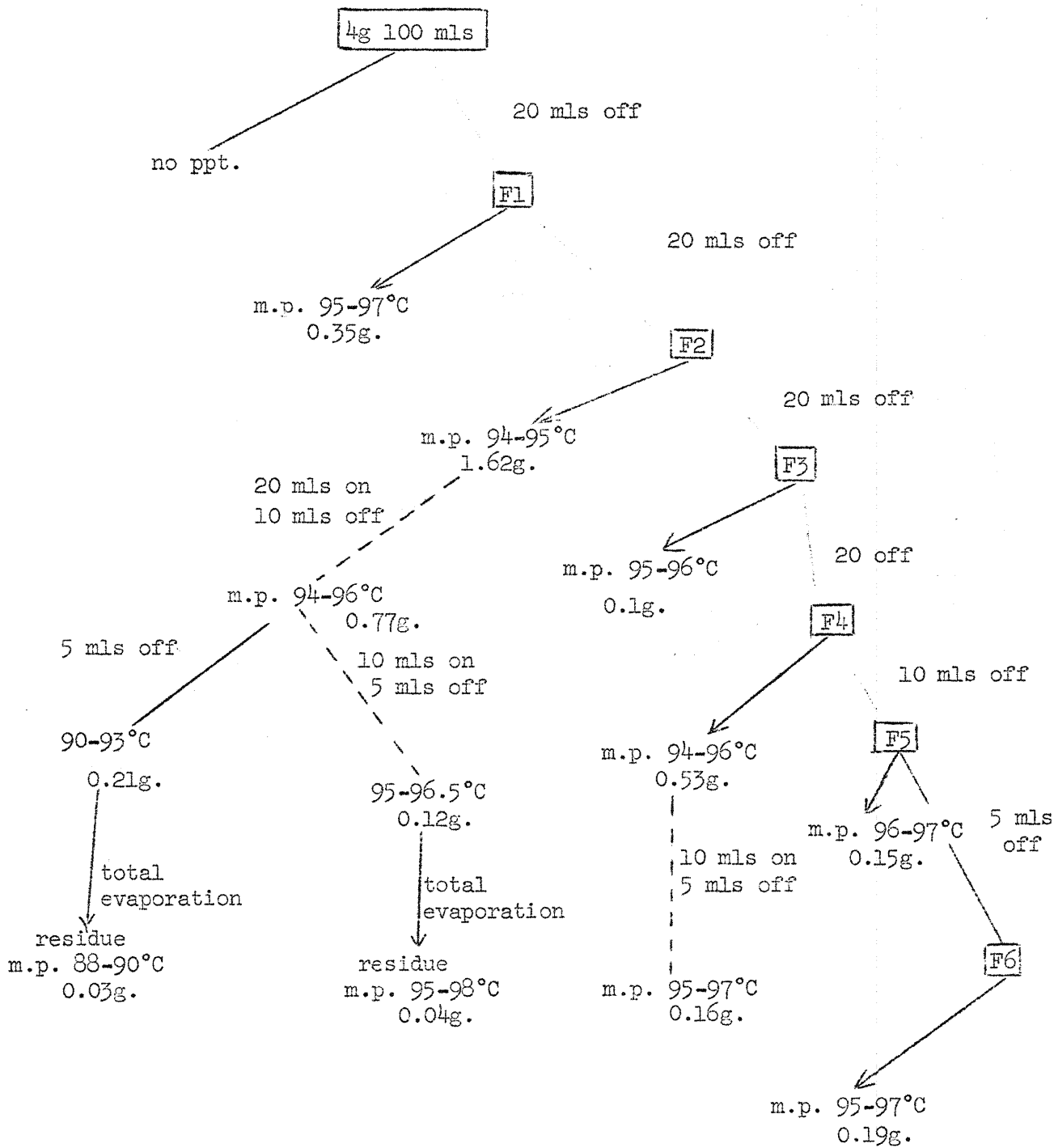
Systematic recrystallisation of DDHP from toluene
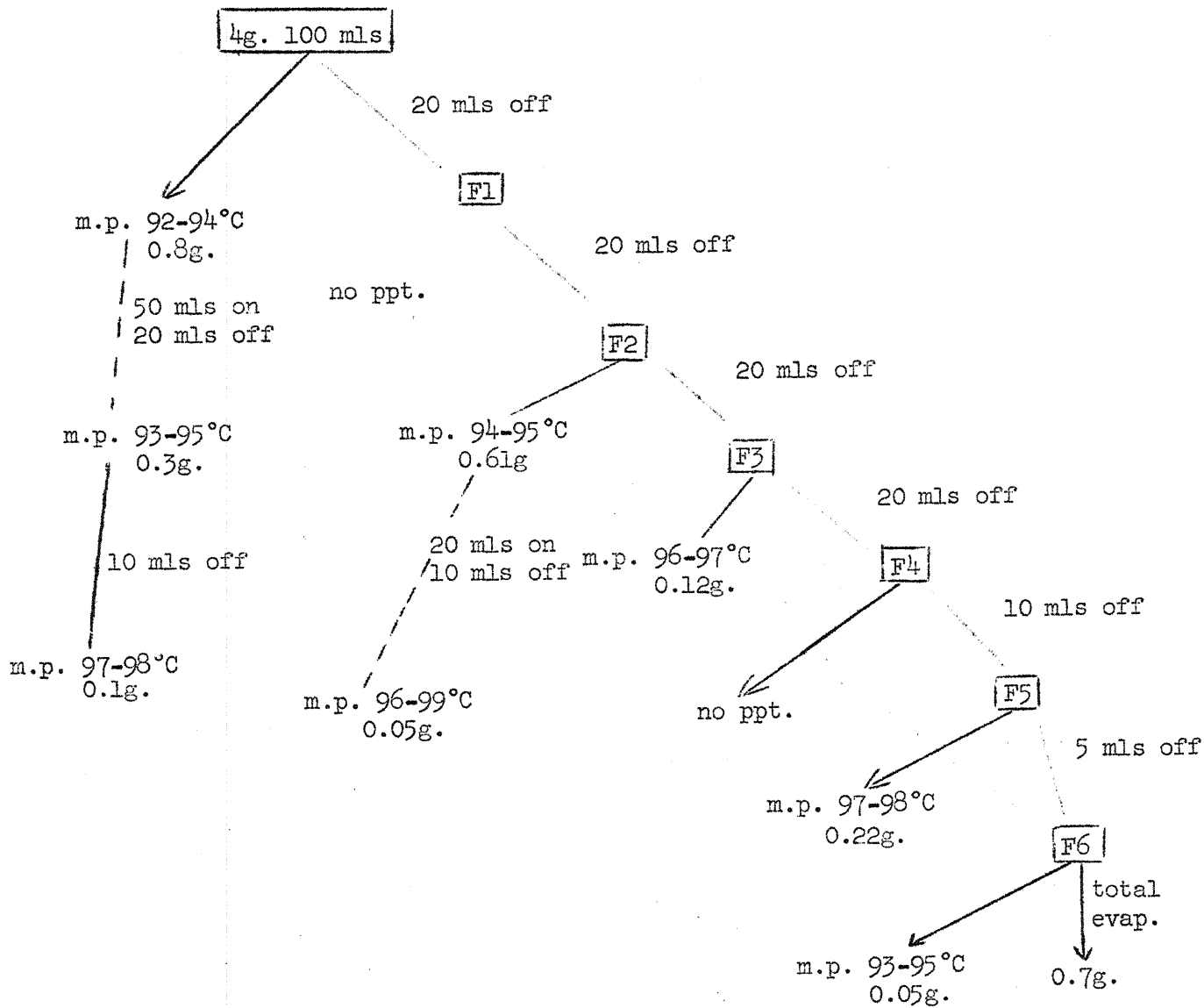
Systematic recrystallisation of DDHP from 80-100 Petroleum


```
                    ┌─────────────┐
                    │ 4g in 100 mls│
                    └─────────────┘              20 mls off
     m.p. 78-79°C                            ┌──┐
           /  yield                          │F1│
          / 50 mls on                        └──┘
         /  20 mls off                              20 mls off
        /                                        ┌──┐
       /                    m.p. 90-91°C         │F2│
      /                                          └──┘
   m.p. 80-80.5°C                                      20 mls off
       1.35g.                                       ┌──┐
  10 mls      \  10 mls on      m.p. 85-86°C        │F3│
  off          \ 5 mls off          0.2g.          └──┘
                \                                         20 mls off
 m.p. 84-86°C                          no ppt.
     0.09g.                                             ┌──┐
                                                        │F4│
                                                        └──┘
                                     no ppt.                10 mls off
                                                          ┌──┐
                                                          │F5│
                                                          └──┘
                                                              5 mls off
                                  m.p. 86-89°C
                                       .01g
                                                            ┌──┐
                                                            │F6│
                                                            └──┘
                                              0.12g. 50-80°C
```
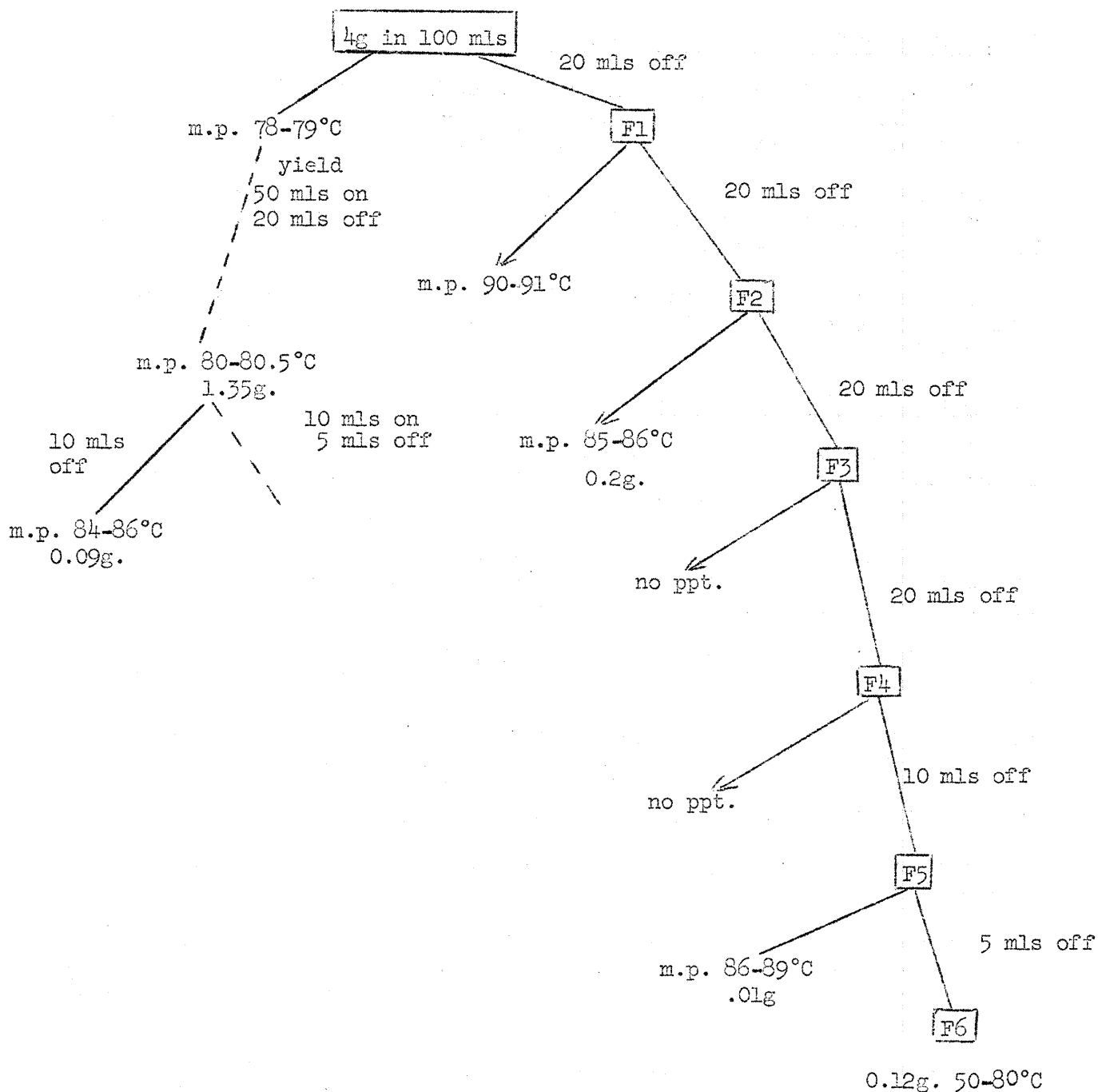
Analysis of material recrystallised from 80-100 petroleum.
Requires for 2,6 dimethyl 2,6 diol perfluoropyran
C 33.1%, H 3.2%
found C 32.7%, H 3.1%

Further recrystallisation experiments on DDHP

Attempts, enumerated below, were made at Cranfield and at Birmingham to repeat sections of the above schemes with a view to obtaining material of m.p. 96-98°C.

1)   Using 80-100 petroleum on material of m.p. ~ 80°C.

4g of this material were dissolved in 100 mls solvent, the liquid taken to reflux, and then cooled overnight at - 12°C.   The ppt was filtered in vacuo over phosphorus pentoxide for 16 hours.   Yield 2.45g m.p. 90-96°C.

The above material was dissolved in 50 mls of 80-100 petroleum.   20 mls of solvent were removed by distillation and the above procedures repeated. Yield 1.9g m.p. 83.5 - 86°C.

This material was redissolved in 30 mls of fresh 80-100 petroleum, 10 mls were removed by distillation and the above process repeated.   Yield 1.6g 84-87°C.

2)   Using chloroform on crude 'as prepared' DDHP.

4g of material were dissolved in 100 mls of chloroform and 40 mls removed by distillation.   The liquid was cooled overnight at - 12°C and the usual procedures carried out.   m.p. 98-99°C.

The liquid was further reduced by distillation by 20 mls and cooled overnight at - 12°C.   Following the usual procedures a further precipitate was obtained.   Yield 1.1g m.p. 98.5-99°C.

The filtrate was further reduced by distillation and a precipitate obtained according to the usual procedures.   Yield 0.49g. m.p. 98.5-99°C.

3)   1g of material of m.p. 98.5-99°C was dissolved in 15 mls of 80-100 petroleum, 7 mls of liquid were removed by distillation, the liquid was then cooled at - 12°C overnight and the previous procedures repeated.   The material obtained had m.p. 99-100°C.   Yield 0.72g.

4)   Recrystallisation experiments on materials obtained by thermal ageing of 96-98°C melting material.

Material of m.p. 68-83°C was dissolved in 10 mls of chloroform, taken to reflux, 5 mls of chloroform removed by distillation and the liquid cooled at - 12°C overnight.   Following the usual procedures a material m.p. 89-91°C was obtained.

Further recrystallisation by redissolving this material in 10 mls of chloroform and removing 7 mls of solvent gave a material of m.p. 87-92°C.

Material of m.p. 60-90°C (obtained by thermally ageing a material of

m.p. 96-98°C) was dissolved in 10 mls of 80-100 petroleum, 5 mls removed by distillation and the liquid cooled to - 12°C overnight. Following the usual procedures a precipitate of m.p. 64-72°C was obtained. Redissolving this in 100 mls of 80-100 petroleum and removing 5 mls and following standard processes gave a material of m.p. 66-73°C.

5) The above experiments were repeated at Birmingham University, but only material melting at 64-79°C could be obtained.

6) (a) 4g of crude material were dissolved in 100 mls of chloroform and 40 mls removed by distillation. The liquid was cooled overnight at - 12°C, the precipitate was obtained in the usual way. Yield 1g. m.p. 90-94°C. (m.p. verified by Dr. J. Burdon).

(b) 4g of crude DDHP were dissolved in 100 mls of 80-100 petroleum, taken to reflux, cooled at -12°C and the precipitate obtained according to standard procedures. Yield 1.75g. m.p. 88-93°C. (m.p. 90-95°C according to Dr. J. Burdon).

Material from experiment(a)were dissolved in 20 mls of chloroform, 10 mls were taken off, the material treated in the usual way giving a material yield 0.32g m.p. 91-93°C.

Material from experiment(b)was taken, and dissolved in 40 mls of petroleum (80-100) and 15 mls taken off. After the usual treatment of cooling at - 12°C etc. material was obtained m.p. 89-91°C yield 1.4g.

7) Repeated recrystallisations from chloroform were performed on a scale of 8g of crude DDHP dissolved in 200 mls of chloroform and following the conventional scheme for chloroform under the systematic recrystallisations. Only materials of m.p. 85-88°C could be obtained. Recrystallisations of this material only yielded further material of m.p. 89-91°C.

A portion of material (1.75g) melting at 85-88°C was dissolved in 10 mls of benzene, 5 mls removed by distillation and the precipitate obtained in the usual way gave m.p. 89-91°C yield 1.4g.

A series of similar experiments were undertaken using benzene. These are summarised in tabular form. In every case 4g of crude DDHP was dissolved in 100 mls of benzene, the material cooled to - 12°C overnight, the benzene melted, filtered, and the resulting material dried over phosphorus pentoxide in vacuo overnight.
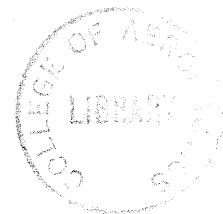
Benzene recrystallisations

Volume of liquid removed from 100 mls	Yields		Melting Range
(1)			
20 mls off	Crop 1	0.25g	96 - 97°C
20 mls off	Crop 2	0.91g	94 - 96°C
(2)			
20 mls off	Crop 1	1.01g	96 - 97°C
20 mls off	Crop 2	0.55g	95 - 96°C
(3)			
20 mls off	Crop 1	1.01g	91 - 92°C
20 mls off	Crop 2	0.54g	96 - 97°C
(4)			
20 mls off	Crop 1	0.46g	95 - 96°C
20 mls off	Crop 2	0.55g.	95 - 97°C
20 mls off	Crop 3 ~	0.02g	95 - 97°C
(5)			
20 mls off	Crop 1	1.35g	m.p. 96 - 98°C
20 mls off	Crop 2	0.55g	m.p. 95 - 96°C
20 mls off	Crop 3	0.55g	m.p. 93.5 - 95°C
20 mls off	1.15g		96 - 98°C
20 mls off	-		93 - 96°C

Attempts were made to recrystallise the crude DDHP at Birmingham University from benzene, but these only gave material melting in the range 64 - 79°C. The work was done according to the above scheme.

Attempts were made to recrystallise crude DDPH from 80-100 petroleum, using reduced pressure to remove the solvent. In both cases similar conditions were used but material of m.p. 85.5 - 89.5°C was obtained in the first case and in the second case material of m.p. 96-100°C was obtained.

Attempts to investigate the erratic nature of products of recrystallisation compared with Birmingham and Cranfield.

The complete neutral products of a Grignard preparation (17-19g) were made up to 300 c.c. using sodium dried ether and then treated according to the following scheme.

At Cranfield

A. 30 c.c. of solution were evaporated down in a Petri dish, exposed

overnight and the material remaining was recrystallised from 6 mls of benzene, material was filtered and dried in the usual way.

m.p. 74 - 76°C   yield 0.1g.

This material was again recrystallised from fresh solvent in the same manner.

m.p. 75 - 77°C   yield ~ .1g.

B.   50 c.c. of material were evaporated down in a round-bottomed flask using a steam bath, the residue was taken up in benzene, the bulk reduced to approx. 6-7 mls and then cooled at - 12°C overnight.   The precipitate was filtered and dried according to the usual procedures.

m.p. 72 - 74°C   yield 0.1g.

On recrystallising the above material from fresh solvent we obtained

m.p. 75 - 76°C   yield negligible

C.   70 c.c. of the above material was stored in a bottle at Cranfield until the completion of the Birmingham experiments.   It was then evaporated down in a Petri dish and the material recrystallised from benzene in the same manner as above.

m.p. 67 - 79°C.

At Birmingham

A.   Repeated exactly.   m.p. 70 - 75°C

B.   Repeated exactly.   m.p. 70 - 76°C

C.   70 c.c. of material were returned to Cranfield, evaporated and re-crystallised as in previous experiment C.   m.p. 81 - 90°C

2.   Attempt to prepare 98°C melting material by exact repetition of previous recrystallisations at Birmingham University and Cranfield.   The neutral products of a Grignard preparation (16-19g) were divided into two parts.

At Cranfield, one part of this solution was evaporated in a Petri dish. Yield 7.4g.   4g of this material were dissolved in 100 mls of benzene, 20 mls removed by distillation and the remaining liquid cooled at - 12°C overnight. After melting the benzene the material was filtered off and dried in the usual manner.   m.p. 96 - 98°C   yield 1.06g.

The remaining liquid was allowed to evaporate slowly over several days

and large discreet crystals were grown. One of these, after conventional drying in vacuo, was ground up and m.p. was 72-80°C. The crystals, which were needle-shaped, were shown to be birefringent.

One half of the solution of the neutral materials was taken to Birmingham and treated precisely in the same way as at Cranfield, in exact detail, using glass-ware taken from Cranfield.

Yield of crude materials 8.34g. 4g recrystallised as in the above experiment. yield 1.1g. m.p. 60-71°C.

Attempted recrystallisations from other solvents

1) It was found impossible to recrystallise the material DDHP from water, it was found to throw out as an oil.

2) Attempts to recrystallise the material from ethanol likewise gave an oil, it was also found that a 50% mixture of benzene and ethanol yielded an oil on attempting the usual recrystallisation procedures.

3) 0.5g of DDHP were dissolved in approx. 10 mls of 1 dichlero 1, monofluoro, 2 monochloro 2, difluoro ethane and the precipitate treated and dried in the usual manner. The yield was 0.27g. m.p. 95 - 96.5°C. Analysis requires for 2,6 dimethyl 2,6 diol tetra-fluoropyran C33.1% H 3.2% Found C33.0% H 2.9%

4) The material was found to be very sparingly soluble in trifluoromethyl benzene, though a very small quantity of material melting at 79-86°C was obtained.

Systematic ageing experiments on the form of DDHP melting at 96-98°C

1) Three samples of material of melting-point 96-98°C, obtained by re-crystallisation from chloroform were aged for 48 hours at 45°C.

m.p. Sample 1		73-95°C
m.p. Sample 2		75-97°C
m.p. Sample 3		68-83°C

0.37g of material of m.p. 68-83°C (previously of m.p. 98°C before thermal ageing were dissolved in 10 mls of chloroform and refluxed, 5 mls were removed by distillation and the precipitate obtained in the usual way. m.p. 89-91°C.

This material was redissolved in 10 mls of chloroform and 6 mls were taken off and the residue cooled overnight at - 12°C ~ the ppt processed in the usual way. m.p. 87-92°C.

A second sample of thermally aged material was treated in an identical manner to the above.

1st recrystallisation m.p. 64-72°C
2nd recrystallisation m.p. 66-75°C

It was not found possible to regenerate 98°C m.p. DDHP in this experiment.

2) Thermal ageing of material of m.p. 84-87°C

Material melting at 84-87°C was aged for 5 days at 50°C with the following results:

after 1 day   melting point was 79-87°C
after 2 days melting point was 79-87°C
after 3 days melting point was 74-87°C
after 4 days melting point was   -
after 5 days melting point was 55-81°C.

Analysis after ageing.   Requires for 2,6 dimethyl 2,6 diol hexafluoro-pyran
C 33.1% H 3.2% Found C 32.7% H 3.2%.

3) It had been observed that material of m.p. 96-98°C when sent to Birmingham University acquired the melting range 64-80°C overnight, i.e. in the post.   It was suspected that the material could be affected by mechanical shaking.

Material of m.p. 90-95°C was subjected to the following test.   It was divided into two parts, one part as a control, the other being kept in a car, and then shaken in a shaker.

M.p. standing at R.T.	M.p. car rides (25 miles daily)	M.p. in Refrigerator - 12°C
after 3 days 83-87°C	after 3 days 79-85°C	1 day 83-86°C
after 4 days 84-88°C	after 4 days 80-86°C	-
after 6 days 85-88°C	after 6 days 82-86°C	-
+ 24 hrs 85-88°C	+ 24 hrs 77-80°C in shaker	-

It appeared that the material was affected by mechanical vibration.

Dr. J. Burdon attempted to place material m.p. 95-98°C in small bottles, weighed down under the surface of liquid nitrogen in Dewar flasks, the material on arrival at Birmingham had m.p. 64-80°C.

4) Attempts to regenerate material of m.p. 98°C from thermally aged material

Two samples of material DDHP, original m.p. 95-96°C were continuously aged at 45°C as reported below:-

1st Sample		2nd Sample	
1 day	m.p. 87-95°C	4 days	78-85°C
5 days	m.p. 78-92°C	6 days	64-85°C
6 days	m.p. 64-78°C	7 days	65-85°C
7 days	m.p. 65-73°C	8 days	58-71°C

The combined weight of the two samples was 0.88g. This material was dissolved in 20 mls of benzene, 5 mls were removed by distillation, the liquid was then cooled at - 12°C overnight. The precipitate was taken and treated in the usual way. Yield 0.41g. m.p. 78-81°C.

The material was similarly recrystallised from 10 mls of benzene, 5 mls being removed by distillation. M.p. 78-81°C. A repetition of this process gave a material of m.p. 78-80°C. It was not possible in this experiment to regenerate material of m.p. 98°C once it had been thermally aged.

5. Ageing of material at 70°C

1g of material m.p. 64-79°C was aged for 7 hours at 70°C. The material became liquid and was cooled overnight at - 12°C to solidify. m.p. 58-80°C. The lower end of the melting range was lowered by this process.

6) Repitition of ageing of material at 45°C

Material DDHP of melting point 94-96°C was aged for 3 days at 45°C. Resultant m.p. 58-75°C. Attempts to regenerate material of m.p. 95-98°C did not succeed.

Experiments designed to investigate possible reactions of crude DDPH with water

1) 4g of crude (m.p. 64-79°C) DDHP were placed in 50 mls distilled water and shaken for 4 hours. The aqueous part was decanted off, remaining solid matter and then continuously extracted with ether for 24 hours. Ether was evaporated off by distillation and the crude remaining material was re-crystallised in the usual manner from 80-100 petroleum m.p. 94°C. This was recrystallised a second time and gave a material of m.p. 96-98°C.

2) 3g of material were dissolved in 100 mls of wet ether (previously made by shaking ether and water together for several hours) and stood for 64 hours to gain conversion. Anhydrous sodium sulphate was then added to the solution and the material stood for a further 24 hours. The sodium sulphate was filtered off and ether then removed by evaporation under reduced pressure.

Material was recrystallised, using the usual procedures, from 80-100 petroleum.   yield 1.88g m.p. 96-99°C.

A similar second recrystallisation from 80-100 petroleum gave material m.p. 99-100°C.   yield 1.32g.

3)   4g of crude DDHP were dissolved in 100 mls of distilled water and shaken at room temperature for 6 hours.

The undissolved residue (which was slight) was removed by filtration and the liquid continuously extracted with ether for 24 hours.   No effort was made to dry the ether.

25 mls of the above solution was exposed in a Petri dish overnight to evaporate off the ether and the resultant material recrystallised in the standard manner from approx. 8 mls of 80-100 petroleum.   m.p. 81-85°C. A second similar recrystallisation from 80-100 petroleum gave a material of m.p. 88-90°C.   yield 0.31g.

A second portion (25 mls) of the ether solution was evaporated down in a Petri dish, as in the previous experiment, and then recrystallised from benzene in the usual manner.   Melting range 88-90°C.   yield 0.25g.

A further portion (25 mls) was transferred to Birmingham University where the identical evaporation process was performed and the resultant material was recrystallised from benzene.   m. range 70-75°C.

3g of crude DDHP were dissolved in 100 mls of wet ether and left for 3 days.   Anhydrous sodium sulphate was then added and the material left overnight.   The solution was transferred to Birmingham, sodium sulphate removed by filtration and ether stripped off under reduced pressure. The material so obtained was recrystallised from 80-100 petroleum after 3 hours cooling and normal overnight drying.   m.p. 76-80°C.

Remaining material was cooled overnight in the deep freeze, filtered, and placed in a vac. desiccator for 4 hours.   m.p. 82-86°C.

Infra-red sprectra of the above materials were identical to each other and also identical with the spectrum of standard material of m.p. 64-79°C.

Experiments on distillation of crude DDPH

1)   3g of crude DDHP were distilled under atmospheric pressure and the material collected in two cuts.

> Cut 1   distillation range 95-120°C
> Cut 2   distillation range 120-170°C.

Some liquid from Cut 1 was left in the collecting flask, some was placed in

the open air in a watch glass, the same was done for Cut 2 and the materials were then left overnight.

m.p.'s   Cut 1 Flask   mushy liquid
          Cut 1 Watch glass   63-67°C
          Cut 2 Flask   87-90°C
          Cut 2 Watch glass   70-77°C.

The solid materials were then dried overnight, in vacuo, over phosphorous pentoxide and the melting points retaken:

Cut 1 Flask   78-89°C
Cut 1 Watch glass   92-93°C
Cut 2 Flask   93-95°C
Cut 2 Watch glass   87-90°C.

A sample of material of m.p. 93-95°C was aged for 48 hours at 45°C.

m.p. 69-75°C.

2)   Distillation of a sample of DDHP of melting point 90-93°C

1g of the above material was distilled under atmospheric pressure. Most of the material boiled between 140-160°C and the only cut examined was in this range.

Some liquid was left in the flask overnight and some material was exposed on a watch glass overnight.

Material was dried according to the usual procedure and melting points were taken:

m.p. material in flask   92-94°C
m.p. material on watch glass   92-94°C.

X-ray crystallography studies on material of m.p. 98°C, comparisons with material of melting range 64-79°C.

4g of crude DDHP were dissolved in 100 ml of benzene, 20 mls were removed by distillation, the liquid cooled at -12°C overnight and the solid material obtained according to normal filtering and drying procedures.

m.p. 96-98°C.

A sample of material of melting range 64-79°C was also examined. The method was the rotating crystal method using CuKα radiation. Two photographs of the material of melting range 64-79°C were taken. (Photographs I and II).

Figure 2.   The first photograph shows the material in a more finely divided state, than in the second photograph.   Both show a reasonable, crystalline pattern.

Figure 2.   Photograph III shows material of m.p. 96-98°C after sieving and placing inside the small glass tube of the X-ray instrument.

Figure 2.   Photograph IV shows material of m.p. 96-98°C which was not sieved, the particles of which were stuck on the outside of the instruments tube.

Figure 2.   Photograph V shows material of m.p. 96-98°C, which was not sieved, but which was forced inside the tube of the instrument.

Several of the photographs showed marked asterism, and it was shown using nickle powder that this was not due to an instrumental effect, and may therefore be due to some form of distorted or strained crystalline lattice.

Material of m.p. 96-98°C was found to have a m.p. of 91-96°C after 24 hours at room temperature.

Material of m.p. 91-96°C was forced through the sieve used for X-ray powders, m.p. immediately after sieving 69-74°C.

A m.p. was done on the non-sieved material stuck on the outside of the tube, after the X-ray photograph, m.p. 78-82°C.

A m.p. was done on the non-sieved material placed inside the glass tube of the X°ray equipment.   m.p. 78-87°C.   It may be doubtful if the material had a m.p. of 96-98°C whilst the photographs were being taken.

The photographs are shown on Plate 1 at the end of the Note. Measurements on ring diameters as far as could be done, showed no difference between the photographs.   The lattice is not one of the simple cubic systems.

Analysis on LDPH recrystallised from solvents

Crude DDHP was recrystallised from 80-100 petroleum and had initially the m range 96-98°C, which subsequently fell to 64-79°C.

Analysis   Found C 32.7%   H 3.1%
          Requires C 33.1%   H 3.2%

Crude DDHP (p.   ) was recrystallised from 1 dichloro 1, monofluoro, 2 monochlero 2, difluoroethane and had a m.p. 95-96.5°C.   This subsequently changed to 64-80°C and analysis taken

Found C 33.0%   H 2.9%
Requires C 33.1%   H 3.2%

Gas chromatography studies on the ethereal solution of neutral materials

Using a Perkin-Elmer model 452 gas chromatograph the ethereal solution of neutral materials was examined.

a) Using the polyethylene glycol column at a temperature of 150°C (See chart I). It will be noted that there is one peak, other than the ether peak. The initial negative peak is due to air.

b) Using a silicone based column at a temperature of 150°C (see Chart II). Apart from the ether peak it will be noted that the second peak, due to the dissolved substance, is divided, possibly suggesting the resolution of two very similar materials.

Derivatives of the neutral material 2,6 diol, 2,6 dimethyl 3,4,5 hexafluoro-pyran (DDHP)

1) Using a methanolic medium two 2:4 dinitro phenyl hydrazones were prepared from the solid material DDHP of melting range 64-79°C. Using a methanolic acidic medium and an excess of 2:4 dinitro phenyl hydrazine reagent a bright yellow material was obtained, filtered and dried in the usual way. Various recrystallisation procedures proved unsuccessful. m.p. 203-4°C.

<blockquote>
Found for   di 2:4 dinitro phenyl hydrazone
             C 38.12%   H 2.58%
Required   C 38.25%   H 2.37%
</blockquote>

It has also been found possible to prepare this material in an aqueous medium.

2) Using a methanolic medium and an approximate 1:1 molar ratio of 2:4 dinitro phenyl hydrazone to DDHP an orange material was obtained, filtered and dried in the usual way. Again various recrystallisation procedures proved unsuccessful. m.p. 140-1°C.

Found for the mono 2:4 dinitro phenyl hydrazone   C 37.70%   H 2.36%. Required C 37.50%   H 2.42%. The di (2:4 DNPH) showed the C = N stretching frequency at 1630 cms^{-1}.

The mono (2:4 DNPH shewed the C = N stretching frequency at 1630 cms^{-1}, but no carbonyl frequency in the 1700-1750 cms^{-1} range. This suggests a cyclic structure.

3) Attempts to prepare tosyl derivatives were unsuccessful.

4) 3:5 dinitro benzoates were only obtained in very low yield and were not analysed. The system of preparation in pyridine was used.

5)   A semi-carbazone was successfully prepared as follows:-

0.2g of semi-carbazide hydrochloride was dissolved in approx. 10 mls of a saturated solution of sodium acetate.   To this 0.1g of crude DDHP (m range 64-79°C) was added.   The material was heated using a water bath for $\frac{1}{2}$ hour, and then cooled for several days at - 12°C.   White crystals appeared, washed with water, filtered, dried 16 hours over phosphorus pentoxide in vacuo.   m.p. 201-2°C.

Required for

$$CH_3.C.CF_2-CF_2-CF_2-C-CH_3$$

with HO and OH above, and N.NH.CO.NH$_2$ below

Required for   C 30.91%   H 3.56%
Found   C 31.31%   H 3.50%

An infra-red analysis of the material was found to have a broad C = N absorption at 1700 cms^{-1} similar to that of 1,1,1 trifluoroacetone semi-carbazone.   There was no carbonyl frequency.

Derivatives of acid product of the reaction.   1,2,3 hexafluoro 4-one caproic acid (or a cyclic form).

1)   Using an aqueous medium, and an excess of an aqueous acidic solution of 2:4 dinitro phenyl hydrazone, a yellow material, long needle-like crystals, was obtained, filtered and dried in the usual manner.   It was found impossible to recrystallise the material.   m.p. 124°C.

Required for 4 one 1,2,3 hexafluorocoproic acid 2:4 dinitro
phenyl hydrazone   C 34.45%   H 1.93%
Found   C 34.17%   H 2.25%.

The Lassaigne test was positive for fluorine and nitrogen.

2)   An attempt to prepare a tosyl derivative was unsuccessful.

3)   0.5g of the material was dissolved in 4 mls of water and titrated to an orange colour using 10% caustic soda solution.   One drop of dilute sulphuric acid was then added, followed by 5-6 mls of a saturated solution of S benzyl thio-uronium chloride.   The material obtained was filtered off, and recrystallised from 80% aqueous ethanol, dried in the usual manner. m.p. 144-145°C.

Required for 4-one, 1,2,3, hexafluoro-caproic acid
S benzyl thio-uronium salt.   C 30.91%   H 3.56%.
                    Found   C 31.31%   H 3.50%.

Infra-red analysis showed a carbonyl frequency at 1760 cm^{-1} and showed a marked similarity to the S benzyl thio-uronium salt of pentafluoropropionic acid.

Reactions of 2,6 diol 2,6 dimethyl hexafluoropyran

1) Reductions with Lithium Aluminium hydride.

Attempts at reduction under mild conditions, using a reaction time
of 15 minutes at room temperature were not successful.

1.5g of lithium aluminium hydride was placed in a 3 necked flask fitted
for reflux, and with a stirrer and made into a slurry using sodium dried
ether.   3g of DDHP (m.p. 64-78°C) were dissolved in 30 mls of sodium dried
ether, the solution was then run into the slurry of lithium aluminium hydride
in the cold, exercising some caution.   The reactants were stirred cold for
2½ hours and then refluxed without stirring for 24 hours.

12 mls of water (distilled) were added to the ether layer, followed by
50 mls of 20% sulphuric acid to remove all solid matter.   The ether layer
was separated, and then washed with 20 mls of 20% sulphuric acid followed
by 20 mls of water.   The ether layer was dried overnight over anhydrous
sodium sulphate.   Ether was removed by distillation leaving a brown liquid
which crystallised over a period of 10 days.   Attempts to recrystallise this
material from 80-100 petroleum gave a brown liquid layer.   Ether was added
and the solution decolourised with charcoal.   On removing the ether under
reduced pressure an oil appeared which crystallised at - 12°C overnight.
Yield 1.35g.   m.p. 56-65°C.

Recrystallisation was repeated according to the above procedure.
Yield 0.30g.   m.p. 56-61°C.
Required for 2,6 diol 3,4,5 hexafluoro n-heptane   C 35.0%   H 4.2%
Found   C 35.0%   H 4.1%.

The infra-red spectrum was consistent with the proposed structure.

2) Reduction using sodium borohydride.

3g of DDHP of m.p. 65-79°C were dissolved in 90g of water, with warming
and shaking.   The small amount of material which did not dissolve was
separated out with a separating funnel.

1.5g of sodium borohydride was dissolved in the above solution and shaken.
There was some initial effervescence and the material was left at room
temperature for 5 days.

Using diluted sulphuric acid the liquid was turned acid (to litmus)
and continuously extracted with ether for 24 hours.   The ether extract was
dried overnight over anhydrous sodium sulphate, ether was removed by dis-
tillation and the solid remaining was dissolved in 80-100 petroleum, and
after decolourisation with charcoal was recrystallised from the petroleum.
Yield 0.7g   m.p. 52-64°C.

The material was again recrystallised from 80-100 petroleum.

<u>Yield 0.3g. m.p. 54-68°C.</u> Mixed m.p. with material from lithium
aluminium hydride 55-66°C. Required for 2,6 diol 3,4,5 hexafluoro
n- heptane.

        C 35.0% H 4.2%
Found   C 35.0% H 4.3%

The infra-red spectrum was identical with that of reduction product from
lithium aluminium hydride.

3) <u>Reaction of DDHP (m.p. 64-79°C) with benzoyl chloride</u>
    (ratio of 1 mole of DDHP to 2 moles of benzoyl chloride).

    Pyridine was dried by distillation off phosphorus pentoxide.

    2g of DDHP were dissolved in dry pyridine (20 mls) and 2.22g of
benzoyl chloride were dissolved in 20 mls of dry pyridine.

    The two solutions were mixed and in 10 minutes crystals appeared.
The solution was left overnight and the crystals filtered off. An attempt
to recrystallise them from pyridine was unsuccessful.

    Several drops of water were added to the filtrate which was left for
3 hours. 100 mls of saturated aqueous sodium bicarbonate solution were
now added and stirred in. Insoluble sodium bicarbonate was filtered off.

    The pyridine/aqueous layer was hand extracted with ether (3 x 100 mls),
the combined ethereal extracts were washed with 15% dilute sulphuric acid,
a strong exothern was noted, which causes considerable, dangerous volatal-
isation of the ether. This process was continued until the washings were
acid to litmus. The ethereal layer was then extracted with aqueous sodium
bicarbonate solution.

    The remaining ethereal layer was decolourised using charcoal and
dehydrated with anhydrous sodium sulphate. After removal of ether by
distillation over a steam-bath a viscous liquid remained behind. This
formed a waxy solid overnight.
            Yield of crude material 1.7g
                    m range 37-44°C.

1g of the above material was recrystallised from 80-100 petroleum using
normal procedures.
            Yield 0.5g   m.p. 46-49°C.

Analysis requires for the dibenzoate C 53.55% H 3.6%
                            Found C 49.3% H 2.75%

Repurification of the material was attempted by further recrystallisation

in the usual way from 80-100 petroleum.   Solvent was removed by distillation under reduced pressure.   Material was dried in vacuo over phosphorus pentoxide.   m.p. 48-50°C.

As the analysis was not correct, fresh crude benzoate was taken and twice recrystallised from 80-100 petroleum.   m.p. 48-50°C.

Once again the analysis was not correct, this was presumed to be due to the fact that it is extremely difficult to crystallise this material. It normally comes down as an oil,   It was found impossible to recrystallise the above material from benzene, owing to extreme solubility in that solvent.

Preparation of a phenyl urethane

4)   Attempts to prepare a urethane, using phenyl isocyanate proved unsuccessful.

5)   Dehydration reactions.   Preliminary experiments.

Attempts were made to dehydrate DDHP (m range 64-79°C) by distillation of the material from several dehydrating agents at atmospheric pressure.

a)   from anhydrous calcium sulphate.   A liquid distilling at 98°C was observed, this formed two layers in the receiving vessel.   There was no sign of decomposition in the distillation flask.

b)   from magnesium perchlorate.   A violent reaction took place suddenly at an oil bath temperature of 160°C producing much charring in the flask. A small quantity of brown oil distilled over at 150°C.

c)   using phosphorus pentoxide.   A small quantity of liquid distilled over covering a distillation range from 80-150°C.   The liquids were pink, but were decolourised by standing for several days over precipitated silver. Most of the material did not distil and the contents of the flask were violently charred.

d)   using calcium hydride.   Material in very small yield distilled over continuously between 60°C and 150°C.   Very considerable charring in the distillation vessel was observed.

e)   using boric anhydride.   This material was previously dried before use for 1 hour at 100°C.   On attempted distillation it was found that nothing could be distilled off at all, and that a glassy material was formed in the distillation vessel which made distillation very difficult.

f)   using dried silica gel.   The silica gel was dried prior to use for $1\frac{1}{2}$ hours at 170°C and ground to a fine powder.

On distillation it was found that hardly any material could be distilled over at all.

Detailed examination of distillation using calcium sulphate

Several experiments showed that in order to get better results it was necessary to roast the calcium sulphate overnight at 650°C. Distillation was done by intimately mixing the calcium sulphate and crude DDHP, using previously dried apparatus; the method of heating the flask was by means of an oil-bath. 3g of DDHP were reacted with 30g of calcium sulphate. Initially, by tilting the apparatus backwards the material was allowed to reflux before distillation commenced. Material distilled off at 94-96°C and the liquid collected in the receiving vessel was seen to be in two layers. Even on several days standing these liquids did not mix or crystallise out. Using a semi-micro separating funnel the two liquids were separated.

Upper layer	n_D^{21}	1.3751
Lower layer	n_D^{21}	1.3343
Distilled water	n_D^{21}	1.3327

Quoted n_D^{20} distilled water 1.3333. An infra-red spectrum of the lower layer was that of water, thus the lower layer was water. A repitition of the above experiment gave similar results, upper layer n_D^{18} 1.3754.

As a control experiment crude DDHP m.p. 65-81°C was distilled without calcium sulphate being present, distillation occurring over a range 80-160°C.

Distillate having a refractive index of n_D^{18} 1.3523.

A third repitition of the dehydration experiment described above gave upper layer b.p. 96°C at atmospheric pressure n_D^{18} 1.3756.

An attempt to prepare a 2:4 dinitro phenyl hydrazone using the methanolic medium gave a viscous reddish oil, which did not form crystals, but separated out in droplets.

Analysis for 1:2 ene 2, methyl 6 one 3,4,5 hexafluoro cyclohexane.

Found   C 40.13%   H 1.87%
Requires   C 38.55%   H 1.85%.

Spectroscopic data

The infra-red shows the carbonyl frequency at 1700 cm^{-1} and a double bond frequency at 1600 cm^{-1}.

There are two peaks in the N.M.R. spectrum, one at 2.2 p.p.m. (CH$_3$) and the other at 6.4 p.p.m. (H adjacent to double band) in approximate ratio 3:1. This is consistent with the proposed structure.

More detailed examination of dehydration using phosphorus pentoxide.

3g of the above material were placed in a dried round bottomed flask with 30g of phosphorus pentoxide and distilled, giving 15 minutes reflux, by tilting the apparatus back before distillation. Temperature of reflux was 150-160°C.

Two cuts were taken for distillation

1st Cut   distilled 140-150°C n_D^{20} 1.36350

2nd Cut   distilled 140-150°C n_D^{20} 1.36465

The combined yield was 0.25g, there was very great charring and decomposition in the reaction vessel.

Haloform reaction with DDHP, m range 64-79°C

Varying quantities of crude DDHP and aqueous caustic soda were refluxed together. Attempts were made to prepare S benzyl thio-uronium derivatives of any organic acids formed and also, using cerous nitrate attempts were made to test for fluoride ion, in certain cases. The results of these experiments are summarised in the tables below:-

Quantity of crude DDHP	Quantity of Caustic Soda	Normality of Caustic Soda	Reflux Time	Fluoride Ion	S benzyl thio uronium salt
0.3g.	5 mls.	2N	70°C for 1hr.	–	v. small yield
0.2g.	3 mls.	2N	$\frac{1}{2}$ hr. reflux	–	yield .01g m.p.187°C
0.13g.	3 mls.	2N	$\frac{1}{2}$ hr. reflux	–	no material
0.49g.	8 mls.	4N	3 hrs reflux	–	8 mg. m.p. 152°C
4g.	64 mls.	4N	3 hrs reflux	–	0.145g. m.p.162-4°C
2g.	32 mls.	4N	6 hrs. shaken at r. temp. 12 hrs. standing	–	m.p. 172-4°C
4g.	64 mls.	4N	3 hrs. reflux	–	m.p. 166-7°C
2g.	32 mls.	4N	3 hrs. reflux	positive	m.p. 190°C
2g.	32 mls.	2N	3 hrs. reflux	positive	m.p. 181°C
2g.	32 mls.	N	3 hrs. reflux	dubious	m.p. 186-7°C
1g.	16 mls.	N	2 hrs. reflux	positive	no derivative

S benzyl thio-uronium salts appeared in low yields and with
extremely erratic melting points.   The S benzyl salts of formic acid
(m.p. 151°-2°) and acetic acid (132-4°C) were prepared in the usual way,
but material of m.p. 152°C gave a depression of 6°C when a mixed m.p.
with S benzyl thio uronium formate was done.   There was no evidence at
any stage for the presence of S benzyl thio-uronium acetate.

Fluoride ion was tested by reaction with a solution of cerous nitrate
in acetic acid, the precipitate being tested with dilute nitric acid, when
it should remain insoluble if fluoride ion is present.   It may be noted
that fluoride is present, even after reaction with N caustic soda.

Reaction of DDHP with Phosgene, attempted carbonate formation

Attempts were made to react crude DDHP (m.p. 64-79°C) with phosgene,
by dissolving the material in toluene and mixing this solution with a 12%
solution of phosgene in toluene.   The product of this reaction, after
working up, was a brown liquid which decomposed on attempted vacuum
distillation at 15 mm pressure.

Reaction of crude DDHP with malanoyl chloride

An attempt was made to react the above material with malanoyl chloride
formed by the reaction of malonic acid and phosphorus pentachloride.   The
end product of this reaction was a tarry material, which was not worked up.

Condensation of crude DDHP with acetone to form a ketone acetal

An attempt was made to react the crude DDHP (m range 64-79°C) with acetone,
in an ethereal medium, using p-toluene sulphuric acid as a catalyst.
This reaction was not successful.

Attempted preparation using crude DDHP, of a copper chelate, according to the method of Calrin and Reid (JACS 72, p. 2948)

Attempts were made, using the method of the above authors, to react
crude DDHP with copper acetate in a water/ethanol medium.   This reaction
yielded no definite compound, but a brown material, insoluble in ethanol
and xylene, was obtained melting between 300 - 340°C.   The flame test
suggested this material was a copper compound but it did not appear to be
one of the copper oxides.   The material may be of a polymeric nature.

Acknowledgments

References
----

1. Henne and Zimmerschied, J. Amer. Chem. Soc. 67, p. 1235 (1945).

2. McBee, Wiseman and Bachman. Ind. Eng. Chem. 39, p. 415-7 (1947).

3. Evans and Tatlow. J. Chem. Soc. 178, (1955) p. 1184.

4. Murray, Hauptschein and Groth. J. Amer. Chem. Soc. 73, p. 2461-3 (1951).

5. Huston and Bailey. J. Amer. Chem. Soc. 68, p. 1382 et seq. (1946).

6. German Patent 166, 698-9 (1906).

7. Grignard. Compt. rend. Acad. Sc., Paris, 138, p. 152 (1904).

8. Salkind and Beburischwili. Ber. dtsch. chem. Ges. 42, p. 4500 (1909).

9. Sykes, Tatlow and Thomas. J. Chem. Soc. 179, (1956) p. 835.

10. Dishart and Levine. J. Amer. Chem. Soc. 78, p. 2269 (1956).

11. Groth. J. Org. Chem. 24, p. 1709 (1959).

12. Rigby. J. Chem. Soc. 172, p. 1586, p. 1588 (1949).

13. Sebatier and Mailke. Compt. rend. Acad. Sc., Paris 146, p. 1193 (1908).

14. Lindemann and Baumann. Ann. Chem. 477, p. 78 (1929).

15. Rothstein. Ann. Chem. 14, p. 461 (1930).

16. Coops, Dienske and Aten. Rec. Trav. chim. 57, p. 303 (1938).

17. Dimroth and Resin. Ber. dtsch. Chem. Ges. 75 (1942)B, p. 322.

18. Cope and Fourier. J. Amer. Chem. Soc. 79 (1957) p. 3896.

19. Czorndola. Roczniki Chem. 16 (1936) p. 459. C.A. 31, 1807 (1937)

20. Henne, Shepherd and Young. J. Amer. Chem. Soc. 72, (1950) p. 3577.

21. Hauptschein and Braun. J. Amer. Chem. Soc. 77, (1955) p. 4930.

22. Reid and Calvin. J. Amer. Chem. Soc. 72, (1950) p. 2948.

23. Hauptschein, Stokes and Grosse. J. Amer. Chem. Soc. 74, (1952), p. 1974.

24. 'Organic Chemistry'. Julius Schmidt, p. 318.

25. Sayers, Stephens and Tatlow. J. Chem. Soc. (1964) 187, p. 3035.

FIG. I   SOME REACTIONS OF PERFLUORO-GLUTARIC ACID.

Key to X-ray photographs 2,6 diol 2,6 dimethyl hexafluoropyran

All photographs were taken using CuKα radiation.

I   Range-melting material, sieved.

II   Range-melting material, sieved.

III   Material m.p. 98°C after sieving and placed in the tube of the instrument.

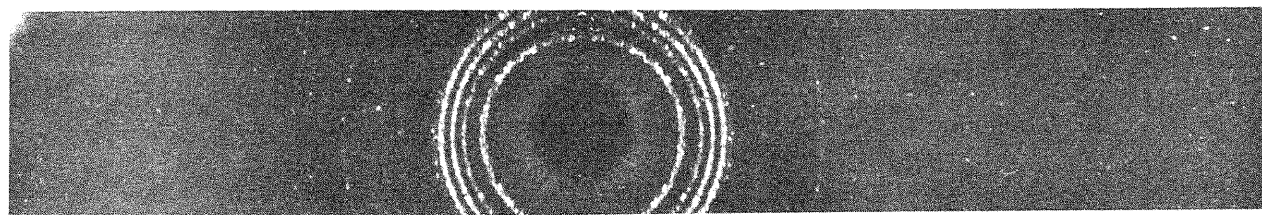IV   Material m.p. 98°C, not sieved, particles stuck to the outside of the instrument tube.

V   Material m.p. 98°C, not sieved, forced inside the tube.

FIG.2

I
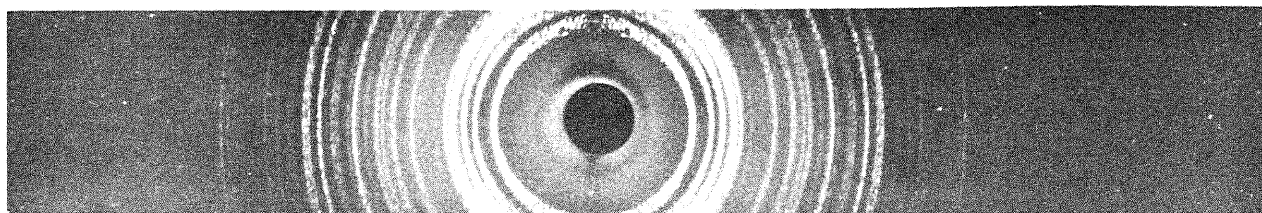
II

III

IV

V

WAVELENGTH (MICRONS)

(1) 2,6, diol 2,6 dimethyl hexafluoropyran melting range
64 - 79°C

TRANSMITTANCE (%)

CM-1

WAVELENGTH (MICRONS)

(2) 2,6 diol 2,6 dimethyl hexafluoropyran original m.p.
99°C

TRANSMITTANCE (%)

INFRACORD ™ PE

WAVELENGTH (MICRONS)

(3) 2,6 diol 2,6 dimethyl hexafluoropyran treated with
water

TRANSMITTANCE (%)

INFRACORD ™ PE

CM-1

WAVELENGTH (MICRONS)

(4) 1,2,3 hexafluoro 4-one caproic acid

INFRACORD ™ PE

WAVELENGTH (MICRONS)

(5) 2,6 diol 2,6 dimethyl hexafluoropyran mono
(2:4 dinitro phenyl hydrazone)

INFRACORD ™ PE

WAVELENGTH (MICRONS)

(6) 2,6 diol 2,6 dimethyl hexafluoropyran di
(2:4 dinitro phenyl hydrazone)

INFRACORD ™ PE

CM-1

WAVELENGTH (MICRONS)

(7) trifluoromethyl ethyl ketone 2:4 dinitro phenyl
hydrazone

WAVELENGTH (MICRONS)

(8)   2,6 diol 2,6 dimethyl hexafluoropyran mono semi
carbazone

WAVELENGTH (MICRONS)

(9)   2,6 diol 3,4,5 hexafluoro n-heptane prepared using
sodium borohydride

CM-1

WAVELENGTH (MICRONS)

(10) 2,6 diol 3,4,5 hexafluoro n-heptane prepared using lithium aluminium hydride

WAVELENGTH (MICRONS)

(11) 1, 2-ene, 2 methyl, 3, 4, 5 hexafluoro 6-one cyclo-hexane

WAVELENGTH (MICRONS)

(12) S benzyl thio-uranium 1, 2, 3, hexafluoro 4-one caproate

CM-1

WAVELENGTH (MICRONS)

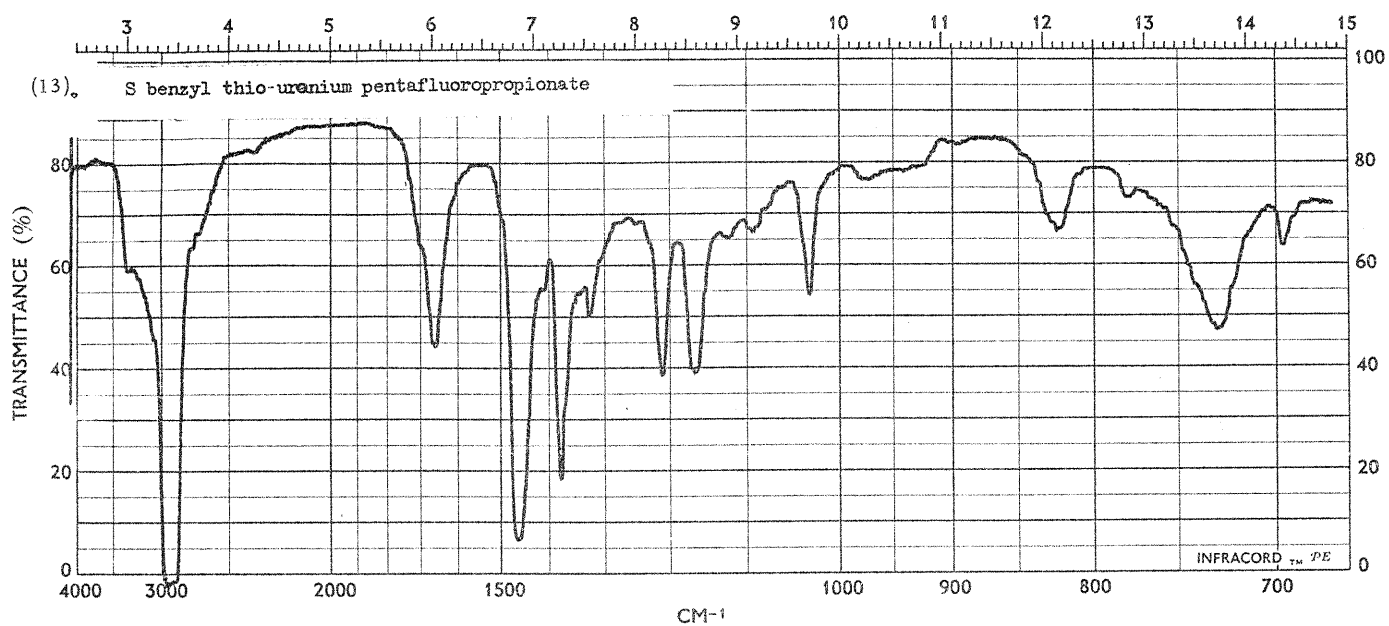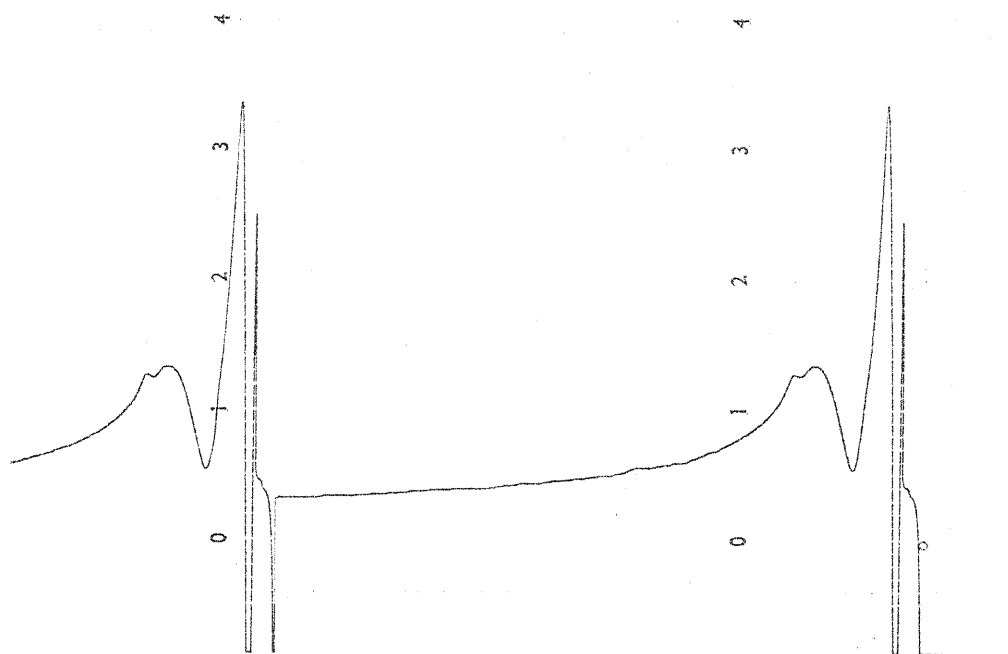(13). S benzyl thio-uranium pentafluoropropionate

INFRACORD ™ PE

TRANSMITTANCE (%)

CM-1

GAS CHROMATOGRAPHY TRACE

(14)

(2) 2,6 diol 2,6 dimethyl hexafluoropyran in ether,
passed through a silicone grease column at 150°C