

combustion data, which may be in error by as much as 5 kcal. per mole.

Table I presents the measured values of the specific heat of the compound expressed in calories per mole with the corresponding temperatures. The factor used for converting electrical energy to calories was 0.23895.

Summary

1. The heat capacity of beta-lactose was

measured over the temperature range from 83 to 298°K.

2. The value of the entropy of the compound has been estimated from these measurements and certain other data.

3. The free energy of formation of the compound has also been calculated by the use of the entropy and the combustion data which appeared to be the most reliable.

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Reactivity and Influence of Fluorine in Aliphatic Compounds

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Organic compounds containing fluorine, quite often fail to follow empirical generalizations derived from the behavior of similar organic combinations containing some other halogen in place of fluorine. Many such contradictions are particularly emphasized by a study of the stability and the reactivity of the simple aliphatic fluorides. The preparation and physical properties of all the compounds used as a basis for the present study have been reported by Swarts (see Beilstein) and by workers of this Laboratory.¹ All of Swarts' data used herein have been verified.

The discovery of the inertness of CCl_2F_2 was a distinct surprise to organic chemists. The fluorine in this molecule is not only quite inert but its presence seemingly strengthens the C-Cl bonds so that the chlorine is much less reactive than in any other similar chlorine compound such as CH_2Cl_2 or CBr_2Cl_2 . This, naturally, suggests that the C-F bond is unusually strong; it is therefore again surprising to find that great stability and inertness is not an invariable function of the C-F bond.

The first four members of the normal alkyl monofluoride series are stable and distil without decomposition. Members of the series higher than amyl fluoride show a tendency to decompose spontaneously to hydrogen fluoride and ethylenic hydrocarbons. This tendency increases with the structural complexity and becomes so marked in secondary and tertiary fluorides that it is impossible to prepare them free from olefins. Similarly

cyclohexyl fluoride² decomposes spontaneously to cyclohexylene.

Monofluorides of saturated hydrocarbons hydrolyze quite easily. It is to be noted that they are more sensitive to hydrolysis by concentrated acids than by concentrated bases. Acids act simultaneously in two ways, both saponifying and removing hydrogen fluoride. The experimental conditions determine which effect predominates.

The physiological effect of the alkyl fluorides is a further demonstration of their tendency to lose hydrogen fluoride. Inhalation of a 30% concentration of ethyl fluoride in air (by volume) is needed to produce anesthesia, and is invariably fatal; death is caused by a severe oedema of the lungs and upper respiratory tract; this oedema is characteristic of hydrogen fluoride burns.

The recurrence of a monofluoride group increases the instability of the molecule very markedly: ethylene fluoride decomposes spontaneously to hydrogen fluoride and butadiene at 0°, and merely passing it through water gives ethylene glycol. Similarly 1,2-difluorocyclohexane yields cyclohexadiene at room temperature, and its reaction with water yields 1,2-dihydroxycyclohexane; 1,2-difluorodioxane is likewise unstable.

The stability of a CH_2F group may be affected by the presence of another group in the molecule: for instance, monofluoroethanol and monofluoroacetic acid are quite stable.

A striking improvement in the stability of a molecule containing fluorine and decrease in the reactivity of the halogens is observed when the

(1) *THIS JOURNAL*, **56**, 1726 (1934); **58**, 402, 404 (1936).

(2) Confirming a verbal communication from Dr. Swarts.

compound contains several halogens linked to the same carbon atom. Methyl fluoride is less stable than methyl chloride, but CH_2ClF is more stable than CH_2Cl_2 while CH_2F_2 is so stable that its fluorine is inert to practically every reagent. The stabilizing effect is most marked when the second halogen is also a fluorine atom. A demonstration of this change is offered by a comparison of ethylene fluoride and its isomer ethylidene fluoride. The former, as before mentioned, hydrolyzes and decomposes with great ease whereas the latter resists hydrolysis and is so stable that it may be administered to animals in 50% concentration without any ill effect.

The stabilizing effect exerted by fluorine in a group carrying a second halogen atom is by no means confined to this group but extends to adjacent groups. For instance, $\text{CH}_2\text{BrCH}_2\text{F}$ is easily hydrolyzed to glycol, but $\text{CH}_2\text{BrCHF}_2$ is rendered so resistant by the CHF_2 group that a long heating with aqueous mercuric hydroxide at 150° is required to hydrolyze the bromine in the adjacent group and thus obtain difluoroethanol, and it is only at about 200° that the fluorine starts to hydrolyze, to yield a small amount of glycolaldehyde. In the case of CH_2FCHF_2 , the fluorine atom in the CH_2F group is by no means as labile as fluorine in methyl or ethyl fluoride, thus illustrating the stabilizing influence of the adjacent CHF_2 group. How far along the chain this influence is exerted cannot at present be definitely stated, but in propane derivatives it has been detected two carbon atoms away.

The stabilizing influence is placed in evidence by the course of the fluorination when chloro derivatives of ethane are treated with antimony fluorides. Hexachloroethane gives successively $\text{CCl}_2\text{FCCl}_3 \rightarrow \text{CCl}_2\text{FCCl}_2\text{F} \rightarrow \text{CClF}_2\text{CCl}_2\text{F} \rightarrow \text{CClF}_2\text{CClF}_2$, where fluorination stops, and at no stage is there any formation of an isomer. In $\text{CCl}_2\text{FCCl}_3$ the chlorine atoms in the CCl_3 group are more reactive than in the CCl_2F group, and if they have been stabilized at all, it is only to an amount insufficient to be detected by fluorination. After the difluoride stage has been reached, there is only one trifluoride that can be formed, and it is formed easily, thus indicating that the single fluorine on each carbon is insufficient to prevent further replacement of the chlorine atoms. But as soon as the trifluoride has been formed, the reaction stops, showing that the presence of

the two fluorine atoms on one of the carbon atoms has immunized the remaining chlorine on that carbon against further fluorination; moreover, this has so strengthened the bonds of the chlorine atoms on the adjacent carbon atom that further fluorination proceeds only when conditions are made severe. To illustrate: the reaction proceeds of its own accord as far as the trifluoride stage by mere mixing of the reactants but it takes temperatures of about 140 to 150° , and the use of SbF_3Cl_2 as a fluorinating agent to cause the formation of the tetrafluoride from the trifluoride; despite the most severe conditions tried, neither the penta- nor the hexafluoride can be obtained by these methods.

A similar treatment of pentachloroethane yields successively $\text{CCl}_2\text{FCHCl}_2 \rightarrow \text{CClF}_2\text{CHCl}_2 \rightarrow \text{CClF}_2\text{CHClF} \rightarrow \text{CClF}_2\text{CHF}_2$. The first two stages are easily obtained, while the latter two require severe fluorinating conditions. As a CHCl_2 group is always more difficult to fluorinate than a CCl_3 group, the mild stabilizing effect exerted by the CCl_2F group is here sufficient to prevent fluorination of the adjacent CHCl_2 group, while in $\text{CCl}_3\text{CCl}_2\text{F}$ it was insufficient to protect the adjacent CCl_3 group; consequently, the next fluorination step transforms the CCl_2F group into a CClF_2 group, and as the stabilizing influence of this group on itself and on its neighbor is quite considerable, fluorination stops.

This explanation agrees well with the fluorination of $\text{CHCl}_2\text{CHCl}_2$ which yields successively CHClFCHCl_2 and $\text{CHF}_2\text{CHCl}_2$, where the reaction stops. Here again the presence of the first fluorine atom stabilizes the chlorine on the adjacent carbon atom, and the presence of the second fluorine strengthens the C-Cl bonds in the adjacent group to such an extent that attempts at further fluorination by means of antimony fluorides fail or bring about an unexpected rearrangement to CH_2ClCF_3 .

In line with the two preceding cases $\text{CH}_2\text{ClCCl}_3$ yields successively $\text{CH}_2\text{ClCCl}_2\text{F}$ and $\text{CH}_2\text{ClCClF}_2$ where the reaction stops. Similarly, $\text{CH}_2\text{ClCHCl}_2$ yields $\text{CH}_2\text{ClCHClF}$ and $\text{CH}_2\text{ClCHF}_2$ where the reaction stops.

As it is impossible to fluorinate a CH_2Cl group by means of antimony fluoride (or for that matter a CH_2Br or CH_2I group) the above reasoning would be incomplete if it could not be shown that reactants capable of transforming a CH_2Cl group into a CH_2F group, fail to perform that transfor-

mation or are at least considerably retarded after the CH_2Cl group has been "stabilized" by the presence of the two fluorine atoms on the adjacent carbon. The use of mercuric³ fluoride supplied the needed demonstration. This salt fluorinates $\text{C}_2\text{H}_5\text{Cl}$ easily but affects $\text{CH}_2\text{ClCHClF}$ very little, and $\text{CH}_2\text{ClCHF}_2$ not at all. Similarly, it reacts quantitatively with $\text{C}_2\text{H}_5\text{Br}$, but not at all with $\text{CH}_2\text{BrCHF}_2$; it reacts violently with $\text{C}_2\text{H}_5\text{I}$ but to affect CH_2ICHF_2 , it must be heated for a long time at 160° , and yields only some 60% of $\text{CH}_2\text{-FCHF}_2$. It cannot be held that mercuric fluoride causes fluorination to proceed along different lines, as it reacts with $\text{CHBr}_2\text{CHBr}_2$ to yield successively $\text{CHBr}_2\text{CHBrF} \rightarrow \text{CHBr}_2\text{CHF}_2$ (where the reaction stops when using SbF_3), then $\text{CHBrFCHF}_2 \rightarrow \text{CHF}_2\text{CHF}_2$, while its reaction with $\text{CH}_2\text{BrCHBr}_2$ yields successively $\text{CH}_2\text{BrCHBrF}$ and $\text{CH}_2\text{BrCHF}_2$, where the reaction stops just as it does with antimony fluoride.

The fluorination of CH_3CCl_3 gives successively $\text{CH}_3\text{CCl}_2\text{F} \rightarrow \text{CH}_3\text{CClF}_2 \rightarrow \text{CH}_3\text{CF}_3$. There is one other example of fluorinating directly to a CF_3 group, and that is $\text{C}_6\text{H}_5\text{CCl}_3 \rightarrow \text{C}_6\text{H}_5\text{-CF}_3$. In both cases, the passage from the CClF_2 stage to the CF_3 stage is rapid, an indication that the last chlorine had not been rendered inert by the two fluorine atoms. It should be noted that in both cases there is no halogen atom on the adjacent carbon.

The "stabilization" hypothesis is in good agreement with experimental evidence derived from the interaction of fluorochlorides and zinc in

(3) See following paper, *THIS JOURNAL*, **58**, 884 (1936).

alcohol. From $\text{CCl}_2\text{FCCl}_3$, $\text{CCl}_2\text{FCCl}_2\text{F}$, $\text{CHCl}_2\text{-CCl}_2\text{F}$, $\text{CH}_2\text{ClCHClF}$, $\text{CHCl}_2\text{CHClF}$ and $\text{CH}_2\text{ClCCl}_2\text{F}$, it is extremely easy quantitatively to obtain $\text{CClF}=\text{CCl}_2$, $\text{CClF}=\text{CClF}$, $\text{CHCl}=\text{CClF}$, $\text{CH}_2=\text{CHF}$, $\text{CHCl}=\text{CHF}$ and $\text{CH}_2=\text{CClF}$, respectively. It is, however, quite difficult to obtain $\text{CClF}=\text{CF}_2$, $\text{CH}_2=\text{CHF}$, $\text{CHCl}=\text{CHF}$ and $\text{CH}_2=\text{CF}_2$, from $\text{CCl}_2\text{FCClF}_2$, $\text{CH}_2\text{ClCHClF}_2$, $\text{CHCl}_2\text{CHF}_2$ and $\text{CH}_2\text{ClCClF}_2$, respectively, and the yields are not good. It is almost impossible to obtain $\text{CF}_2=\text{CF}_2$ from $\text{CF}_2\text{ClCF}_2\text{Cl}$, and even at 1000 pounds pressure, the yield is only 30-35%.

Summing up the above observations the conclusion is reached that the presence of a lone fluorine atom in an aliphatic molecule produces an unstable compound, which shows a great tendency to liberate hydrogen fluoride. In contradistinction, compounds having a halogen atom on the carbon bearing the fluorine are more stable. The presence of two fluorine atoms on the same carbon is attended with (1) a very great increase of the strength of the carbon-fluorine bonds; (2) a strengthening of the linking of any third halogen atom that may be present on this same carbon; and (3) a great increase of the stability of any halogen atoms present on adjacent carbon atoms.

Summary

A general survey is presented of the effects that the presence of fluorine has on the stability and reactivity of aliphatic compounds.

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Mercuric Fluoride, a New Fluorinating Agent

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Antimony, silver and mercurous fluorides have been the most important fluorinating agents used to replace halogens by fluorine in organic halides. Antimony fluoride is preferred for fluorinating compounds rich in halogen atoms, as for instance, carbon tetrachloride, chloroform or acetylene tetrabromide. It is a convenient reagent to obtain groups such as $-\text{CX}_2\text{F}$, $-\text{CXF}_2$, $-\text{CHXF}$ and $-\text{CHF}_2$, and, in rare cases, a $-\text{CF}_3$ group. Silver and mercurous fluorides have been used

with some success on bromides or iodides containing not more than one halogen atom.

It is now found that mercuric fluoride can be substituted for silver or mercurous fluorides in every case where these salts have or could have been used; the yields are considerably increased, most reactions take place swiftly at room temperature, and side reactions are minimized, or absent. Moreover, mercuric fluoride can be used in many cases where antimony fluoride has been