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

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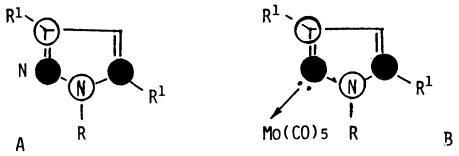
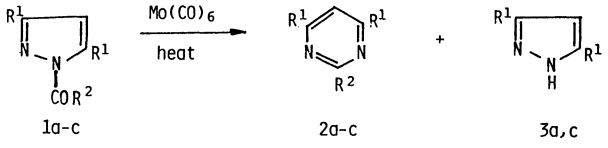
Synopsis. [$Mo(CO)_6$]-induced reactions of 1-acyl-3,5-disubstituted pyrazoles underwent N-N bond cleavage and subsequent cyclocondensation to give pyrimidines as well as deacylation to give 3,5-disubstituted pyrazoles. Under similar conditions, 1,3,5-trisubstituted pyrazoles, which have no electron-withdrawing 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 [$Mo(CO)_6$], [$Fe_2(CO)_9$], or [$Fe(CO)_5$] 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 [$Mo(CO)_5$] 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 [$Mo(CO)_6$]-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 [$Mo(CO)_6$] 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



a: R^1 = Ph; R^2 = Me, b: R^1 = R^2 = Ph, c: R^1 = Me; R^2 = Ph

Scheme 1.

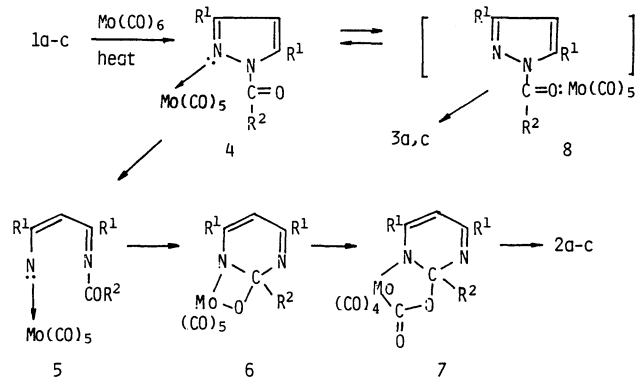
reaction conditions and the yields of the products are summarized in Table 1 (Entries 1—3). Since compound **1a** underwent no reaction under heating in the absence of [$Mo(CO)_6$], [$Mo(CO)_6$] is indispensable for the formation of **2** and **3**. The structures of the pyrimidines **3a**,[6] **3b**,[7] 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 [$Mo(CO)_6$] has been shown to give an *N*-complexed isoxazoles, the

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

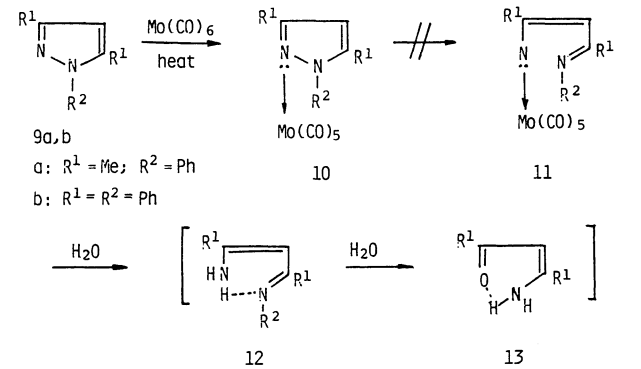
a) A molar equivalent amount of [$Mo(CO)_6$] was used, being heated under reflux for 24 h. b) DMB denotes 1,2-dimethylbenzene. c) Benzoic acid was isolated as ethyl benzoate albeit in low yields (ca. 1—12 %) (see Experimental).



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 $[Mo(CO)_6]$ 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 $[Mo(CO)_6]$, 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). 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**.



Scheme 3.

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 $[Mo(CO)_6]$ in 1,2-Dimethylbenzene. A solution of **1** (0.5 mmol) and $[Mo(CO)_6]$ (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 $[Mo(CO)_6]$ in Toluene. A solution of **1a** (132 mg, 0.5 mmol) and $[Mo(CO)_6]$ (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 $[Mo(CO)_6]$ in Acetonitrile. A solution of **1** (1 mmol) and $[Mo(CO)_6]$ (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 cm^3). 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 cm^3) and H_2SO_4 (0.2 cm^3) 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 cm^3) and/or acetonitrile (5 cm^3) 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).

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