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A theoretical and experimental study of the flash vacuum pyrolysis (FVP) of trifluoromethylpyrazoles

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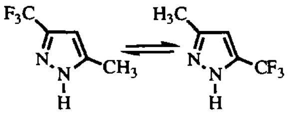
Abstract

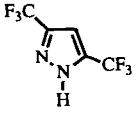
Flash vacuum experiments have been carried out on 3(5)-trifluoromethyl-5(3)-methylpyrazole and 3,5-bis(trifluoromethyl)pyrazole. In both cases, the reaction proceeds with elimination of nitrogen and the formation of complex mixtures of fluorinated olefins and acetylenes. The Arrhenius parameters have been determined and discussed. The first step of the reaction, a pyrazole/pyrazolenine tautomerization process, has been calculated theoretically (STO-3G).

Introduction

Our interest in pyrazole chemistry was focused on the effect of replacing methyl by trifluoromethyl groups. Since the change in electronegativity is very large, their reactivities should be different. In the synthesis of trifluoromethylpyrazoles from fluorinated β-diketones and hydrazine, the intermediate hydroxypyrazolines are sufficiently stabilized to be isolated in a crystalline form [1]. In addition, the solution and gas-phase acid–base properties are very different from the methyl homologues [2]. To complete these studies, we decided to investigate the kinetics of the flash vacuum pyrolytic reactions of 3(5)-trifluoromethyl-5(3)-methylpyrazole (**1**) and 3,5-bis(trifluoromethyl)pyrazole (**2**).



1a **1b**



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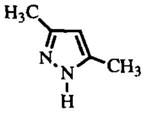

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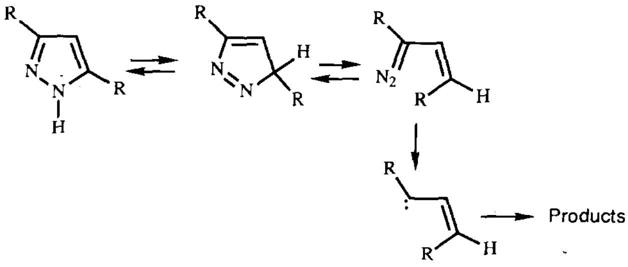


Scheme 1.

As has been established by some of us [3], *N*–H pyrazoles afford nitrogen and unsaturated hydrocarbons under FVP conditions. These reactions begin with a tautomerization process that leads to a 3*H*-pyrazole (pyrazolenine), which isomerizes to a vinyldiazomethane followed by loss of nitrogen to form a vinylcarbene. The nitrogen extrusion is the slowest step of the whole process which is summarized in Scheme 1.

In the case of 3,5-dimethylpyrazole (**3**), the only reaction product is 1,3-pentadiene (**4**). The experiments carried out with deuterated **3** demonstrated that the reaction product is formed by a [1,4] shift of the intermediate vinylcarbene [4].

The comparison of the reaction products and kinetic parameters of the fluorinated and non-fluorinated pyrazoles should give useful information regarding the effect of these substituents on FVP reactions.

Results and discussion

Reactions were carried out in the FVP system previously described [5], with the usual control so that reactions were homogeneous. In all the reactions, the carrier gas was nitrogen unless otherwise indicated. In these experiments with fluorinated derivatives, caution must be taken in view of the rapid deterioration of the quartz tubes.

FVP reactions of pyrazole **1** ($C_5H_5N_2F_3$, M = 150) were carried out between 640 °C and 700 °C and at a pressure of 10^{-2} Torr; they afford mixtures of volatile and solid products. The MS of the volatile products, with a molecular peak at *m/z* 122, corresponds to the loss of nitrogen (M − 28). The solid product was identified as **1**. Reaction products were identified by MS and ^1H NMR spectroscopy as 4,4,4-trifluoro-3-methylbutyne-1 (**5**), 5,5,5-trifluoro-1,3-pentadiene (**6**), 1,4-difluoro-3-enpentyne-1 (**7**) and 5,5,5-trifluoropentyne-2 (**8**). The corresponding kinetic results are gathered in Table 1. The specific rate constants were determined by UV methods measuring the disappearance of **1**.

FVP reactions of pyrazole **2** ($C_5H_2N_2F_6$, M = 204) were carried out under the same conditions. As in the case of **1**, only volatile products and unreacted **2** were detected. MS of the volatile products, *m/z* 176, corresponded to

TABLE 1

Kinetic measurements from FVP of pyrazole **1**[a]

$(T\pm1)$ (°C)	k (s^{-1})
640	11.0 ± 0.6
660	21.9 ± 0.4
680	44 ± 6
700	63 ± 6

[a] $r=0.993$; $E_a=(52.6\pm0.7)$ kcal mol^{-1}; $\log[A\ (s^{-1})]=13.7\pm0.8$.

TABLE 2

Kinetic measurements from FVP of pyrazole **2**[a]

$(T\pm1)$ (°C)	k (s^{-1})
640	5.41 ± 0.01
660	10.5 ± 0.5
680	24 ± 2
700	40 ± 2

[a] $r=0.996$; $E_a=(60.5\pm0.5)$ kcal mol^{-1}; $\log[A\ (s^{-1})]=15.2\pm0.5$.

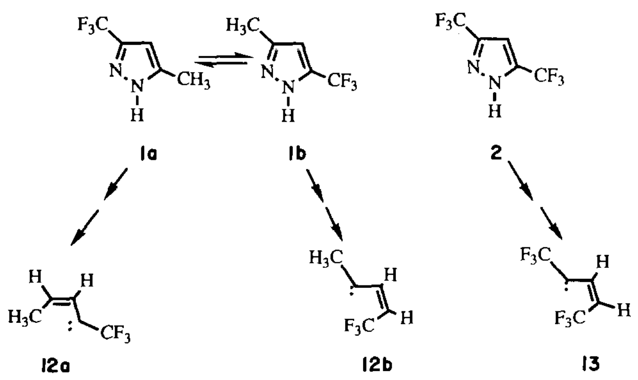
nitrogen extrusion ($M-28$). These products were identified by MS and ^1H NMR spectroscopy as 1,1,1,5,5,5-hexafluoropentyne-2 (**9**), 4,4,4-trifluoro-3-(trifluoromethyl)-butyne-1 (**10**) and 1,4,5,5,5-pentafluoro-3-enpentyne-1 (**11**). The specific rate constants were measured by UV methods, quantifying the disappearance of **2**, and are collected in Table 2.

Although trifluoromethylated pyrazoles lost nitrogen under FVP conditions, as do other *N*–H pyrazoles, the variety of products formed are much more complex and need some special consideration. In both cases with compounds **1** and **2**, reactions products may arise from the mechanism depicted in Scheme 1, through a vinyl carbene. When toluene was used as carrier gas, no bibenzyl was detected; thus, a radical reaction can be excluded.

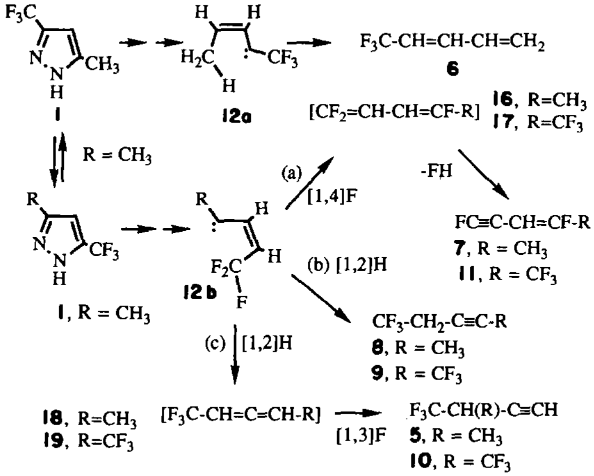
In the case of **1**, two isomeric vinyl carbenes, **12a** and **12b**, can be formed, each one arising from a different tautomer (respectively **1a** and **1b**), while only **13** can be obtained from **2** (Scheme 2).

Looking at the reaction products of compound **1**, one of them, namely **6**, is the equivalent of **4**; it can arise from **12b** by a [1,2] H-shift or from **12a** by a [1,4] H-shift. The [1,4] H-shift is expected to be the preferred route taking into account our previous results [3]. Compounds **8** and **9** may be formed by a [1,2] H-shift from **12b** as in the reactions of pyrazole **14** itself where propyne **15** was the only reaction product [3].

There was no evidence of alkyne formation in reactions of compound **3**, perhaps due to the possibility of a less strained transition state in the [1,4] H-shift. Compounds **7** and **11** could result from hydrogen fluoride



Scheme 2.



Scheme 3.

elimination from 1,1,4-trifluoro-1,3-pentadiene (**16**) and 1,1,4,5,5,5-hexafluoro-1,3-pentadiene (**17**), respectively. Compound **16** may arise from a [1,2] F-shift from **12b** or a [1,4] F-shift from **12a**, whereas **17** may result from [1,2] or [1,4] F-shifts from **13**. Hydrogen halide elimination is a well-known thermal reaction of halogenated compounds [6]. There is some evidence of [1,2] F-shifts from a trifluoromethyl group to a carbene [6]. *Ab initio* calculations indicate that the barrier to a [1,2] F-shift in fluorovinylidene is about 40.4 kcal mol^{-1} [7]. This value is lower than the activation energy of the pryolysis reaction, hence a fluorine migration is possible in the present case, even a [1,4] F-shift.

The origin of compounds **5** and **10** (Scheme 3) can only be explained through the intermediacy of allenes: 1,1,1-trifluoro-2,3-pentadiene (**18**) and 1,1,1,5,5,5-hexafluoro-2,3-pentadiene (**19**), respectively. Allene/acetylene isomerization is known to occur with an activation energy of 61.2 kcal mol^{-1}

for the direct reaction [8], but other authors propose that the reaction takes place with the intermediacy of a cyclopropene and a vinyl carbene [9] which is present in this reaction. The fact that there is no equivalent of compounds **5** and **10** in the reaction of **3** may be due to the fact that [1,3] CF_3-shifts are comparable to [1,3] H-shifts, both being lower than the [1,3] CH_3-shifts. These results agree with some experimental observations in the FVP of isoxazoles where there is a CF_3 migration in the azirine to form a nitrile [10]. According to Woodward–Hoffmann's rules, a [1,3] CH_3-suprafacial-shift is energetically forbidden unless inversion of the migrating group takes place [11], this process being of higher energy than an H-shift. However, it is possible for [1,3] CF_3-shifts to be thermally allowed. The difference in electronegativity between a hydrocarbon derivative, such as a CH_3, and the CF_3 group, makes it possible to include this last system in Type III AX of Epiotis' classification [12], and for these systems [1,3] shifts are allowed. This could be the reason why this reaction is absent in the FVP of 3,5-dimethylpyrazole (**3**) [3].

Once the reaction products have been rationalized, the analysis of the experimental activation energies can proceed. Table 3 contains the values for these reactions, including the already reported values for 3,5-dimethylpyrazole (**3**) and for pyrazole **1** itself [3].

We have carried out STO-3G *ab initio* calculations [13] of the energies involved in the first step of the reaction, i.e. the tautomerization process to form the non-aromatic pyrazolenines. The results are shown in Table 4. The $\Delta\Delta E$ values are probably underestimated since a 6-31G//STO-3G calculation on the 3,5-dimethylpyrazole/3,5-dimethylpyrazolenine pair yields a difference of 36.34 kcal mol^{-1}; nevertheless, the relative values should be correct.

As can be seen, there is no relation between the electronegativity of the substituent on the pyrazole ring and the difference in energy between aromatic and non-aromatic tautomers; there is an average value of *c.* 18.3 ± 0.5 kcal mol^{-1}. These results confirm that even with trifluoromethyl substituents the determinant step is the formation of the vinyl carbene. Calculations also showed that tautomer **1a** is more stable than **1b** by 2 kcal mol^{-1}.

An examination of the results listed in Table 3 shows that there is not a simple relationship between the substitution pattern and the Arrhenius parameters. The activation energy falls when hydrogen atoms are replaced

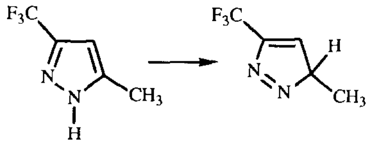
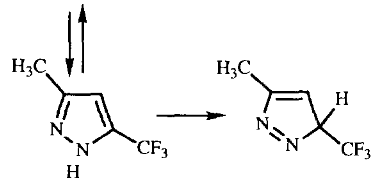
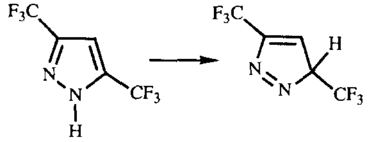
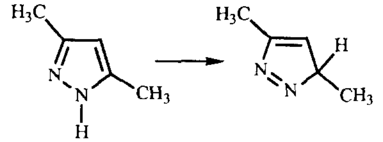
TABLE 3

Arrhenius parameters for the FVP experiments of pyrazoles **1**, **2**, **3** and **14**

Compound	E_a (kcal mol^{-1})	log[A (s^{-1})]
1	52.6 ± 0.7	13.7 ± 0.8
2	60.5 ± 0.5	15.2 ± 0.5
3	66.9 ± 0.7	15.1 ± 0.5
14	71.3 ± 0.3	15.44 ± 0.03

TABLE 4

Energy differences (kcal mol^{-1}) between pyrazoles and pyrazolenines

Reaction	$\Delta\Delta E$
 **1a**	18.72
 **1b**	17.78 (with regard to **1a**: 19.84)
 **2**	18.72
 **3**	18.44

by electron-donor groups, such as methyl groups (from 71.3 to 66.9 kcal mol^{-1}). When a methyl group of compound **3** is replaced by an electron-withdrawing trifluoromethyl group, as in compound **1**, there is a lowering of about 13 kcal mol^{-1} in the activation energy, but when the second CH_3 group is replaced by another CF_3 (**1** → **2**) the energy increases by 8 kcal mol^{-1}. Perhaps the influence of trifluoromethyl groups is stronger in the vinyl carbenes than in the pyrazoles.

Experimental

Methods and materials

UV spectra were determined using a Shimadzu 260 spectrophotometer; mass spectra were recorded using a Finnigan 3300 spectrometer with a 1500 INCOS data system; ^1H NMR spectra were recorded either on a Bruker WPSY

(80 MHz) spectrometer (IQUIOS, Rosario, R. Argentina) (compounds **5**, **6**, **7** and **8**) or a Bruker AC200 (200 MHz) spectrometer (UNED, Madrid, Spain) (compounds **5**, **9**, **10** and **11**) (chemical shifts in δ and coupling constants in Hz). All solvents were of analytical grade. Compounds **1** and **2** were prepared as previously described [2].

FVP reactions of compound 1

Due to the fact that the reaction products are volatile and unstable, their structures were determined by MS and ^{1}H NMR spectroscopy on the mixture. MS (*m/z*) (%): 122 (56.60; 121 (15.2); 107 (3.4); 103 (11.7); 102 (20.7); 101 (30.0); 95 (5.8); 86 (33.4); 84 (57.5); 69 (7.1); 44 (14.5); 40 (10.6); and 32 (100.0). ^{1}H NMR data are listed in Table 5.

Kinetic measurements were carried out by UV methods, quantifying the presence of **1** (λ_{max}, MeOH, 218.2 nm).

FVP reactions of compound 2

As in the case of compound **1**, the product structures were determined by MS and ^{1}H NMR spectroscopy on the reaction mixtures. MS (*m/z*) (%): 176 (1.7); 156 (54.2); 137 (44.8); 117 (5.3); 106 (32.2); 93 (2.9); 87 (18.0); 75 (5.2); 69 (27.5); 56 (11.8); and 44 (100). ^{1}H NMR data are reported in Table 5.

The kinetic experiments followed the same procedure as above by following the quantity of **2** by UV methods (λ_{max}, MeOH, 205.4 nm).

Samples for ^{1}H NMR spectral investigation were collected as follows: 0.5 ml $CDCl_3$ was introduced into the reaction trap at the beginning of the experiment and cooled with liquid air. Once the reaction had ceased, the

TABLE 5

^{1}H NMR data of FVP products (chemical shifts δ in ppm and coupling constants in Hz)[a] (internal reference compound TMS)

CF_3–CH(CH_3)–C≡CH (**5**) M=122	CH(sp)=2.00 (s); CH(sp^3)=2.98 (q,q); $^4J_{HH}=2.5$, $^4J_{HF}=9.7$, $^4J_{HH}=2.5$; $CH_3=1.81$ (d)
H_2C=CH–CH=CH–CF_3 (**6**) M=122	$CH_2=5.10$ (m); CH(2)=5.10 (m); CH(3)=6.40 (m); CH(4)=6.75 (m)
FC≡C–CH=CF–CH_3 (**7**) M=102	CH=5.10 (m); $CH_3=1.78$ (d,d); $^4J_{HF}=7.4$
F_3C–CH_2–C≡C–CH_3 (**8**) M=122	$CH_2=5.10$ (m); $CH_3=1.79$ (s); $^4J_{HH}$(allylic)=3.4
F_3C–CH_2–C≡C–CF_3 (**9**) M=176	$CH_2=5.04$ (q); $^4J_{HF}=2.9$
F_3C–CH(CF_3)–C≡CH (**10**) M=176	CH(sp)=6.02 (q); $^4J_{HF}=4.6$; CH(sp^3)=2.2 (s)
F_3C–CF=CH–C≡CF (**11**) M=156	CH=4.70 (d,d,q); $^4J_{HF}=22.5$, $^5J_{HF}=1.4$, $^4J_{HF}$(allylic)=2.7

[a] s: singlet, d: doublet, q: quartet, m: multiplet.

trap with $CDCl_3$ containing the reaction products was sealed and allowed to reach room temperature. The NMR spectra were then recorded.

Theoretical calculations

The total energies of the pyrazoles and pyrazolenines have been calculated at the STO-3G level [13] after complete optimization of the geometry at the same level (STO-3G//STO-3G calculations; only the planarity of the aromatic pyrazole ring was assumed). All the calculations were carried out with the Hondo package [14] on the IBM 4381 computer of the CC/UAM. The pyrazolenines adopt an envelope conformation with calculated N=N and C=C bond lengths of 1.273 and 1.315 Å, respectively. These values agree with those reported for pyrazolenines (X-ray determinations): 1.257–1.265 and 1.345–1.356 Å, respectively, taking into account that the reported structures are conjugated polycyclic compounds [15, 16].

The calculated energies and dipole moments of the compounds of Table 4 are: **1a** (−591.53309 hartrees, $\mu = 4.28$ D) (the corresponding pyrazolenine, −591.50327 hartrees, $\mu = 3.31$ D); **1b** (−591.52981 hartrees, $\mu = 0.26$ D) (the corresponding pyrazolenine, −591.50148 hartrees, $\mu = 3.85$ D); **2** (−883.90773 hartrees, $\mu = 2.24$ D) (the corresponding pyrazolenine, −883.87836 hartrees, $\mu = 3.10$ D); **3** (−299.15316 hartrees, $\mu = 2.27$ D) (the corresponding pyrazolenine, −299.12405 hartrees, $\mu = 3.20$ D).

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