

Hexacarbonylmolybdenum-Induced N-N Bond Cleavage of Pyrazoles. Conversion of 1-Acylpyrazoles to Pyrimidines

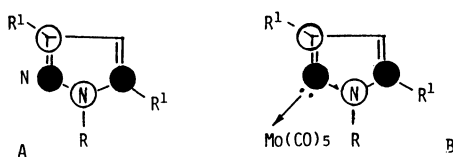
Makoto NITTA,* Tatsuo HAMAMATSU, and Hiroyuki MIYANO

Department of Chemistry, School of Science and Engineering, Waseda University, Shinjuku-ku, Tokyo 160

(Received June 17, 1988)

Synopsis. $[\text{Mo}(\text{CO})_6]$ -induced reactions of 1-acyl-3,5-disubstituted pyrazoles underwent N-N bond cleavage and subsequent cyclocondensation to give pyrimidines as well as deacylation to give 3,5-disubstituted pyrazoles. Under similar conditions, 1,3,5-trisubstituted pyrazoles, which have no electron-withdrawing substituent on N1, gave no product, except for the starting materials.

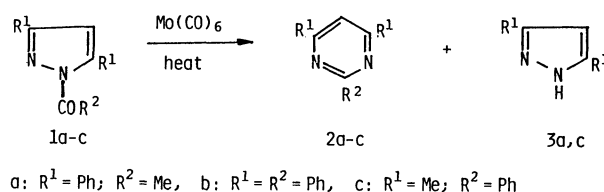
Previous studies in this series have included papers involving a system which formally contains a C=N-O group. The reaction of substituted 2-isoxazolines with $[\text{Mo}(\text{CO})_6]$, $[\text{Fe}_2(\text{CO})_9]$, or $[\text{Fe}(\text{CO})_5]$ under thermal conditions or photo-irradiations has been shown to undergo N-O and C4-C5 bond cleavages to give two fragments of aldehydes (or ketones) and complexed vinylnitrenes, which could collapse to ketones in a protic media.^{1,2)} Similarly substituted isoxazoles underwent a reductive cleavage of the N-O bond to give β -amino enones in good yields.³⁾ The N-complexed isoxazole has been isolated as a reasonable intermediate in the reaction.³⁾ The easy, metal-carbonyl prompted N-O bond cleavage has a strong resemblance to the photochemically induced N-O bond cleavage of isoxazoles to give oxoazirines.⁴⁾ The photochemical reaction of a pyrazole has also been known to undergo a possible N-N bond cleavage to give an imidazole.⁵⁾ In pyrazoles the nitrogen-nitrogen linkage appears to be antibonding in character



(LUMO shown as A in the Figure), and this seems to cause a possible photochemical N-N bond cleavage. Considering the pyrazoles N-complexed B to a $[\text{Mo}(\text{CO})_5]$ species, a possible delocalization of a π -d electron from the central metal to the π^* (LUMO) of

the pyrazole is expected to facilitate an N-N bond cleavage. This paper describes the $[\text{Mo}(\text{CO})_6]$ -induced N-N bond cleavage of 1-acetyl- and 1-benzoyl-3,5-disubstituted pyrazoles and a subsequent cyclocondensation to give 2,4,6-trisubstituted pyrimidines.

The thermal reaction of 1-acetyl-3,5-diphenyl-, 1-benzoyl-3,5-diphenyl-, and 1-benzoyl-3,5-dimethylpyrazoles (**1a—c**) with $[\text{Mo}(\text{CO})_6]$ in dry 1,2-dimethylbenzene underwent an N-N bond cleavage and a subsequent cyclocondensation to give pyrimidine derivatives **2a—c** as well as deacylation to give 3,5-disubstituted pyrazoles **3a, c** (Scheme 1). The detailed



Scheme 1.

reaction conditions and the yields of the products are summarized in Table 1 (Entries 1—3). Since compound **1a** underwent no reaction under heating in the absence of $[\text{Mo}(\text{CO})_6]$, $[\text{Mo}(\text{CO})_6]$ is indispensable for the formation of **2** and **3**. The structures of the pyrimidines **3a**,⁶⁾ **3b**,⁷⁾ and **3c**⁶⁾ were confirmed by comparisons of their physical data with those found in the literature. On the other hand, reactions proceeded slowly in dry toluene or acetonitrile in place of 1,2-dimethylbenzene, and gave pyrimidines **2a—c** as well as pyrazoles **3a, c**, in addition to the unreacted starting materials **1a—c** (Table 1, Entries 4—7). Compound **1c** does not seem to be labile, as compound with **1a, b**, in N-N cleavage reactions (Entries 3 and 7).

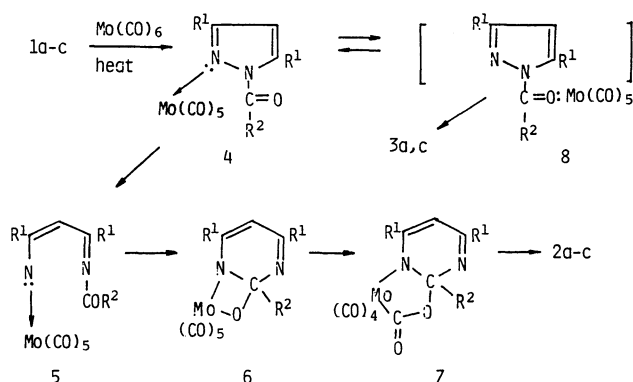
The formation of pyrimidines **2a—c** and pyrazoles **3a, c** can be explained as follows. Since $[\text{Mo}(\text{CO})_6]$ has been shown to give an N-complexed isoxazoles, the

Table 1. Experimental Results Obtained in the Reaction of **1a—c** with $[\text{Mo}(\text{CO})_6]$ ^{a)}

Entry	Pyrazole			Solvent	Product (yield/%)		Recovery (%)
	1	R^1	R^2		2	3	1
1	1a	Ph	Me	DMB ^{b)}	2a (30)	3a (37)	(0)
2 ^{c)}	1b	Ph	Ph	DMB ^{b)}	2b (30)	3a (40)	(0)
3 ^{c)}	1c	Me	Ph	DMB ^{b)}	2c (12)	3c (34)	(0)
4	1a			Toluene	2a (18)	3a (47)	1a (8)
5	1a			CH_3CN	2a (9)	3a (60)	1a (10)
6 ^{c)}	1b			CH_3CH	2b (5)	3a (47)	1b (45)
7 ^{c)}	1c			CH_3CN	2c (0)	3c (82)	1c (15)

a) A molar equivalent amount of $[\text{Mo}(\text{CO})_6]$ was used, being heated under reflux for 24 h.

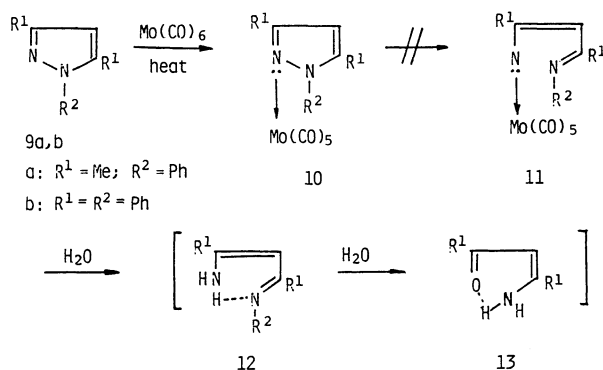
b) DMB denotes 1,2-dimethylbenzene. c) Benzoic acid was isolated as ethyl benzoate albeit in low yields (ca. 1—12 %) (see Experimental).



Scheme 2.

initial step is a complexation of **1** to give **4**.³⁾ The following N-N bond cleavage of **4** gives complexed nitrene **5**. The intermediate **5** can cyclize to give **6**, a ligand migration of which is followed by decomplexation would give pyrimidines **2a-c**.⁸⁾ Although isolated yields of benzoic acid (Entries 2,3,6, and 7) were very low, pyrazoles **3a,c** presumably originate from the formally postulated complex **8**, which undergoes deacylation with contaminated water or under workup conditions. Even a reaction in a dry solvent can not eliminate the possibility of stray water. In a deacylation reaction, a molybdenum moiety seems to act as a Lewis acid. The carbonyl ligand of $[\text{Mo}(\text{CO})_6]$ is easily substituted by acetonitrile,^{3,9)} several carbonyl ligands in each of the postulated complexes **4-8** are possibly exchanged with acetonitrile in the reactions of Entries 5-7. The formation of pyrazoles **3a,c** predominates over pyrimidines **2a-c**. This fact is suggestive of a high energy barrier of N-N bond cleavage, as compared to that of deacylation, and a possible existence of equilibrium between **4** and **8**. Although the N-N bond cleavage of **1a-c** was enhanced by $[\text{Mo}(\text{CO})_6]$, the reaction seems to require a higher temperature, compared to that of isoxazoles.³⁾ This fact is ascribed to the large resonance energy of pyrazole, as compared to that of isoxazole.¹⁰⁾ Thus, the appreciable delocalization of a d electron from the central metal to the π^* (LUMO) of the pyrazole is actually suggested by the present reactions (figure).

Similarly, a reaction of 1-phenyl-3,5-dimethyl- and 1,3,5-triphenylpyrazoles (**9a, b**), both of which have no electron-withdrawing substituent at N1, was studied



Scheme 3.

(Scheme 3). In this case, the expected vinylnitrene complex **11** can not collapse to pyrimidine. Thus, reactions expected N-N bond cleavage in moist solvents to give such products as **12** (and/or **13**) were carried out as in reactions of isoxazoles to give β -amino enones.³⁾ However, the reactions gave no product, except for the starting materials (see Experimental). This fact is suggestive of an enhanced resonance energy and a strong N-N bond of **9a, b**, compared to those of 1-acyl-substituted pyrazoles **1a-c**.

Experimental

The ^1H NMR spectra were recorded on a Hitachi R-24 spectrometer and the chemical shifts are given in ppm (δ) relative to the internal SiMe_4 standard. The desired compounds, 1-acylpyrazole derivatives **1a-c**, 1-phenyl-3,5-dimethylpyrazole (**9a**), and 1,3,5-triphenylpyrazole (**9b**), were prepared according to methods described in the literature.¹¹⁾ All of the reactions were carried out under a dry nitrogen atmosphere.

General Procedure for the Reaction of Acylpyrazoles **1a-c with $[\text{Mo}(\text{CO})_6]$ in 1,2-Dimethylbenzene.** A solution of **1** (0.5 mmol) and $[\text{Mo}(\text{CO})_6]$ (133 mg, 0.5 mmol) in 1,2-dimethylbenzene (5 cm^3) was refluxed for 24 h. After the solvent was evaporated, the residue was dissolved in chloroform (10 cm^3); it was then filtered through Celite to remove insoluble materials. After the filtrate was concentrated, the residue was separated by TLC on silica gel. In the reaction of **1a**, the first band (R_f 0.3) from the TLC plates developed by hexane-chloroform (1/3) gave pyrimidine **2**. The second band (R_f 0.1) gave **3a**. In reactions of **1b, c**, the first band (R_f 0.8 for **2b**; 0.6 for **2c**) from the TLC plates developed by hexane-AcOEt (6/1) gave pyrimidine **2b,c**. The second band (R_f 0.3 for **3b**; 0.2 for **3c**) gave a mixture containing **3b,c**. This mixture was heated in ethanol (5 cm^3) and H_2SO_4 (0.2 cm^3) for 3.5 h. After the usual workup, the pyrazole and ethyl benzoate (ca. 7%) were obtained. The yields of the products are summarized in Table 1. For **2a**: mp 91–92°C (lit, mp 96–97°C); ^1H NMR (CDCl_3) δ =2.83 (3H, s), 7.3–7.6 (6H, m), 7.79 (1H, s), 7.9–8.0 (4H, m).⁶⁾ For **2b**: mp 183–184°C (lit, mp 183–184°C); ^1H NMR (CDCl_3) δ =7.3–7.7 (9H, m), 7.98 (1H, s), 8.0–8.5 (4H, m), 8.5–8.9 (2H, m).⁷⁾ For **2c**: mp 74–78°C (lit, mp 81–83°C); ^1H NMR (CDCl_3) δ =2.62 (6H, s), 6.95 (1H, s), 7.3–7.7 (3H, m), 8.3–8.7 (2H, m).⁶⁾

Thermal Reaction of 1-Acetyl-3,5-diphenylpyrazole **1a in 1,2-Dimethylbenzene.** A solution of **1a** (131 mg, 0.5 mmol) in 1,2-dimethylbenzene (5 cm^3) was heated under reflux for 24 h. After the solvent was evaporated, the residue was purified by TLC on silica gel using hexane-AcOEt (5/1) as a developer to give **1a** (111 mg, 85%).

Reaction of 1-Acetyl-3,5-diphenylpyrazole **1a with $[\text{Mo}(\text{CO})_6]$ in Toluene.** A solution of **1a** (132 mg, 0.5 mmol) and $[\text{Mo}(\text{CO})_6]$ (133 mg, 0.5 mmol) in dry toluene (5 cm^3) was heated under reflux for 24 h. After the solvent was evaporated, the residue was dissolved in dichloromethane (10 cm^3), and the solution was filtered through Celite to remove insoluble materials. The filtrate was concentrated and the resulting residue was separated by TLC on silica gel using hexane-chloroform (1/2) as a developer. The first band (R_f 0.6) from the TLC plates gave the starting material **1a**. The second band (R_f 0.2) gave the pyrimidine **2a**. The third band (R_f 0.1) gave the pyrazole **3a**. The yields are summarized in Table 1.

General Procedure for the Reaction of **1a-c with $[\text{Mo}(\text{CO})_6]$ in Acetonitrile.** A solution of **1** (1 mmol) and $[\text{Mo}(\text{CO})_6]$ (266 mg, 1 mmol) in dry acetonitrile (5 cm^3) was

heated under reflux for 24 h. The acetonitrile was evaporated and the residue was dissolved in dichloromethane (10 cm³). After the solution was filtered through Celite to remove insoluble materials, the filtrate was concentrated and the residue was separated by TLC on silica gel. In the reaction of **1a**, the first band (*R_f* 0.6) from the TLC plates developed by hexane-chloroform (1/3) gave **1a**. The second band (*R_f* 0.3) gave pyrimidine **2a**. The third band (*R_f* 0.1) gave pyrazole **3a**. In reactions of **1b**, **c**, the first band (*R_f* 0.6 for **1b**; 0.7 for **1c**) from the TLC plates developed by hexane-AcOEt (6/1) gave **1b**, **c**. The second band (*R_f* 0.3 for **2b**) gave pyrimidine **2b**. The third band (*R_f* 0.3 for **3b**; 0.2 for **3c**) gave a mixture containing **3b**, **c**. This mixture was then heated in ethanol (5 cm³) and H₂SO₄ (0.2 cm³) under reflux. The usual workup afforded pyrazole **2** and ethyl benzoate (ca. 1–12%).

General Procedure for the Reaction of Pyrazoles 9a, b with [Mo(CO)₆] in Moist Toluene and/or Acetonitrile. A solution of **9** (0.5 mmol) and [Mo(CO)₆] (133 mg, 0.5 mmol) in moist toluene (5 cm³) and/or acetonitrile (5 cm³) was heated under reflux for 24 h. After the reaction mixture was concentrated, the resulting residue was purified by TLC on silica gel using hexane-AcOEt (3/1) as a developer to give the starting material: **9a** (84% in acetonitrile); **9b** (96% in acetonitrile and 94% in toluene).

References

- 1) M. Nitta and T. Kobayashi, *Chem. Lett.*, **1983**, 51; M. Nitta and T. Kobayashi, *J. Chem. Soc., Perkin Trans. 1*, **1984**, 2103.
- 2) M. Nitta, A. Yi, and T. Kobayashi, *Bull. Chem. Soc. Jpn.*, **58**, 991 (1985).
- 3) M. Nitta and T. Kobayashi, *J. Chem. Soc., Perkin Trans. 1*, **1985**, 1401.
- 4) E. F. Ullman and B. Singh, *J. Am. Chem. Soc.*, **88**, 1844 (1966); B. Singh and E. F. Ullman, *J. Am. Chem. Soc.*, **89**, 6911 (1967).
- 5) P. Beak, J. L. Miesel, and W. R. Messer, *Tetrahedron Lett.*, **1967**, 5315.
- 6) H. Yamanaka, K. Edo, F. Shoji, S. Konno, T. Sakamoto, and M. Mizugaki, *Chem. Pharm. Bull.*, **26**, 2160 (1978); T. Nishio, T. Tokunaga, and Y. Omote, *J. Heterocycl. Chem.*, **22**, 405 (1985).
- 7) A. L. Weis and V. Rosenbach, *Tetrahedron Lett.*, **22**, 1453 (1981); A. -A. Pourzal, *Synthesis*, **1983**, 717.
- 8) T. Kobayashi and M. Nitta, *Bull. Chem. Soc. Jpn.*, **58**, 1057 (1985); T. Kobayashi and M. Nitta, *Bull. Chem. Soc. Jpn.*, **58**, 3099 (1985); and references cited therein.
- 9) D. P. Tate, W. R. Knipple, and J. M. Augl, *Inorg. Chem.*, **1**, 433 (1962).
- 10) A. G. Anastassiou, S. W. Eachus, R. P. Cellura, and J. H. Gebrian, *J. Chem. Soc., Chem. Commun.*, **1970**, 1133; A. V. Chapman, M. J. Cook, A. R. Katritzky, M. H. Abraham, A. F. Danil DE Namor, L. Dumont, and J. Reisse, *Tetrahedron*, **34**, 1571 (1978).
- 11) K. T. Potts, "Comprehensive Heterocyclic Chemistry," Vol. 5, Pergamon Press, Oxford, New York, Toronto, Sydney, Paris, and Frankfurt; and references cited therein.