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REACTIONS OF 1,2-DICHLORO-3,3-DIFLUOROCYCLOPROPENE WITH METHANOLIC SODIUM METHOXIDE

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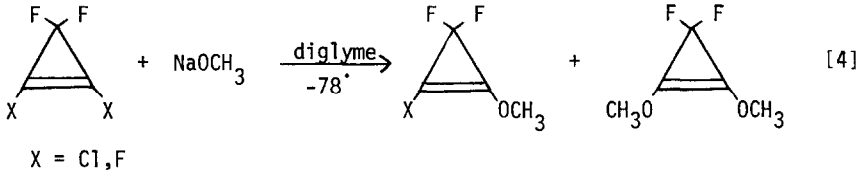
SUMMARY

Slow addition of sodium methoxide in methanol to 1,2-dichloro-3,3-difluorocyclopropene yields initially 1-chloro-2-methoxy-3,3-difluorocyclopropene. Further addition of methoxide in methanol yields preferentially Z 1-chloro-2-fluoro-3,3,3-trimethoxypropene and a small amount of dimethyl malonate. The ortho ester undergoes facile hydrolysis during the reaction and work up to form the acrylate ester, Z methyl 2-fluoro-3-chloroacrylate. A mechanism is suggested to account for the selective isomer formation.

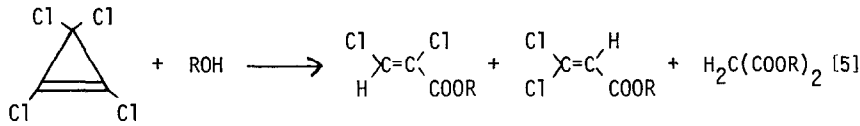
INTRODUCTION

Previous reports on the reactions of tetrahalocyclopropenes with nucleophilic reagents have been limited to the following nucleophiles; iodide [1] , fluoride [2], amines [3] and methoxide [4]. In the last work, the reaction of sodium methoxide and 1,2-dichloro-3,3-difluorocyclopropene in diglyme at -78° was reported.



[4]

It is of interest to compare these results with those of West [5] and others [6] who have observed the spontaneous solvolysis of tetrachlorocyclopropene with various alcohols.



[5]

In this paper, the reaction of 1,2-dichloro-3,3-difluorocyclopropene with sodium methoxide in methanol has been studied in an attempt to determine the reaction pathway which leads to ring opening and the fate of the allylic fluorine in the final product.

RESULTS AND DISCUSSION

In contrast to the highly exothermic reaction of tetrachlorocyclopropene and methanol at room temperature, we have found that a solution of 1,2-dichloro-3,3-difluorocyclopropene (I) in methanol gave only trace quantities of products after four hours reflux. However, sodium methoxide in methanol reacted with I at 0° to form various products depending on the reaction conditions.

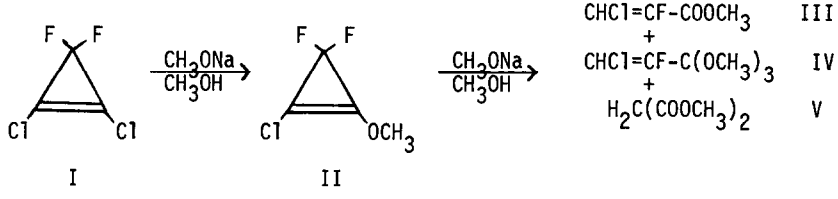
When methanolic sodium methoxide was added dropwise to I only a single product was formed up to the point at which one equivalent of methoxide ion had been added. This was determined by periodic analysis of the reaction mixture by a gas chromatograph.

Although the addition of methoxide would take up to several hours, none of the reported [4] extreme instability of the initial product was observed. The reaction mixture was worked up by quickly adding water, extraction with methylene chloride and drying. A single product (1-chloro-2-methoxy-3,3-difluorocyclopropene,II) in up to 63% yield was isolated from the extracts.

The cyclopropenyl ether II is quite volatile, nevertheless we found it to be sufficiently stable to obtain satisfactory data on samples which had been sent away for chemical analysis. Spectral analyses were performed on samples which had remained for a day or more at room temperature. The property values which we found are quite similar to those previously reported [4] for II.

It was interesting to note that the base peak in the mass spectrum of II corresponded to the loss of CH_3 from the parent molecule. This is in agreement with our earlier findings that loss of allylic fluorine to generate the cyclopropenium ion is not a preferred mode of fragmentation [1].

When more than one equivalent of methoxide was added to I the reaction pathway was quite sensitive to the presence of sodium hydroxide and/or water in the methanol solution. For example, the addition of a solution of commercially available sodium methoxide in methanol to I in a 3:1 ratio gave nearly equal quantities of three products.



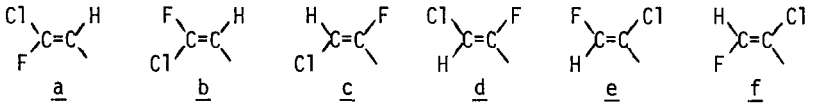
I II

When strictly anhydrous conditions were employed in the reaction, using sodium methoxide prepared from sodium metal and methanol, the second step in the reaction pathway became more selective. Again, the slow addition of one equivalent of methoxide in methanol to I gave only a single product (II) by G.C. analysis. Further addition of a second equivalent of methoxide converted II to the ortho ester IV in about 90%. Less than 10% of the reaction products appeared as the acrylate III and the malonate V.

The ortho ester is extremely sensitive to hydrolysis and much of this product was converted to the acrylate during work up of the reaction mixture

Dimethyl malonate (V) was identified by matching the IR and NMR spectra with a known sample.

The structure of Z methyl 2-fluoro-3-chloro-acrylate (III) was determined from the following information. The infrared spectrum established the presence of an acrylate ester containing a vinylic proton. This was further supported by the proton NMR spectrum which showed a singlet at 3.87 ppm (O-C<u>H</u>$_3$) and a widely split doublet (J=20 Hz) at 6.87 ppm (=C<u>H</u>). The fluorine spectrum also showed a doublet at -124.2 ppm (J=20 Hz). Mass spectrum and elemental analysis confirmed the molecular formula $C_4H_4O_2FCl$ for which there are six structural possibilities for a methyl acrylate.



<u>a</u> <u>b</u> <u>c</u> <u>d</u> <u>e</u> <u>f</u>

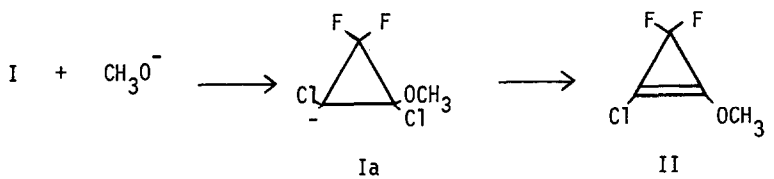
Structure e and f may be excluded from the possibilities as the observed F-H coupling constant of 20 Hertz lies outside the general range for <u>geminal</u> F-H coupling constants [7]. However, the reported ranges for <u>cis</u> coupling (0-20 Hz) and <u>trans</u> coupling (12-53 Hz) do not permit a ready discrimination among the remaining isomers. Fortunately, Reilly [8] has studied F-H coupling constants of a similar molecule, 1-chloro-2-fluoropro-

pene and reports F-H J values of 10.8 Hz for cis and 24.2 Hz for trans isomers. Thus the trans relation of H and F is preferred. Calculated chemical shifts [9] for the olefinic proton in the trans F-H isomers a and d are 4.96 and 6.11 ppm respectively. Thus, structure d was selected as isomer which best fit the observed spectra data. The reaction mechanism proposed below also suggest the preferential formation of this isomer.

The structure of the ortho ester IV was established through its mass spectrum, NMR proton and fluorine spectra and the facile hydrolysis of IV to the acrylate ester III.

A previous study on the mechanism of the reaction of alcohols with tetrachlorocyclopropene have strongly implicated the trichlorocyclopropenium ion as an intermediate in solvolysis process [6]. Smart has also suggested that the solvolysis of II may proceed through the initial loss of allylic fluorine to form a cyclopropenium ion [4]. In this work, the high degree of selectivity in isomer formation suggests an alternate mechanism.

In the initial step the methoxide ion attack on I produces the intermediate carbonion Ia. Collapse of Ia occurs selectively through the Sn-2ae process rather than the Sn-2' process.

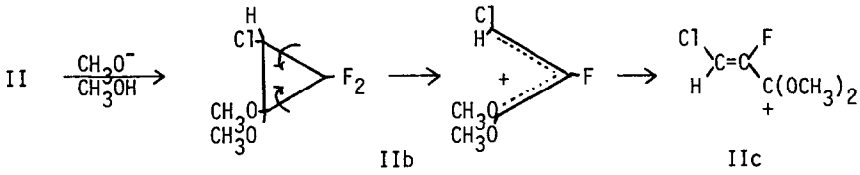


Ia II

The observed tendency for allylic substitution in larger ring systems [10] appears to be decreased by ring strain. The absence of any fluorine substitution products also eliminates the possibility of a dichlorofluorocyclopropenium ion in the first step.

In contrast to the work by Smart [4], there is no indication that the second methoxide ion attack occured at the vinylic carbon bearing chlorine.

Instead, II appears to follow the pathway of activated vinyl ethers [11] and a molecule of alcohol is added across the double bond to produce the ketal IIb. Although many possible modes of ring opening of IIb may be envisioned, the preferred process should occur by a disrotatory breaking of the CHCl--$C(OCH_3)_2$ bond and the concerted elimination of a fluoride ion.



Rotation of the chlorine atom away from the methoxyl groups produces the isomer with F-H trans [12]. The carbonium ion II_c may then react with methanol to produce the ortho ester IV or the ester III if water is present.

Ring opening by breaking the $C(OCH_3)_2$-CF_2 bond and concerted loss of chloride ion would lead to a 3,3-difluoroacrylate. The expected rapid solvolysis of this intermediate would lead to the malonate IV.

EXPERIMENTAL

Apparatus

Commercially available sodium methoxide and methanol previously distilled from calcium hydride were mixed under dry box conditions. Preparation of the 1,2-dichloro-3,3-difluorocyclopropene has been described previously [1]. Elemental analyses were performed by Huffman Laboratories, Wheatridge, Colorado, and by P.C.R. Inc., Gainesville, Florida. Fluorine NMR were obtained on a Varian 56/60 using fluorotrichloromethane as an internal standard. Proton NMR were obtained on a Perkin Elmer R-12A using TMS as an internal standard. The mass spectra were obtained on a DuPont

21-491 instrument and the ir spectra were obtained on a Beckman IR-8 using a polystyrene film for calibration. Gas chromatograph analysis of the reaction mixtures were performed on a Varian 202B using a 5 ft. X 0.25 inch SS column packed with 20 wt. % SF-1265 on Chromosorb W.

In contrast to a recent report [4] which described the spontaneous reaction between 1-methoxytrifluorocyclopropene and methanol, we were unable to observe any significant reaction between 1 and methanol after four hours reflux.

Reaction of sodium methoxide with I (1:1 ratio)

A solution of sodium methoxide in methanol (4.57 ml; 2.11 N) was slowly added dropwise to 1.40g (9.6 mmol) of I. The reaction mixture was stirred rapidly at 0° and repeatedly monitored by vpc analysis. After methoxide addition was complete (ca 2 hr.) the reaction mixture was poured into water and the organic layer was quickly removed and dried over 5A molecular sieves. VPC analysis of the product (0.82g, 63%) indicated a single compound (1-chloro-2-methoxy-3,3-difluorocyclopropene, II) was present: IR (neat film) 2960(w), 2850(w), 1835(s), 1440(w), 1300(s), 1250(s), 1010(s), 850(s) and 760(m) cm^{-1}; ^{19}F NMR($CDCl_3$)-99.0 ppm (singlet); ^{1}H NMR($CDCl_3$) 4.07 ppm (singlet). Mass spectrum gave weak molecular ions at 142 and 140 with fragmentation ions appearing at 127, 125 (base peak), 123, 121, 111, 109, and 105 mass units. Calcd. for $C_4H_3OF_2Cl$: C, 34.19 H, 2.15; F, 27.04; Cl, 25.23; Found: C, 35.09; H, 2.43; F, 27.00; Cl, 25.85. (lit., [4] NMR (CCl_4) ^{1}H δ=3.97(s), ^{19}F -99.1(s), ir (neat) 1832 cm^{-1}).

Reaction of sodium methoxide with I (3:1 ratio)

A solution of sodium methoxide in methanol (61.0 ml, 1.65N) was slowly added dropwise to 5.0g (34.4 mmol) of I at 0°. Periodic vpc analysis of

the reaction mixture indicated only one product was formed up to 1.0 equivalent of methoxide addition. Addition of the second and third equivalent of methoxide caused the initial product peak to disappear with the concurrent formation of three new products. The reaction mixture was stirred at 0° for 4 hours then concentrated in a rotary film evaporator. The organic residue was extracted from the salts with 25 ml of methylene chloride then quickly washed with 100 ml water and dried over 5A molecular sieves. Preparative vpc separation of the methylene chloride soln on a 25 ft. X ½ in. column containing 20% SF-1265 on Chromosorb W gave three peaks in the ratio 1.3:1.7:1.9.

The first peak was identified as Z methyl 2-fluoro-3-chloroacrylate (12.3%)nc(III):IR(neat film) 3130(m), 2960(m), 2850(w), 1750(vs), 1640(s), 1440(s), 1340(s), 1250(s), 1110(s), 980(s), 890(m), 870(m), 830(s), 760(s) and 740(s) cm^{-1}; ^{19}F NMR ($CDCl_3$)-124.2 ppm (doublet, J=20 Hz); ^{1}H NMR ($CDCl_3$) 3.87 ppm (3H, singlet), 6.87 ppm (1H, doublet, J=20 Hz). Mass spectrum gave strong molecular ions at 138 and 140 with fragmentation ions appearing at 109, 107 (base peak), 103, 81, 79 and 59 mass units. Calcd. for $C_4H_4O_2FCl$: C, 34.68; H, 2.91; F, 13.71; Cl, 25.59; Found: C, 34.46; H, 3.19; F, 13.4; Cl, 25.38.

The second peak was identified as Z 1-chloro-1-fluoro-3,3,3-trimethoxypropene (12.1%)nc(IV):IR (neat film) 3130(w), 2960(m), 2860(w), 1685(w), 1310(s), 1191(s), 1100(broad, vs), 798(s) and 610(m) cm^{-1}; ^{19}F NMR ($CDCl_3$) -122.4 ppm (doublet, J=23 Hz); ^{1}H NMR ($CDCl_3$) 3.25 ppm (9H, singlet), 6.25 ppm (1H, doublet, J=23 Hz). Mass spectrum gave a weak molecular ion at 184, 186 and strong fragmentation ions at 155, 153, 149, 140, 138, 109, 107 (base peak) and 103 mass units.

The third peak was identified as methyl malonate (18.6%)V by matching the NMR and IR spectra with a known sample.

Reaction of sodium methoxide with I (ratio 2:1)

A solution of sodium methoxide in methanol (11.8 ml, 4.37N), prepared from sodium metal and anhydrous methanol, was added dropwise to 4.0g (27.6 mmol.) of I at 0°. VPC monitoring of the reaction mixture indicated that a single product (II) was formed during the addition of one equivalent of methoxide. Addition of the second equivalent converted II into principally III with less than 5% of the acrylate IV and the malonate V appearing in the reaction mixture. After the addition was complete (ca 3 hr.) the reaction mixture was poured in 75 ml cold water and extracted twice with 25 ml portions of methylene chloride. The extracts were combined, dried and carefully concentrated to remove the methylene chloride. VPC analysis of the residue (2.0 g) indicated a small amount of solvent, acrylate IV (30.6%), ortho ester III (11.0%) and malonate V (0.4%). Attempted fractional distillation of the mixture caused further conversion of the ortho ester III to the acrylate IV, bp 65° (131mm), 101=102° (747 mm).

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