# 2-FLUORO-4,4,5,5-TETRAMETHYL-1,3-DIOXOLANE: A COMPOUND CARRYING TWO INDEPENDENT PROBES FOR DETERMINING RATES OF FORMATIONS OF CONTACT AND SOLVENT-SEPARATED ION PAIRS

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*Abstract*: 2-Fluoro-4,4,5,5-tetramethyl-1,3-dioxolane was shown to be a useful compound for independently determining the rate constants of contact ion pair and solvent-separated ion pair formations. The compound was used to determine rate constants for toluene-$d_8$ and chloroform-$d$ solutions and they were found to be identical for each solution. © 1998 Elsevier Science Ltd. All rights reserved.

Winstein et al.'s proposal [1] that solvolyses of organic halides and sulfonates proceed via contact (CIP) and solvent-separated ion pairs (SSIP) has attracted the interest of many investigators. Among the works devoted to the elucidation of intermediates, Goering et al. were successful in dichotomizing the formations of CIP and SSIP using optically active carboxylate esters, in which the scrambling of $^{18}O$ in the ester moiety is the probe for the formation of CIP, and the loss of optical activity is the probe for the formation of SSIP. [2] However, this methodology has a number of problems, such as the accuracy in mass spectrometry and specific rotation measurements.

In recent years, dynamic NMR spectroscopy, which utilizes the change in lineshapes of NMR signals, has received increasing interest, especially because of the ease in which data can be handled due to advances in computer technology. [3] The method has advantages over the classical method developed by Goering et al. in that the substrate can be used as a racemate rather than as an optically resolved form, and analyses of the products and/or the starting materials are not necessary. In this communication, we wish to report a successful application of the dynamic NMR technique to the problem of CIP and SSIP formations.

In an earlier work, we have demonstrated that the dynamic NMR technique can be used for determining the rates of dissociation of organic halides [3] and have extended applications of the method to various dissociation problems. Among the applications, the dissociation of 4,4,5,5-tetramethyl-1,3-dioxolan-2-yl acetate (**1a**), as reported by Capon and Grieve, [4] was found to be rather slow but the corresponding chloroacetate (**1b**) exhibited suitable rates of dissociation. [5]



**1a**: R = $CH_3$
**1b**: R = $CH_2Cl$

**2**
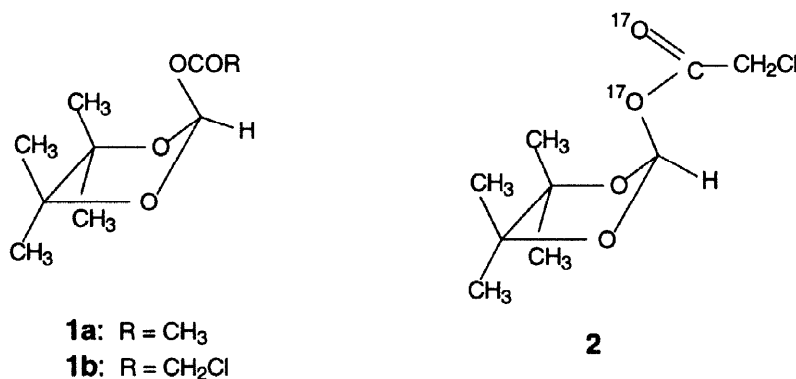
At the outset of this investigation, we synthesized 4,4,5,5-tetramethyl-1,3-dioxolan-2-yl chloroacetate (2) for the dynamic NMR measurement. Whereas Goering et al. used $^{18}O$ scrambling as a probe for CIP formation and loss of optical activity as that for SSIP formation, in this compound the $^{17}O$'s in the ester group and the 4,4,5,5-tetramethyl groups would serve as probes for CIP and SSIP formations, respectively. Unfortunately, the $^{17}O$ signals in the ester moiety were found to have very large half-bandwidths and were not suitable for obtaining reliable data by lineshape analysis. [6]

An alternative method for obtaining the kinetic data for the CIP formation is to take advantage of the loss of coupling [7] when the CIP is formed. For example, if an organic fluoride carries a proton which is attached to the same carbon to which the fluorine atom is attached, and a pair of protons which become diastereotopic due to the substitution pattern, the compound is suitable for measuring the rates of CIP and SSIP formations, provided that the diastereotopic nature of the protons is lost by ionization of the C-F bond: If the dissociation is fast, the $^1H$-$^{19}F$ coupling should not be observed, whereas if the ionization is slow, the $^1H$-$^{19}F$ coupling should be observed. Also the rates of dissociation should be appropriate on the NMR time scale. The p$K$a of hydrogen fluoride is 3.2, [8] whereas those of acetic acid and chloroacetic acid are 4.75 and 2.85, respectively. [9] Therefore the leaving ability of the fluoride ion is not far from that of the chloroacetate ion. From our experience of compound 1, a fluoro compound in which the fluoro substituent is attached to a carbon atom bonded to two oxygen atoms should be a good candidate for our purpose.

A compound which meets these requirements is diethoxyfluoromethane (3). [10] However, we could not obtain compound 3 in a pure enough form for our purpose despite a great deal of effort: The ionized fluoride ion seemed to attack the ethyl group in the ionized intermediate and a large amount of ethyl formate was formed.
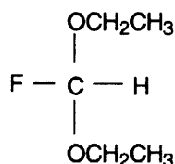


3
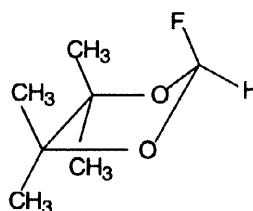


4

Compounds 1a and 1b are said to be stable, though they ionize rapidly at room temperature due to the steric effects of the two pairs of vicinal methyl groups. This is because $S_N2$ type reactions within the reaction intermediates (the carboxylate anion and 4,4,5,5-tetramethyl-1,3-dioxolanyl cation) are slow. We hoped that these steric effects would also be effective in the case where a fluoride anion and 4,4,5,5-tetramethyl-1,3-dioxolan-2-yl cation are formed. Therefore, we decided to synthesize 2-fluoro-4,4,5,5-tetramethyl-1,3-dioxolane (4).

After various trials, we found that the reaction of 4,4,5,5-tetramethyl-1,3-dioxolan-2-yl acetate (1a) [11] with cesium fluoride afforded the desired compound 4 with sufficient purity. [12] In the $^1H$ NMR spectrum of this compound at ambient temperature, the proton at the 2-position and the methyl protons showed broad singlet signals in chloroform-$d$. At lower temperatures than the ambient, the lineshapes changed to show the dynamics, and finally at -60 °C two sharp singlets for each of the 2-H and the methyl protons were observed. The results indicate that the dissociation of the C-F bond is slow enough at this temperature, showing that the compound is suitable for our purpose.

When compound 4 is successfully prepared, the dynamics we expect to observe can be summarized as in Fig. 1. When compound 4 ionizes to CIP, H-F coupling should be lost, and when solvent molecule(s) intervene, the molecular species (positive and negative ions) should become free for independent tumbling. Then, when SSIP changes into SSIP', the site exchange of the *gem*-dimethyl groups can set in. The SSIP'
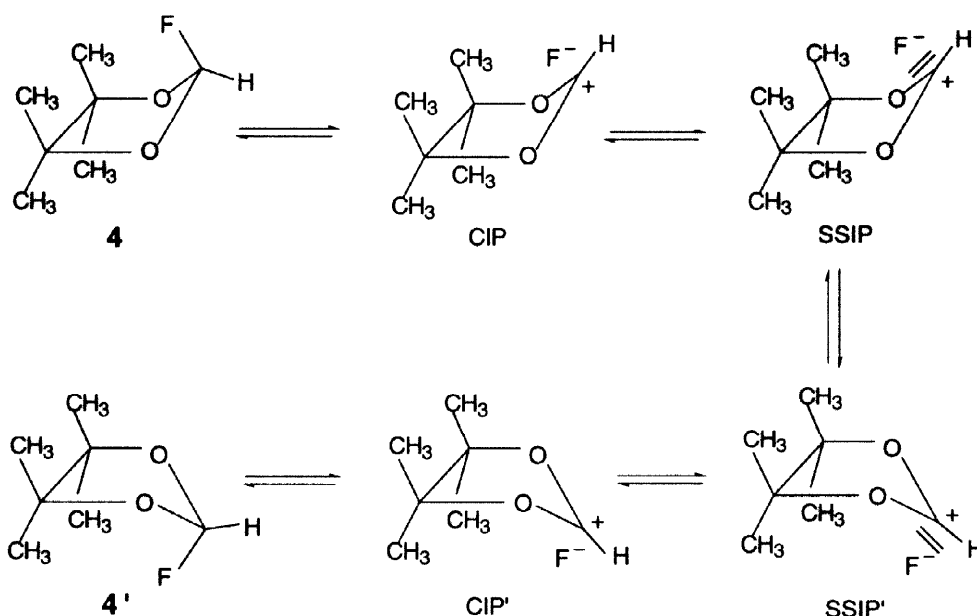
Fig. 1 Steps involved in topomerization of compound **4**

species can lose solvent molecule(s) to proceed to CIP', which then forms a covalent bond to complete the topomerization of the molecule. Here, we assume that the exchange between SSIP and SSIP' is fast.

The rates of formations of CIP and SSIP were obtained by simulating the lineshapes at various temperatures using the DNMR3K program. [13] The data for dissociation to CIP were additionally obtained by observing ^{19}F NMR at various temperatures, because the ^{19}F nucleus also loses coupling with the proton at the 2-position on dissociation to CIP. Comparison of the data obtained with ^{1}H and ^{19}F probes provides a measure of the reliability of the technique applied to the dynamics in question.

The kinetic parameters obtained with the use of the three probes are shown in Table 1. Comparing the rates and other kinetic parameters of CIP formation obtained by the [1]H(2) probe and the ^{19}F probe for chloroform-$d$ solutions, one notices that they are the same within experimental error. This shows the high reliability of the technique used here. The rates of topomerization in CDCl$_3$ solutions obtained by the use of themethyl signals seems to be a little larger than those obtained by [1]H(2) and ^{19}F probes, though other kinetic

Table 1. Kinetic Parameters for Formation of Contact Ion Pairs and Solvent-Separated Ion Pairs from **4** in Two Solvents [15]

| Solvent | Probe | $k_{253}$/s$^{-1}$ | $\Delta G^{\ddagger}_{253}$/kcal mol$^{-1}$ | $\Delta H^{\ddagger}$/kcal mol$^{-1}$ | $\Delta S^{\ddagger}$/cal mol$^{-1}$ K$^{-1}$ |
|---|---|---|---|---|---|
| CDCl$_3$ | 2-H | 249 | 12.0 | 7.8±0.4 | -16.5±1.9 |
| | 2-F | 267 | 11.9 | 7.9±1.0 | -15.9±4.2 |
| | 4,5-Me | 309 | 11.9 | 7.1±0.2 | -18.7±0.9 |
| C$_7$D$_8$ [a] | 2-H | 14.4 | 13.4 | 8.9±1.1 | -17.8±4.1 |
| | 2-F | 14.7 | 13.4 | 8.9±0.9 | -17.7±3.3 |
| | 4,5-Me | 9.2 | 13.6 | 9.0±0.3 | -18.2±1.3 |

a) toluene-$d_8$

parameters agree. However, if the topomerization rates are significantly larger than those for the loss of coupling, but faster reaction rates than those of the rate-limiting step are detected, it is contradictory to the general belief that only the rate-limiting step is observed. Thus, the topomerization rates must be the same as the loss of coupling rates. That is, we must assume that the difference in rate constants of 20% should be allowed as an error, and the rate-limiting step is the CIP formation. Another feature of the kinetic parameters is a fairly large, negative entropy of activation. Ionic dissociation of a covalent species is known to exhibit this tendency because the freedom of motion of solvent molecules is decreased due to strong solvation to the incipient ionic species in the transition state. [16] The reactions we observe here also show this general tendency.

For the toluene-$d_8$ solutions, the rates of dissociation are clearly smaller than those in chloroform-$d$ solutions. This is consistent with the general idea that ionic dissociation proceeds slowly in a solvent of low polarity. Again, we believe the rates obtained for the three probes are identical. Kinetic studies of compound **4** in other solvents are in progress in order to search for the generality in ionization, and for possible demonstrations of the case where SSIP formation is rate-limiting due to the dimensiosolvatic effects. [17]

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