ELIMINATION OF HYDROGEN FLUORIDE FROM FLUOROSUCCINIC ACIDS. KINETICS OF DEHYDROFLUORINATION OF 2,2-DIFLUOROSUCCINIC ACID

M. HUDLICKY and J. A. HALL

Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061 (U.S.A.)
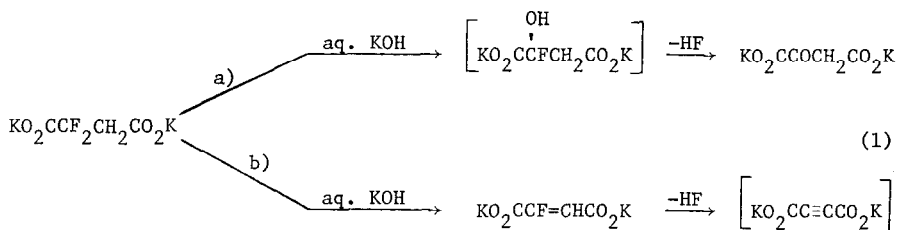
SUMMARY

Elimination of hydrogen fluoride from 2,2-difluorosuccinic acid was found to follow second order kinetics with the activation energy of 16.9 kcal/mol. The probable mechanism is bimolecular trans-elimination giving fluorofumaric acid. No hydrogen-deuterium exchange was observed.

INTRODUCTION

Some time ago one of the authors described a rather unexpected and unique elimination of hydrogen fluoride in preference to hydrogen bromide when dimethyl or diethyl 2-bromo-3-fluorosuccinates were heated with a base [1]. Kinetic measurements of the base-promoted dehydrofluorination of the esters were rather difficult to interpret because of the complexity of the reactions. In order to gain some insight into the mechanism of elimination of hydrogen fluoride from fluorinated succinic acids, base-promoted elimination of hydrogen fluoride from 2,2-difluorosuccinic acid was now studied in some detail.

When 2,2-difluorosuccinic acid is exposed to an excess of aqueous alkali the following reactions can be anticipated:

1. Nucleophilic displacement of fluorine in the geminal difluoro group by hydroxyl followed by elimination of hydrogen fluoride to give an alkali salt of oxalacetic acid (route a in equation 1).
Based on the examples available in the literature [2] such a reaction cannot be completely ruled out but is not very likely.

$$\text{KO}_2\text{CCF}_2\text{CH}_2\text{CO}_2\text{K}
\begin{cases}
\xrightarrow[]{\text{a) aq. KOH}} \left[\text{KO}_2\text{CCFCH}_2\text{CO}_2\text{K}\;(\overset{\text{OH}}{|})\right] \xrightarrow{-\text{HF}} \text{KO}_2\text{CCOCH}_2\text{CO}_2\text{K} \\[2em]
\xrightarrow[]{\text{b) aq. KOH}} \text{KO}_2\text{CCF=CHCO}_2\text{K} \xrightarrow{-\text{HF}} \left[\text{KO}_2\text{CC}\equiv\text{CCO}_2\text{K}\right]
\end{cases} \quad (1)$$

2. The other possible reaction of 2,2-difluorosuccinic acid with aqueous alkali is elimination of hydrogen fluoride to give alkali salts of fluoromaleic or fluorofumaric acid which might react further with the excess of base to give ultimately alkali salt of acetylenedicarboxylic acid (route b in equation 1).

Spectral analysis of the products of the action of aqueous alkali on 2,2-difluorosuccinic acid using proton NMR showed that the only reaction which occurred was elimination of one molecule of hydrogen fluoride to give fluorofumaric acid. Fluorofumaric acid heated with an excess of aqueous alkali under comparable conditions (75°, 3.5 hours) did not eliminate hydrogen fluoride. (This finding makes, at the same time, doubtful the claim that 2,3-difluorosuccinic acid by mere heating with water gives acetylenedicarboxylic acid [3]).

EXPERIMENTAL

Apparatus

Kinetic measurements were carried out by potentiometric titration using Orion Research Specific Ion Electrode for fluorine, model 94-09A, and Orion Research Digital pH Meter model 701. ^{1}H and ^{19}F NMR spectra were taken on Varian EM 390 spectrophotometer at 90 MHz and 84.6 MHz frequencies, respectively. TMS and sodium 3-trimethylsilylpropanesulfonate were used as internal standards for proton, and HFB and TFA for fluorine.

Chemicals

2,2-Difluorosuccinic acid was the commercial product of PCR and was found to be 100% ±0.2% pure by alkalimetric titration. Its purity was moreover checked by ^{1}H and ^{19}F NMR.

Solutions of sodium hydroxide and sodium fluoride (used as a standard) were analytically certified solutions from Fisher and Orion Companies.

Measurements

2,2-Difluorosuccinic acid was weighed, transferred into a 50 ml volumetric flask, neutralized to phenolphthalein by 0.1 N potassium hydroxide, a desired excess of 0.1 N potassium hydroxide was added, and the solution was diluted with distilled water to 50 ml. The flask was heated in a water bath at 45.0°, 60.0°, or 75.0° ±0.1°, aliquots were pipetted into a 5 ml polyethylene beaker fitted with a Teflon[R]-coated magnetic stirring microbar, the fluorine selective electrode was inserted, and the contents of fluorine were determined by potentiometric measurements using a calibration curve.

The results of the individual series of measurements are plotted graphically in Fig. 1 using least square plot based on the second order kinetics. Numerical data are listed in Tables 1-3.

RESULTS AND DISCUSSION

The reaction of 2,2-difluorosuccinic acid with potassium hydroxide follows second order kinetics as evidenced by the linearity of the plot of ln [B]/[A] versus time (Fig. 1). Rate constants of the reaction at different temperatures and different concentrations are listed in Tables 1-3. The reaction rate increases with increasing concentration of the base as illustrated by quarter-life data (Experiments 9-11, Table 3).

Examination of the data in Tables 1-3 shows that the rate constants are functions of the concentrations of reactants. They increase as the starting concentrations increase. The range of values of k is much larger than the experimental error expected indicating that this effect is real. The interpretation offered is that this is an ionic strength effect and not a change in rate law or mechanism. Although a quantitative treatment has not been done, a simple plot of log k versus $\sqrt{\mu}$ shows that the trend can be accounted for in this way (Fig. 2). The variation in k seems to be explicable on this basis.

For this reason, activation energy (E_{act}=16.9 kcal/mol) was calculated only from data obtained from measurements at the same concentrations. (Experiments 1-3, Table 1; 6-7, Table 2 ; and 13-16, Table 3) (Fig. 3).

TABLE 1

Rate constants $k_2 \times 10^3$ mol/L/sec at 45°

Exp. No.	Concn. of Acid mol/L	Concn. of Base mol/L	Ratio Base/Acid (equiv.)	Half-life min.	$k_2 \times 10^3$
1	0.0315	0.1890	6	154.5	0.447 ± 0.7%
2	0.0315	0.1890	6	152.3	0.458 ± 1.4%
3	0.0313	0.1878	6	156.1	0.440 ± 1.6%
4	0.0507	0.2028	4	131	0.467 ± 1.1%

TABLE 2

Rate constants $k_2 \times 10^3$ mol/L/sec at 60°

Exp. No.	Concn. of Acid mol/L	Concn. of Base mol/L	Ratio Base/Acid (equiv.)	Half-life min.	$k_2 \times 10^3$
5	0.0208	0.0832	4	169.1	0.897 + 5.4%
6	0.0315	0.1890	6	53.9	1.430 ± 0.4%
7	0.0314	0.1884	6	55.7	1.297 ± 6.5%
8	0.0501	0.2004	4	43.6	1.683 ± 1.2%

TABLE 3

Rate constants $k_2 \times 10^3$ mol/L/sec at 75°

Exp. No.	Concn. of Acid mol/L	Concn. of Base mol/L	Ratio Base/Acid (equiv.)	Half-life min.	$k_2 \times 10^3$
9	0.00919	0.01838	2	190*	1.523 ± 0.8%
10	0.00913	0.03650	4	74.3*	2.050 ± 3.4%
11	0.00938	0.05630	6	47*	2.050 ± 1.0%
12	0.0280	0.1680	6	32.5	5.100 ± 6.6%
13	0.0314	0.1884	6	25.9	3.967 ± 2.5%
14	0.0314	0.1884	6	23.2	4.250 ± 2.7%
15	0.0316	0.1896	6	21.9	4.133 ± 2.6%
16	0.0313	0.1878	6	23.5	4.600 ± 3.2%

*Quarter-life time.
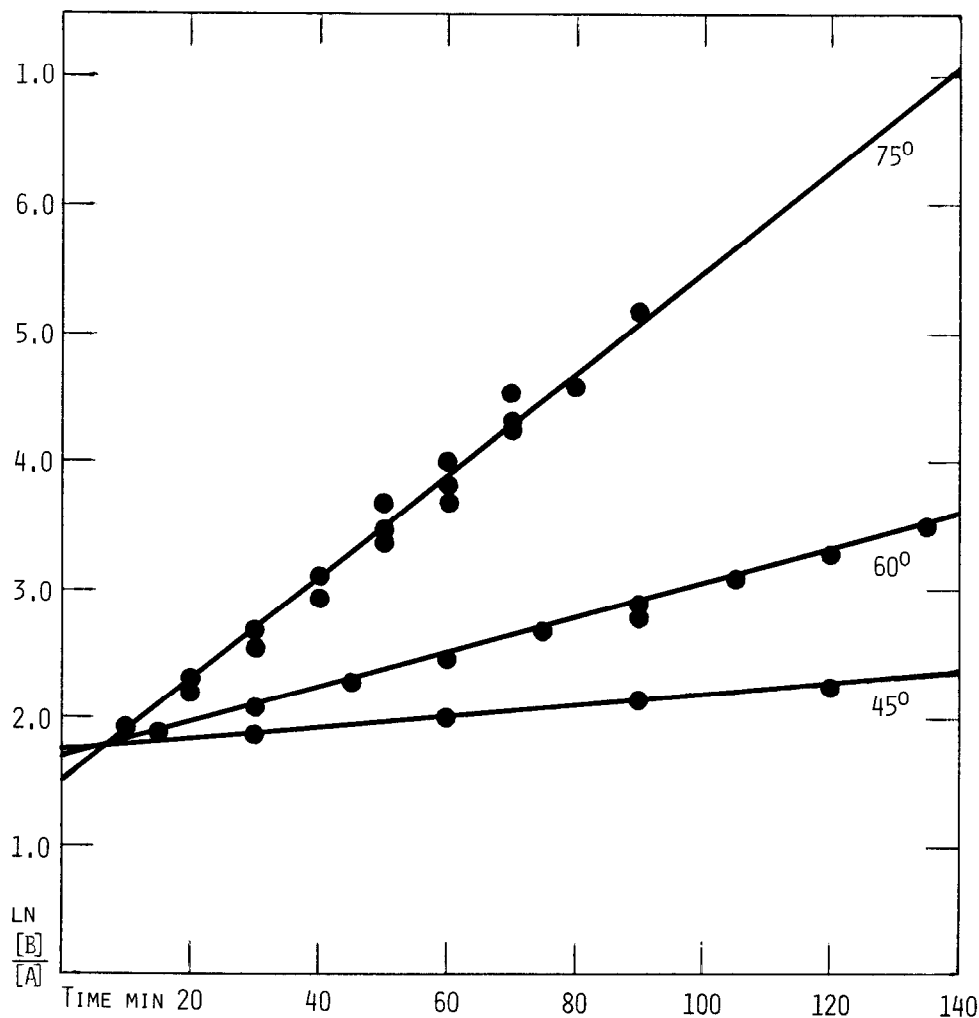
Fig. 1. Plot of ln [B]/[A] versus time in minutes at 45°, 60° and 75°.
([B] concentration of potassium hydroxide, [A] concentration of 2,2-difluorosuccinic acid).

The second order kinetics suggests E2 mechanism for the elimination of hydrogen fluoride from 2,2-difluorosuccinic acid. The product results from bimolecular trans elimination: In the transition state with 2-fluorine and 3-hydrogen in anti-periplanar conformation both carboxylic groups are trans to each other giving fluorofumaric acid as the final product. E1 anionic mechanism can be ruled out based on the kinetic measurements and on complete lack of exchange of 3-hydrogen for 3-deuterium in deuterium oxide in the presence of alkali.
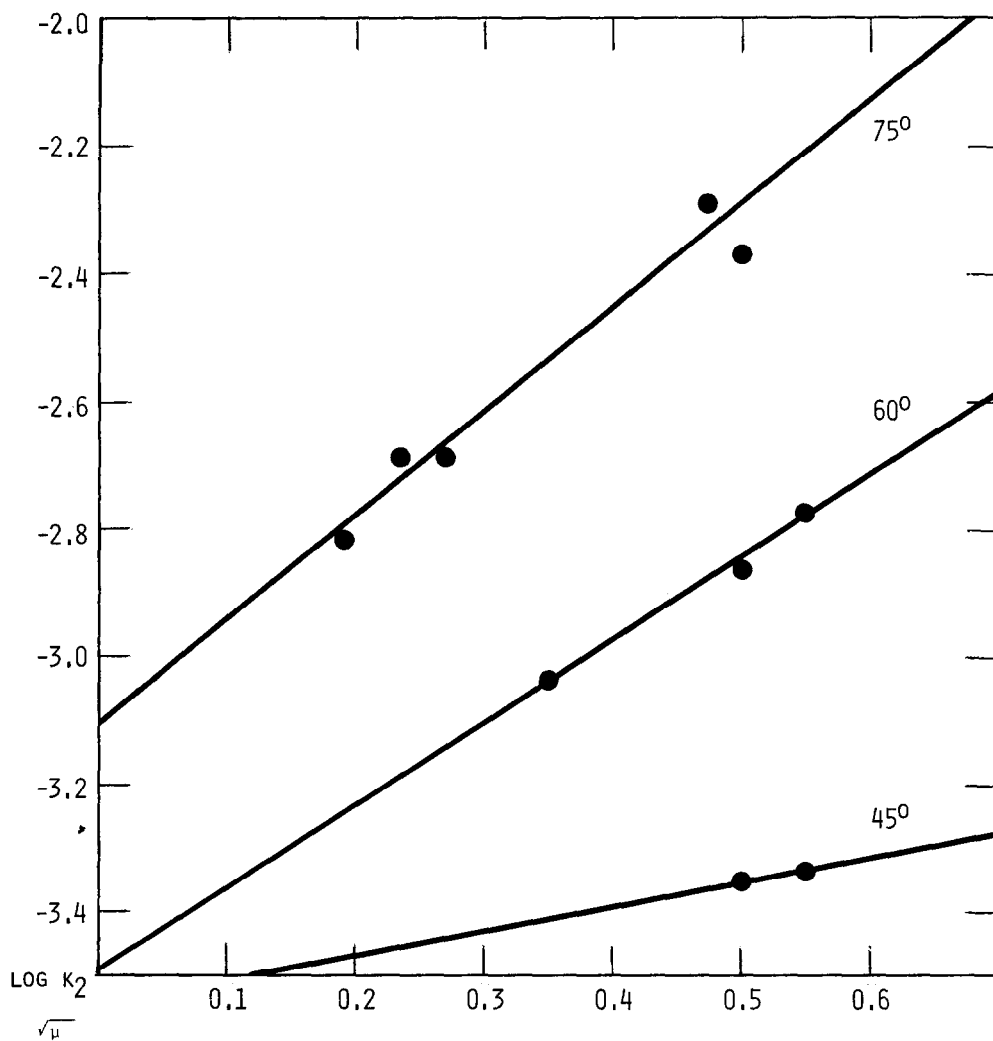
Fig. 2. Plot of log k_2 versus square root of ionic strength at 45°, 60° and 75°
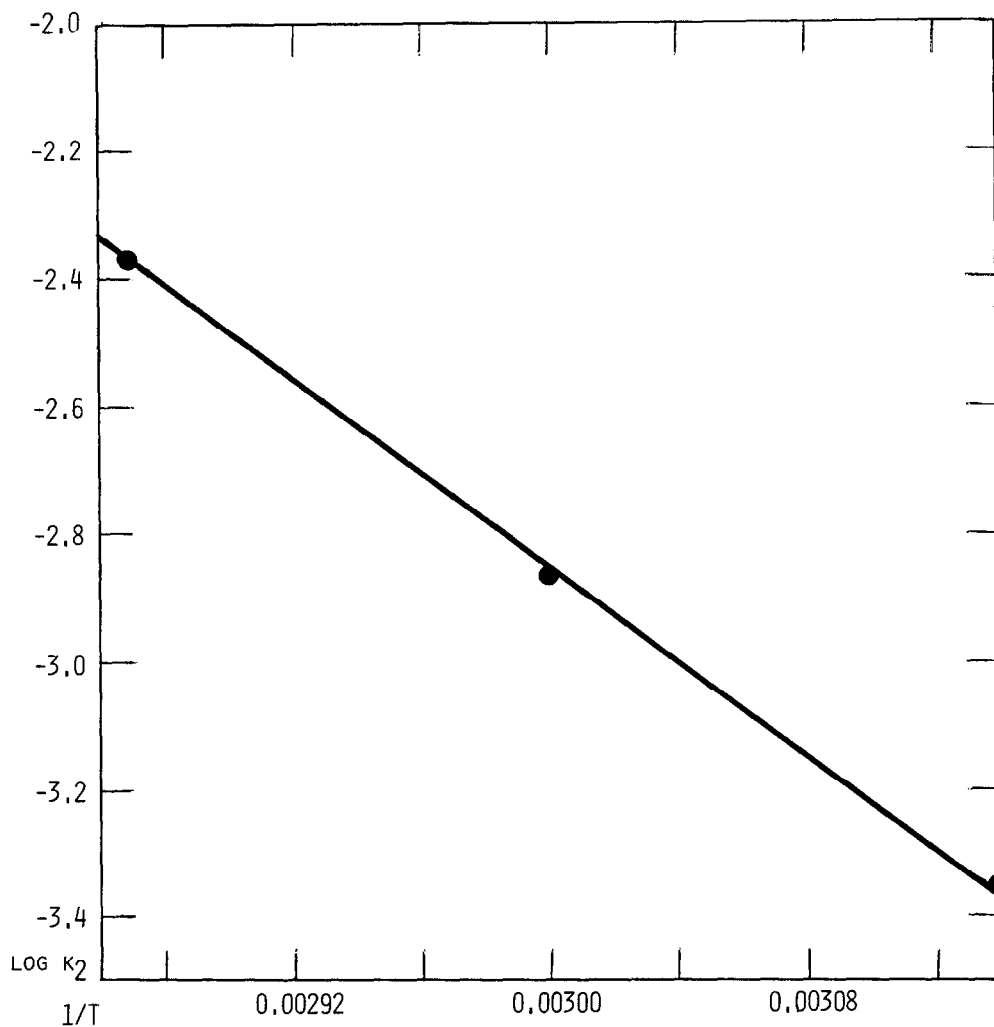
Fig. 3. Arrhenius plot of k_2 versus reciprocal absolute temperature.

REFERENCES

1 M. Hudlicky, J. Fluorine Chem., 2 (1972) 1.
2 M. Hudlicky, Chemistry of Organic Fluorine Compounds, 2nd Ed., Ellis Horwood, Chichester, England, 1976, p. 266-272.
3 M. S. Kharasch, U.S. Pat. 2,426,224 (1947); Chem. Abstr., 42, 213b (1948).