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ELIMINATION REACTIONS OF 1,2-DIHALO-2,3,3-TRIFLUOROCYCLOBUTANES

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SUMMARY

Elimination reactions on isomeric mixtures of cis and trans 1,2-dihalo-2,3,3-trifluorocyclobutanes are reported. In zinc-promoted dehalogenations a steady decrease in the relative amount of the trans isomers compared to the cis isomers occured, with 2,3,3-trifluorocyclobutene as the sole product. The cis isomers reacted at a faster rate in potassium hydroxide induced eliminations to yield a slight predominance of 1-halo-2,3,3-trifluorocyclobutenes over 3-halo-3,4,4-trifluorocyclobutenes. However, with triethylamine as the inducing base, an increased rate of elimination from the trans isomers was noted along with almost exclusive formation of 3-halo-3,4,4-trifluorocyclobutenes.

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INTRODUCTION

Considerable evidence from physical data has indicated a significantly nonplanar conformation for cyclobutane derivatives with a psuedo-axial and pseudo-equatorial positioning possible for each substituent.[2] This conformational similarity to cyclohexane has been increasingly applied to account for the chemical reactivity in this system.[2-4] Fluorinated ethylenes react readily with activated alkenes to yield fluorocyclobutanes by 1,2-cycloaddition[5] and, in some cases, cis and trans isomers have been examined[4,6-9] but the fate of the geometrical isomers in elimination reactions has not been widely investigated. In the present study, 1,2-dihalo-2,3,3-trifluorocyclobutanes, prepared from the codimerization of chlorotrifluoroethylene and vinyl chloride or bromide, were found to be a mixture of cis and trans isomers. The reactivity differences between the stereoisomers under elimination conditions was then examined.

RESULTS AND DISCUSSION

During a zinc-promoted dechlorination reaction on an equal isomeric mixture (or nearly so) of 1,2-dichloro-2,3,3-trifluorocyclobutane (I), the isomer with the longer retention time in the glpc‡ trace (Ib) reacted faster than the other isomer (Ia). There was a steady decrease in the relative amount of Ib compared to Ia, resulting in almost pure Ia after 80% reaction, with 2,3,3-trifluorocyclobutene[10] (II) as the sole product (see Figure 1)

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‡ gas liquid partition chromatography.

Since zinc-promoted dehalogenations are often stereoselective anti-processes,[11] the trans isomer with pseudo-axial chlorines would be expected to have the preferred orientation and thus react faster. This would indicate that Ib was the trans dichloro isomer. An nmr analysis[12] confirmed this geometrical assignment by suggesting that Ib had a trans arrangement of the chlorines with an equilibrium mixture of pseudo-diequatorial or pseudo-diaxial chlorines. Finally, chlorination of II led to a ratio of Ia to Ib of 15 to 85, as would be expected since stereospecific trans addition of halogens occurs even under free radical conditions[13] with fluorocyclobutenes.[6,8]

Examination of a potassium hydroxide induced dehydrohalogenation reaction on the codimerization 50:50 isomer mixture of I using glpc techniques showed that Ia reacted faster than Ib under these conditions. Thus, with the reaction near completion, 80% of the remaining cyclobutane was isomer Ib and the product consisted of 55% 1-chloro-2,3,3-trifluorocyclobutene (III) and 45% 3-chloro-3,4,4-trifluorocyclobutene (IV) (see Figure 1 for the general sequence and Table 1 for product ratios). Sufficient quantities of each geometric isomer were isolated for analytical, physical, and nmr characterization but the difficulty of separation allowed only an approximate indication of the product yields produced from each isomer under elimination conditions. Ia gave almost exclusive formation of III whereas Ib led to about 90% IV with only 10% III being produced. Isomerization between the products under these conditions was not observed. Therefore, from the 50:50 codimerization mixture, one would predict the formation of larger amounts of III over IV, as was experimentally demonstrated.

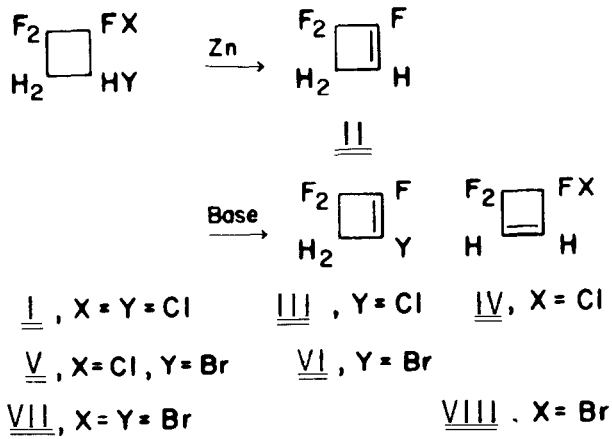
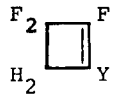
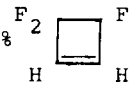


Fig. 1. Elimination reactions with 1,2-dihalo-2,3,3-trifluorocyclobutanes

TABLE 1

Results of Base Induced Dehydrohalogenations of Fluorocyclobutanes

Cyclobutane (Isomer ratio)	Base	Product Ratios % 	% 
Iab (50:50)	KOH	55	45
Ia	KOH	ca. 95	ca. 5
Ib	KOH	ca. 10	ca. 90
Vab (50:50)	KOH	55	45
VIIb	KOH	50	50
Iab (50:50)	Et_3N	7	93
Vab (50:50)	Et_3N	2	98

Note: The isomer and product ratios were determined by glpc analysis.

The flexible puckered cyclobutane ring can attain the preferred anti-coplanar geometry for elimination[13] with the result that anti-elimination has been predicted to be favored over the syn-pathway.[11] The nmr analysis[12] indicated that the predominant conformer of the cis isomer (Ia) exists with a pseudo-axial proton (C-1) and a pseudo-axial chlorine (C-2). This is consistent with formation of III upon dehydrohalogenation of Ia due to the involvement of the hydrogen atom at C-1 in a stereoelectronically preferred anti-coplanar elimination.

For elimination from the trans isomer Ib to embrace an anti-coplanar arrangement of a pseudo-axial proton and chlorine, base attack must occur at the proton at C-4, leading to the predominant product, IV. Cis elimination evidently does take place to a much smaller degree through the proton at C-1 to lead to III, presumably attaining the necessary cis-coplanar geometry by a flattening of the ring. The tendency for a syn-coplanar elimination with the dihedral angle near 0° to proceed somewhat slower than the anti-coplanar pathway close to 180° has been proposed by DePuy.[14] Syn-elimination can compete effectively with the anti-pathway as the ring size decreases from six to five carbon atoms,[11,15] a trend continued with cyclobutane derivatives.[16]

These results are similar to those noted for cis and trans dibromocyclobutane where anti-elimination from the cis isomer took place faster than syn-elimination from the trans isomer.[11] With polyfluorocyclohexanes,[17] a rapid reaction occured for an anti-coplanar dehydrofluorination; whereas, with polyfluorocyclopentanes,[15] although an anti-coplanar arrangement gave the easiest elimination, a competitive syn-coplanar reaction

took place. In all cases, the most acidic hydrogen atom was abstracted.

The results with the triethylamine dehydrohalogenation of I listed in Table 1 offer striking differences from the potassium hydroxide case. After 60% reaction with the codimerization product I, recovery of the remaining starting material revealed that the relative proportion of the isomers Ia to Ib had changed from 50:50 to 77:23, indicating that now the trans isomer was reacting preferentially to yield largely IV, 93:7 over III. These data may be due to an increased steric requirement for the attacking base which would result in a greater tendency to interact with the least hindered proton at C-4 (CH_2).[18] The steric bulk of the halogens relative to hydrogen could also be considered to shield C-1.[19] Since potassium hydroxide is a stronger base than triethylamine, those conditions would be expected to be the most sensitive to the relative acidities of the protons of I since it has been established that the stronger the base, the greater the tendency to remove the more acidic proton.[20] Based upon the general acidities of fluorocarbon substrates[21] and a review[22] concerning the carbanion stabilizing effect of halogens on the cyclobutyl system, one would predict activation of the proton at C-1 (CHCl). At any rate, with predominate proton abstraction at C-4, a faster rate of elimination might be expected from the trans isomer with an anti-coplanar pathway.

The potassium hydroxide induced dehydrohalogenation of 1-bromo-2-chloro-2,3,3-trifluorocyclobutane (V)[23] which was a near 50:50 mixture of geometrical isomers, led generally to the same results as I in that the isomer with the shorter

retention time (Va) reacted faster than the other isomer (Vb). However, the change from chlorine to bromine at C-1 (CHX) would be expected to increase the acidity of that proton[21] which also should facilitate cis-elimination.[24] On the other hand, a better leaving group, bromine vs chlorine,[22] would now be involved. A 55:45 ratio of the products, 1-bromo-2,3,3-trifluorocyclobutene (VI) to IV resulted.

Again, in a triethylamine induced elimination with V, the trans-isomer (Vb) reacted faster than the cis (Va). From this trans-isomer, not only would the preferred anti-coplanar arrangement be available with the 4-proton and 1-halogen but also a better leaving group, bromine vs chlorine.[22] This resulted in almost exclusive dehydrobromination to yield 98% IV to 2% VI. As before, a slower syn-coplanar process may have operated from the cis-isomer also involving the 4-proton.

Bromination of 2,3,3,-trifluorocyclobutene yielded the expected trans 1,2-dibromo-2,3,3-trifluorocyclobutane (VIIb)[10] by the preferred trans addition which occurs with fluorocyclobutenes.[8,25] The ratio of VI to 3-bromo-3,4,4-trifluorocyclobutene (VIII) was 50:50 from a hydroxide induced dehydrobromination, a significant increase in the syn-elimination pathway over that of trans Ib. This may be ascribed not only to the increased acidity at C-1 expected from the change of chlorine to bromine as outlined earlier for the trans IVb but also to the better leaving group ability of bromine over chlorine at C-2.

The results of this study involving elimination reactions may be rationalized by conformational and acidic considerations and, therefore, support the geometrical assignment of isomers by nmr analysis.[12]

EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer Infracord spectrophotometer and product analyses and preparative scale separations were carried out on a F and M Model 300 Programmed Temperature Gas Chromatograph with a Texas Instruments Inc. Servariter model recorder and disc integrator, utilizing a column with a fluorosilicone 1265 (QF-1) substrate. A Bausch and Lomb refractometer was used to measure the refractive indices and densities were determined by weight difference with a calibrated 10 μl syringe. Microanalyses were performed by the Galbraith Laboratories, Knoxville, Tenn. NMR spectra for the fluorocyclobutanes of this study are reported elsewhere[12] but other spectra, obtained on a Varian Model A-60, using tetramethylsilane as reference, are given. The nmr spectrum of 3-chloro-3,4,4-trifluorocyclobutene (III) has been published elsewhere.[26] Table 2 summarizes the physical properties and analytical verifications. Care should be excerised to exclude oxygen from the codimerization reactions.

1,2-Dichloro-2,3,3-trifluorocyclobutane (I). A one liter stainless steel high-pressure shaker reactor was evacuated, cooled, and charged with 225 g of vinyl chloride, about 1 g of dl-limonene (to prevent polymerization) and 300 g of chlorotrifluoroethylene. After heating at 190-200°C for 14 hours, the reactor was cooled, the excess pressure vented, and the crude product distilled to yield 269

g of I. Analysis by glpc techniques indicated I to be a 50:50 mixture of geometrical isomers, Ia (isomer with the shorter retention time) and Ib.

Reaction of I with potassium hydroxide. Over a five hour period, 179 g of I (50% Ia to 50% Ib) was added dropwise to 132 g of crushed potassium hydroxide in 300 ml of heavy mineral oil maintained at 45°C ± 3°. Using glpc techniques, samples were analyzed periodically to compare the rate of reaction of the two isomers [(time in hours, percent I remaining, percent Ia:Ib): 5,75,50:50; 9,63,40:60; 21,40,36:64; 27,27,25:75; 31,8,20:80]. After 33 hours, work up gave 51 g of 1-chloro-2,3,3-trifluorocyclobutene (III), bp 47-8° (630 mm), infrared spectrum identical to that of an authentic sample,[27] and 42.5 g of 3-chloro-3,4,4-trifluorocyclobutene (IV).

Reaction of I with zinc. Into 72 g of zinc dust in 250 ml of dibutoxytetraglycol and a few drops of hydrochloric acid maintained at 105°C ± 5 was added 197 g of I dropwise over a period of 13 hours. Analysis of periodic samples by glpc techniques gave the following data [(time in hours, percent Ia:Ib): 13,50:50, 26,53:47; 45,59:41; 83,62:38; 107, 66:34]. After 170 hours, in a Dry-Ice condenser connected to the reaction flask was collected 75 g of 2,3,3-trifluorocyclobutene, bp 24-6°/630 mm, infrared spectrum identical to an authentic sample.[10] Also recovered was 20 g of I (95% Ia to 5% Ib).

TABLE 2

Properties of New Compounds

Compd.	$N^{25}D$	d^{25}	bp °C/630 mm	%C		%H		%F	
				Calcd	Found	Calcd	Found	Calcd.	Found
Ia	1.392	1.47	98-98.5	26.8	26.6	1.7	1.6	31.8	32.0
Ib	1.394	1.48	100-101.5	26.8	26.9	1.7	1.6	31.8	32.0
IV	1.327	1.61	74.5-76	33.7	33.7	1.4	1.3	40.0	39.8
Va	1.420	1.85	115.5-116	21.5	21.7	1.3	1.3	25.5	25.7
Vb	1.423	1.83	118.5-119	21.5	21.6	1.3	1.4	25.5	25.6
VI	1.394	1.72	65-65.5	25.7	25.8	1.1	1.1	30.5	30.6
VIII	1.404	1.73	94.5-95	25.7	25.8	1.1	1.0	30.5	30.4

Reaction of Ia with potassium hydroxide. After heating 0.89 g of Ia with 0.66 g of crushed potassium hydroxide in 1.5 ml of mineral oil held at 45°C ± 3° for 35 hours, 0.59 g of III and 0.03 g of IV were identified from the reaction.

Reaction of Ib with potassium hydroxide. Heating 0.9 g of Ib with 0.66 g of crushed potassium hydroxide in 1.5 ml of mineral oil maintained at 45°C ± 3° for 40 hours led to 0.44 g of IV and 0.05 g of III.

Addition of chlorine to II. Chlorine gas was slowly bubbled for ten hours into a solution of 25 g of 2,3,3-trifluorocyclobutene in 50 ml of carbon tetrachloride at room temperature. After washing with aqueous sodium bisulfite and drying, distillation gave 21 g of I (15% Ia to 85% Ib).

Reaction of I with triethylamine. A mixture of 28.5 g of I and 20 g of triethylamine in 50 ml of chloroform was heated to heavy reflux for 29 hours. After washing with dilute hydrochloric acid and drying, distillation gave 0.5 g of III and 7.8 g of IV. Also recovered was 10 g of I (77% Ia to 23% Ib).

1-Bromo-2-chloro-2,3,3-trifluorocyclobutane (V). Following the procedure of Gini,[23] 465 g of chlorotrifluoroethylene, 534 g of vinyl bromide, and about 1 g of dl-limonene were charged into a stainless steel reactor and heated to 190 to 200°C for 16 hours. Distillation gave

185 g of V. Glpc analysis showed V to be a 50:50 mixture of Va (isomer with the shorter retention time) and Vb.

Reaction of V with potassium hydroxide. Into a mixture of crushed potassium hydroxide in 250 ml of mineral oil, heated to 55°C, 112 g of V was added slowly over two hours. Periodic sampling by glpc gave the following data [(time in hours, percent V remaining, percent Va:Vb): 4.5,62, 42:58; 8.25,38, 34:66; 10.25, 24, 32:68]. After 25 hours, work up gave 24 g of IV and 39 g of 1-bromo-2,3,3-trifluorocyclobutene (VI); ir 1710 (C=C); nmr ($CDCl_3/CFCl_3$) 7.07τ (d,t,J=11.7 and 2.9 Hz), 110.6φ(t,t,J=11.7 and 4.5 Hz), 114.1φ(d,t,J=4.5 and 2.9 Hz)

Reaction of V with triethylamine. After holding a mixture of 22 g of V and 15 g of triethylamine in 35 ml of chloroform at mild reflux for 12 hours, 5.3 g of IV and 0.085 g of VI were isolated. At five and one-half hours the ratio of Va to Vb was 93:7.

1,2-Dibromo-2,3,3-trifluorocyclobutane (VIIb). The procedure of Park, Holler, and Lacher[10] was used to prepare VIIb.

Reaction of VIIb with potassium hydroxide. Heating 102 g of VIIb and 92 g of crushed potassium hydroxide in 100 ml of mineral oil to 85°C ± 5 for six hours led to 18.7 g of VI and 18.6 of 3-bromo-3,4,4-trifluorocyclobutene (VIII); nmr (CCl_4) 3.05 τ (m) and 3.49 τ (m).

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REFERENCES

1 Taken in part from the Ph.D.Dissertation of T.S. Croft, University of Colorado, 1967

2 D.B. Miller, P.W. Flanagan and M. Shechter, J. Amer. Chem. Soc. 94, 3919 (1972) and references cited therein

3 I.Lillien and R.A. Doughty, Tetrahedron Letters 3953 (1967).

4 G. Fuller and J.C. Tatlow, J. Chem. Soc. 3198 (1961)

5 W.H. Sharkey in "Fluorine Chemistry Reviews" (P. Tarrant, Ed.), Vol. 2, Chap. 1, Marcel Dekker, Inc., New York, N.Y. (1968)

6 J.R. Lacher, A. Buchler, and J.D. Park, J. Chem. Phys. 20, 1014 (1952)

7 W.C. Soloman and L.A. Dee, J. Org. Chem. 29, 2790 (1964)

8 W.R. Cullen and P. Singh, Can. J. Chem. 41, 2397 (1963)

9 J.D. Park, R.O. Michael, and R.A. Newmark, J. Org. Chem. 34, 2526 (1969)

10 J.D. Park, H.V. Holler, and J.R. Lacher, ibid. 25, 990 (1960)

11 N.A. LeBel in "Advances in Alicyclic Chemistry" (H. Hart and G.J. Karabatos, Eds.) Vol. 3, Chap. 3, Academic Press, New York N.Y. (1971)

12 R.A. Newmark, R.E. Watson, and T.S. Croft, Tetrahedron, in press.

13 J. March, "Advanced Organic Chemistry:Reactions, Mechanism and Structure", Chapter 15 and 17, McGraw-Hill, Inc., New York, N.Y. (1968).

14 C.H. DePuy, R.D. Thurn, and G.F. Morris, J. Amer. Chem. Soc. 84, 1314 (1962)

15 J. Burdon, T.M. Hodgins, R. Stephens, and J.C. Tatlow, J. Chem. Soc. 2382 (1965) and references cited therein

16 C.H. DePuy, C.G. Naylor, and J.A. Beckman, J. Org. Chem. 35, 2750 (1970)

17 S.F. Campbell, F. Lancashire, R. Stephens, and J.C. Tatlow, Tetrahedron 23, 4435, (1967) and references cited therein

18 H.C. Brown and M. Nakagawa, J. Amer. Chem. Soc. 78, 2197 (1956)

19 J.E. Anderson and H. Pearson, Tetrahedron Letters 2779 (1972)

20 R.A. Bartsch, K.E. Wiegers, and D.M. Guritz, J. Amer. Chem. Soc. 96, 430 (1974)

21 K.J. Klubunde and D.J. Burton, J. Amer. Chem. Soc. 94, 5985 (1972)

22 J.D. Park, R.J. McMurtry, and J.H. Adams in "Fluorine Chemical Reviews" (P. Tarrant, Ed.), Vol. 2,Chapter 2, Marcel Dekker, Inc., New York, N.Y. (1968)

23 Synthesis described in unpublished results from this laboratory; see D.C. Gini, PhD dissertation, University of Colorado, 1961

24 J. Weinstock, R.G. Pearson, and F.G. Bordwell, J. Amer. Chem. Soc. 78, 3468 (1956)

25 J.D. Park, J.R. Dick, and J.H. Adams, ibid. 30, 400 (1965)

26 R.A. Newmark, G.R. Apai, and R.O. Michael, J. Magnetic Resonance 1, 418 (1969)

27 M.S. Raasch, R.E. Miegel, and J.E. Castle, J. Amer. Chem. Soc. 81, 2678 (1959)