Kinetics, Deuterium Isotope Effect and Mechanism of the Reaction of 1,1,1-Trifluoro-2,2-bis(4-nitrophenyl)ethane with 1,1,3,3-Tetramethylguanidine in Aprotic Solvents

Arnold Jarczewski,* Grzegorz Schroeder, Mieczyslaw Waligorski and Miroslaw Dworniczak
Faculty of Chemistry, Adam Mickiewicz University, 60-780 Poznań, Poland

The reaction of 1,1,1-trifluoro-2,2-bis(4-nitrophenyl)ethane with 1,1,3,3-tetramethylguanidine (TMG) in different solvents gives *N*-[bis(dimethylamino)methylene]-1-fluoro-2,2-bis(4-nitrophenyl)ethenylamine $\{(O_2NC_6H_4)_2C{=}CF[N{=}C(NMe_2)_2]\}$ as the final product. No intermediates were isolated in the reaction mixture.

The kinetics of this reaction in a series of solvents—acetonitrile (MeCN), benzonitrile (PhCN), tetrahydrofuran (THF) and hexane—are reported. In acetonitrile kinetic curves showed non-exponential behaviour in the first 10–20% of the kinetic run. The rate constants, deuterium isotope effect and activation parameters are discussed in terms of a multistep mechanism. Non-exponential behaviour of kinetic curves in acetonitrile and the lack of intermediate is explained.

The kinetics of the reaction of 1,1,1-trifluoro-2,2-bis(4-nitrophenyl)ethane with piperidine and pyrrolidine bases in a series of solvents—acetonitrile, benzonitrile and dimethyl sulphoxide—have been investigated previously.[1] The reaction is complex, leading to 1-amino-1-fluoro-2,2-bis(4-nitrophenyl)ethene as the final product *via* the intermediate 1,1-difluoro-2,2-bis(4-nitrophenyl)ethene. The results obtained are discussed in terms of a multistep mechanism, $(E1cB)_{ip}$, consisting of a pre-equilibrium followed by fast addition–elimination steps.

The reaction of primary and secondary amines with 1,1-difluoro-2,2-bis(4-nitrophenyl)ethene in acetonitrile gives initially 1-amino-1-fluoro-2,2-bis(4-nitrophenyl)ethene and then 1-amino-1,1-difluoro-2,2-bis(4-nitrophenyl)ethane.[2] It is concluded that the reaction proceeds *via* a pre-equilibrium step leading to a zwitterion, followed by another equilibrium giving a carbanion that yields the product 1-amino-1-fluoro-2,2-bis(4-nitrophenyl)ethene by a rate-determining cleavage of the carbon–fluorine bond.

The kinetics and mechanism of the reaction of 1,1-difluoro-2,2-bis(4-nitrophenyl)ethene with TMG in different solvents to give the final product *N*-[bis(dimethylamino)methylene]-1-fluoro-2,2-bis(4-nitrophenyl)ethenylamine $\{(O_2NC_6H_4)_2C{=}CF[N{=}C(NMe_2)_2]\}$ have been investigated.[3]

Table 1 Rate constants and kinetic isotope effects for the reaction of $[(O_2N)_2C_6H_4]_2CHCF_3$ (H) and $[(O_2N)_2C_6H_4]_2CDCF_3$ (D) with TMG in acetonitrile. The initial concentration of the fluoroethane was 5×10^{-5} mol dm^{-3}.

(*a*)

		$k_{obs}/10^{-5}$ s^{-1}			
Substrate	[TMG]/mol dm^{-3}	20 °C	30 °C	40 °C	50 °C
H	0.001	38	66	119	190
D	0.001	—	42	80	131
H	0.003	136	185	326	547
D	0.003	36	115	219	371
H	0.005	200	342	643	873
D	0.005	75	167	411	595
H	0.007	265	493	825	1298
D	0.007	116	248	451	864
H	0.009	370	640	1090	1684
D	0.009	123	292	585	1085

(*b*)

T/°C	k_H/dm^3 mol^{-1} s^{-1}	k_D/dm^3 mol^{-1} s^{-1}	k_H/k_D
20	0.40 ± 0.02	0.15 ± 0.02	2.7 ± 0.4
30	0.73 ± 0.02	0.32 ± 0.02	2.3 ± 0.2
40	1.22 ± 0.05	0.62 ± 0.02	2.0 ± 0.2
50	1.87 ± 0.05	1.20 ± 0.02	1.6 ± 0.1

In previous papers[4–6] the products, kinetics and mechanism of the reaction of 1,1,1-trifluoro-2,2-bis(4-nitrophenyl)ethane with alkoxide bases in alcohols have been determined. The first unstable reaction product obtained is the alkene $Ar_2C{=}CF_2$. As a result of fast consecutive addition–elimination reactions, this compound is transformed into the alkoxyalkene $Ar_2C{=}CF(OR)$, before undergoing further transformation into the stable final product, $Ar_2C{=}C(OR)_2$.

Similar results have been reported by Koch *et al.*[7] and Dmowski[8] for the reaction of fluoroethanes with alkoxide ions in alcohols.

Jarczewski *et al.*[9] have reported the kinetics and mechanism of the β-elimination reaction of 1,1,1-trichloro-2,2-bis(4-nitrophenyl)ethane (analogous to fluoroalkane) promoted by TMG in a series of aprotic solvents. The results are interpreted as indicating an $(E1cB)_I$ mechanism for both substrates in acetonitrile solvent and an E2H or mixed $(E1cB)_I$–E2H mechanism in the less polar solvents, tetrahydrofuran and hexane.

Results and Discussion

1,1,1-Trifluoro-2,2-bis(4-nitrophenyl)ethane reacts with TMG in a series of solvents to give only one product, *N*- [bis(dimethylamino)methylene]-1-fluoro-2,2-bis(4-nitrophenyl)ethenylamine. No intermediates were isolated in the reaction mixture.

The reactions were followed spectrophotometrically by monitoring the appearance of the final product. In acetonitrile kinetic curves showed non-exponential behaviour in the first 10–20% of the kinetic run for both protonated and deuteriated compounds. This effect was not observed for the other solvents used.

Calculations of the pseudo-first-order rate constants (k_{obs}) were made by means of the Guggenheim method using only the exponential part of the kinetic curve.

From the dependence of k_{obs} on base concentration the second-order rate constants (k_H, k_D) were calculated. Rate constants for the reaction of $[(O_2N)_2C_6H_4]_2CHCF_3$ with TMG in different solvents are collected in Tables 1–4. The activation parameters for the reaction of Ar_2CHCF_3 with TMG are shown in Table 5.

Table 2 Rate constants and kinetic isotope effects for the reaction of $[(O_2N)_2C_6H_4]_2CHCF_3$ (H) and $[(O_2N)_2C_6H_4]_2CDCF_3$ (D) with TMG in benzonitrile. The initial concentration of the fluoroethane was 5×10^{-5} mol dm^{-3}.

(*a*)

Substrate	[TMG]/mol dm^{-3}	$k_{obs}/10^{-4}$ s^{-1}				
		10 °C	20 °C	30 °C	40 °C	50 °C
H	0.001	—	1.25	1.90	4.22	5.76
D	0.001	—	0.69	1.43	2.30	4.95
H	0.003	1.88	4.10	6.56	11.52	18.04
D	0.003	0.88	2.34	4.84	8.44	15.35
H	0.005	3.03	5.95	10.67	19.20	30.71
D	0.005	1.73	3.72	7.48	14.66	27.25
H	0.007	4.39	8.75	15.28	27.40	44.14
D	0.007	2.23	5.45	11.32	20.84	38.20
H	0.009	5.87	11.32	19.96	35.22	56.14
D	0.009	2.96	6.95	14.11	26.87	48.80
H	0.011	7.20	14.10	24.08	43.18	90.00
D	0.011	4.07	8.44	17.12	32.62	60.45

(*b*)

T/°C	$k_H/10^{-2}$ dm^3 mol^{-1} s^{-1}	$k_D/10^{-2}$ dm^3 mol^{-1} s^{-1}	k_H/k_D
10	6.7 ± 0.2	3.8 ± 0.3	1.8 ± 0.1
20	12.7 ± 0.3	7.8 ± 0.1	1.6 ± 0.1
30	22.2 ± 0.2	15.7 ± 0.3	1.4 ± 0.1
40	39.2 ± 0.3	30.4 ± 0.2	1.3 ± 0.1
50	64.9 ± 0.5	55.5 ± 0.5	1.2 ± 0.1

Table 3 Rate constants and kinetic isotope effects for the reaction of $[(O_2N)_2C_6H_4]_2CHCF_3$ (H) and $[(O_2N)_2C_6H_4]_2CDCF_3$ (D) with TMG in THF. The initial concentration of the fluoroethane was 5×10^{-5} mol dm^{-3}.

(*a*)

Substrate	[TMG]/mol dm^{-3}	$k_{obs}/10^{-4}$ s^{-1}				
		10 °C	20 °C	30 °C	40 °C	50 °C
H	0.004	0.84	1.50	2.69	3.90	6.72
D	0.004	0.38	0.96	1.77	2.82	5.28
H	0.008	1.77	3.03	5.26	8.29	13.28
D	0.008	1.06	2.19	4.18	7.10	11.62
H	0.012	2.65	4.41	7.89	12.74	20.82
D	0.012	1.80	3.76	6.53	11.28	18.12
H	0.016	3.47	6.08	11.09	16.89	27.92
D	0.016	2.53	5.09	9.12	14.97	24.41
H	0.020	4.34	7.79	13.59	21.30	34.93
D	0.020	3.39	6.31	11.32	18.81	31.19

(*b*)

T/°C	$k_H/10^{-2}$ dm^3 mol^{-1} s^{-1}	$k_D/10^{-2}$ dm^3 mol^{-1} s^{-1}	k_H/k_D
10	2.17 ± 0.03	1.87 ± 0.04	1.16 ± 0.05
20	3.91 ± 0.09	3.40 ± 0.08	1.15 ± 0.05
30	6.9 ± 0	6.01 ± 0.07	1.15 ± 0.05
40	10.8 ± 0.1	10.0 ± 0.2	1.09 ± 0.05
50	17.8 ± 0.2	16.2 ± 0.1	1.1 ± 0.1

For all the reactions of Ar_2CHCF_3 promoted by alkoxide[6] and phenolate[10] bases $Ar_2C{=}CF_2$ was isolated as an intermediate, as shown in eqn. (1).

$$Ar_2CHCF_3 + B \xrightarrow{k_f} Ar_2C{=}CF_2 \xrightarrow{k_d} Ar_2C{=}CFB \qquad (1)$$

In the case of the reaction of Ar_2CHCF_3 promoted by TMG derivatives $[R\text{–}N{=}C(NMe_2)_2$ (R = Me or Ph)] and amidines $[R\text{–}N{=}CMe(NMe_2)]$ difluoroalkene $Ar_2C{=}CF_2$ was isolated as a final product.

Table 4 Rate constants and kinetic isotope effects for the reaction of $[(O_2N)_2C_6H_4]_2CHCF_3$ (H) and $[(O_2N)_2C_6H_4]_2CDCF_3$ (D) with TMG in hexane. The initial concentration of the fluoroethane was 5×10^{-5} mol dm^{-3}.

(*a*)

Substrate	[TMG]/mol dm^{-3}	$k_{obs}/10^{-4}$ s^{-1}				
		30 °C	35 °C	40 °C	45 °C	50 °C
H	0.03	1.35	1.65	2.25	3.10	3.85
D	0.03	0.37	0.81	1.10	2.00	3.00
H	0.04	1.85	2.34	3.15	4.25	5.30
D	0.04	0.66	1.20	1.60	2.81	4.01
H	0.05	2.30	2.89	3.85	5.30	6.60
D	0.05	0.95	1.59	2.00	3.51	5.10
H	0.06	2.80	3.50	4.65	6.30	7.50
D	0.06	1.22	1.95	2.85	4.25	6.00

(*b*)

T/°C	$k_H/10^{-3}$ dm^3 mol^{-1} s^{-1}	$k_D/10^{-3}$ dm^3 mol^{-1} s^{-1}	k_H/k_D
30	4.8 ± 0.1	2.8 ± 0.1	1.7 ± 0.1
35	6.1 ± 0.2	3.8 ± 0.1	1.6 ± 0.1
40	7.9 ± 0.3	5.7 ± 0.7	1.4 ± 0.2
45	10.7 ± 0.2	7.5 ± 0.2	1.4 ± 0.1
50	12.9 ± 0.9	10.1 ± 0.3	1.2 ± 0.1

Table 5 Activation parameters for the reaction of 1,1,1-trifluoro-2,2-bis(4-nitrophenyl)ethane with TMG in different solvents (25 °C)

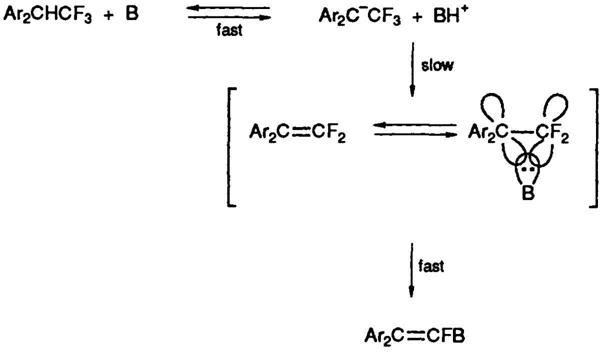
Solvent	Substrate	$\Delta H^{\ddagger}$/kJ mol^{-1}	$-\Delta S^{\ddagger}$/J mol^{-1} K^{-1}	$\Delta G^{\ddagger}$/kJ mol^{-1}
Acetonitrile	H	38.5 ± 1.7	122 ± 1	75.0 ± 1.7
Acetonitrile	D	51.5 ± 0.4	84 ± 1	76.7 ± 0.4
Benzonitrile	H	40.6 ± 0.4	124 ± 1	77.5 ± 0.4
Benzonitrile	D	48.6 ± 0.4	101 ± 1	78.6 ± 0.4
THF	H	37.3 ± 0.4	145 ± 2	80.4 ± 0.8
THF	D	38.5 ± 0.4	142 ± 1	80.9 ± 0.4
Hexane	H	37.3 ± 2.0	168 ± 8	87.2 ± 2.0
Hexane	D	49.9 ± 1.7	130 ± 4	88.4 ± 1.7

An attempt to detect the difluoroalkene in our reaction mixture was not successful. If $Ar_2C{=}CF_2$ is the intermediate in the reaction studied, then the ratio of the rate of its formation to that of its decay determines the possibility of its detection in the reaction mixture.

In a previous paper[3] rate constants (k_d) for the reaction of $Ar_2C{=}CF_2$ with TMG in acetonitrile, benzonitrile, tetrahydrofuran and hexane were determined at 10–50 °C. The appropriate values are: 1.88, 2.68, 2.55 and 1.84 dm^3 mol^{-1} s^{-1}. Rate constants obtained in the recent study (Tables 1–4) allow us to determine the ratio of the rates of decay and formation (k_d/k_f) of $Ar_2C{=}CF_2$, assuming that this compound is an intermediate in the reaction studied. The values of this ratio are: 5 in acetonitrile, 20 in benzonitrile, 65 in THF and 920 in hexane. Theoretical calculations show that when this ratio is 3–5, non-exponential behaviour of the kinetic curve for the first 10–20% of the kinetic run can be observed. This clearly explains why this disturbance is observed only in acetonitrile.

Taking into account the mechanism of the reaction of $Ar_2C{=}CF_2$ with TMG, and of Ar_2CHCF_3 with aliphatic amines[1] and alkoxide bases[6,10] we proposed the reaction mechanism shown in Scheme 1.

The possibility of detecting $Ar_2C{=}CF_2$ in the reaction mixture depends upon the equilibrium constant for addition of amine to the difluoroalkene. In polar solvents the value of this constant is large and, even if the rate constant ratio k_f/k_d [eqn. (1)] formally allows $Ar_2C{=}CF_2$ to exist, this intermediate cannot be detected in the reaction mixture.



Scheme 1

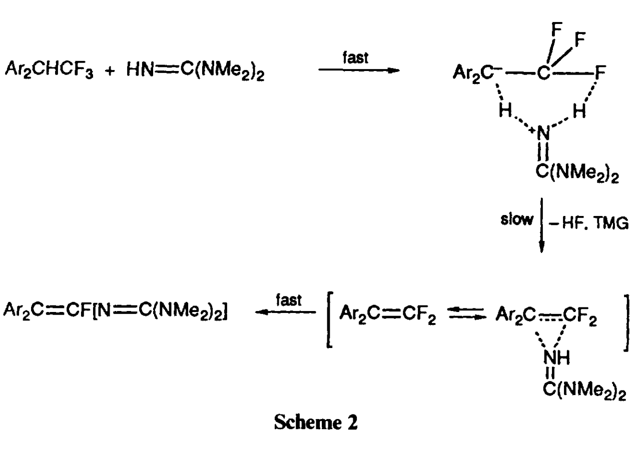
Reported rate constants and activation parameters given in Tables 1–5 refer to the elimination reaction, which is the rate-determining step in the mechanism proposed.

The rate constants k_H (Tables 1–4) show clearly that the elimination reaction is very sensitive towards solvent polarity. When the solvent polarity is increased the rate constants increase rapidly. For the reaction of the chloro analogue Ar_2CHCCl_3 with TMG the ratio of the rate constants in hexane and acetonitrile $k_{AN}/k_{hex} = 8.5$, while for our reaction system $k_{AN}/k_{hex} = 152$. Strong dependence of k_H on solvent polarity was also found for the reaction of Ar_2CHCF_3 with cyclic amines.[1] Such differences in the influence of solvent on the reaction rate for chloro- and fluoro-alkanes can be attributed to the different mechanism of the reaction.

Reaction of the chloroethane exhibits a considerable kinetic deuterium isotope effect: 8.7 in acetonitrile, 5.1 in hexane, while for the fluoroethane the values are 2.3 and 1.71, respectively. For the reaction of Ar_2CHCF_3 with pyrrolidine and piperidine the values of the kinetic isotope effects in acetonitrile are 1.05 and 1.25, respectively.[1] These values show that the rate of the proton abstraction process does not determine the overall rate of reaction. Kinetic isotope effects for the reaction of Ar_2CHCF_3 with TMG are, however, larger than for the reaction with cyclic aliphatic amines. Therefore we can say that the role of proton transfer in the rate-determining step is more important in the reaction with TMG.

The kinetic isotope effect values are characteristic of an elimination reaction of E1cB type, without isotopic exchange.[11] For the reaction system studied we do not observe H–D exchange in the unreacted substrate. However, one can observe such exchange for the reaction with alkoxide bases.

Activation parameters (Table 5) show large $\Delta H^‡$ values and large negative $\Delta S^‡$ values in all solvents. The large negative values of the entropy of activation are compatible with considerable change in the charge distribution between the ground and the transition states. This is consistent with earlier observations[12,13] and similar to the $(E1cB)_{ip}$ or ion-assisted elimination mechanisms of HCN where the appropriate $\Delta S^‡$ values are -55 and -125 J mol^{-1} K^{-1}, respectively. Generally the $\Delta S^‡$ values are more negative for the bimolecular process where BH_2^+ participates in the transition state.



Scheme 2

Activation parameters similar to the values found for the reaction of Ar_2CHCF_3 with cyclic amines allow us to propose a mechanism for the reaction as shown in Scheme 2. The rate-determining step is the elimination of the ion pair (TMG, HF) from the hydrogen-bonded intermediate. Difluoroethene obtained in this step reacts to give the final product.[3]

Reaction of Ar_2CHCF_3 with tetramethylguanidine is a typical example of the multistep process in which not only the rates of individual steps, but also equilibrium processes determine the possibility of the detection of intermediates.

Experimental

1,1,1-Trifluoro-2,2-bis(4-nitrophenyl)ethane and its deuteriated analogue were prepared according to the procedure described previously.[4,6]

1,1,3,3-Tetramethylguanidine (TMG) was dried (KOH) for several days and fractionally distilled under reduced pressure.

The acetonitrile was purified by the method of O'Donnell[14] with a final fractional distillation over P_2O_5. Reagent grade benzonitrile was purified by the method of Coetzee[15] by drying (CaH_2) followed by fractional distillation at reduced pressure. Reagent grade tetrahydrofuran was purified by Paul's[16] procedure. After work-up with NaOH and Al_2O_3, the solvent was fractionally distilled over sodium, with collection of the fraction distilling at 66.0 °C. The hexane was purified by the method of Tonberg and Johnson.[17]

Product Analyses.—1,1,1-Trifluoro-2,2-bis(4-nitrophenyl)ethane (0.5 g) was treated with TMG (2.0 g) in acetonitrile (50 cm^3) by refluxing the reaction mixture for 2 h. The mixture was cooled, poured into water, and the alkene product extracted with diethyl ether. The product, *N*-[bis(dimethylamino)methylene]-1-fluoro-2,2-bis(4-nitrophenyl)ethenylamine $\{(O_2NC_6H_4)_2C{=}CF[N{=}C(NMe_2)_2]\}$, was isolated by evaporation of the solvent, and was recrystallised several times from ethanol. The purity of the product was checked by means of high resolution MS and NMR spectroscopy (Found: M^+, 401.151 89. Calc. for $C_{19}H_{20}FN_5O_4$: *M*, 401.149 79); δ_H 7.3 (4 H, d), 8.5 (4 H, d) and 2.8 (12 H, s). The mass and NMR spectra were measured with JEOL-D-100 and VARIAN-60 spectrometers, respectively.

Kinetic Measurements.—The kinetics of the reaction of Ar_2CHCF_3 with TMG were followed at $\lambda = 430$ nm (AN), 420 nm (THF), 410 nm (BN) and 385 nm (hexane) using a Specord UV–VIS spectrophotometer. The rate constants and activation parameters were calculated by the method described previously.[4–6]

Acknowledgements

Financial support from CPBP 01.19.04.16 is gratefully acknowledged.

References

1 A. Jarczewski, G. Schroeder and M. Dworniczak, *J. Chem. Soc., Perkin Trans. 2*, 1986, 55.
2 K. T. Leffek and U. Maciejewska, *Can. J. Chem.*, 1986, **64**, 2274.
3 A. Jarczewski, G. Schroeder, M. Waligorski and M. Dworniczak, in press.
4 K. T. Leffek and G. Schroeder, *Can. J. Chem.*, 1982, **60**, 1696.
5 K. T. Leffek and G. Schroeder, *Can. J. Chem.*, 1982, **60**, 3077.

6 A. Jarczewski, G. Schroeder, W. Galezowski, K. T. Leffek and U. Maciejewska, *Can. J. Chem.*, 1985, **63**, 576.

7 H. F. Koch, J. G. Koch, N. H. Koch and A. S. Koch, *J. Am. Chem. Soc.*, 1983, **105**, 2388.

8 W. Dmowski, *J. Fluorine Chem.*, 1980, **15**, 299.

9 A. Jarczewski, M. Waligorska and K. T. Leffek, *Can. J. Chem.*, 1985, **63**, 1194.

10 G. Schroeder, *Acta Chim. Hungarica*, 1988, 125; 181.

11 F. G. Bordwell, *Acc. Chem. Res.*, 1972, **5**, 374.

12 M. Albeck, S. Hoz and Z. Rappoport, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1248.

13 Z. Rappoport and E. Shohamy, *J. Chem. Soc. B*, 1971, 2060.

14 J. F. O'Donnell, J. T. Ayers and C. K. Mann, *Anal. Chem.*, 1965, **37**, 1161.

15 J. F. Coetzee and G. R. Padmanabhan, *J. Am. Chem. Soc.*, 1965, **87**, 5005.

16 J. A. Riddick and W. B. Bunger, *Techniques of Organic Chemistry*, Wiley-Interscience, New York, 2nd edn., 1979, vol. II, p. 594.

17 J. A. Riddick and W. B. Bunger, *Techniques of Organic Chemistry*, Wiley-Interscience, New York, 2nd edn., 1979, vol. II, p. 705.

Paper 0/04662K
Received 16*th October* 1990
Accepted 14*th December* 1990