Chinese Chemical Letters Vol. 10, No. 8, pp. 643–646, 1999

A Convenient Synthesis of Pyrazolylpyrazoles Using α-Oxo Ketene S,S- and N,S-Acetals

Han Song CHEN, Zheng Ming LI*, Zhong Wen WANG

State Key Laboratory of Elemento-Organic Chemistry,
Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071

Abstract: Substituted pyrazolylpyrazoles were synthesized through the reaction of hydrazine hydrate and α-oxo-(3,5-dimethyl-1H-pyrazole-1-yl) ketene S,S- and N,S-acetals, which were obtained from α-oxo-(3,5-dimethyl-1H-pyrazole-1-yl) acetophenone. Pyrazolylpyrazole was also prepared *via* α-oxo ketene N,O-acetal by way of ring chain transformation.

Keywords: Pyrazole, pyrazolylpyrazole, α-oxo-ketene dithioacetal, ring chain transformation.

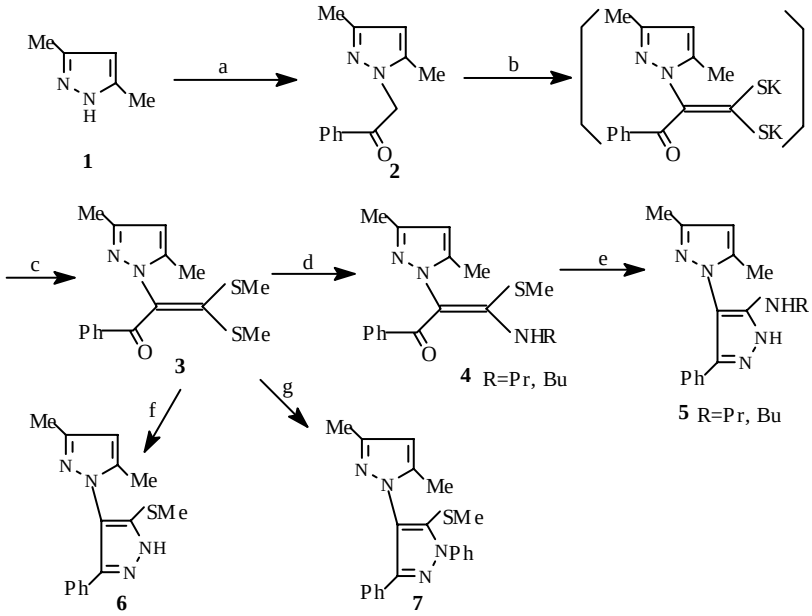
Aryl-substituted pyrazole derivatives have already attracted wide attention in recent decades because they were reported to show a broad spectrum of biological activities. For instance, several substituted pyrazolylpyrazoles demonstrated high preemergent herbicidal activity against a wide variety of broadleaf weed species[1,2]. Pyrazolyl-pyrimidines exhibited some fungicidal activity[3]. Fripronil (5-amino-3-cyano-1-(2′,6′-dichloro-4′-trifluoromethylphenyl)-4-trifluoromethylsulfinylp yrazole) is a new pyrazole insecticide that provides excellent control of many soil and foliar insects on a wide variety of crops and noncrops[4].

α-Oxo ketene dithioacetals and related compounds are versatile synthons in organic synthesis, when they reacted with bifunctional reactants, many 5 or 6-membered ring heterocyclic compounds are readily obtained[5,6]. α-Oxo-α-(1,2,4-triazol-1-yl) ketene dithioacetals and α-oxo-α-imidazolylketene dithioacetals were investigated by our research group[7,8], and the corresponding di-heterocyclic compounds were synthesized. However, a survey of the literature revealed that α-oxo-α-(1H-pyrazol-1-yl) ketene dithioacetals have up to now not been reported. Prompted by these studies and in connection with a program devoted to the preparation of biologically active heterocycles we reported herein a convenient method to prepare pyrazolylprazoles *via* α-oxo-α-(1H-pyrazole-1-yl) ketene dithioacetals or their derivatives.

α-(3,5-Dimethyl-1H-pyrazol-1-yl) acetophenone **2** was prepared by treatment of 3,5-dimethyl-1H-pyrazole with 2-bromoacetophenone in acetone containing potassium carbonate. Then **2** reacted with potassium hydroxide and carbon disulfide, followed by alkylation to afford α-oxo-α-(3,5-dimethyl-1H-pyrazole-1-yl) ketene dithioacetal **3**. When **3** reacted with hydrazine hydrate or phenyl hydrazine in refluxing ethanol,

pyrazolylpyrazoles **6** and **7** were produced respectively. When **3** reacted with excess alkyl amine at room temperature, the corresponding N,S-acetals were obtained, which underwent cyclization with hydrazine hydrate to give compounds **5** (**Scheme 1**).

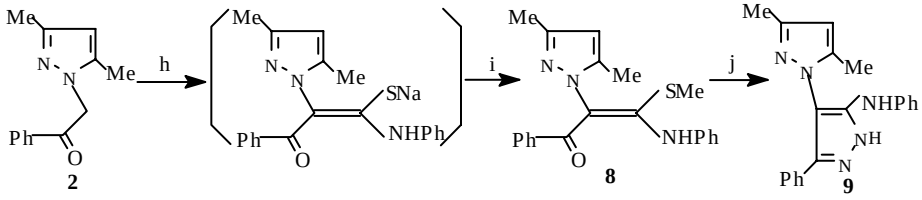
Scheme 1



a. $PhCOCH_2Br/K_2CO_3$/Acetone, reflux; b. KOH/CS_2/DMSO, r.t.; c. MeI, r.t.; d. RNH_2/EtOH, reflux; e. f. $NH_2NH_2.H_2O$/EtOH, reflux; g. $PhNHNH_2$/EtOH, reflux.

Another way to synthesize N,S-acetal was shown in **Scheme 2**. The reaction of **2** with phenyl isothiocyanate in anhydrous THF using sodium hydride as base, followed by alkylation to yield N,S-acetal **8**. On further reaction with hydrazine hydrate, new pyrazolylpyrazole compound **9** was prepared.

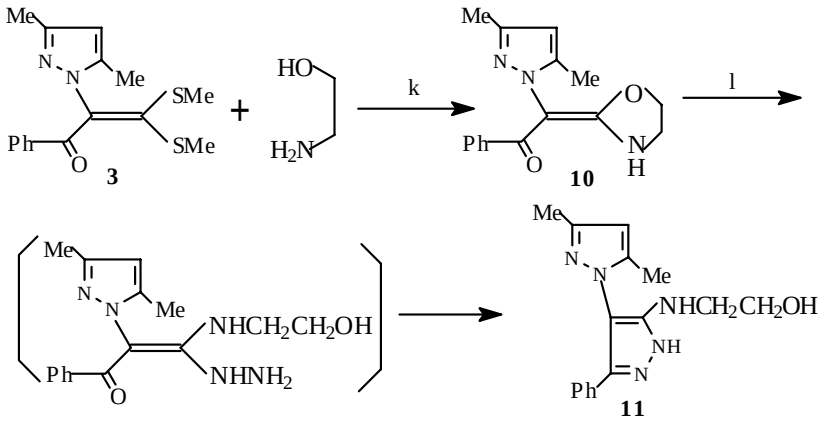
Scheme 2



h. PhNCS/NaH/THF, -5°C; i. MeI, r.t.; j. $NH_2NH_2.H_2O$/EtOH, reflux.

Pyrazolylpyrazole was prepared by the ring chain transformation of cyclic α-oxo-α-(3,5-dimethyl-1H-pyrazole-1-yl) ketene N,O-acetal, too. The concept of ring chain transformation is based on the opening of a saturated heterocyclic ring in the starting material while immediately afterward a new heteroaromatic ring is formed by condensation[9]. As starting intermediates, 1,3-dicarbonyl heteroanalogs were used. These substrates were "ring-chain" transformed by reaction with binucleophiles. We applied **10** as C-C-C building block and hydrazine as the binucleophile[10,11]. As shown in **Scheme 3**, the S,S-acetal **3** reacted with ethanolamine to afford cyclic N,O-acetal **10**, then **10** reacted with hydrazine hydrate in refluxing ethanol to yield compound **11** by way of ring chain transformation.

Scheme 3



k. EtOH, r.t.; l. $NH_2NH_2.H_2O$/EtOH, reflux.

The structures of all new products were characterized by ^{1}H NMR and elemental analysis. Compounds **3** and **11** were taken as examples: ^{1}H NMR spectrum of the former showed δ value: 2.15 (s, 3H, CH_3), 2.19 (s, 3H, SCH_3), 2.21 (s, 3H, SCH_3), 2.26 (s, 3H, CH_3), 5.83 (s, 1H, H_4-pyrazole), 7.37~7.89 (m, 5H, Ph), and the ^{1}H NMR spectrum of the latter showed: 1.84 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 3.12 (t, 2H, NH$\underline{CH_2}$), 3.84 (t, 2H, $\underline{CH_2}$OH), 5.93 (s, 1H, H_4-pyrazole), 7.03~7.13 (m, 5H, Ph).

Biological activities of all new compounds are being investigated.

References:

1. U. Hartfiel, G. Dorfmeister, H. Franke, *et al*., EP 542, 388, **1991**.
1. G. Dorfmeister, H Franke, J. Geisler, *et al.*, WO 94, 08, 999, **1994** .
2. K. Konishi and T. Kuragano, *J. Pesticide Sci.*, **1990**, *15*, 13.
3. F. Colliot, K. A. Kukorowski, D. W. Hawkins, *et al*. , *Brighton Crop Prot. Conf.-Pest Dis.*, **1992**, *1*, 29.
4. R. K. Dieter, *Tetrahedron*, **1986**, *42*(12), 3029.
5. H. Junjappa, H. Ila and C. V. Asokan, *Tetrahedron*, **1990**, *46*(16), 5423.
6. Z. N. Huang and Z. M. Li, *Chem. J. Chin. Universities*, **1995**, *16*(12), 1888.
7. Z. M. Li, J. M. Li and G. F. Jia, *Heteroatom Chem*., **1998**, *9*(3), 317.
8. M. Patzel, A. Ushmajev, J. Liebscher, *Synthesis*, **1993**, *5*, 525.
9. Z.N. Huang, Z.M. Li, *Synth. Commun.*, **1995**, *25*(20), 3219.
10. Z.N. Huang, Z.M. Li, *Synth. Commun.*, **1995**, *25*(22), 3603.

Received 8 February 1999