Studies of Thermal Rearrangements of Methyl 3-Alkyl-3-methyl-3*H*-pyrazole-5-carboxylates. Concerted, Stepwise, and Unclassified Mechanisms

Elizabeth A. Jefferson and John Warkentin*

Department of Chemistry, McMaster University, Hamilton, Ontario, L8S 4M1 Canada

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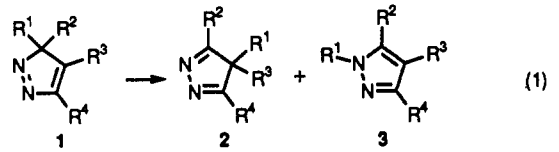
Studies of the thermal rearrangements of five 3*H*-pyrazoles are described, in which the migrating groups were methoxymethyl, *tert*-butyl, 1-adamantyl, *p*-methoxybenzyl, and benzyl. On the basis of reaction products, rearrangement of the (methoxymethyl)pyrazole in benzene, dichloromethane, and methanol at room temperature occurs by a stepwise mechanism, involving discrete ion-pair intermediates. Observed first-order rate constants, for the rearrangement of four of the 3*H*-pyrazoles in benzene-d_6 and acetone-d_6 at higher temperatures, were determined. The *tert*-butyl compound also rearranges by a stepwise mechanism in benzene-d_6, acetone-d_6, and methanol-d_4 based on the fact that isobutene and *tert*-butyl methyl ether (in methanol) are coproducts of rearrangement. The mechanism of rearrangement of the adamantyl and methoxybenzyl systems, in both benzene-d_6 and acetone-d_6 solvents, is ambiguous, the distinction between stepwise, with tight ion-pair intermediates, and concerted, with some charge separation, being unclear. However, both afforded a methyl ether in low yield during rearrangement in methanol solvent, which suggests a stepwise, ion-pair mechanism for rearrangement in that medium. No methanolysis product could be detected from the rearrangement of the benzyl compound in methanol, which suggests concerted rearrangement. Additional evidence that it rearranges by a concerted mechanism is the fact that it affords only one pyrazole product, whereas the others afford two or more.

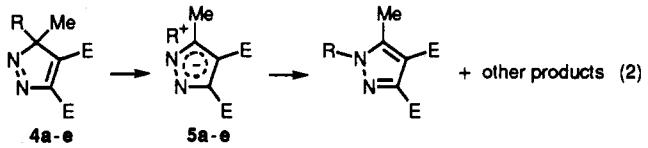
Introduction

Studies of the thermal rearrangements of several 3*H*-pyrazoles led to the conclusion that rearrangement occurs via competitive [1,5]-sigmatropic shifts of an alkyl substituent from the sp^3-hybridized ring carbon center.[1] In general, according to eq 1, 3*H*-pyrazole **1** affords 4*H*-pyrazole **2** and 1*H*-pyrazole **3** by clockwise and counterclockwise [1,5]-sigmatropic migrations of R^1, respectively. According to Woodward–Hoffmann orbital symmetry theory, these rearrangements are thermally allowed processes involving 6π-electron transition states.[2] The migrating group remains continuously and covalently bonded to the rest of the molecule as transfer from one ring atom to another proceeds.



1 2 3 (1)

We recently reported exceptions to the above generality; some dimethyl 3-alkyl-3-methyl-3*H*-pyrazole-4,5-dicarboxylates (**4a–e**) undergo thermal rearrangement by a stepwise mechanism involving ion-pair intermediates **5a–e** rather than by a concerted process involving [1,5]-sigmatropic shifts of substituent R (eq 2).[3] Evidence in support of such a mechanism came from product studies, from structure–reactivity data, and from observation of trapping of the migrating group by methanol. The R substituents of 3*H*-pyrazoles **4a–e** are known to form cations readily in solvolysis reactions of R–X (X = halogen).[4] Presumably, these 3*H*-pyrazoles undergo stepwise rearrangement because the migrating groups are relatively stable in cationic form and because the pyrazole nucleus, substituted with two methoxycarbonyl groups, is relatively stable in anionic form as an aromatic species.



4a-e **5a-e**

E = CO_2Me

a, R = $CHPh_2$; **b**, R = CH_2OMe; **c**, R = *t*-Bu; **d**, R = 1-adamantyl; **e**, R = *p*-$CH_2C_6H_4OMe$

In contrast to the rearrangements of **4a–e**, dimethyl 3-alkyl-3-methyl-3*H*-pyrazole-4,5-dicarboxylates, where alkyl = Me and Et, rearrange by concerted [1,5]-sigmatropic shifts.[5] Similarly, 3*H*-pyrazole **6**, substituted with only one methoxycarbonyl substituent, was reported to

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(1) (a) Dürr, H.; Sergio, R. *Tetrahedron Lett.* **1972**, 3479. (b) Franck-Neumann, M.; Buchecker, C. *Tetrahedron Lett.* **1972**, 937. (c) Katner, A. S. *J. Org. Chem.* **1973**, *38*, 825. (d) Franck-Neumann, M.; Dietrich-Buchecker, C. *Tetrahedron Lett.* **1976**, 2069. (e) Huisgen, R.; Verderol, M. P. B.; Gieren, A.; Lamm, V. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 694. (f) Huisgen, R.; Reissig, H.-U.; Huber, H. *J. Am. Chem. Soc.* **1979**, *101*, 3647. (g) Mataka, S.; Takahashi, K.; Tashiro, M. *Chem. Lett.* **1979**, 1033. (h) Mataka, S.; Ohshima, T.; Tashiro, M. *J. Org. Chem.* **1981**, *46*, 3960. (i) Leigh, W. J.; Arnold, D. R. *Can. J. Chem.* **1979**, *57*, 1186. (j) Schiess, P.; Stalder, H. *Tetrahedron Lett.* **1980**, *21*, 1417.

(2) (a) Woodward, R. B.; Hoffmann, R. *J. Am. Chem. Soc.* **1965**, *87*, 395. (b) Hoffmann, R.; Woodward, R. B. *J. Am. Chem. Soc.* **1965**, *87*, 2046. (c) Hoffmann, R.; Woodward, R. B. *Acc. Chem. Res.* **1968**, *1*, 17. (d) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.

(3) (a) Majchrzak, M. W.; Jefferson, E.; Warkentin, J. *J. Am. Chem. Soc.* **1990**, *112*, 2449. (b) Jefferson, E. A.; Warkentin, J. *J. Am. Chem. Soc.* **1992**, *114*, 6318.

(4) (a) Streitwieser, A., Jr. *Solvolytic Displacement Reactions*; McGraw-Hill: New York, 1962. (b) Thornton, E. R. *Solvolysis Mechanisms*; Ronald Press: New York, 1964. (c) Ingold, C. K. *Structure and Mechanism in Organic Chemistry*, 2nd ed.; Cornell University Press: Ithaca, New York, 1969. (d) Hartshorn, S. R. *Aliphatic Nucleophilic Substitution*; Cambridge University Press: New York, 1973. (e) Raber, D. J.; Harris, J. M.; Schleyer, P. v. R. In *Ions and Ion-Pairs in Organic Reactions*; Szwarc, M., Ed.; Wiley: New York, 1974.

(5) Frampton, C. S.; Majchrzak, M. W.; Warkentin, J. *Can. J. Chem.* **1991**, *69*, 373.

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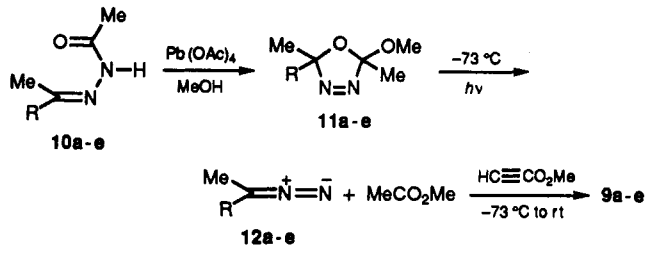
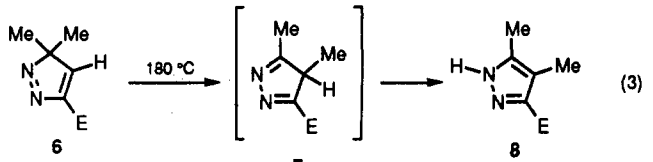
Scheme 1[a]



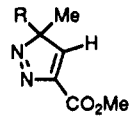
[a] a, R = CH_2OMe; b, R = *t*-Bu; c, R = 1-adamantyl; d, R = *p*-$CH_2C_6H_4OMe$; e, R = Bn.

undergo concerted thermal rearrangement. At 180 °C, rearrangement of **6** afforded only 1*H*-pyrazole **8** (eq 3).[1d] The product was accounted for in terms of an initial [1,5]-sigmatropic migration of Me to C-4 to form 4*H*-pyrazole **7**, which then rearranged further by sequential migration of hydrogen to carbon and to nitrogen.



(3)

Herein we report a study of the thermal rearrangement of 3*H*-pyrazoles **9a–e**. Do they rearrange by a two-step mechanism like 3*H*-pyrazoles **4a–e** or by a concerted mechanism like 3*H*-pyrazole **6**? The study provides insight into the sensitivity of the stepwise mechanism to the stabilization of the ionic form of both the pyrazole nucleus and the migrating group.



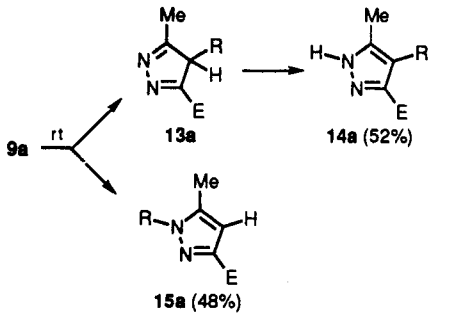
9a-e

a, R = CH_2OMe; **b**, R = *t*-Bu; **c**, R = 1-adamantyl; **d**, R = *p*-$CH_2C_6H_4OMe$; **e**, R = Bn

Results and Discussion

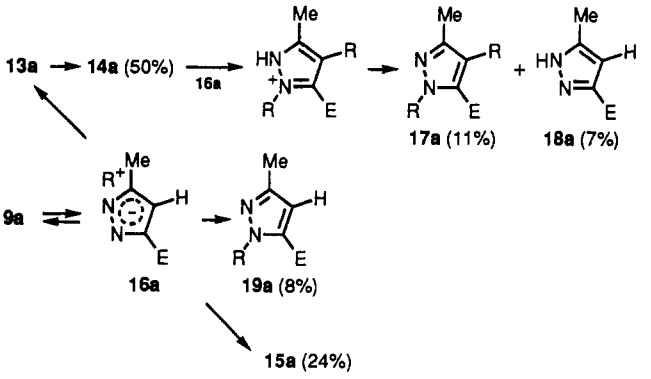
Synthesis of 3*H*-Pyrazoles 9. 3*H*-Pyrazoles **9** were synthesized by the method outlined in Scheme 1. Acetylhydrazones **10a–e** underwent oxidative cyclization with lead tetraacetate in methanol to afford oxadiazolines **11a–e**.[6,7] These oxadiazolines were then photolyzed with 300-nm light at −73 °C in toluene solvent for 6 h to generate solutions of the appropriate diazo compounds (**12a–e**) as well as methyl acetate.[8] Methyl propiolate was added to the photolysis solutions, at −73 °C in the dark, and then the solutions were left to warm to room temperature.[9,10] Diazo compounds **12a–e** underwent 1,3-dipolar cycloaddition reactions to methyl propiolate to afford 3*H*-pyrazoles **9a–e**. 3*H*-Pyrazoles **9b–e** were isolated in fair to good yields (43–65%) and were found to be stable compounds at room temperature. In contrast, 3*H*-pyrazoles **4c–e** were not thermally stable at room temperature.[3b] 3*H*-Pyrazoles **9b–e** were identified on the basis of their ^1H and ^{13}C NMR spectra, as well as their mass spectrometric masses, but **9a** could not be isolated as it rearranged in the media in which it was generated. To avoid complications from acid-catalyzed reactions of the pyrazoles, acid-free solvents and base-washed glassware were used throughout.

Scheme 2[a]



[a] R = CH_2OMe.

Scheme 3[a]



[a] R = CH_2OMe.

Synthesis and Rearrangement of 3*H*-Pyrazole 9a. In Benzene-d_6. A solution of oxadiazoline **11a** (0.5 M) and methyl propiolate in benzene-d_6 was irradiated at 300 nm for 6 h. According to ^1H NMR spectroscopy, **14a** and **15a** were formed in roughly equal amounts (Scheme 2). Presumably, 1*H*-pyrazole **14a** was formed by hydrogen migrations in unstable 4*H*-pyrazole **13a**. Since the rearrangement of **9a** is fast at room temperature, as it is for **4b**, it is reasonable to assume that an ion-pair mechanism is operating in this rearrangement,[3] especially since 3*H*-pyrazole **6** requires a temperature of 180 °C for thermal rearrangement.[1d] Furthermore, **6** affords only **8** while **9a** affords 1*H*-pyrazoles **14a** and **15a**.[1d]

In Dichloromethane. A solution of oxadiazoline **11a** (1.8 M) and methyl propiolate in dichloromethane was irradiated at 300 nm for 6 h. 3*H*-Pyrazole **9a**, a presumed intermediate, rearranged to give several products when generated in CH_2Cl_2. Scheme 3 reveals the percentages (by ^1H NMR spectroscopy) of those products as well as

(6) The synthesis of oxadiazolines **6a–e** is described in ref 3b.

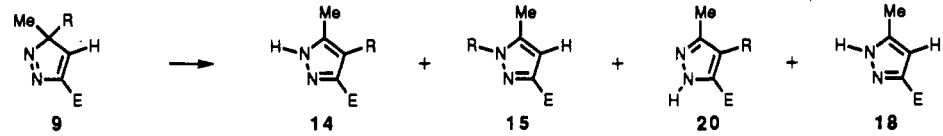
(7) The synthesis of oxadiazoline **6f** has been described. Majchrzak, M. W.; Warkentin, J.; Woollard, J. M. R. *Struct. Chem.* **1991**, *2*, 137.

(8) Majchrzak, M. W.; Békhazi, M.; Tse-Sheepy, I.; Warkentin, J. *J. Org. Chem.* **1989**, *54*, 1842.

(9) The cycloaddition between diazo compound and methyl propiolate was regioselective; the other regioisomer could not be detected. Others have found cycloaddition of other diazo compounds to methyl propiolate to be regioselective. Franck-Neumann, M.; Buchecker, C. *Tetrahedron Lett.* **1969**, 15.

(10) 3*H*-Pyrazoles **9b–e** could not be isolated in very good yields when the photolysis of oxadiazolines **11b–e** was carried out in the presence of methyl propiolate. Nitogen extrusion yielding cyclopropenes occurred even when a substantial amount of the starting oxadiazoline was still present.

Table 1. Products and Product Yields[a] from the Thermal Rearrangements of 9b–e in Benzene-d_6 and Acetone-d_6



9	14	15	20	18	+ others
9b,[b] R = *t*-Bu	28 (38)	15 (15)	2 (7)	55 (41)	isobutene, 55 (34)
9c,[c] R = 1-adamantyl	72 (72)	28 (28)	nil (nil)	nil (nil)	
9d,[d] R = *p*-$CH_2C_6H_4OMe$	78 (91)	22 (9)	nil (nil)	nil (nil)	
9e,[e] R = Bn	100 (100)	nil (nil)	nil (nil)	nil (nil)	

[a] At the level of detection afforded by ^1H NMR spectroscopy, the products listed were the only products from rearrangement and the yield numbers (%) reflect materials balance prior to opening of a tube. The numbers without (parentheses) are percentages determined in C_6D_6 while the numbers in (parentheses) are percentages determined in acetone-d_6. [b] Rearrangement at 90 °C with $k(C_6D_6) = (1.06 \pm 0.03) \times 10^{-4}$ s^{-1}; k(acetone-d_6) = $(9.7 \pm 0.3) \times 10^{-5}$ s^{-1}. [c] Rearrangement at 90 °C with $k(C_6D_6) = (1.10 \pm 0.09) \times 10^{-4}$ s^{-1}; k(acetone-d_6) = $(8.9 \pm 0.4) \times 10^{-5}$ s^{-1}. [d] Rearrangement at 60 °C with $k(C_6D_6) = (3.3 \pm 0.2) \times 10^{-4}$ s^{-1}; k(acetone-d_6) = $(2.1 \pm 0.1) \times 10^{-4}$ s^{-1}. [e] Rearrangement at 90 °C with $k(C_6D_6)$ = $(2.8 \pm 0.1) \times 10^{-4}$ s^{-1}; k(acetone-d_6) = $(2.80 \pm 0.05) \times 10^{-4}$ s^{-1}.

a mechanistic proposal for their formation. 3*H*-Pyrazole **9a** dissociates to ion-pair **16a**, the cation of which collapses on C-4, N-1, and N-2 of the anion. Collapse of the methoxymethyl cation at C-4 affords unstable 4*H*-pyrazole **13a**, and fast migration of hydrogen to nitrogen in this pyrazole gives 1*H*-pyrazole **14a**. Alkylation of **14a** with the cation of ion-pair **16a** results in proton loss and the formation of **17a**, while protonation of the anion of ion-pair **16a** gives rise to compound **18a**. The methoxymethyl cation of ion-pair **16a** also collapses on both nitrogen atoms of the pyrazole anion to give **15a** and **19a**. Dichloromethane, a more polar solvent than benzene, apparently increases ion-pair separation during rearrangement which, in turn, increases the probability of cation collapse on the nitrogen furthest from the migration origin. Since coupling of the migrating group occurs preferentially on the nitrogen nearest the migration origin, rather than equally on both nitrogen atoms, rather tight ion pairs are implicated. However, since **14a** was apparently alkylated by **16a**, separation of some of the ion pairs must be occurring. This product study implies the presence of both solvent-separated ion pairs and tight ion pairs as reaction intermediates. Both the increase in solvent polarity and the higher concentration of 3*H*-pyrazole **9a** in CH_2Cl_2 (Experimental Section) appear to be contributing factors leading to the different product distribution from rearrangement of **9a** in dichloromethane compared to those from its rearrangement in benzene. ^1H NMR NOE difference experiments, described in the Experimental Section, were very useful in characterizing compounds **15a**, **17a**, and **19a**.

Rearrangement of 3*H*-Pyrazoles 9b–e in Benzene-d_6. Unlike 3*H*-pyrazole **9a**, 3*H*-pyrazoles **9b–e** are stable compounds at room temperature and required higher temperatures for thermal rearrangement. Table 1 reveals both the products and observed rate constants of these thermal rearrangements in benzene-d_6 solvent. Those rearrangements led to very clean product solutions and the numbers reported are percentages determined by ^1H NMR spectroscopy.

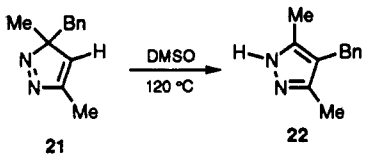
A fragmentation reaction of 3*H*-pyrazole **9b** gave 18 and isobutene as thermolysis products. The presence of isobutene was confirmed by an ^1H NMR spectroscopy decoupling experiment on the thermolysis mixture (sealed NMR tube). Presumably, isobutene came from formation and subsequent deprotonation of a *tert*-butyl cation intermediate. 1*H*-Pyrazoles **14b** and **20b**, from initial migration of *tert*-butyl to C-4, and **15b**, from migration of *tert*-butyl to N-2, were also products of thermal rearrangement. The conclusion, from the product study, is that 3*H*-pyrazole **9b** rearranges in benzene-d_6 solvent by a stepwise mechanism, involving the formation of an ion-pair intermediate.

3*H*-Pyrazole **9c** underwent thermal rearrangement at 90 °C with an observed rate constant similar to that obtained for the rearrangement of 3*H*-pyrazole **9b**, and rearrangement afforded both **14c** and **15c**. Solvolysis of adamantyl systems is normally slower than solvolysis of *tert*-butyl analogues, especially in nucleophilic solvents, but Bentley and co-workers[11] have predicted that the reverse should be true for pure S_N1 reactions. Rearrangement of **9b** and **9c** in benzene appears to be the first case in which adamantyl has caught up with *tert*-butyl. The fact that **9d** rearranges approximately 24 times[12] faster than both **9b** and **9c** is consistent with a stepwise mechanism since the *p*-methoxybenzyl chloride solvolyzes faster than *tert*-butyl chloride in 80% aqueous ethanol.

The thermal rearrangement of **9e** afforded only **14e**, from exclusive benzyl substituent migration to C-4. In contrast, the rearrangements of **9a–d** gave a mixture of 1*H*-pyrazoles **14** and **15**, the result of R substituent migration to both C-4 and N-2. 3*H*-Pyrazole **9e** (R = Bn) rearranged approximately 10 times more slowly than 3*H*-pyrazole **9d** (R = *p*-$CH_2C_6H_4OMe$). The rate enhancement for **9d**, compared to **9e**, suggests the development of some positive charge in the migrating group at the transition state for thermal rearrangement.

The thermal rearrangement of a 3*H*-pyrazole analogue of **9e** had been investigated previously. Schiess and Stalder studied the thermal rearrangement of 3*H*-pyrazole **21** and reported that rearrangement occurred at 120 °C, in DMSO solvent, with an overall first-order rate constant of 3.05×10^{-4} s^{-1} (eq 4).[1j] Thermal rearrangement afforded only **22** from initial migration of benzyl to C-4 followed by hydrogen migration to nitrogen. 3*H*-Pyrazole **9e**, which rearranges with $k_{obsd} = 2.8 \times 10^{-4}$ s^{-1}, at 90 °C in benzene, is considerably more reactive than **21**. The methoxycarbonyl substituent at C-5 of **9e** is rate enhancing, compared to the methyl group at C-5 of **21**, and a simple explanation is that there is more negative charge developed within the pyrazole nucleus at the transition state for thermal rearrangement of **9e**.

(11) Bentley, T. W.; Carter, G. E. *J. Am. Chem. Soc.* **1982**, *104*, 5741.
(12) A 2-fold increase in the observed rate of rearrangement for every 10 °C increase in temperature was assumed in order to compare observed rate constant data when such data were not determined at identical temperatures.
(13) Streitwieser, A. *Chem. Rev.* **1956**, *56*, 571.



(4)

Whether 3*H*-pyrazoles **9c–e** undergo rearrangement by a stepwise or a concerted mechanism in benzene solvent is uncertain. 3*H*-Pyrazoles **9b–e** all rearrange with large rate enhancements compared to the thermal rearrangement of **6**, for which a concerted mechanism for rearrangement is assumed. The approximate relative order of rates of rearrangement for **9b–e** is the following: **9b** (1.0), **9c** (1.0), **9d** (24), and **9e** (2.5). With the exception of **9e**, these compounds afford products from migration of R to both C-4 and N-2. In contrast, the thermal rearrangement of **6** affords only **8** from migration of methyl to C-4.[1d]

Rearrangement of 3*H*-Pyrazoles 9b–e in Acetone-d_6. The rearrangements of 3*H*-pyrazoles **9b–e** in acetone-d_6 were also investigated. It was possible to determine the effect of a change of solvent polarity (benzene-d_6 to acetone-d_6) on the observed rates of rearrangement and on the product distribution. A more polar solvent should increase ion-pair separations and possibly even lead to different products of rearrangement, if ion pairs are indeed involved.

Table 1 gives the products and observed rate constants of the rearrangement of 3*H*-pyrazoles **9b–e** in acetone-d_6 solvent. The percentage yields were determined by ^{1}H NMR spectroscopy after the completion of thermal rearrangement.

Surprisingly, 3*H*-pyrazoles **9b–e** rearranged in acetone-d_6 with similar and even lower (for **9c** and **9d**) observed rate constants compared to those for rearrangement in benzene-d_6. This unusual result is not easily explained, especially for **9b** which presumably proceeds via an ion-pair intermediate, based on the presence of **18** and isobutene in the product solutions. A change to a more polar solvent should increase the overall rate of rearrangement if the ground state is less polar than the transition state. In a sense that expectation was met with the finding that 3*H*-pyrazole **9d** (R = *p*-$CH_2C_6H_4OMe$) rearranges approximately 10 times faster than **9e** (R = Bn). This substituent effect on the rate of rearrangement in acetone again suggests some development of positive charge on R at the transition state for migration. However, the fact that the absolute values of the rate constants for rearrangement in acetone do not exceed those for rearrangement in benzene suggests that ground-state solvation is important.

The similar overall rates of rearrangement of these 3*H*-pyrazoles in benzene and in acetone can be rationalized if the ground states are assumed to be comparable to the transition states in polarity or if benzene is assumed to be especially good at solvating organic ion pairs, one ion of which is an aromatic species. It is known that for the thermal decomposition of cis-azo isobutane to isobutyl radicals, an increase in solvent polarity decreases the overall rate of rearrangement, the ground state of the cis-azo compound being more polar than the transition state for decomposition.[14] The 3*H*-pyrazoles presumably also have substantial net dipole moments, from the vector contributions of the two C–N(azo) bonds and the ester function.

The product distribution from the rearrangements of **9b–e** in acetone-d_6 is similar to that found from their rearrangements in benzene-d_6 solvent. Thus the change to a more polar solvent did not lead to formation of a second N-substituted 1*H*-pyrazole. Rearrangements of 3*H*-pyrazoles **4a–e** in chloroform solvent,[3b] and of **9a** in dichloromethane, do afford both possible N-substituted 1*H*-pyrazoles but such 1*H*-pyrazole isomers of **15b–e** could not be detected in the product solutions from **9b–e**. Possibly, two N-substituted 1*H*-pyrazoles are not formed if contact ion pairs are involved.

Rearrangement of 3*H*-Pyrazoles 9a–e in Methanol or Methanol-d_4. In an effort to trap any potential intermediate ion pairs from the rearrangements of **9a–e**, and to observe the effect of a hydrogen-bonding nucleophilic solvent on the rates, those rearrangements were carried out in methanol solvent.

Table 2 reveals the products from the rearrangement of 3*H*-pyrazoles **9a–e** in methanol or methanol-d_4 solvents. The percentages reported were determined by ^{1}H NMR spectroscopy, after the completion of thermal rearrangement.

3*H*-Pyrazole **9a** rearranged at ambient temperature in the methanol-d_4 solvent in which it was generated to afford **14a**, **15a**, 1*H*-pyrazole **18** (D analogue, 26%), and **23** (dimethoxymethane-d_3, 26%). Dimethoxymethane-d_3 was confirmed by ^{1}H NMR spectroscopy and gas chromatography spiking experiments with an authentic sample of the nondeuterated analogue. The trapping of the methoxymethyl group from **9a** provides strong evidence that rearrangement occurs by an ion-pair mechanism.

A reactive fragment from 3*H*-pyrazole **9b** also was intercepted by methanol-d_4. After only 20 min at 90 °C, **9b** had rearranged completely (^{1}H NMR spectroscopy) to form *tert*-butyl methyl-d_3 ether (**23b**, 31%), **18** (together with D analogue), **14b**, **15b**, **20b**, and isobutene. The presence of **23b** was confirmed by ^{1}H NMR spectroscopy and gas chromatography spiking experiments with an authentic sample of the nondeuterated analogue. The products listed above force the conclusion that an ion-pair intermediate was generated during the rearrangement of **9b** in methanol-d_4. In another experiment, the rate constant [k_{obsd} = (4.7 ± 0.1) × 10^{-4} s^{-1}] was determined for the rearrangement of **9b** in methanol-d_4 at 50 °C. That value is approximately 75 times greater than those for rearrangement of **9b** in acetone or in benzene, if a factor of 2 per 10 degrees is used to correct for the 40 °C temperature difference.

Thermal rearrangement of both **9c** and **9d** during 0.5 h in refluxing methanol afforded only small amounts (<2%) of **18** and **23**. The presence of the methyl ethers (**23c** and **23d**) was confirmed by ^{1}H NMR and gas chromatography spiking experiments with authentic samples prepared by another route.[15,16] Since rearrangement is complete after 0.5 h at 65 °C, there is a rearrangement rate enhancement for both these 3*H*-pyrazoles, compared to their rearrangements in benzene-d_6 or acetone-d_6. Presumably, an ion-pair mechanism operates in these

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(15) Owens, P. H.; Gleicher, G. J.; Smith, L. M., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4122.

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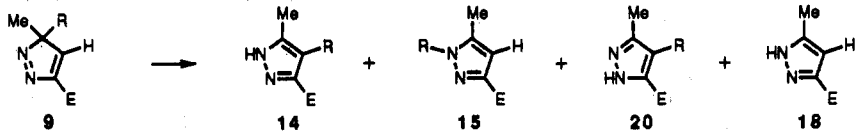
Table 2. Products and Product Yields[a] from the Thermal Rearrangements of 9a–e in Methanol



9	14	15	20	18	ROMe (23)	+ other
9a,[b] R = CH_2OMe	53	21	nil	26[c]	26[d]	
9b,[e] R = *t*-Bu	18	16	6	60[f]	31[d]	isobutene, 27
9c,[g] R = 1-adamantyl	81	19	nil	<2	<2	
9d,[g] R = *p*-$CH_2C_6H_4OMe$	75	25	nil	<2	<2	
9e,[g] R = Bn	100	nil	nil	nil	nil	

[a] At the level of detection afforded by ^1H NMR spectroscopy, the products listed were the only products from rearrangement and the yield numbers (%) reflect materials balance prior to opening of a tube. [b] Rearrangement at ambient temperature. [c] D analogue. [d] CD_3OR, from rearrangement in CD_3OD at ambient temperature. [e] Rearrangement at 90 °C. [f] Mixture of H and D analogues. [g] Rearrangement in MeOH 65 °C.

rearrangements, but the ion pairs in these cases are very "tight" and only a small percentage are scavenged by methanol.

3*H*-Pyrazole **9e** rearranged completely, during refluxing in methanol for 0.5 h, to afford only **14e**. Benzyl methyl ether and **18** could not be detected by gas chromatography. Since rearrangement was complete after only 0.5 h at 65 °C, there is also a rate enhancement (*ca.* 40-fold) in methanol, relative to acetone or benzene (Table 1). The simplest explanation is that 3*H*-pyrazole **9e** rearranges by a concerted mechanism, even in methanol, and that there is enough charge separation in this polar solvent to cause a rate enhancement. Such a mechanism is not operationally distinguishable from one that invokes a very tight ion pair, not interceptable by methanol.

Conclusions

The 3*H*-pyrazoles **9a–d** rearrange by a stepwise mechanism in methanol solvent since, in each case, some of the migrating groups were intercepted. Large rate enhancements for the rearrangements of 3*H*-pyrazoles **9b–d** in methanol, compared to benzene, also provide support for a stepwise mechanism for rearrangement in methanol solvent. 3*H*-Pyrazole **9a** rearranges by a stepwise mechanism also in both benzene and dichloromethane as inferred from the large rate enhancements for those rearrangements and from the fact that, in dichloromethane solvent, **9a** affords some products (**17a**, **18**, and **19a**) that could not have arisen from a concerted mechanism. 3*H*-Pyrazole **9b** also must rearrange by a stepwise mechanism in both benzene-d_6 and acetone-d_6, because isobutene and **18** were reaction products. For 3*H*-pyrazoles **9c** and **9d**, which rearrange in acetone-d_6 or in benzene-d_6 to afford only "normal" products, it is unclear whether a concerted mechanism, with some charge separation, or a stepwise mechanism, involving tight ion pairs, operates. It is likely that 3*H*-pyrazole **9e** rearranges by "normal" [1,5]-sigmatropic shifts of benzyl in benzene-d_6, acetone-d_6, and methanol solvents. Its rearrangement in methanol seems to involve some charge separation because of the rate enhancement observed in this solvent of higher polarity but there was no evidence, from trapping, that an ion-pair intermediate was involved.

A logical conclusion is that a range of transition-state structures exists for rearrangements of cyclopentadiene-like systems. At the one extreme are true [1,5]-sigmatropic rearrangement mechanisms, by definition concerted but not necessarily synchronous. Motion along the reaction coordinate presumably resembles a bending mode. At the other extreme is a two-step mechanism, involving a discrete ion-pair intermediate, formed by C–C bond stretching, to which the term "sigmatropic" does not apply. In between are rearrangements that are not easily classified, showing evidence of significant charge separation at the transition state but not compelling evidence of the existence of discrete ion-pair intermediates. Except for those rearrangements that are concerted, the thermal rearrangements of 3*H*-pyrazoles probably fit into the mechanistically-rich manifold of S_N1 reactions, involving tight ion pairs, ion-pair return, solvent separated ion pairs, and free ions. A reviewer has suggested that concerted and ion-pair mechanisms may compete in some cases.

Heterolysis of C–C bonds has drawn considerable attention in recent years. Heteroatom-free organic compounds that are covalent in the solid state but ionic as solutions in polar organic solvents have been reported.[17,18] The reverse case, a crystalline salt that becomes a covalent organic compound on dissolution, is also known.[19] Evidence for facile C–C bond heterolysis of *tert*-butyl(nitro)-malononitrile in DMSO has been published,[20] as well as a computational study of heterolysis of so-called "push-pull" ethanes.[21] Moreover, extensive correlations have been developed by Arnett and his group, between the energies of homolysis and heterolysis of C–C bonds.[22] The formation of ion pairs from 3*H*-pyrazoles bearing only one ester group (**9**) as well as from pyrazoles bearing two,[3] in moderately polar or nonpolar organic solvents, illustrates further the important role that CC bond heterolysis can play.

Experimental Section

General. Melting points were determined on a Thomas-Hoover capillary melting point apparatus. Centrifugal chromatography was performed with silica gel (Merck kieselgel 60 PF_{254}) coated plates (2-mm or 4-mm thick) spinning in a Chromatotron Model 7924T apparatus. Analytical TLC was performed with silica gel plates (E. Merck, D-Plastikfolien, kieselgel 60 F_{254}). ^1H NMR data were obtained on Varian EM-390, Bruker AC-200, Bruker WM-250, or Bruker AM-500 spectrometers. Chemical shifts are reported in ppm (δ) units downfield from TMS or relative to the singlet at 7.24 ppm for chloroform in chloroform-d_1, or in ppm relative to the singlet at

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7.15 ppm for benzene-d_5 in benzene-d_6. ^{13}C NMR spectra were obtained at 50 MHz on a Bruker AC-200 or at 125 MHz on a Bruker AM-500 spectrometer and are reported in ppm relative to the center line of a triplet at 77.0 ppm for chloroform-*d* or a triplet at 128.0 for benzene-d_6. High resolution mass spectra were recorded on a VG ZAB-E double focusing mass spectrometer. Samples were run at 70 eV, source temperature 200 °C, and resolution 5000. Samples were introduced by direct insertion probe. Photolyses employed a Rayonet photochemical reactor fitted with 300-nm lamps. Purity of all products was established by ^1H and ^{13}C NMR spectroscopy and melting point, where appropriate. The syntheses of acetylhydrazones **10a–e** and oxadiazolines **11a–e** were described previously.[3b,7]

General Procedure for the Preparation of 3-Alkyl-3-methyl-3*H*-pyrazole-5-carboxylic Acid, Methyl Esters 9b–e. The oxadiazolines **11b–e** (0.25 mmol) were dissolved in toluene (0.5 mL) and irradiated at −73 °C with 300-nm light (Rayonet apparatus) for 7 h. At −73 °C, with the Rayonet bulbs switched off, methyl propiolate (0.50 mmol in 0.1 mL of toluene) was added to the photolysis mixtures. The mixtures were warmed to room temperature, the volatiles were removed in vacuo, and the residues were dissolved in hexane. The solid 3*H*-pyrazoles were filtered and washed with hexane.

3-*tert*-Butyl-3-methyl-3*H*-pyrazole-5-carboxylic acid, methyl ester (9b): 43% yield, mp 55–58 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.77 (s, 1 H, CH), 3.99 (s, 3 H, CO_2Me), 1.38 (s, 3 H, Me), 1.06 (s, 9 H, *t*-Bu); ^{13}C NMR (spin sort, 50 MHz, $CDCl_3$) δ 161.38 (+ve), 154.37(−ve), 147.02 (+ve), 105.08 (+ve), 52.38 (−ve), 37.45 (+ve), 26.77 (3C, −ve), 15.06 (−ve); MS *m/z* (M^+) for $C_{10}H_{16}N_2O_2$ calcd 196.1212, found 196.1211.

3-(1-Adamantyl)-3-methyl-3*H*-pyrazole-5-carboxylic acid, methyl ester (9c): 52% yield, mp 120–121 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.77 (s, 1 H, CH), 3.98 (s, 3 H, CO_2Me), 1.99 (br s, 3 H, CH), 1.68 (br s, 12 H, CH_2), 1.33 (s, 3 H, Me); ^{13}C NMR spin sort (50 MHz, $CDCl_3$) δ 161.39 (+ve), 154.47 (−ve), 147.01 (+ve), 105.60 (+ve), 52.33 (−ve), 40.60 (+ve), 38.59 (3C, +ve), 36.68 (3C, +ve), 28.72 (3C, −ve), 13.73 (−ve); MS *m/z* (M^+) for $C_{16}H_{22}N_2O_2$ calcd 274.1681, found 274.1690.

3-(4-Methoxybenzyl)-3-methyl-3*H*-pyrazole-5-carboxylic acid, methyl ester (9d): 45% yield, mp 127–130 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.66 (s, 1 H, CH), 7.00 (d, 2 H, J = 8.2 Hz), 6.78 (d, 2 H, J = 8.2 Hz), 3.94 (s, 3 H, CO_2Me), 3.77 (s, 3 H, OMe), 3.29 (d, 1 H, CH, J = −13.7 Hz), 3.07 (d, 1 H, CH, J = −13.7 Hz), 1.46 (s, 3 H, Me); ^{13}C NMR (200 MHz, $CDCl_3$) δ 161.09, 158.65, 153.11, 147.66, 130.70 (2), 129.07, 113.66, 99.30, 55.14, 52.40, 40.45, 18.01; MS *m/z* (M^+) for $C_{14}H_{16}N_2O_3$ calcd 260.1161, found 260.1155.

3-Benzyl-3-methyl-3*H*-pyrazole-5-carboxylic acid, methyl ester (9e): 65% yield, mp 114–116 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.66 (s, 1 H, CH), 7.26–7.07 (m, 5 H, Ph), 3.93 (s, 3 H, CO_2Me), 3.34 (d, 1 H, J = −13.4 Hz), 3.10 (d, 1 H, J = −13.4 Hz), 1.47 (s, 3 H, Me); ^{13}C NMR (200 MHz, $CDCl_3$) δ 161.00, 152.86, 147.60, 134.72, 129.60 (2), 128.25 (2), 127.17, 98.96, 52.34, 41.12, 18.03; MS *m/z* (M^+) for $C_{13}H_{14}N_2O_2$ calcd 230.1055, found 230.1065.

Rearrangement of 3*H*-Pyrazoles 9a–e in Benzene-d_6. Rearrangement of 9a. Oxadiazoline **11a** (0.25 mmol) and methyl propiolate (0.50 mmol) in C_6D_6 (0.5 mL) were irradiated at room temperature with 300-nm light (Rayonet apparatus) for 6 h. A 1.1:1.0 ratio of **14a**:**15a** was indicated by ^1H NMR spectroscopy. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give **14a** (28%) and **15a** (31%).

4-(Methoxymethyl)-5-methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (14a): mp 85–88 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 4.62 (s, 2 H, CH_2), 3.92 (s, 3 H, CO_2Me), 3.37 (s, 3 H, OMe), 2.36 (s, 3 H, Me); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.93, 144.31, 137.95, 117.88, 63.41, 57.88, 51.92, 10.39; MS *m/z* (M^+) for $C_8H_{12}N_2O_3$ calcd 184.0848, found 184.0841.

1-(Methoxymethyl)-5-methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (15a): ^1H NMR (500 MHz, $CDCl_3$) δ 6.63 (s, 1 H, CH), 5.45 (s, 2 H, CH_2), 3.92 (s, 3 H, CO_2Me), 3.32 (s, 3 H, OMe), 2.38 (s, 3 H, Me); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.85, 142.66, 140.88, 109.23, 80.33, 56.40, 51.97, 10.69; MS *m/z* (M^+) for $C_8H_{12}N_2O_3$ calcd 184.0848, found 184.0843.

In an ^1H NOE experiment, irradiation of the methyl singlet at 2.38 ppm caused enhancement of singlets at 5.45 ppm (CH_2) and 6.63 ppm (vinyl proton).

Rearrangement of 9b. 3*H*-Pyrazole **9b** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in C_6D_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube. The tube was heated at 90 °C for 15 h. The percentages of **14b**, **15b**, **20b**, **18**, and isobutene by ^1H NMR spectroscopy were 28, 15, 2, 55, and 25, respectively. The presence of isobutene was confirmed by an ^1H NMR decoupling experiment on the reaction mixture following the rearrangement of **9b**. Irradiation of the multiplet at 4.74 ppm (CH_2) caused collapse of the triplet at 1.60 ppm (2 Me). The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give **14b** (19%), **15b** (7%), **20b** (1%), and **18** (42%).

4-*tert*-Butyl-5-methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (14b): mp 145–148 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 3.88 (s, 3 H, CO_2Me), 2.42 (s, 3 H, Me), 1.42 (s, 9 H, *t*-Bu); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.01, 142.49, 139.91, 129.12, 51.92, 31.49, 31.12 (3), 14.16; MS *m/z* (M^+) for $C_{10}H_{16}N_2O_2$ calcd 196.1211, found 196.1197.

1-*tert*-Butyl-5-methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (15b): ^1H NMR (200 MHz, $CDCl_3$) δ 6.58 (s, 1 H, CH), 3.89 (s, 3 H, CO_2Me), 2.47 (s, 3 H, Me), 1.67 (s, 9 H, *t*-Bu); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.24, 139.99, 139.42, 111.27, 61.12, 51.76, 29.82 (3), 14.65; MS *m/z* (M^+) for $C_{10}H_{16}N_2O_2$ calcd 196.1211, found 196.1212.

4-*tert*-Butyl-3-methyl-1*H*-pyrazole-5-carboxylic acid, methyl ester (20b): ^1H NMR (200 MHz, $CDCl_3$) δ 3.90 (s, 3 H, CO_2Me), 2.41 (s, 3 H, Me), 1.39 (s, 9 H, *t*-Bu); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.12, 154.00, 137.11, 116.81, 51.66, 31.08, 29.16, 10.13; MS *m/z* (M^+) for $C_{10}H_{16}N_2O_2$ calcd 196.1211, found 196.1204.

5-Methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (18):[23] mp 74–76 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 6.57 (s, 1 H, CH), 3.89 (s, 3 H, CO_2Me), 2.38 (s, 3 H, Me); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.51, 142.61, 141.77, 107.19, 51.78, 11.22; MS *m/z* (M^+) for $C_6H_8N_2O_2$ calcd 140.0586, found 140.0570.

Rearrangement of 9c. 3*H*-Pyrazole **9c** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in C_6D_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube. The tube was heated at 90 °C for 14 h. The percentages of **14c** and **15c** by ^1H NMR spectroscopy were 72 and 28. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give **14c** (55%) and **15c** (18%).

4-(1-Adamantyl)-5-methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (14c): mp 239–241 °C (sublimes); ^1H NMR (200 MHz, $CDCl_3$) δ 4.50 (s, 1 H, NH), 3.90 (s, 3 H, CO_2Me), 2.46 (s, 3 H, Me), 2.14 (br s, 6 H, CH_2), 2.03 (br s, 3H, CH), 1.76 (br s, 6 H, CH_2); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.71, 137.23, 130.03, 114.50, 52.05, 41.76 (3), 36.67 (3), 34.14, 28.87 (3), 15.37; MS *m/z* (M^+) for $C_{16}H_{22}N_2O_2$ calcd 274.1681, found 274.1688.

1-(1-Adamantyl)-5-methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (15c): ^1H NMR (200 MHz, $CDCl_3$) δ 6.57 (s, 1 H, CH), 3.89 (s, 3 H, COOMe), 2.51 (s, 3 H, Me), 2.32 (bs, 6 H, CH_2), 2.23 (bs, 3 H, CH), 1.75 (bs, 6 H, CH_2); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.30, 140.16, 139.50, 111.26, 62.28, 51.80, 41.64 (3), 36.08 (3), 29.71 (3), 15.00; MS *m/z* (M^+) for $C_{16}H_{22}N_2O_2$ calcd 274.1681, found 274.1685.

Rearrangement of 9d. 3*H*-Pyrazole **9d** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in C_6D_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube. The tube was heated at 60 °C for 5 h. The percentages of **14d** and **15d** by ^1H NMR spectroscopy were 78 and 22. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 70:30 hexane/ethyl acetate) to give **14d** (60%) and **15d** (15%).

4-(4-Methoxybenzyl)-5-methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (14d): mp 129–131 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.07 (d, 2 H, CH, J = 8.6 Hz), 6.78 (d, 2 H, CH,

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J = 8.6 Hz), 4.03 (s, 2 H, CH_2), 3.85 (s, 3 H, CO_2Me), 3.76 (s, 3 H, OMe), 2.21 (s, 3 H, Me); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.21, 157.68, 143.21, 136.75, 132.46, 129.05 (2), 120.91, 113.62 (2), 55.16, 51.63, 28.12, 10.50; MS m/z (M^+) for $C_{14}H_{16}N_2O_3$ calcd 260.1161, found 260.1164.

1-(4-Methoxybenzyl)-5-methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (15d): ^1H NMR (200 MHz, $CDCl_3$) δ 7.01 (d, 2 H, CH, J = 8.8 Hz), 6.77 (d, 2 H, CH, J = 8.8 Hz), 6.54 (s, 1 H, CH), 5.24 (s, 2 H, CH_2), 3.86 (s, 3 H, CO_2Me), 3.71 (s, 3 H, OMe), 2.12 (s, 3 H, Me); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.01, 159.24, 142.03, 128.26 (2), 127.78, 114.14 (2), 108.94, 55.23, 53.63, 51.91, 11.29; MS m/z (M^+) for $C_{14}H_{16}N_2O_3$ calcd 260.1161, found 260.1149.

Rearrangement of 9e. 3*H*-Pyrazole **9e** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in C_6D_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube which was heated at 90 °C for 6 h. 1*H*-Pyrazole **14e** appeared, by ^1H NMR spectroscopy, to be formed in quantitative yield. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 60:40 hexane/ethyl acetate) to give **14e** (81%).

4-Benzyl-5-methyl-1*H*-pyrazole-3-carboxylic acid, methyl ester (14e): mp 102-104 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.17–7.36 (m, 5 H, Ph), 5.10 (s, 1 H, NH), 4.11 (s, 2 H, CH_2), 3.88 (s, 3 H, CO_2Me), 2.21 (s, 3 H, Me); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.22, 143.31, 140.34, 136.91, 128.24, 128.15 (2), 125.84 (2), 120.45, 51.61, 29.05, 10.48; MS m/z (M^+) for $C_{13}H_{14}N_2O_2$ calcd 230.1055, found 230.1062.

Determination of k_{obs} for the Rearrangement of 3*H*-Pyrazoles 9b–e in Benzene-d_6. 3*H*-Pyrazole **9** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in C_6D_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube. The tube was heated at 90 °C for **9b**, **9c**, and **9e** and at 60 °C for **9d**, and progress of the rearrangement of **9** was monitored by ^1H NMR spectroscopy. Concentration vs time data were obtained by normalizing the integrated intensity of the CH_2 singlet of phenoxy-2-propanone against the integrated intensity of the C-3 methyl singlet of 3*H*-pyrazole **9**. The decrease in concentration of **9** was monitored to at least 2 half-lives. The resultant plots of $\ln([9]/[9]_0)$ vs t, where $[9]_0$ is the initial concentration of **9**, gave the following observed rate constants: $k^{90\ °C}$(**9b**) = (1.06 ± 0.03) × 10^{-4} s^{-1} (correlation coefficient = 0.9975); $k^{90\ °C}$(**9c**) = (1.10 ± 0.09) × 10^{-4} s^{-1} (correlation coefficient = 0.9850); $k^{60\ °C}$(**9d**) = (3.3 ± 0.2) × 10^{-4} s^{-1} (correlation coefficient = 0.9898); $k^{90\ °C}$(**9e**) = (2.8 ± 0.1) × 10^{-4} s^{-1} (correlation coefficient = 0.9955).

Rearrangement of 9a in Dichloromethane. Oxadiazoline **11a** (0.92 mmol) and methyl propiolate (1.21 mmol) were dissolved in CH_2Cl_2 (0.5 mL, base washed with $NaHCO_3$ and distilled) and irradiated at room temperature with 300-nm light (Rayonet apparatus) for 6 h. After volatiles were removed in vacuo and the residue was dissolved in $CDCl_3$, the percentages (determined by ^1H NMR spectroscopy) were **14a** (50), **15a** (24), 18 (7), **19a** (8), and **17a** (11). The residue was subjected to centrifugal chromatography (silica gel, 2:1 diethyl ether/hexanes) to give **14a** (32%), **15a** (18%), 18 (4%), **19a** (5%), and **17a** (7%).

1-(Methoxymethyl)-3-methyl-1*H*-pyrazole-5-carboxylic acid, methyl ester (19a): ^1H NMR (500 MHz, $CDCl_3$) δ 6.69 (s, 1 H, CH), 5.75 (s, 2 H, CH_2), 3.88 (s, 3 H, CO_2Me), 3.35 (s, 3 H, OMe), 2.30 (s, 3 H, Me); ^{13}C NMR (50 MHz, $CDCl_3$) δ 159.95, 148.30, 133.09, 112.20, 80.52, 56.75, 51.99, 13.34; MS (CI, CH_4) m/z (M^+) for $C_8H_{12}N_2O_3$-H calcd 183.0770, found 183.0759. In an ^1H NOE experiment, irradiation of the methyl singlet at 2.30 ppm caused enhancement at 6.69 ppm (vinyl proton) but not at 5.75 ppm.

1,4-Bis(methoxymethyl)-3-methyl-1*H*-pyrazole-5-carboxylic acid, methyl ester (17a): ^1H NMR (500 MHz, $CDCl_3$) δ 5.72 (s, 2 H, N-CH_2), 4.55 (s, 2 H, C-CH_2), 3.93 (s, 3 H, CO_2Me), 3.35 (s, 3 H, C-CH_2OMe), 3.32 (s, 3 H, N-CH_2OMe), 2.32 (s, 3 H, Me); ^{13}C NMR (50 MHz, $CDCl_3$) δ 160.22, 148.96, 130.98, 121.78, 81.23, 64.06, 57.94, 56.77, 52.08, 11.77; MS (CI, CH_4) m/z (M^+) for $C_{10}H_{16}N_2O_4$ calcd 228.1110, found 228.1096. In an ^1H NOE experiment, irradiation of the methyl singlet at 2.32 ppm caused enhancement of the singlet at 4.55 ppm (C-CH_2), while irradiation of the methylene singlet at 5.72 caused enhancement of the singlet at 3.32 (N-CH_2OMe). Furthermore, irradiation of the methylene singlet at 4.55 caused enhancement of the singlet at 3.35 ppm (C-CH_2OMe).

Rearrangement of 3*H*-Pyrazoles 9b–e in Acetone-d_6. Rearrangement of 9b. 3*H*-Pyrazole **9b** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-d_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube, which was then heated at 90 °C for 16 h. The percentages of **14b**, **15b**, **20b**, 18, and isobutene by ^1H NMR spectroscopy (200 MHz) were 38, 15, 7, 41, and 34, respectively. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give **14b** (24%), **15b** (8%), **20b** (3%), and 18 (32%).

Rearrangement of 9c. 3*H*-Pyrazole **9c** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-d_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube, which was then heated at 90 °C for 16 h. The percentages of **14c** and **15c** by ^1H NMR spectroscopy were 72 and 28, respectively. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give **14c** (58%) and **15c** (21%).

Rearrangement of 9d. 3*H*-Pyrazole **9d** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-d_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube. The tube was heated at 60 °C for 6 h. The percentages of **14d** and **15d** by ^1H NMR spectroscopy were 90 and 9, respectively. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 70:30 hexane/ethyl acetate) to give **14d** (80%) and **15d** (5%).

Rearrangement of 9e. 3*H*-Pyrazole **9e** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-d_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube, which was then heated at 90 °C for 6 h. 1*H*-Pyrazole **14e** appeared to be formed in quantitative yield as inferred by means of ^1H NMR spectroscopy. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 60:40 hexane/ethyl acetate) to give **14e** (84%).

Determination of k_{obs} for the Rearrangement of 3*H*-Pyrazoles 9b–e in Acetone-d_6. 3*H*-Pyrazole **9** (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-d_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube. The tube was heated at 90 °C for **9b**, **9c**, and **9d** and at 60 °C for **9e**, and progress of the rearrangement of **9** was monitored by ^1H NMR spectroscopy. Concentration vs time data were obtained by normalizing the integrated intensity of the CH_2 singlet of phenoxy-2-propanone against the integrated intensity of the C-3 methyl singlet of 3*H*-pyrazole **9**. The decrease in concentration of **9** was monitored to at least 2 half-lives. The resultant plots of $\ln([9]/[9]_0)$ vs t gave the following observed rate constants: $k^{90\ °C}$(**9b**) = (9.7 ± 0.3) × 10^{-5} s^{-1} (correlation coefficient = 0.9954); $k^{90\ °C}$(**9c**) = (8.9 ± 0.4) × 10^{-5} s^{-1} (correlation coefficient = 0.9924); $k^{60\ °C}$(**9d**) = (2.1 ± 0.1) × 10^{-4} s^{-1} (correlation coefficient = 0.9990); $k^{90\ °C}$(**9e**) = (2.80 ± 0.05) × 10^{-4} s^{-1} (correlation coefficient = 0.9988).

Rearrangement of 3*H*-Pyrazoles 9a–e in Methanol. Rearrangement of 9a. Oxadiazoline **11a** (0.25 mmol) and methyl propiolate (0.50 mmol) were dissolved in methanol-d_4 (0.5 mL) and irradiated at room temperature with 300-nm light (Rayonet apparatus) for 6 h. By ^1H NMR spectroscopy the relative yields of **14a**, **15a**, 18, and dimethoxymethane-d_3 were 53%, 21%, 26% and 26%, respectively. Bulb to bulb distillation at 0.01 mmHg separated the volatiles from the pyrazoles. Dimethoxymethane-d_3 was confirmed by ^1H NMR and gas chromatography spiking experiments with an authentic sample of dimethoxymethane. The residue was subjected to centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give **14a** (48%), **15a** (16%), and 18 (24%).

Rearrangement of 9b. 3*H*-Pyrazole **9b** (0.200 mmol) was dissolved in C_6D_6 (0.5 mL), degassed (three freeze–pump–thaw cycles), and sealed into an NMR tube, which was subsequently heated at 90 °C for 20 min. The percentages of **14b**, **15b**, **20b**, 18, *tert*-butyl methyl ether-d_3, and isobutene by ^1H NMR spectroscopy were 18, 16, 6, 60, 31, and 27, respectively. *tert*-

Butyl methyl ether-d_3 was confirmed by ^{1}H NMR and gas chromatography spiking experiments. The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give **14b** (11%), **15b** (12%), **20b** (4%), and 18 (55%).

In another experiment 3*H*-pyrazole **9b** (20 mg, 0.102 mmol) and 2-phenoxy-2-propanone (7.7 mg, 0.05 mmol, internal standard) were dissolved in methanol-d_4. The tube was heated at 50 °C for 1 h and the progress of the rearrangement of **9b** was monitored by ^{1}H NMR spectroscopy. Concentration vs time data were obtained by normalizing the integrated intensity of the CH_2 singlet of phenoxy-2-propanone against the integrated intensity of the methyl singlet of 3*H*-pyrazole **9b**. The decrease in concentration of **9b** was monitored for 2.4 half-lives. The resultant plot of $\ln([\mathbf{9b}]/[\mathbf{9b}]_0)$ vs t with 5 data points gave an observed rate constant of $4.7 \pm 0.1 \times 10^{-4}$ s^{-1} (correlation coefficient = 0.9993).

Rearrangement of 9c. 3*H*-Pyrazole **9c** (0.200 mmol) was dissolved in methanol (5 mL) and the solution was refluxed for 0.5 h. The percentages of **14c** and **15c** by ^{1}H NMR spectroscopy were 81 and 19. Both 1*H*-pyrazole 18 and 1-adamantyl methyl ether (<2%) were detected by gas chromatography and ^{1}H NMR spectroscopy. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give **14c** (70%) and **15c** (13%).

In another experiment **9c** (0.100 mmol) and phenoxy-2-propanone (0.05 mmol, internal standard) were dissolved in methanol-d_4 and the solution was heated at 50 °C for 30 min. ^{1}H NMR spectroscopy revealed **9c** (7%), **14c** (76%), and **15c** (17%).

Rearrangement of 9d. 3*H*-Pyrazole 9d (0.200 mmol) was dissolved in methanol (5 mL) and the solution was refluxed for 0.5 h. The percentages of **14d** and **15d** by ^{1}H NMR spectroscopy were 75 and 25, respectively. Both 1*H*-pyrazole 18 and *p*-methoxybenzyl methyl ether (<2%) were detected by gas chromatography and ^{1}H NMR spectroscopy. The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 70:30 hexane/ethyl acetate) to give **14d** (63%) and **15d** (16%).

In another experiment, **9d** (0.100 mmol) and phenoxy-2-propanone (0.05 mmol, internal standard) were dissolved in 0.5 mL of methanol-d_4. After 9 min at ambient temperature, ^{1}H NMR spectroscopy revealed **9d** (8%), **14d** (65%), and **15d** (27%). After 15 min at ambient temperature, the solution consisted of **14d** (81%) and **15d** (19%).

Rearrangement of 9e. A solution of 3*H*-pyrazole **9e** (0.200 mmol) in methanol (5 mL) was refluxed for 0.5 h. 1*H*-Pyrazole **14e** appeared to be formed in quantitative yield by ^{1}H NMR spectroscopy. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 60:40 hexane/ethyl acetate) to give **14e** (86%).

In another experiment, **9e** (0.100 mmol) and phenoxy-2-propanone (0.05 mmol, internal standard) in 0.5 mL of methanol-d_4 were placed in a NMR tube. Initially the solution was not homogeneous. However, the solution was homogeneous after 1.6 h at 40 °C and it contained **9e** (42%) and **14e** (58%). The solution was then heated at 50 °C for an additional 30 min after which it consisted of **9e** (21%) and **14e** (79%) according to ^{1}H NMR spectroscopy.

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