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Pyrazoles. XII. The Preparation of 3(5)-Nitropyrazoles by Thermal Rearrangement of *N*-Nitropyrazoles[1,2]

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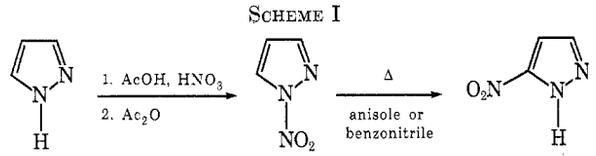
3(5)-Nitropyrazoles, such as 3,5-dinitropyrazole (**2f**), can be readily synthesized by thermal rearrangement of *N*-nitropyrazoles. In turn, 3(5),4-dinitropyrazoles are obtained by further nitration of some 3(5)-nitropyrazoles.

The direct nitration of pyrazole, using nitric acid or mixtures of nitric acid and sulfuric acid,[4,5] leads to substitution in the 4 position, in line with the behavior of other electrophilic reagents. Moreover, no further nitration of 4-nitropyrazoles has been reported in the literature. Reports on formation of 3-nitropyrazoles either concern compounds synthesized by other methods such as ring closure reactions[4,6] or by nitration of 1,4-disubstituted pyrazoles,[7,8a,b] neither of which appear to be general methods for the synthesis of 3-nitropyrazoles. It is worth notice that in the latter case further nitration to 3,5-dinitropyrazoles can occur.[7]

Recently three different groups of workers independently reported on the synthesis of the unsubstituted 3(5)-nitropyrazole (**2a**). Bagal, *et al.*,[9] obtained **2a** *via* diazotation of 3(5)-aminopyrazole, and Birkofer[10] substituted the trimethylsilyl group in 3(5)-trimethylsilylpyrazole by a nitroso group, which in turn was oxidized to give **2a**. We reported on a novel reaction, the thermal isomerization of *N*-nitropyrazoles into their corresponding 3(5)-nitro derivatives,[11] an example of an apparently characteristic property of *N*-nitroazoles to rearrange thermally into *C*-nitro compounds.[12,13] Using this rearrangement reaction, **2a** was obtained from pyrazole in a simple two-step synthesis in very high yield (see Scheme I).

SCHEME I



1a **2a**

The intramolecular migration of the nitro group can be visualized as a [1,5] sigmatropic shift giving a 3*H*-pyrazole followed by a fast tautomerization (see Scheme II).[13,14]

(1) Part XI: P. B. M. W. M. Timmermans, A. P. Uijttewaal, and C. L. Habraken, *J. Heterocycl. Chem.*, **9**, 1347 (1972).

(2) This research was supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for the Advancement of Pure Research (ZWO).

(3) Participant in the Undergraduate Research Project Program, supported by Pieter Langerhuizen Lzn. Fonds, administered by De Hollandsche Maatschappij der Wetenschappen.

(4) R. Fusco in "The Chemistry of Heterocyclic Compounds," Vol. 22, A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1967, p 3.

(5) A. R. Katritzky and J. M. Lagowski, "The Principles of Heterocyclic Chemistry," Methuen, London, 1967, p 148.

(6) W. E. Parham and J. L. Bleasdale, *J. Amer. Chem. Soc.*, **73**, 4664 (1951).

(7) M. D. Coburn, *J. Heterocycl. Chem.*, **7**, 707 (1970); **8**, 153, 293 (1971).

(8) (a) C. L. Habraken and P. Cohen Fernandes, *Recl. Trav. Chim. Pays-Bas*, **91**, 1185 (1972); (b) C. L. Habraken, P. Cohen Fernandes, S. Balian, and K. C. van Erk, *Tetrahedron Lett.*, 479 (1970).

(9) L. I. Bagal, M. S. Pevzner, A. N. Forlov, and N. I. Sheludyakova, *Khim. Geterosikl. Soedin.*, 259 (1970); *Chem. Abstr.*, **72**, 111383h (1970).

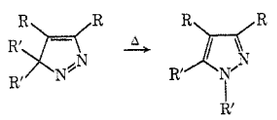
(10) L. Birkofer and M. Franz, *Chem. Ber.*, **104**, 3062 (1971).

(11) J. W. A. M. Janssen and C. L. Habraken, *J. Org. Chem.*, **36**, 3081 (1971).

(12) P. Cohen Fernandes and C. L. Habraken, *J. Org. Chem.*, **36**, 3084 (1971).

(13) C. L. Habraken and P. Cohen Fernandes, *Chem. Commun.*, 37 (1970).

(14) The presumed first step in this isomerization of *N*-nitropyrazoles resembles the reversed process of a van Alphen rearrangement[15] where 3,3,4,5-tetrasubstituted 3*H*-pyrazoles (pyrazolenines) rearrange into N-substituted pyrazoles, a reaction which was reported to be an uncatalyzed



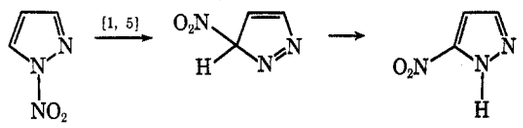
thermal rearrangement.[16] Recently, other examples of the pyrazolenine rearrangement were reported by Dürr and Sergio,[17a] and by Franck-Neumann and Buchecker,[17b] who observed migrations of ester, acyl, and cyano groups which they also explained in terms of [1,5] sigmatropic migrations.

(15) J. van Alphen, *Recl. Trav. Chim. Pays-Bas*, **62**, 485 (1943); **62**, 491 (1943).

(16) R. Hüttel, K. Francke, H. Martin, and J. Riedl, *Chem. Ber.*, **93**, 1433 (1960).

(17) (a) H. Dürr and R. Sergio, *Tetrahedron Lett.*, 3479 (1972); (b) M. Franck-Neumann and C. Buchecker, *ibid.*, 937 (1972).

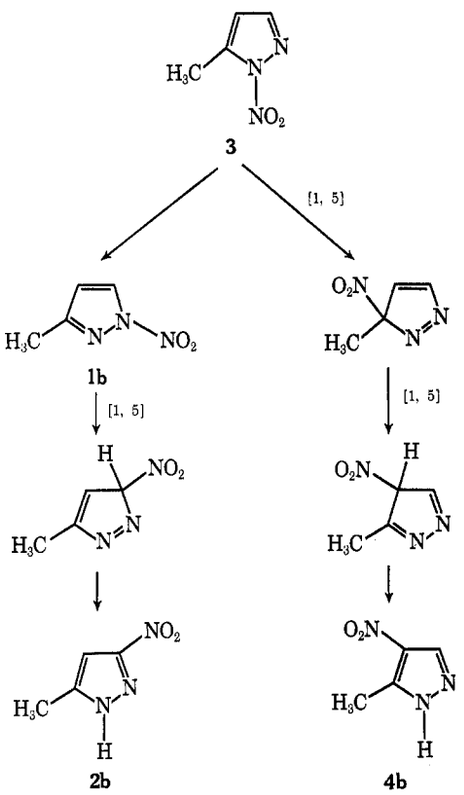
SCHEME II



1a 2a

The thermolysis of 5-methyl-1-nitropyrazole (**3**) affording 3(5)-methyl-4-nitropyrazole (**4b**) in addition to a small amount of 3(5)-methyl-5(3)-nitropyrazole (**2b**),[11] offers the only example so far encountered giving a 4-nitropyrazole. This result can be explained by assuming a subsequent sigmatropic rearrangement from a 3*H*- into a 4*H*-pyrazole followed by tautomerization. The concurrent formation of the 3(5)-methyl-5(3)-nitro isomer **2b** was demonstrated to originate from 3-methyl-1-nitropyrazole (**1b**), which in turn was demonstrated to arise from **3**, presumably by a competing [1,5] migration of the nitro group to the adjacent nitrogen atom (see Scheme III).

SCHEME III



3

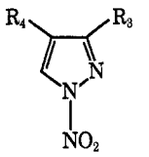
1b

2b **4b**

In this paper we report on the general synthetic implications of this novel isomerization reaction for the preparation of 3(5)-nitropyrazoles.

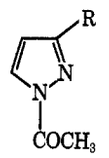
Results and Discussion

The required *N*-nitropyrazoles (**1a–k**) were obtained either by the original N-nitration procedure of Hüttel and Büchele[18] or by nitration of the pyrazole with a preformed mixture of nitric acid and acetic anhydride ("acetyl nitrate"). As described earlier,[11] N-nitration of 3(5)-methylpyrazole gave a mixture of the two isomers 3-methyl- and 5-methyl-1-nitropyrazole. Subsequently



1a, R_3 = H; R_4 = H
b, R_3 = CH_3; R_4 = H
c, R_3 = $C(CH_3)_3$; R_4 = H
d, R_3 = C_6H_5; R_4 = H
e, R_3 = *p*-$NO_2C_6H_4$; R_4 = H
f, R_3 = NO_2; R_4 = H
1g, R_3 = H; R_4 = CH_3
h, R_3 = H; R_4 = C_2H_5
i, R_3 = H; R_4 = C_6H_5
j, R_3 = H; R_4 = NO_2
k, R_3 = C_6H_5; R_4 = NO_2

we found that nitration of 3(5)-methylpyrazole with a large excess of acetyl nitrate *gives the 1,3 isomer* **1b** *as the only product* (see Experimental Section), whereas nitration with an equimolar amount of acetyl nitrate afforded primarily the 1,5 isomer **3** in addition to small amounts of **1b** and 1-acetyl-3-methylpyrazole (**5**).



5, R = CH_3
6, R = C_6H_5

The formation of small quantities of *N*-acetyl compounds as by-products on N-nitration was also observed in some other cases.[8a,11,19] Usually the *N*-nitropyrazoles could be purified by direct crystallization or by very mild acid hydrolysis of the *N*-acetyl derivatives prior to crystallization.[8a] N-Nitration of 3(5)-*tert*-butylpyrazole, 3(5)-phenylpyrazole, and 3(5)-(*p*-nitrophenyl)pyrazole afforded 1-nitro-3-*tert*-butylpyrazole (**1c**), 1-nitro-3-phenylpyrazole (**1d**),[19] and 1-nitro-3-(*p*-nitrophenyl)pyrazole (**1e**) in excellent yields. In these instances the formation of 5-substituted 1-nitropyrazoles is presumably prevented by the bulkiness of the sustituents. An attempt to prepare 1-nitro-5-phenylpyrazole according to the procedure developed for the synthesis of the 5-methyl analog **3** was unsuccessful; the only product obtained was 1-acetyl-3-phenylpyrazole (**6**)[19]. The N-nitration of 4-nitro-3(5)-phenylpyrazole (**4d**) also resulted in the formation of only one isomer, 1,4-dinitro-3-phenylpyrazole (**1k**). Contrary to what was reported by Hüttel and Büchele,[18] N-nitration of 4-nitropyrazole (**4a**) resulted in high yields of 1,4-dinitropyrazole (**1j**). Likewise, N-nitration of 3(5)-nitropyrazole easily afforded 1,3-dinitropyrazole (**1f**).

N-Nitropyrazoles, as in general *N*-nitroazoles, are readily characterized through tlc (see Experimental Section) and ir spectroscopy.[11,12] In addition to the absence of a N–H absorption band, the NO_2 stretching frequencies for a *N*-nitro group (as compared to those of a *C*-nitro group) are found at a lower wavenumber (1270–1295 cm^{-1}) for the symmetric vibration and a higher wavenumber (1600–1650 cm^{-1}) for the asymmetric vibration. In those instances where a decision between two possible isomeric structures was needed, namely compounds **1c–f**, structural assign-

(18) R. Hüttel and F. Büchele, *Chem. Ber.*, **88**, 1586 (1955).

(19) Dal Monte-Casoni[20] N-nitrated 3(5)-phenylpyrazole in two ways: on nitration by Hüttel's procedure she obtained an *N*-nitrophenylpyrazole with unassigned structure, presumably **1d**; on nitration with an excess of acetyl nitrate 1-acetyl-3-(*p*-nitrophenyl)pyrazole was obtained in addition to the same *N*-nitro compound.

(20) D. Dal Monte-Casoni, *Ann. Chim. (Rome)*, **48**, 783 (1958).

TABLE I

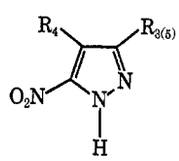
REARRANGEMENT OF *N*-NITROPYRAZOLES 1 INTO 3(5)-NITROPYRAZOLES 2

N-Nitropyrazole	Substituents		3(5)-Nitropyrazole	Rearrangement conditions[a]	Yield[b]
	R_3	R_4			
1a	H	H	**2a**	B, 3 hr, 180°	+++
1b	CH_3	H	**2b**	A, 2 hr, 145°[c]	+++
1c	$C(CH_3)_3$	H	**2c**	A, 2.5 hr, 130°	+++
1d	C_6H_5	H	**2d**	A, 1.5 hr, 130°	+++
1e	p-$NO_2C_6H_4$	H	**2e**	B, 1.5 hr, 140°	+++
1f	NO_2	H	**2f**	B, 110 hr, 140°	+++
1g	H	CH_3	**2g**	B, 20 hr, 160°	++
1h	H	C_2H_5	**2h**	A, 50 hr, 140°[c]	++
1i	H	C_6H_5	**2i**	B, 2.5 hr, 120°	+
1j	H	NO_2	**2j**	B, 6 hr, 191°	+
1k	C_6H_5	NO_2	**2k**	B, 1.5 hr, 140°	+++

[a] A = anisole solution, B = benzonitrile solution; the work-up of the reaction mixture is described in the Experimental Section. [b] See Experimental Section for more detailed information; +++ = 80% and above; ++ = 50–80%; + = low yield (see text). [c] This experiment is described in ref 11.

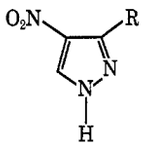
ments were based on their nmr spectral data. The chemical shifts of the 5 protons of these compounds were found at much lower external field as compared to those of the corresponding protons in the N-unsubstituted pyrazoles, owing to the nitro group on the adjacent nitrogen atom.[11,12] Moreover, as is known from investigations of Jacquier and others,[21] the coupling constant between a 4 and a 3 proton differs from that between a 4 and 5 proton ($J_{45} > J_{34}$). The distinct multiplet character of the signal of the phenyl protons in the nmr spectrum of **1d** indicating a phenylpyrazole unsubstituted in the ortho positions[22] furnishes additional support for these assignments.

The best results for the rearrangement reactions were obtained on heating 5–10% solutions of the *N*-nitropyrazole in anisole or benzonitrile. Thin layer chromatographic analysis was used to determine the end of the reaction. In some cases dilution with hexane of the chilled reaction mixture resulted in a nearly quantitative precipitation of the *C*-nitropyrazole. For example, 97% of 3(5)-nitropyrazole was obtained in this way from the rearrangement of 1-nitropyrazole in benzonitrile (see Experimental Section). In most of the remaining cases, *e.g.*, the conversion of 1,3-dinitropyrazole into 3,5-dinitropyrazole (**2f**), high yields were obtained *via* additional extraction with a sodium hydroxide solution (see Experimental Section and Table I). It appeared that isomerization of 4-substituted 1-nitropyrazoles was accompanied by considerable decomposition, resulting in fair to low yields. Thus, 4-methyl- and 4-ethyl-1-nitropyrazole (**1g** and **1h**) led to 4-methyl-3(5)-nitropyrazole (**2g**) and 4-ethyl-3(5)-nitropyrazole (**2h**), respectively, in isolated yields of *ca.* 60%. Likewise, thermolysis of 1-nitro-4-phenylpyrazole (**1i**) afforded (among many decomposition products) only small amounts of the known compound 3(5)-nitro-4-phenylpyrazole (**2i**),[6] as was observed on tlc. Thermolysis of the 1,4-dinitro compound, **1j**, gave but a small yield of 3(5),4-dinitropyrazole (**2j**). [Because it was found (*vide infra*) that the latter compound can be obtained in good yield on nitration of 3(5)-nitropyrazole in sulfuric acid, no further efforts were undertaken to obtain **2j** by preparative themolysis of 1,4-dinitropyrazole]. One of the decomposition reactions observed was a denitration of the *N*-nitropyrazole giving back the N-unsubstituted starting material. Such denitration also occurred in the case of the thermolysis of 1,3-dinitropyrazole, as observed from the presence of 10–15% of 3(5)-nitropyrazole on work-up of the reaction mixture.



2a, $R_{3(5)}$ = H; R_4 = H
b, $R_{3(5)}$ = CH_3; R_4 = H
c, $R_{3(5)}$ = $C(CH_3)_3$; R_4 = H
d, $R_{3(5)}$ = C_6H_5; R_4 = H
e, $R_{3(5)}$ = p-$NO_2C_6H_4$; R_4 = H
f, $R_{3(5)}$ = NO_2; R_4 = H
g, $R_{3(5)}$ = H; R_4 = CH_3
h, $R_{3(5)}$ = H; R_4 = C_2H_5
i, $R_{3(5)}$ = H; R_4 = C_6H_5
j, $R_{3(5)}$ = H; R_4 = NO_2
k, $R_{3(5)}$ = C_6H_5; R_4 = NO_2

As expected, the thermal rearrangement of the 1-nitropyrazoles unsubstituted in the 5 position, **1a–k**, in all cases afforded the corresponding 3(5)-nitropyrazoles **2a–k**. Structural assignments of the 3(5)-*tert*-butyl-, 3(5)-phenyl-, and 3(5)-*p*-nitrophenyl-5(3)-nitropyrazoles (**2c**, **2d**, and **2e**) were based on comparison (tlc, melting points, uv[23] and ir spectra) with the isomeric 4-nitropyrazoles **4c**, **4d**, and **4e**, which were synthesized by unambiguous routes, **4d** being obtained from **4e** after selective reduction to 4-nitro-3(5)-



4a, R = H
b, R = CH_3
c, R = $C(CH_3)_3$
d, R = C_6H_5
e, R = p-$NO_2C_6H_4$

(*p*-aminophenyl)pyrazole followed by deamination. For those compounds originally possessing a substituent in the 4 position, the identifications were based on the presence of a *C*-nitro group in 4-methyl-3(5)-nitropyrazole (**2g**) and of a second *C*-nitro group in 3(5),4-dinitro- and 3(5),4-dinitro-5(3)-phenylpyrazole (**2j** and **2k**) (ir spectra and tlc and mass spectral

(21) J. Elguero, R. Jacquier, and H. C. N. Tien Duc, *Bull. Soc. Chim. Fr.*, 2327 (1966).

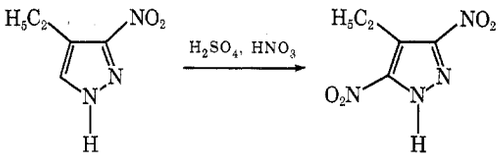
(22) L. G. Tensmeyer and C. Ainsworth, *J. Org. Chem.*, **31**, 1878 (1966).

(23) Uv spectra of a number of nitropyrazoles will be presented and discussed in a separate paper.

or elemental analysis). Compound **2f**, the isomerization product of 1,3-dinitropyrazole, was found to be a *C*-dinitropyrazole differing from the 3(5),4-dinitro isomer **2j** and was consequently assigned the structure of 3,5-dinitropyrazole. All assignments were corroborated by the nmr spectra.

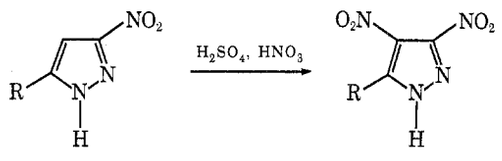
As mentioned before, 4-nitropyrazoles do not undergo further C-nitration, whereas 1,4-disubstituted pyrazoles can undergo dinitration to give 3,5-dinitro derivatives. These findings of Coburn[7] were confirmed by the synthesis of 4-ethyl-3,5-dinitropyrazole (**7**) on further nitration in mixed acid of the mononitropyrazole **2h** (Scheme IV) (see Experimental Section). Moreover, it appeared that the 3(5)-nitropyrazoles **2a** and **2b** on nitration with mixed acid afforded quite readily and in good yields 3(5),4-dinitropyrazole (**2j**) and 3(5),4-dinitro-5(3)-methylpyrazole (**8**) (Scheme V). No trace of 3(5),4-dinitropyrazole (**2j**) could be detected when 4-nitropyrazole was subjected to the same dinitration conditions of the 3(5)-nitropyrazoles. To our knowledge only one other example of further nitration of a 3(5)-nitropyrazole has been described, namely that of 3(5)-nitro-5(3)-(*m*-pyridyl)pyrazole giving the corresponding 3(5),4-dinitro derivative.[24] Apparently, and contrary to what is observed with 4-nitropyrazoles, 3(5)-nitropyrazoles can be C-nitrated further, and again in the 4 position, as readily as other 3(5)-substituted pyrazoles.

SCHEME IV



2h **7**

SCHEME V



2a, R = H **2j**, R = H
2b, R = CH_3 **8**, R = CH_3

In conclusion, thermal rearrangement of *N*-nitropyrazoles offers a convenient method to synthesize 3(5)-nitropyrazoles, which in turn may undergo electrophilic substitution preferably in the 4 position, as we observed for the nitration reaction.

Experimental Section[25]

General.—Nmr spectra (δ expressed in parts per million) were recorded on a JEOL 60-MHz Minimar or on a JEOL PS-100 instrument; ir spectra (KBr technique) were recorded on a Perkin-Elmer IR-137 spectrophotometer. Glc analyses were performed on a Varian Aerograph 1400 instrument. Spraying with Rhodamine B solution (0.05% in ethanol) was used for the detection of nitropyrazoles on tlc; in the case of *N*-nitropyrazoles the purple-colored spots characteristic for all nitroazoles turned into yellow or brownish yellow colored spots on standing. Elemental analyses were performed by Mr. W. J. Buis, TNO Laboratory of Organic Chemistry, Utrecht, The Netherlands; mass spectra were recorded on a AE MS-902 spectrometer. All melting points are uncorrected.

Materials.—3(5)-Methylpyrazole, 3(5)-phenylpyrazole, and 4-nitropyrazole (**4a**) were synthesized by standard procedures. The syntheses of 1-nitropyrazole (**1a**), 5-methyl-1-nitropyrazole (**3**), 4-ethyl-1-nitropyrazole (**1h**), 3(5)-methyl-5(3)-nitropyrazole (**2b**), and 4-ethyl-3(5)-nitropyrazole (**2h**) were described in ref 11; the synthesis of 1-nitro-4-phenylpyrazole (**1i**) was described in ref 8a. 4-Methylpyrazole was prepared by reaction of 1,1,3,3-tetraethoxy-2-methylpropane with hydrazine hydrochloride;[26] 3(5)-*tert*-butylpyrazole was prepared by condensing pivaloyl acetaldehyde[27] with hydrazine hydrate, yield 71%, bp 110–112° (10 mm) [lit.[28] bp 106° (9 mm)]. 3(5)-(*p*-Nitrophenyl)pyrazole was made by nitrating 3(5)-phenylpyrazole with nitric acid (*d* 1.52) in sulfuric acid solution in the cold.[20] 1-Acetyl-3-methylpyrazole (**5**) was obtained by reaction of 3(5)-methylpyrazole with an excess of acetyl chloride.[29]

Acetyl nitrate was prepared freshly before use by adding nitric acid (*d* 1.52) to acetic anhydride.[8a] All chemicals, being high-grade commercial products, were used as such.

4-Nitro-3(5)-(*p*-nitrophenyl)pyrazole (4e).—While cooling, 7 g of 3(5)-phenylpyrazole was added to 100 ml of nitric acid (*d* 1.52); after stirring at 50° for 2 hr the solution was poured onto ice and the precipitated compound was collected by filtration. Ether extraction of the filtrate provided an additional amount of **4e**. Total yield after crystallization from ethanol was 7.5 g (66%): mp 210–212° (lit.[30] mp 212°); nmr (60 MHz, DMSO) δ 8.86 [s, 1, 5(3)-H], 8.37 and 7.97 (doublets, 4, J = 8 Hz, aromatic).

4-Nitro-3(5)-(*p*-aminophenyl)pyrazole.—Hydrogen sulfide was passed through a solution of 7.5 g of **4e** containing 4.2 g of NaOH, at a temperature of 80°; after a few minutes the temperature increased to *ca.* 90° and an orange-colored solid precipitated. H_2S was passed through for an additional 1 hr. The solid, collected by filtration, was washed with water: 4.9 g (75%); after crystallization from water, mp 187–187.5°; ir 3350 (NH_2), 3200 (NH), 1495 and 1320 cm^{-1} (NO_2); nmr (60 MHz, acetone) δ 8.25 [s, 1, 5(3)-H], 7.51 and 6.81 (doublets, 4, J = 8 Hz, aromatic).

Anal. Calcd for $C_9H_8N_4O_2$: C, 52.94; H, 3.95; N, 27.44. Found: C, 53.07; H, 3.76; N, 27.36.

4-Nitro-3(5)-phenylpyrazole (4d).—Sodium nitrite (1.4 g) was very slowly added to a cold solution (−5 to 0°) of 4-nitro-3(5)-(*p*-aminophenyl)pyrazole (4.0 g) in 20% hydrochloric acid; after stirring for 0.5 hr at 0°, 31.2 ml of cooled hypophosphoric acid (50%) was added. The mixture was allowed to stand for 24 hr at room temperature; the reaction mixture was diluted with *ca.* 50 ml of water and the solid was collected by filtration. Crystallization from a large amount of water yielded 3.1 g (84%) of **4d**. The compound was recrystallized from water to give an analytically pure sample: mp 185–185.5°; ir 3200 (NH), 1495 and 1320 cm^{-1} (NO_2); nmr (60 MHz, acetone) δ 8.44 [s, 1, 5(3)-H], 7.75–7.40 (m, 5, aromatic).

Anal. Calcd for $C_9H_7N_3O_2$: C, 57.14; H, 3.73; N, 22.21. Found: C, 57.16; H, 3.63; N, 22.32.

4-Nitro-3(5)-*tert*-butylpyrazole (4c).—A 1.5-g portion of 3(5)-*tert*-butylpyrazole was nitrated with "mixed acid" according to the method of Morgan and Ackerman;[31] the reaction mixture was poured onto ice and extracted with ether; evaporation of the solvent afforded 1.7 g (83%) of **4c**. A pure sample was obtained by crystallization from petroleum ether (bp 60–80°): mp 118.5–119°; ir 3235 (NH), 1510 and 1385 (1311?) cm^{-1} (NO_2); nmr (60 MHz, $CDCl_3$) δ 8.37 [s, 1, 5(3)-H] and 1.44 [s, 9, $C(CH_3)_3$].

Anal. Calcd for $C_7H_{11}N_3O_2$: C, 49.69; H, 6.55; N, 24.84. Found: C, 49.80; H, 6.62; N, 24.93.

3(5)-Nitropyrazole (2a). Rearrangement of 1-Nitropyrazole

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(1a).—A solution of 3.0 g of 1a in 30 ml of benzonitrile was heated for 3 hr at 180°; after cooling and the addition of a threefold quantity of hexane, compound 2a was collected by filtration. The crude yield, after washing with hexane and drying, was 2.9 g (97%), mp 173–174°; recrystallization from water gave mp 174–175° (lit.[9] mp 175°). Additional experiments (up to 10-g scale) afforded 95–99% yields.

Nitration of 3(5)-Methylpyrazole with an Excess of Acetyl Nitrate.—Acetyl nitrate (72 mmol, 3 ml of nitric acid in 7.5 ml of acetic anhydride) was added to a solution of 3(5)-methylpyrazole (2.5 g, 32 mmol) in 3 ml of acetic acid at 0°. After 2 hr the reaction mixture was poured onto ice; the resulting precipitate (0.7 g) appeared to be pure 3-methyl-1-nitropyrazole (1b) (glc, ir, nmr, and melting point); an additional 1.2-g portion of 1b was obtained after neutralization of the filtrate with sodium carbonate and extraction with ether; total yield was 49%.

Nitration of 3(5)-Methylpyrazole with an Equimolar Amount of Acetyl Nitrate.—A 5.9-g (72 mmol) portion of 3(5)-methylpyrazole was treated with 72 mmol of acetyl nitrate as described above; after neutralization and extraction with ether the product mixture was analyzed by glc and nmr; on comparison with authentic samples, it was found to consist of 3, 1b, and 5 (7:1:2).

1-Nitro-3-*tert*-butylpyrazole (1c).—A 3.0-g portion of 3(5)-*tert*-butylpyrazole was dissolved in 9.5 ml of acetic acid and N-nitrated[11,18] with 2.2 ml of nitric acid (*d* 1.52) and 16 ml of acetic anhydride. The crude product was crystallized from petroleum ether to yield 2.6 g (64%) of compound 1c. The analytical sample was obtained by recrystallization from petroleum ether: mp 66°; ir 1600 and 1285 cm^{-1} (NNO_2); nmr (60 MHz, $CDCl_3$) δ 8.23 (d, 1, J = 2.8 Hz, 5-H), 6.37 (d, 1, J = 2.8 Hz, 4-H), and 1.38 [s, 9, $C(CH_3)_3$].

Anal. Calcd for $C_7H_{11}N_3O_2$: C, 49.69; H, 6.55; N, 24.84. Found: C, 49.66; H, 6.45; N, 24.81.

1-Nitro-3-phenylpyrazole (1d) was obtained when 6.0 g of 3(5)-phenylpyrazole, dissolved in 18 ml of acetic acid, was N-nitrated with 3.6 ml of nitric acid and 18 ml of acetic anhydride. The crude yield was 7.3 g (93%). Recrystallization from methanol gave an analytically pure sample: mp 119° (lit.[20] mp 122°); ir 1620 and 1290 cm^{-1} (NNO_2); nmr (60 MHz, $CDCl_3$) δ 8.20 (d, 1, J = 3.0 Hz, 5-H), 6.67 (d, 1, J = 3.0 Hz, 4-H), 7.90–7.65 (m, 2), and 7.45–7.20 (m, 3, aromatic).

Anal. Calcd for $C_9H_7N_3O_2$: C, 57.14; H, 3.73; N, 22.21. Found: C, 57.21; H, 3.75; N, 22.26.

Reaction of 3(5)-Phenylpyrazole with an Equimolar amount of Acetyl Nitrate.—Acetyl nitrate (14 mmol) was carefully added to a solution of 2 g (14 mmol) of 3(5)-phenylpyrazole in 15 ml of acetic acid at 0°. After 1.5 hr the reaction mixture was poured onto ice; the formed precipitate (2.1 g) appeared to be 1-acetyl-3-phenylpyrazole (6). After crystallization from petroleum ether 6 had mp 63° (lit.[32] mp 64–65°); ir 1725 cm^{-1} (C=O); nmr (100 MHz, $CDCl_3$) δ 8.16 (d, 1, J = 2.8 Hz, 5-H), 6.64 (d, 1, J = 2.8 Hz, 4-H), 7.9–7.7 (m, 2) and 7.4–7.3 (m, 3, aromatic), 2.70 (s, 3, CH_3).

1-Nitro-3-(*p*-nitrophenyl)pyrazole (1e).[25]—When 2.0 g of 3(5)-(*p*-nitrophenyl)pyrazole was dissolved in 35 ml of acetic acid and N-nitrated with 0.6 ml of nitric acid and 6 ml of acetic anhydride, 2.3 g (93%) of crude 1e was obtained. The compound was recrystallized from methanol to give a pure sample. A melting point was only observed when the temperature of the sample was raised rapidly, mp 184–186°. When the temperature was increased slowly, compound 1e rearranged into 2e without liquefying: ir 1625 and 1290 cm^{-1} (NNO_2), 1515 and 1340 cm^{-1} (CNO_2); nmr (60 MHz, DMSO) δ 8.86 (d, 1, J = 2.8 Hz, 5-H), 7.42 (d, 1, J = 2.8 Hz, 4-H), and 8.27 (symmetrical AA'BB' spectrum, 4, aromatic).

Anal. Calcd for $C_9H_6N_4O_4$: C, 46.16; H, 2.58; N, 23.93. Found: C, 46.15; H, 2.46; N, 23.86.

1,3-Dinitropyrazole (1f).[25]—A 2.9-g portion of 2a was suspended in 18 ml of acetic acid and N-nitrated with 2.4 ml of nitric acid and 6 ml of acetic anhydride. After 2.5 hr the reaction mixture was poured onto ice and the *N*-nitro compound was collected by filtration: 2.3 g (57%) of 1f; white crystals from hexane; mp 67°; ir 1645 and 1285 cm^{-1} (NNO_2), 1550 and 1350 cm^{-1} (CNO_2); nmr (60 MHz, $CDCl_3$) δ 8.45 (d, 1, J = 2.8 Hz, 5-H) and 7.17 (d, 1, J = 2.8 Hz, 4-H); mol wt, 158.0079 (calcd for $C_3H_2N_4O_4$, 158.0075).

4-Methyl-1-nitropyrazole (1g).—A 4.0-g portion of 4-methylpyrazole was dissolved in 15 ml of acetic acid and N-nitrated with 3 ml of nitric acid and 9 ml of acetic anhydride. After 2 hr the reaction mixture was poured on ice; 3.75 g (61%) of 1g precipitated from the solution after saturation with NaCl. Recrystallization from petroleum ether (bp 40–60°) gave an analytically pure sample: mp 42.5°; ir 1600 and 1290 cm^{-1} (NNO_2); nmr (60 MHz, $CDCl_3$) δ 8.11 (s, 1, 5-H), 7.48 (s, 1, 3-H), and 2.17 (s, 3, CH_3).

Anal. Calcd for $C_4H_5N_3O_2$: C, 37.80; H, 3.97; N, 33.06. Found: C, 39.02; H, 3.85; N, 33.24.

1,4-Dinitropyrazole (1j).—4-Nitropyrazole (4a, 3.0 g) was suspended in 15 ml of acetic acid and N-nitrated with 3.5 ml of nitric acid and 5.5 ml of acetic anhydride; after 0.5 hr the reaction mixture was poured onto ice, neutralized with sodium carbonate, and repeatedly extracted with ether. The combined extracts were dried on $MgSO_4$ and evaporated to dryness: yield 3.4 g (81%) of crude 1j. The product was purified by column chromatography[11] (silica gel H according to Stahl, chloroform–ethyl acetate, 3:1) and crystallization from hexane: mp 54°; ir 1650 and 1280 cm^{-1} (NNO_2), 1515 and 1320 cm^{-1} (CNO_2); nmr (60 MHz, $CDCl_3$) δ 9.00 (s, 1, 5-H) and 8.17 (s, 1, 3-H); mol wt, 158.0079 (calcd for $C_3H_2N_4O_4$, 158.0075).

1,4-Dinitro-3-phenylpyrazole (1k).—Compound 4d (1.0 g) was dissolved in 10 ml of acetic acid and N-nitrated with 0.7 ml of nitric acid and 5 ml of acetic anhydride. After 1.5 hr the reaction mixture was poured onto ice; the resulting solution was saturated with NaCl; and the *N*-nitro compound was collected by filtration and washed with water. A crude yield of 1.2 g (97%) of 1k was obtained. The analytical sample was obtained after crystallization from methanol: mp 163° dec; ir 1650 and 1270 (NNO_2), 1545 (?), 1510 and 1350 cm^{-1} (CNO_2); nmr (100 MHz, $CDCl_3$) δ 9.10 (s, 1, 5-H), 7.8–7.7 (m, 2), and 7.6–7.4 (m, 3, aromatic).

Anal. Calcd for $C_9H_6N_4O_4$: C, 46.16; H, 2.58; N, 23.93. Found: C, 46.53; H, 2.74; N, 23.54.

3(5)-Nitro-5-(3)-*tert*-butylpyrazole (2c). Rearrangement of 1c.—The reaction mixture obtained after rearrangement of 1c (2.0 g in 25 ml of anisole) was diluted with hexane and extracted with 1 *N* NaOH solution; the NaOH layers were acidified with HCl and extracted with ether. The crude product obtained after evaporation of the solvent was crystallized from petroleum ether (bp 80–100°): yield 1.6 g (80%) of 2c; mp 190–190.5°; ir 3150 (NH), 1530 and 1335 cm^{-1} (CNO_2); nmr (60 MHz, $CDCl_3$) δ 6.59 (s, 1, 4-H) and 1.21 [s, 9, $C(CH_3)_3$].

Anal. Calcd for $C_7H_{11}N_3O_2$: C, 49.69; H, 6.55; N, 24.84. Found: C, 49.74; H, 6.54; N, 25.00.

3(5)-Nitro-5(3)-phenylpyrazole (2d). Rearrangement of 1d.—A 4.0-g portion of 1d, dissolved in 40 ml of anisole, was thermolyzed at 130°; compound 2d precipitated from the chilled reaction mixture and was collected by filtration (3.3 g, 83%). An additional portion was obtained by extraction of the filtrate with NaOH solution. Crystallization from methanol gave an analytically pure sample: mp 198°; ir 3225 (NH), 1540 and 1335 cm^{-1} (CNO_2); nmr (60 MHz, acetone) δ 7.9–7.7 (m, 2) and 7.6–7.3 (m, 3, aromatic), 7.26 (s, 1, 4-H).

Anal. Calcd for $C_9H_7N_3O_2$: C, 57.14; H, 3.73; N, 22.21. Found: C, 57.33; H, 3.65; N, 22.35.

3(5)-Nitro-5(3)-(*p*-nitrophenyl)pyrazole (2e).[25] **Rearrangement of 1e.**—The solution obtained after rearrangement of 1e (0.50 g dissolved in 5 ml of benzonitrile) was diluted with hexane; compound 2e precipitated and was collected by filtration. The crude yield was 0.41 g (82%). Recrystallization from methanol gave an analytically pure sample: mp 260°; ir 3230 (NH), 1545, 1520, and 1335 cm^{-1} (CNO_2); nmr (60 MHz, DMSO) δ 8.23 (symmetrical AA'BB' spectrum, 4, aromatic) and 7.75 (s, 1, 4-H).

Anal. Calcd for $C_9H_6N_4O_4$: C, 46.16; H, 2.58; N, 23.93. Found: C, 46.13; H, 2.61; N, 24.10.

3,5-Dinitropyrazole (2f). Rearrangement of 1f.[25]—The reaction mixture that was obtained after thermolysis of 1.0 g of 1f in 20 ml of benzonitrile was worked up by dilution with hexane and extraction with NaOH solution. The product (1 g) was contaminated with 10–15% of 2a (nmr analysis). Crystallization from benzene afforded pure 2f: mp 173–174°; ir 3200 (NH), 1570(?), 1530, 1365, and 1340 cm^{-1} (CNO_2); nmr (60 MHz, acetone) δ 7.64 (s, 4-H).

Anal. Calcd for $C_3H_2N_4O_4$: C, 22.79; H, 1.28; N, 35.45. Found: C, 22.91; H, 1.42; N, 35.51.

4-Methyl-3(5)-nitropyrazole (2g). Rearrangement of 1g.—A 3.0-g portion of 1g, dissolved in 60 ml of benzonitrile, was

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thermolyzed at 160°. **2g** was precipitated from the reaction mixture by the addition of hexane; the compound (1.25 g) was collected by filtration. An additional 0.60 g was obtained by extraction of the filtrate with NaOH solution. The total crude yield was 62%. Crystallization from water gave a pure sample: mp 187°; ir 3175 (NH), 1525 and 1350 (1370?) cm^{-1} (CNO_2); nmr (60 MHz, $CDCl_3$) 7.80 [s, 1, 5(3)-H] and 2.47 (s, 3, CH_3).

Anal. Calcd for $C_4H_5N_3O_2$: C, 37.80; H, 3.97; N, 33.06. Found: C, 37.92; H, 4.07; N, 32.97.

3(5),4-Dinitro-5(3)-phenylpyrazole (2k). Rearrangement of 1k.—A 0.30-g portion of **1k** was dissolved in 5 ml of benzonitrile and thermolyzed at 140°; the resulting solution was worked up by extraction with NaOH solution. The crude yield was 0.24 g (80%). Crystallization from benzene gave an analytically pure sample: mp 149–150°; ir 3280 (NH), 1535 (m), 1370 and 1330 cm^{-1} (CNO_2); nmr (100 MHz, acetone) δ 7.9–7.7 (m, 2) and 7.7–7.5 (m, 3, aromatic).

Anal. Calcd for $C_9H_6N_4O_4$: C, 46.16; H, 2.58; N, 23.93. Found: 46.43; H, 2.72; N, 23.74.

Thermolysis of 1i.—A 2% solution of **1i** in benzonitrile was heated at 120°; the reaction was followed by tlc. Among other products, the rearrangement product 3(5)-nitro-4-phenylpyrazole (**2i**)[33] could be detected.

3(5),4-Dinitropyrazole (2j). Nitration of 2a with Mixed Acid.—Compound **2a** (1.5 g) was dissolved in 2.55 ml of concentrated sulfuric acid and nitrated by the method of Morgan and Ackerman[31] with 1.65 ml of nitric acid and 5.1 ml of sulfuric acid. The reaction mixture was poured on ice and, after saturation with NaCl, extracted with ether. Removal of the solvent gave 1.9 g (86%) of **2j** as white crystals from benzene: mp 87.5–88.5°; ir 3280 (NH), 1550, 1520, 1370, and 1340 cm^{-1} (NO_2); nmr (60 MHz, acetone) δ 8.71 [s, 5(3)-H]; mol wt, 158.0078 (calcd for $C_3H_2N_4O_4$, 158.0075).

Thermolysis of 1j.—The reaction mixture that was obtained when a solution of **1j** in benzonitrile (10%) was refluxed for 6 hr was worked up by extraction with NaOH solution. The oily liquid that was obtained appeared to be mainly a mixture of **2j** and **4a** (8:2, nmr analysis). When a solution of **1j** was heated for a longer time at a lower temperature (130°), other (unknown) products were formed.

3(5),4-Dinitro-5(3)-methylpyrazole (8).—Compound **2b** (0.80 g) was nitrated by the method of Morgan and Ackerman.[31] The reaction mixture was poured onto ice, neutralized with sodium carbonate, and extracted with ether, yield 0.78 g (72%). Crystallization from benzene gave an analytically pure sample: mp 120–121°; ir 3280 (NH), 1550, 1505, 1360, and 1330 cm^{-1} (NO_2); nmr (60 MHz, acetone) δ 2.67 (s, CH_3).

Anal. Calcd for $C_4H_4N_4O_4$: C, 27.91; H, 2.34; N, 32.56. Found: C, 28.33; H, 2.49; N, 32.30.

3,5-Dinitro-4-ethylpyrazole (7).—The reaction mixture that was obtained after nitration of 1.5 g of **2h** by the method of Morgan and Ackerman[31] was poured onto ice; the formed precipitate (unreacted **2h**) was removed by filtration; the filtrate was neutralized with sodium carbonate and extracted with ether to yield 0.48 g (23%) of **7**. The compound was purified by column chromatography[11] (silica gel H according to Stahl, chloroform–methanol–acetic acid, 80:20:0.5, as eluent) and crystallization from water: mp 170–171°; ir 3245 (NH), 1590 (?), 1545 and 1340 cm^{-1} (NO_2); nmr (100 MHz, hexadeuterioacetone) δ 3.19 (q, 2, CH_2) and 2.24 (t, 3, CH_3).

Anal. Calcd for $C_5H_6N_4O_4$: C, 32.26; H, 3.25; N, 30.10. Found: C, 32.71; H, 3.35; N, 30.26.

Nitration of 4-Nitropyrazole (4a).—This compound was treated with mixed acid by the same method that was used for the further nitration of **2a**. Work-up of the reaction mixture afforded the unreacted compound as the only product (tlc analysis).

Registry No.—**1a**, 7119-95-1; **1c**, 38859-25-5; **1d**, 38859-26-6; **1e**, 38859-27-7; **1f**, 38858-81-0; **1g**, 38858-82-1; **1j**, 35852-77-8; **1k**, 38858-84-3; **2a**, 26621-44-3; **2c**, 38858-86-5; **2d**, 38858-87-6; **2e**, 38858-88-7; **2f**, 38858-89-8; **2g**, 38858-90-1; **2h**, 31163-87-8; **2j**, 38858-92-3; **2k**, 38858-93-4; **4a**, 2075-46-9; **4c**, 38858-95-6; **4d**, 38858-96-7; **4e**, 38858-97-8; **6**, 38858-98-9; **7**, 38858-99-0; **8**, 38859-00-6; 3(5)-phenylpyrazole, 2458-26-6; 4-nitro-3(5)-(*p*-aminophenyl)pyrazole, 38859-02-8; 3(5)-methylpyrazole, 1453-58-3; 3(5)-(*p*-nitrophenyl)pyrazole, 20583-31-7; 4-methylpyrazole, 7554-65-6.

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On the Reaction of Carbonyl Compounds with 3,5-Dihydroxy-4-phenylisoxazole. A Novel Type of Noncatalyzed Condensation and Carbon–Carbon Bond Formation

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3,5-Dihydroxy-4-phenylisoxazole reacts spontaneously with a variety of carbonyl compounds yielding with aromatic aldehydes *N*-arylmethylidene-4-phenylisoxazol-5-onium-3-enolates and with acetone a 1:2 condensation product. The latter undergoes reaction with alcohols giving 5-alkoxy-2-oxo-3-phenyl-5,7,7-trimethyl-2*H*,7*H*-isoxazolo[3,2-*b*][1,3]oxazine. Crotonaldehyde, acrolein, and mesityl oxide reacted with the initial isoxazole. Structures and properties of the various products are studied.

The unusual physical properties of 3,5-dihydroxy-4-phenylisoxazole (**1**), prepared from ethyl α-phenylmalonate and hydroxylamine, have been described recently.[1] An interesting chemical property of this compound which is studied here is its reactivity toward carbonyl compounds. It reacts spontaneously either upon dissolution in the neat carbonyl compound or in solution, at room temperature. The stable red products which are obtained from aromatic aldehydes were briefly described in a recent communication[2] and were proved to be *N*-arylmethylidene-4-phenylisoxazol-5-onium-3-enolates (**2**). Additional data about these compounds are given in the Experimental Section below. The formation of **2** is probably initiated by the protonation of the aldehydic oxygen by the very acidic[1] enol of **1**, followed by the elimination of water. Another possible approach is a cyclic concerted mechanism (see Scheme I). In the case of benzaldehyde the re-

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