Flash Vacuum Pyrolysis of Pyrazoles as an Alternative Way to Study Vinylcarbenes

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Flash vacuum pyrolysis (FVP) reactions of 3,5-diphenylpyrazole (**1**) and 3(5)-methyl-5(3)-phenylpyrazole (**2**) were carried out. The reaction products expected for nitrogen extrusion were formed through different rearrangements in the vinylcarbene intermediate. Kinetic parameters for nitrogen extrusion from **1** are reported. To show that FVP reactions of pyrazoles are useful to obtain vinylcarbenes, the reactions of other pyrazoles previously studied are also discussed.

Introduction

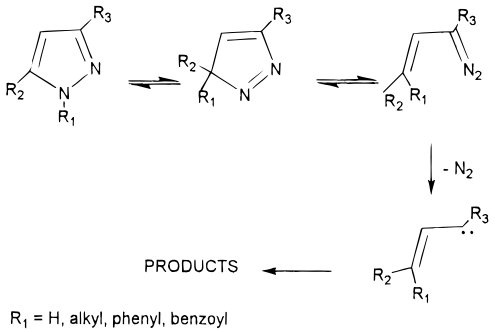
Among five-membered nitrogen heterocycles, pyrazoles have drawn the attention of many chemists due to their many possibilities of study. Searching in the literature, it is possible to see articles concerning spectroscopy, theoretical calculations, organometallic chemistry using pyrazoles as ligands, synthesis in particular of bioactive compounds, reactions in different media and with different partners, etc.[1] On the other hand, studies on their thermal reactions are scarce due to their high stability. For this reason most of these thermal studies are carried out using high energy systems such as FVP (flash vacuum pyrolysis).[2]

It is in this field that we are carrying out our studies on heterocyclic chemistry. In the case of pyrazoles, we found that their thermal reactions may be classified into two types, that is (a) reactions with retention of nitrogen, and (b) reactions with nitrogen extrusion.

Reactions of type a are typical of *N*-substituted compounds, and the kind of reaction depends on the N1 substituent. For example, pyrazole elimination occurs if this is an alkyl group with β H,[3] isomerizations occur if it is aromatic,[4a] benzoyl,[4b] or adamantyl,[4c] and radical formation occurs if it is a benzoyl group[4b] or if the compound is a polyazolylmethane.[5]

On the other hand, reactions of type b are exclusive in the case of NH pyrazoles[6,7] and compete with other reactions[3,4a,b] in *N*-substituted pyrazoles.

Scheme 1



For nitrogen extrusion reactions, we have proposed a mechanism involving several steps through a vinylcarbene intermediate (Scheme 1).[6] The mechanism was partly based on the reactions of 3*H*-pyrazoles[8] and vinyldiazo compounds[9,10] described by other authors.

Vinylcarbenes are normally produced by ring opening of cyclopropenes (thermally and photochemically) and from vinyl-diazo compounds (photochemically).[11] The problem with these last compounds is that in thermal reactions, two competitive reactions are present, that is, cyclization to a 3*H*-pyrazole and nitrogen extrusion, the first one being the lower in energy, as has been demonstrated by Pincock et al.[10]

From these evidences, and our experience in kinetic measurements in FVP reactions, we thought that gas-phase thermal reactions of pyrazoles (*N*-unsubstituted to avoid competitive reactions) may provide information on two obscure topics in this field: (i) the influence of different substituents on the activation energy of vinylcarbenes, and (ii) the participation of different substituents in vinylcarbene rearrangement.

With this in mind, we report on the FVP reactions of 3,5-diphenyl (**1**) and 3(5)-methyl-5(3)-phenylpyrazole (**2**) and the kinetic measurements of **1** and make some considerations on the rearrangements of vinylcarbenes.

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(2) See for example: Brown, R. F. C., Eastwood, F. W., Fallon, G. D., Lee, S. C., McGeary, R. P. *Aust. J. Chem.* **1994**, *47*, 991.

(3) (a) Pérez, J. D., Phagouapé, L. M. *Int. J. Chem. Kinet.* **1988**, *19*, 571. (b) *Ibid.* **1987**, 217. (c) *Ibid.* **1988**, *20*, 603. (d) *Ibid.* **1989**, *21*, 227.

(4) (a) Pérez, J. D., Yranzo, G. I., Phagouapé, L. M. *Bull. Soc. Chim. Fr.* **1986**, 129. (b) Pérez, J. D., Yranzo, G. I. *J. Anal. Appl. Pyrol.* **1989**, *16*, 165. (c) Yranzo, G. I.; Pérez, J. D.; Ferraris, M. A.; Claramunt, R. M.; Cabildo, P.; Sanz, D.; Elguero, J. *Anal. Quimica Int. Ed.* **1996**, *92*, 3.

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Scheme 2

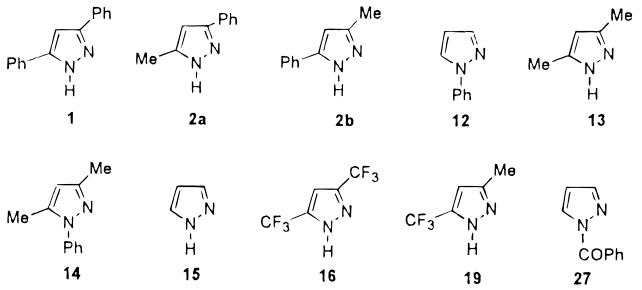


Table 1. FVP of 3,5 Diphenylpyrazole (1)

T, °C	% **1**	% **3**	% **4**	k (s^{-1})[a]
640	80	–	20	25.0 ± 0.8
680	30	–	70	99 ± 1
740	7	9	84	365 ± 1
820	–	78	12	

[a] Average over at least four determinations, contact times from 10^{-1} to 10^{-2} s and pressures from 0.2 to 0.1 torr.

Scheme 3

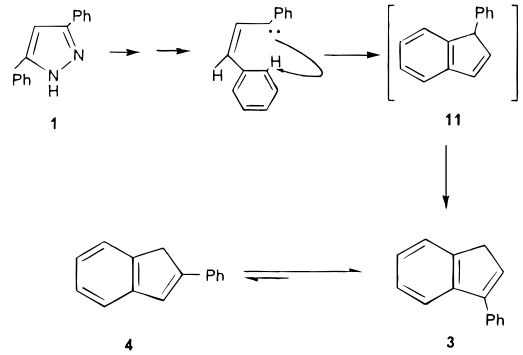


Table 2. FVP of 3(5)-Methyl-5(3)-phenyl Pyrazole (2)

T, °C	% **2**	% **5**	% **6**	% **7**	% **8**	% **9**	% others (10 included)
660	50	13	20	2	2	5	8
700	18	15	35	5	6	17	4
750	5	3	48	11	5	24	4

Results

The pyrazoles discussed in this work are represented in Scheme 2.

FVP Reactions of 3,5-Diphenylpyrazole (1). The reactions were carried out between 640 and 820 °C. Reaction products as well as reaction conditions are reported in Table 1 and Scheme 3.

The isolated reaction products are 3-phenylindene (**3**) and 2-phenylindene (**4**). These two indenes arise from the expected nitrogen extrusion reaction. No traces of other products were detected.

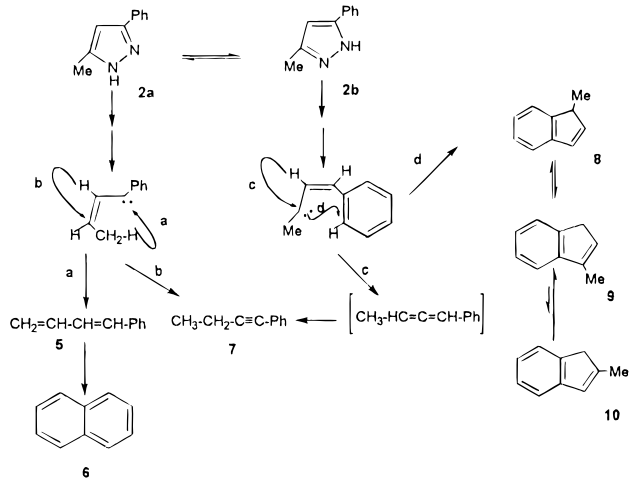
FVP Reactions of 3(5)-Methyl-5(3)-phenylpyrazole (2). The reactions were carried out between 660 and 750 °C. The reaction products and experimental conditions are shown in Table 2 and Scheme 4.

It is interesting to note that the reaction products isolated in these reactions (**5**−**10**) are isomers arising from nitrogen extrusion reactions, like in the case of **1**. As it will be discussed later, they are formed from the two different tautomers present in pyrazole **2**.

Discussion

In Scheme 3, 1-phenylindene (**11**) is represented as a nondetected product, but it is the indene expected for carbene insertion into an aryl C−H bond. Isomerization of 1-phenylindene to 3-phenylindene which is in equilibrium with 2-phenylindene is a well-known thermal reaction.[12] Table 1 shows the different amounts of **3** and **4** at different temperatures; it is clear that the thermodynamically controlled product is 3-phenylindene (**3**).

Scheme 4



It is worth mentioning that this cyclization reaction to indene was already reported in the FVP of 1-phenylpyrazole (**12**), where nitrogen extrusion is of higher energy than isomerization.[4a] It should also be mentioned that no alkyne isomer was detected at any temperature in that study, which a priori precludes an alkyne precursor for the phenylindenes.

As mentioned above, several products were isolated or detected in reactions of pyrazole **2**. As in other asymmetric pyrazoles,[7] two tautomers are present [3-phenyl-5-methylpyrazole (**2a**) and 3-methyl-5-phenylpyrazole (**2b**)],[13] and two different intermediates arise from them. These two vinylcarbenes and the different pathways that afford the reaction products are described in Scheme 4.

One of the tautomers, **2a**, is responsible for the formation of 1-phenylbutadiene (**5**) through a [1,4] hydrogen shift, as was already proposed for 3,5-dimethylpyrazole (**13**).[14] Cyclization of compound **5** to naphthalene (**6**) has been described[15] and it is confirmed in the present study because the amount of **6** increased as the temperature was raised, and 1-phenylbutadiene concentration decreased (see Table 2). Compound **6** was also found in reactions of 1-phenyl-3,5-dimethylpyrazole (**14**) at higher temperatures than occur for isomerization.[4a]

The intermediate arising from the other tautomer (**2b**, Scheme 4) leads to two different reactions: insertion into a aryl C−H bond and hydrogen shift. In reactions of compound **2**, 1-methylindene (**8**), 3-methylindene (**9**), and 2-methylindene (**10**) were found, **9** being the most abundant at higher temperatures as shown in Table 2. The fact that in these reactions the three isomers are present may be attributed to the lower migration ability of the methyl group compared with the phenyl group.[12] Concerning the hydrogen shift, 1-phenyl-1-butyne (**7**) may

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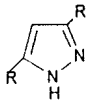
(13) Aguilar-Parrilla, F., Cativiela, C., Díaz de Villegas, M. D., Elguero, J., Foces-Foces, C., García, J. I., Cano, F. H., Limbach, H. H., Smith, J. A. S., Toiron, C. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1737.
(14) Pérez, J. D., Yranzo, G. I. *J. Org. Chem.* **1982**, *47*, 2221.
(15) Badger, G.M., Spotswood, T. N. *J. Chem. Soc.* **1959**, 1635.

Table 3. Kinetic Parameters for Nitrogen Extrusion from Pyrazoles



R	pyrazole	E_a (kJ/mol)	log A (s^{-1})
H	15	298 ± 1	15.44 ± 0.03
CH_3	13	280 ± 3	15.1 ± 0.5
CF_3	16	253 ± 2	15.2 ± 0.5
C_6H_5	1	205 ± 3	13.1 ± 0.1

be formed from one of these two reactions: [1,2] hydrogen shift to afford an allene and then [1,3] hydrogen shift (route c in Scheme 4) or a direct [1,2] hydrogen shift in the vinylcarbene (route b in Scheme 4). If the allene were formed, two different products should arise from [1,3] hydrogen shift, which is not the case. No products arising from [1,3] phenyl nor methyl group migrations were detected in these reactions, as happened in other pyrazoles previously reported.[4a,6]

Influence of Different Substituents on the Activation Energy of Vinylcarbene. We list in Table 3 the kinetic parameters of pyrazole (**15**),[6] **13**,[6] 3,5-bis-(trifluoromethyl)pyrazole (**16**),[7] and **1** in order to compare the activation energies of these reactions and establish the influence of the different substituents on them.

The measured parameters show that the reaction is sensitive to substituent effect. Pincock et al.[10] have reported the activation parameters of thermal reactions of some phenyl-substituted vinyldiazomethanes with different substituents on the phenyl rings. These authors measured the two competitive reactions: nitrogen extrusion and cyclization to cyclopropene. Their results showed that both electron-donating and electron-withdrawing groups increase the reaction constant (i.e. lower the energy of activation). Inspection of Table 3 shows that the results we describe agree with theirs, where methyl and trifluoromethyl groups lower the E_a compared with hydrogen.

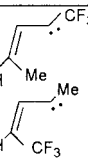
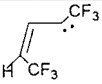
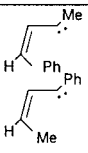
To check the possibility of a change in the mechanism with *C*-phenyl pyrazoles, the ab initio caculations of the first step (isomerization to 3*H*-pyrazole with concomitant loss of aromaticity) previously carried out for pyrazoles **13** and **16** were also taken into account.[7] Those results showed that there was no important change so the slowest step was assumed to be the same, i.e. nitrogen extrusion from the vinyldiazo compound (Scheme 1). If there is no change with CF_3, then no change can be expected with the phenyl group.

Examination of Table 3 also reveals the lower log *A* value for reactions of pyrazole **1** compared with the other pyrazoles, which have almost the same value within experimental error. This fact may be caused by a loss of free rotation of the phenyl group to stabilize the transition state, something related to neighboring group assistance.

Participation of the Different Substituents in Vinylcarbene Rearrangement. The different vinylcarbenes studied are described in Table 4.

First, we will discuss the case of the unsubstituted vinylcarbene, arising from **15**. The only reaction product was propyne (**17**). This compound may be formed through a [1,2] hydrogen shift to the carbene carbon to form an allene (which was not detected) and then a [1,3] hydrogen shift to afford **17.** It has been previously proposed that

Table 4. Different Thermal Reactions of Vinylcarbenes from Pyrazoles

Pyrazole	Vinylcarbene	Reaction	Reference
15		1,2H shift	6
13		1,4H shift	6
19		1,4H shift 1,4F shift 1,3CF_3 shift (in allene) 1,4H shift	7
16		1,4F shift 1,2H shift 1,3CF_3 shift (in allene)	7
27		addition to CO	4b
1		insertion into aromatic C-H	this work
2		1,4H shift 1,2H shift insertion into aromatic C-H	this work

the reaction allene → acetylene takes place through a vinylcarbene.[16]

In the reactions of **13**, the only reaction product was 1,3-pentadiene (**18**). In this case, the product may be formed by two alternative routes: a [1,4] or a [1,2] hydrogen shift. Reactions of **13**-d_1 showed that the product was formed through a [1,4] hydrogen shift.[14] It is important to remark that no product arising from a possible allene was detected, which supports the direct formation of **17** from the carbene.

Continuing the analysis, we will examine the case of trifluoromethylated carbenes. As in the case of **2**, two different intermediates may be formed from the asymmetric compound 3(5)methyl-5(3)-(trifluoromethyl)pyrazole (**19**) and only one from the symmetric of **16** as in **1**, In the case of **16**, 5,5,5-trifluoro-1,3-pentadiene (**20**) was proposed to arise from a [1,4] hydrogen shift as in reactions of **13**. Besides, the other products formed from **19** and the ones from the symmetric one, **16**, may be explained as arising from reactions from similar intermediates. Compounds 1,5,6,6,6-pentafluoro-4-ene-hexyne-1 (**21**) and 1,5-difluoro-4-ene-hexyne-1 (**22**) are proposed[7] to arise from hydrogen fluoride elimination from the diene formed through a [1,4] fluorine shift to the carbene atom. Both reactions are known in fluorinated compounds.[17,18] Furthermore, 5,5,5-trifluoropentyne-2 (**23**) and 1,1,1,5,5,5-hexafluoropentyne-2 (**24**) may be

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(17) Chambers, R. D. *Fluorine in Organic Chemistry*; John Wiley & Sons: New York, 1973; pp 109 and 130.
(18) (a) Holmes, B. E.; Rakestraw, D. J. *J. Phys. Chem.* **1992**, *96*, 2210. (b) So, S. P., *J. Phys. Chem.* **1993**, *97*, 11908. (c) Honjou, N.; Pakansky, J.; Yoshimine, M. *J. Mol. Struct. (THEOCHEM)* **1994**, *312*, 23.

formed from a direct [1,2] hydrogen shift to a sp^2 carbon or through a [1,3] hydrogen shift in the undetected allene. On the other hand, 3-(trifluoromethyl)butyne-1 (**25**) and 3-(trifluoromethyl)-4,4,4-trifluorobutyne-1 (**26**) are undoubtedly formed from the undetected allene through a [1,3] CF_3 shift.

It is known that methyl groups have poor migration ability,[12] and probably [1,3] shifts of trifluoromethyl groups are comparable to [1,3] hydrogen shifts, both being of lower energy than those of the methyl groups. This trifluoromethyl group shift was also detected in some thermal reactions of isoxazoles.[19]

Nitrogen extrusion reactions from 1-benzoylpyrazole (**27**) should also be considered. FVP reactions of **27** show three competitive ways, all of them taking place at the same reaction temperature, indicating that they have similar energies: isomerization, radical fission, and nitrogen extrusion.[4b] Of these reactions, the one important for our present purpose is nitrogen extrusion, affording 2-phenylfuran (**28**). This is an interesting result because it indicates that addition to a carbonyl bond is exclusive over H shift and insertion into Csp^2-H bond.

Conclusion

The fact that FVP reactions of pyrazoles may be used to study vinylcarbenes arising from vinyldiazo compounds should be remarked. This alternative opens a new way to study these intermediates, considering that synthesis of NH pyrazoles is easier than that of the corresponding vinyldiazo isomer and that no competitive reactions are present in thermal studies.

Some conclusions on the thermal reactions of vinylcarbenes can also be drawn:

(1) With at least two aliphatic substituents, the lower energy reaction is a hydrogen shift. (2) With at least two aromatic substituents, insertion into an aryl C−H bond is the lower energy reaction. (3) With asymmetric substituents (aliphatic and aromatic), a hydrogen shift as well as insertion into an aryl C−H bond are competitive reactions, which may be evidence that at least two substituents of the same kind should be present to get a selective reaction. (4) In fluorinated vinylcarbenes, a hydrogen shift is of similar energy as fluorine and CF_3 shifts. (5) In vinylcarbenes with a carbonyl bond, if the geometry is optimum, the only reaction is addition to the carbonyl bond; neither insertion nor hydrogen shifts are competitive reactions.

Experimental Section

General. Reactions were carried out in a Vycor glass flash vacuum thermolysis equipment, using a GAYNOR PRDH temperature controller and a Thermolyne 21100 furnace. Oxygen free dry nitrogen or a nitrogen/toluene mixture was used as carrier gas. Products were trapped at the liquid air temperature, extracted with the appropriate solvent, and submitted to the different analyses or separation techniques. Samples to be pyrolyzed were 30−50 mg. Contact times were 10^{-2} s, and pressures were 0.2 to 0.1 Torr. Column chromatography and TLC were performed on silica gel.

FVP of 1. Compound **1** was prepared as described in the literature.[20] After the reaction was finished, reaction products were separated by column chromatography (petroleum ether) and then submitted to spectroscopy, affording the following data. Compound **3**: ^{1}H NMR (Cl_4C), δ (ppm) 3.50 (2H, d, J = 2 Hz), 6.65 (1H, t, J = 2 Hz), 7.50 (9H, m). MS m/z (relative intensity) 192 (M^+, 100), 165 (18), 115 (8). These results agreed with those previously reported for **3**.[21] Compound **4**: ^{1}H NMR (Cl_4C), δ (ppm) 3.75 (2H, s), 6.90−7.60 (10H, m).[22] MS m/z (relative intensity) 192 (M^+, 100), 165 (13), 115 (5). Kinetic measurements were done with ^{1}H NMR. After the reaction was finished, the entire crude reaction mixture was extracted with CCl_4 and suitably diluted for ^{1}H NMR measurement. After choosing a proton signal for **1**, **3**, and **4**, the total amount was taken as C_o (100%), and then the percentage of **1** was calculated. These ^{1}H NMR experiments were carried out in CCl_4 solution with a capillary tube filled with acetone-d_6 inside the NMR tube.

FVP of 2. Compound **2** was synthesized as described in the literature.[20] The FVP reaction crude was submitted to column chromatography (petroleum ether and petroleum ether:chloroform, 60:40), and the different isolated products afforded the following spectral data. Compound **5**: ^{1}H NMR (DMSO-d_6) δ (ppm) 5.70 (2H, m), 7.10 (3H, m), 7.30−7.90 (5H, m). These results agree with previous ones.[23] Compound **6** was identified by comparison with an authentic sample. ^{1}H NMR (DMSO-d_6), δ (ppm) 7.65 (4H, m), 8.05 (4H, m). Compound **7**: ^{1}H NMR (DMSO-d_6), δ (ppm) 1.27 (3H, t, J = 8 Hz), 2.45 (2H, q, J = 8 Hz), 7.10−7.80 (5H, m).[24] IR (NaBr) 2259 cm^{-1} (C≡C). Compound **8**: ^{1}H NMR (DMSO-d_6), δ (ppm) 1.33 (3H, d, J = 7 Hz), 3.15 (1H, q, J = 7 Hz), 6.15 (2H, dd, J = 2 and 6 Hz), 7.10 (4H, m).[25] MS m/z (relative intensity) 130 (M^+, 100). Compound **9**: ^{1}H NMR (DMSO-d_6) δ (ppm) 2.25 (3H, s), 3.35 (2H, m), 6.38 (1H, m), 7.20−7.50 (4H, m);[25] MS m/z (relative intensity) 130 (M^+, 100). Compound **10**: ^{1}H NMR (DMSO-d_6) δ (ppm) 2.18 (3H, s), 3.30 (2H, s), 6.50 (1H, s), 7.10−7.40 (4H, m);[25] MS (relative intensity) 130 (M^+, 100).

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