HETEROCYCLES, Vol. 89, No. 7, 2014, pp.1645 - 1655. © 2014 The Japan Institute of Heterocyclic Chemistry
Received, 13th September, 2013, Accepted, 12th May, 2014, Published online, 20th May, 2014
DOI: 10.3987/COM-13-12840

THE SYNTHESIS OF DIPYRAZOLYLMETHANES, X-RAY STRUCTURE ANALYSIS

Yuan Ma, Jinxia Wang, and Hengchang Ma*

Key Laboratory of Polymer Materials of Gansu Province, Key Laboratory of Eco-Environment-Related Polymer Materials Ministry of Education, College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou 730070, People's Republic of China; E-mail: mayuan_2012@yeah.net

Abstract – A small dipyrazoylmethane compounds library was established *via* the reaction of 5-alkyl- and 5-aryl-2-aryl-3*H*-pyrazol-3-ones with DMSO in the presence of $NaOAc·3H_2O$ as base using $LiBr·H_2O$ as additive at 100 °C.

Dipyrazoylmethane derivatives are important functional or bioactive materials.[1,2] The synthesis of dipyrazoylmethane by the reaction of 5-methyl-6-phenyl-1,2,4-triazine 4-oxide with pyazolone in dimethyl sulfoxide (DMSO) has been reported by Yurii Azev in 1995.[3] And in 2012, they reported the synthesis of dipyrazoylmethane by the reaction of unsubstituted quinoxaline with 3-methyl-1-phenylpyrazol-5-one (**1a**) in DMSO in the presence of triethylamine, or **1a** with glyoxal.[4] Wong and Huang reported the preparation method of dipyrazolylmethane derivatives by using formamide and phosphoryl chloride ($POCl_3$).[5] These findings confirmed the formation of the key intermediate of **1a**, which is produced from the reaction between **1a** and DMSO or Vilsmeier-type methylenation reactions from **1a** and *N*-methylformamide in the presence of $POCl_3$. However, tedious synthetic procedures and very limited functional group tolerance prevented it from real application.

DMSO has been developed as very useful synthetic reagents, which was extensively employed in the well known Pummerer and related rearragement reactions as well as the formation of thionium ion intermediate.[6] For example, Fei disclosed that DMSO could be applied as a powerful carbon source, leading to the formylation of indoles.[7] Liu also reported a quite similar reaction using DMSO involving Pummerer type reaction.[8]

Considering the significance to establish a library of structurally diversified dipyrazoylmethane derivatives, we found that treatment of 3-methyl-1-(*m*-tolyl)-1*H*-pyrazol-5(4*H*)-one (**1f**) with $NaOAc·3H_2O$ and $LiBr·H_2O$ in the solvent of DMSO at 90-100 °C could led to a new transformation. The resulted product **2f** was fully characterized by IR, ^1H, ^{13}C NMR spectroscopies and mass spectrometry. In IR spectrum, a reactively strong C=O absorption band stretch at 1616 cm^{-1}. Meanwhile,

a cluster of bands between 2922 and 2852 cm^{-1} were detected, which are demonstrated as the most intensed peaks in the spectrum. And also, a broad weak absorption band centered at 3446 cm^{-1}. NMR spectrum of **2f** indicated one set of chemical shifts for the two halves of the molecule. Of some significance was the δ 1H (OH) value in $CDCl_3$ solution of 18.00 ppm.[9-11] The crystal structure revealed (Figure 1) that the corresponding bonds in the two pyrazolone moieties have essentially the same lengths (see values in Table 1), with an extensive delocalization in the central O-C-C-C-C-C-O fragment of the molecule.[12] As a result, an octatomic ring formed *via* a hydrogen bond[13-15] between C=O and H-O-C with near linear O-H…O bond angles, and all C-O bond lengths were in the narrow range of 1.281(4)-1.290(4) Å values between those expected for single and double bonds, and two pairs of C8-C9 and C11-C13, C10-C11 and C10-C8 bond lengths are mensurated in the region of 1.437(4)-1.434(4), and 1.381(5)-1.382(5) respectively. These results confirmed that the two independent molecules exhibit only subtle differences in bond angles and lengths. Each molecule is of extensive delocalization and overall the molecule exhibits a structure almost midway between the two tautomeric forms **2f** and **2f'** (Scheme 1).

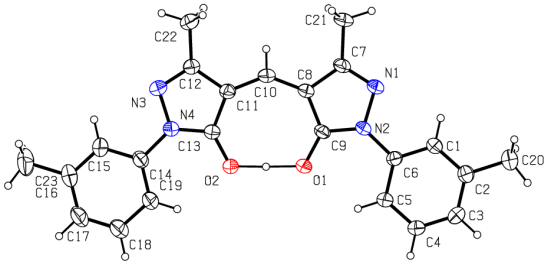
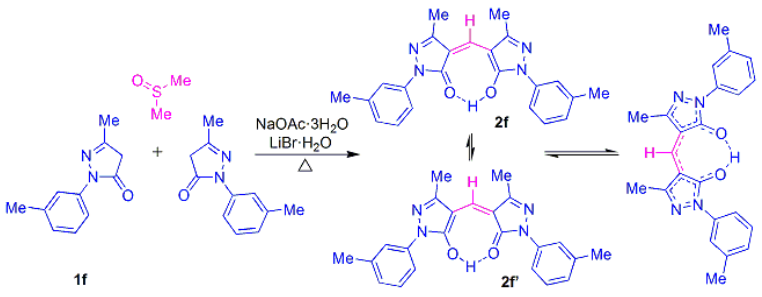


Figure 1. X-Ray crystallographic structure of **2f**

As we found that the presense of dimethyl sulfoxide is critical to the reaction. Therefore, in order to elucidate how DMSO is involved in the procedure, the deuteration experiments were conducted by using DMSO-d_6 as reaction medium. Then, the D-labeled product was obtained predominantly. The reliable results indicated that dimethyl sulfoxide is served as the reaction participate in this transformation. And an active species generated from DMSO couples two 2,4-dihydro-5-methyl-2-(3-methylphenyl)-3*H*-pyrazol-3-one motifs to produce the three rings fused compound. The discrepancy of the typical peak in the DEPT NMR shifted at 137 ppm confirmed the result.



Scheme 1

We commenced our study by examining the intermolecular cyclization of pyrazolone **1a** to dipyrazolylmethane **2a** in the presence of different bases and additives. The results were summarized in Table 1. From Table 1, it was observed that higher temperature is very necessary in the activation of DMSO in the presence of the more weak base $NaOAc·3H_2O$. Heating of **1a** at 60 ^oC for 7 h generates a trace amount of **2a**, and an increase of the reaction temperature up to 100 ^oC could raise the yield up to 70% (Entries 8 and 9). However, elevating the reaction temperature to 120 ^oC produces lower yield of **2a** (60%), accompanied by substantial starting material decomposition (Entry 10). Note that Cs_2CO_3 is not favored in the reaction possibly because Cs_2CO_3 is too hygroscopic under the air conditions. Pyridine and Et_3N could not be available in the transformation (Entries 1, 2, and 3). As tested that CF_3CO_2Na is also suitable for the transformation, product **2a** could be achieved in 72% isolated yield. Considering that $NaOAc·3H_2O$ is relatively cheap compared to CF_3CO_2Na, therefore $NaOAc·3H_2O$ was tested as the base for the following experiments. Additionally, bromine salts were found to improve the reaction efficiency. Comparably, $LiBr·H_2O$ demonstrated slightly better performance and the corresponding product was obtained in 70% yield (Entry 7). In the cases of KBr and NaBr, **2a** was produced with lower yield of 55 and 58%, respectively. Therefore the most efficient conditions for carrying out the reaction were addition of pyrazolone derivatives in DMSO solution and in the presence of 1.5 equiv. of $NaOAc·3H_2O$ and $LiBr·H_2O$ and warmed at 100 ^oC.

Table 1. Optimization of the Reaction Conditions

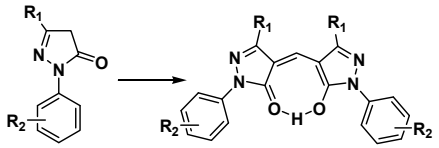
Entry	Base	Additive	T (^oC)	Yield (%)
1	Et_3N	-	100	trace
2	K_2CO_3	-	100	25
3	Cs_2CO_3	-	100	trace
4	$NaOAc·3H_2O$	-	100	53
5	$NaOAc·3H_2O$	KBr	100	55
6	$NaOAc·3H_2O$	NaBr	100	58
7	$NaOAc·3H_2O$	$LiBr·H_2O$	100	70
8	$NaOAc·3H_2O$	$LiBr·H_2O$	60	trace
9	$NaOAc·3H_2O$	$LiBr·H_2O$	80	24
10	$NaOAc·3H_2O$	$LiBr·H_2O$	120	60

[a] Reactions were performed at substrate **1a** (0.1 mmol), base (0.15 mmol), additive (0.15 mmol) in DMSO (2 mL).

With the optimized set of reaction conditions, a variety of dipyrazoylmethanes were synthesized and the corresponding products **2b-s** were produced in good to excellent yields (Table 2). Electron-donating groups, such as Me, *n*-propyl, isopropyl, and phenyl were tolerated in the reaction system. Alkyl and aryl substituents at the 5-positions did not adversely affect for the reaction. It was obvious that the yield of the product decrease along with the increase of chain length the aliphatic substituents. For instance, the yields of **2a** and **2c** were decreased to 70 and 47%, respectively (Entries 1 and 3). Isopropyl apparently

disfavored the formation of the more sterically hindered products, (**2d**: 68%, **2q**: 46%, **2r**: 50%, **2s**: 42%) (Entries 4, 17, 18, and 19). As can be seen from Table 2, the reactions of Cl and Br groups substituted reactants proceeded smoothly to afford the corresponding products in average to excellent yields. Especially, Cl and Br located on the *meta*-position of aromatic rings accelerated the formation of **2g** (92%), **2h** (88%), and **2n** (90%) (Entries 7, 8, and 14). However, in the cases of **2o**, **2q**, and **2r**, the isolated yields decreased to 46, 46, and 50%, respectively, which presumably due to the existence of more sterically hindered *n*-propyl, isopropyl in 3*H*-pyrazol-3-one ring (Entries 15, 17, and 18). The more electron-donating MeO group in benzene ring could slightly promote the transformation, and better results were achieved (**2e**: 94%, **2j**: 67%, **2l**: 71%) (Entries 5, 10, and 12).

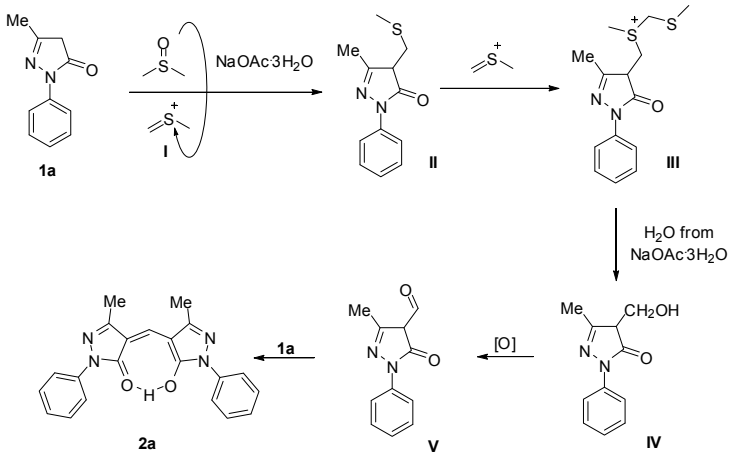
Table 2. The scope of reaction



Entry	Compound	R^1	R^2	Time (h)	Yield (%)
1	**2a**	Me	H	7	70
2	**2b**	Ph	H	7	62
3	**2c**	*n*-Pr	H	7	47
4	**2d**	Me_2CH	H	7.5	68
5	**2e**	Me	4-OMe	7.5	94
6	**2f**	Me	3-Me	7.5	46
7	**2g**	Me	3-Br	8	92
8	**2h**	Me	3-Cl	8	88
9	**2i**	Me	3,5-di-Me	7.5	73
10	**2j**	Ph	4-OMe	7.5	67
11	**2k**	Ph	3-Me	7.5	61
12	**2l**	*n*-Pr	4-OMe	6	71
13	**2m**	*n*-Pr	3-Me	6	57
14	**2n**	*n*-Pr	3-Br	7.5	90
15	**2o**	*n*-Pr	3-Cl	7.5	46
16	**2p**	*n*-Pr	3,5-di-Me	6.5	70
17	**2q**	Me_2CH	3-Br	6	46
18	**2r**	Me_2CH	3-Cl	6	50
19	**2s**	Me_2CH	3,5-di-Me	6	42

A plausible mechanism for this reaction was proposed in Scheme 2. It may involve a Pummerer rearrangement of DMSO in the presence of NaOAc under elevated temperature, affording the active species of **I**. Then, an intermolecular nucleophilic addition of **1a** to the C=S bond of **I** takes place to afford the intermediate **II**.[8] Subsequently, the second nucleophilic addition between **II** and **I** occurs, leading to the formation of sulfonium **III**. Finally, the S_N2 nucleophilic reaction of intermediate **III** attacked by H_2O takes place to form the hydroxymethylation product **IV**, which is oxidized to the formylation product **V** by Swern oxidation.[7] Meanwhile, the nucleophilic attack of **V** by another molecule

1a affords the final product **2a**.[5]



Scheme 2. The plausible reaction pathway

In conclusion, a novel, simple, and highly efficient method for the establishment of a library of structurally diversified dipyrazoylmethane derivatives with 5-alkyl- and 5-aryl-2-aryl-3*H*-pyrazol-3-ones and DMSO under relatively mild conditions has been developed. A detailed mechanistic study and further investigation on the application of this reaction system are currently underway in our laboratory.

EXPERIMENTAL

General. All NMR spectra were recorded on MERCURY (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectrometers; chemical shifts were expressed in parts per million relative to TMS signal as an internal reference in $CDCl_3$. Fourier transform infrared (FT-IR) spectra for the solids were recorded over the wavenumber range from 400 to 4000 cm^{-1} on a Nicolet AVATAR 360 FT-IR spectrophotometer. Samples were prepared by mixing the powdered solids with KBr (the blank). Mass spectra were recorded on a HP5989B mass spectrometer. The crystal structure was recorded on a Bruker APEX-II CCD. All reagents and starting materials were obtained from commercial suppliers and were used without further purification.

General Procedure for the Synthesis of 1a-d. Dicarbonyl compound (1.1 mmol) and phenylhydrazine (108.2 mg, 1.0 mmol) were added in 2 mL of EtOH, and the mixture was stirred at 75 ^{o}C until complete reaction of the phenylhydrazine (observed by TLC, 5-7 h). At the end of the reaction, the solution was concentrated under reduced pressure to afford crude product. The corresponding compounds **1a-d** were obtained by simple recrystallizing from a mixture of EtOAc and petroleum ether.

General Procedure for the Synthesis of 1e-s. Dicarbonyl compound (1.0 mmol) and phenylhydrazine hydrochloride (144.6 mg, 1.0 mmol) were added into 2 mL of EtOH, and the mixture was stirred at 75 ^{o}C

until complete reaction of the dicarbonyl compound (observed by TLC, 6-9 h). The solution was purified by column chromatography on silica gel with a mixture of EtOAc and petroleum ether as eluent to afford the corresponding compounds.

General Procedure for the Synthesis of 2a-s. Pyrazolone (1.0 mmol), $NaOAc·3H_2O$ (136 mg, 1.5 mmol), and $LiBr·H_2O$ (103.9 mg, 1.5 mmol) were added in a 10 mL flask containing 2 mL of DMSO, and the mixture was stirred at 100 ^oC under natural condition until complete consumption of the pyrazolone (observed by TLC, 6-8 h). At the end of the reaction, 5 mL of water was charged, and the solution was extracted with CH_2Cl_2 (3×5 mL). The organic phases were then dried with anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with a mixture of EtOAc and petroleum ether as eluent.

Because the **1a-m**, **1o**,[16] **2a-d**, and **2j, k** have been obtained by published methods and are well characterized and described in the reports, so the detailed spectral analysis of them are not necessary in the EXPERIMENTAL (**2a-d**, and **2j, k** see the Supporting Information).

1-(3-Bromophenyl)-3-propyl-1*H*-pyrazol-5(4*H*)-one (1n) White solid; Mp 110-112 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.08 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.34-7.18 (m, 2H), 2.50 (dt, *J* = 15.2, 7.5 Hz, 2H), 1.76-1.62 (m, 2H), 1.10-0.96 (m, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 170.46, 160.20, 139.24, 130.08, 127.70, 122.47, 121.39, 116.91, 41.72, 33.09, 19.91, 13.73; MS (FAB): *m/z* = 280.02 $[M+H]^+$; IR (KBr): 3440, 2962, 2926, 2870, 1578, 1550, 1476, 1437, 1384, 1316, 1196, 1151, 1091, 845, 803, 771, 726, 622 cm^{-1}. Anal. Calcd for $C_{12}H_{13}BrN_2O$; C, 51.26; H, 4.66; Br, 28.42; N, 9.96. Found: C, 51.24; H, 4.68; Br, 28.44; N, 9.94.

1-(3,5-Dimethylphenyl)-3-propyl-1*H*-pyrazol-5(4*H*)-one (1p) White solid; Mp 105-107 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.37 (d, *J* = 84.9 Hz, 2H), 6.83 (s, 1H), 2.48 (t, *J* = 7.6 Hz, 2H), 2.34 (s, 6H), 1.75-1.62 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 170.47, 159.70, 138.47, 137.88, 126.83, 116.80, 41.65, 33.12, 21.45, 20.12, 13.75; MS (FAB): *m/z* = 230.14 $[M+H]^+$; IR (KBr): 3450, 2962, 2921, 2872, 2620, 1609, 1552, 1467, 1393, 1335, 1240, 1144, 1006, 837, 743, 626 cm^{-1}. Anal. Calcd for $C_{14}H_{18}N_2O$; C, 73.01; H, 7.88; N, 12.16. Found: C, 73.00; H, 7.86; N, 12.14.

1-(3-Bromophenyl)-3-isopropyl-1*H*-pyrazol-5(4*H*)-one (1q) Yellow solid; Mp 84-86 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.08 (s, 1H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.27 (dd, *J* = 16.3, 8.3 Hz, 2H), 2.79 (dt, *J* = 13.6, 6.8 Hz, 1H), 2.17 (s, 2H), 1.25 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 170.51, 164.60, 139.33, 130.08, 127.69, 122.47, 121.40, 116.93, 39.87, 30.82, 20.04; MS (FAB): *m/z* = 280.02 $[M+H]^+$; IR (KBr): 3436, 2966, 2870, 2748, 1717, 1616, 1475, 1398, 1334, 1270, 1186, 1074, 991, 875,

770, 712 cm^{-1}. Anal. Calcd for $C_{12}H_{13}BrN_2O$; C, 51.26; H, 4.66; Br, 28.42; N, 9.96. Found: C, 51.25; H, 4.67; Br, 28.45; N, 9.95.

1-(3-Chlorophenyl)-3-isopropyl-1*H*-pyrazol-5(4*H*)-one (1r) Yellow solid; Mp 80-82 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.94 (s, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.33-7.26 (m, 1H), 7.14 (d, *J* = 7.9 Hz, 1H), 3.44 (s, 2H), 2.78 (dd, *J* = 13.7, 6.8 Hz, 1H), 1.26 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 170.51, 164.56, 139.23, 134.48, 129.80, 124.73, 118.56, 116.44, 39.88, 30.81, 20.02; MS (FAB): *m/z* = 236.07 $[M+H]^+$; IR (KBr): 3072, 2967, 2868, 2749, 1616, 1589, 1479, 1401, 1338, 1269, 1186, 1077, 874, 770, 729, 681 cm^{-1}. Anal. Calcd for $C_{12}H_{13}ClN_2O$; C, 60.89; H, 5.54; Cl, 14.98; N, 11.84. Found: C, 60.90; H, 5.55; Cl, 14.96; N, 11.88.

1-(3,5-Dimethylphenyl)-3-isopropyl-1*H*-pyrazol-5(4*H*)-one (1s) Yellow solid; Mp 80-81 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.59 (s, 2H), 6.80 (s, 1H), 2.62 (s, 2H), 2.34 (s, 6H), 1.59 (d, *J*= 12.0 Hz, 1H), 1.38-1.30 (m, 6H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 164.00, 155.49, 138.48, 138.26, 126.29, 124.64, 116.77, 30.88, 29.88, 21.51, 20.92; MS (FAB): *m/z* = 230.14 $[M+H]^+$; IR (KBr): 3069, 2967, 2869, 2748, 1609, 1588, 1477, 1400, 1393, 1335, 1270, 1240, 1140, 1076, 874, 837 cm^{-1}. Anal. Calcd for $C_{14}H_{18}N_2O$; C, 73.01; H, 7.88; N, 12.16. Found: C, 73.03; H, 7.89; N, 12.17.

(4*Z*)-2,4-Dihydro-4-[[5-hydroxy-3-methyl-1-(4-methoxyphenyl)-1*H*-pyrazol-4-yl]methylene]-5-methyl-2-(4-methoxyphenyl)-3*H*-pyrazol-3-one (2e) Yellow solid; Mp 212-214 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 17.82 (s, 1H), 7.79-7.76 (d, *J* = 8.8 Hz, 4H), 7.24 (s, 1H), 6.97-6.94 (d, *J* = 9.2 Hz, 4H), 3.84 (s, 6H), 2.36 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.7, 158.0, 152.4, 138.1, 130.8, 122.8, 114.0, 109.2, 55.5, 12.9; MS (FAB): *m/z* = 418.16 $[M+H]^+$; IR (KBr): 3447, 2921, 2846, 1618, 1546, 1508, 1440, 1331, 1246, 1168, 1117, 1079, 1034, 1006, 827 cm^{-1}. Anal. Calcd for $C_{23}H_{22}N_4O_4$; C, 66.02; H, 5.30; N, 13.39. Found: C, 66.05; H, 5.32; N, 13.37.

(4*Z*)-2,4-Dihydro-4-[[5-hydroxy-3-methyl-1-(3-methylphenyl)-1*H*-pyrazol-4-yl]methylene]-5-methyl-2-(3-methylphenyl)-3*H*-pyrazol-3-one (2f) Yellow solid; Mp 155-157 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 17.96 (s, 1H), 7.71-7.69 (d, *J* = 8.8 Hz, 4H), 7.35-7.33 (m, 2H), 7.30 (s, 1H), 7.11-7.09 (d, *J* = 7.6 Hz, 4H), 2.41 (s, 6H), 2.38 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.2, 152.6, 138.9, 138.2, 137.5, 128.7, 127.4, 121.7, 118.3, 109.4, 21.5, 12.9; MS (FAB): *m/z* = 386.3 $[M+H]^+$; IR (KBr): 3446, 2922, 2852, 1616, 1546, 1493, 1457, 1418, 1382, 1327, 1103, 1010, 923, 785, 687 cm^{-1}. Anal. Calcd for $C_{23}H_{22}N_4O_2$; C, 71.48; H, 5.74; N, 14.50. Found: C, 71.46; H, 5.71; N, 14.53.

(4*Z*)-2-(3-Bromophenyl)-4-[[1-(3-bromophenyl)-5-hydroxy-3-methyl-1*H*-pyrazol-4-yl]methylene]-2-4-dihydro-5-methyl-3*H*-pyrazol-3-one (2g) Yellow solid; Mp 238-240 ^oC; ^1H NMR ($CDCl_3$, 400 MHz):

δ = 17.82 (s, 1H), 8.16-8.15 (m, 2H), 7.94-7.91 (d, *J* = 8.6 Hz, 2H), 7.42-7.40 (d, *J* = 9.2 Hz, 4H), 7.33-7.29 (m, 2H), 7.25 (s, 1H), 2.38 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz):δ = 161.2, 152.9, 138.8, 138.6, 134.4, 129.1, 126.8, 120.1, 118.3, 109.4, 12.9; MS (FAB): *m/z* = 515.96 $[M+H]^+$; IR (KBr): 3447, 2922, 2857, 1621, 1586, 1552, 1478, 1449, 1377, 1329, 1077, 1013, 903, 772, 716 cm^{-1}. Anal. Calcd for $C_{21}H_{16}Br_2N_4O_2$; C, 48.86; H, 3.12; Br, 30.96; N, 10.85. Found: C, 48.90; H, 3.11; Br, 30.94; N, 10.86.

(4*Z*)-2-(3-Chlorophenyl)-4-[[1-(3-chlorophenyl)-5-hydroxy-3-methyl-1*H*-pyrazol-4-yl]methylene]-2-4-dihydro-5-methyl-3*H*-pyrazol-3-one (2h) Yellow solid; Mp 208-210 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 17.82 (s, 1H), 8.00-7.99 (m, 2H), 7.88-7.86 (d, *J* = 8.0 Hz, 2H), 7.38-7.37 (d, *J* = 7.6 Hz, 2H), 7.35 (s, 1H), 7.24-7.23 (m, 2H), 2.35 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.5, 153.0, 138.6, 138.4, 134.6, 129.9, 126.4, 120.8, 118.7, 109.6, 12.9; MS (FAB): *m/z* = 426.07 $[M+H]^+$; IR (KBr): 3446, 2920, 2852, 1618, 1588, 1547, 1482, 1418, 1381, 1327, 1087, 1006, 779, 737, 681 cm^{-1}. Anal. Calcd for $C_{21}H_{16}Cl_2N_4O_2$; C, 59.03; H, 3.77; Cl, 16.59; N, 13.11. Found: C, 59.01; H, 3.76; Cl, 16.57; N, 13.15.

(4*Z*)-2,4-Dihydro-4-[[5-hydroxy-3-methyl-1-(3,5-dimethylphenyl)-1*H*-pyrazol-4-yl]methylene]-5-methyl-2-(3,5-dimethylphenyl)-3*H*-pyrazol-3-one (2i) Yellow solid; Mp 233-235 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 17.86 (s, 1H), 7.51 (s, 4H), 7.24 (s, 1H), 6.92 (s, 2H), 2.36 (s, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.1, 152.5, 138.6, 138.1, 137.5, 128.3, 119.0, 109.4, 21.4, 12.9; MS (FAB): *m/z* = 414.4 $[M+H]^+$; IR (KBr): 3447, 2922, 2853, 1620, 1593, 1551, 1470, 1372, 1372, 1326, 1154, 1097, 1013, 805, 690 cm^{-1}. Anal. Calcd for $C_{25}H_{26}N_4O_2$; C, 72.44; H, 6.32; N, 13.52. Found: C, 72.41; H, 6.33; N, 13.50.

(4*Z*)-2,4-Dihydro-4-[[5-hydroxy-1-(4-methoxyphenyl)-3-propyl-1*H*-pyrazol-4-yl]methylene]-2-(4-methoxyphenyl)-5-propyl-3*H*-pyrazol-3-one (2l) Yellow solid; Mp 138-140 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 17.88 (s, 1H), 7.79-7.77 (d, *J* = 8.0 Hz, 4H), 7.32 (s, 1H), 6.96-6.94 (d, *J* = 8.0 Hz, 4H), 3.83 (s, 6H), 2.69-2.66 (m, 4H), 1.81-1.75 (m, 4H), 1.08-1.05 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.7, 158.0, 155.9, 137.8, 130.9, 122.8, 114.0, 108.5, 55.5, 29.1, 22.1, 14.1; MS (FAB): *m/z* = 474.23 $[M+H]^+$; IR (KBr): 3443, 2959, 2931, 1609, 1533, 1512, 1443, 1357, 1248, 1218, 1171, 1121, 1089, 1036, 832 cm^{-1}. Anal. Calcd for $C_{27}H_{30}N_4O_4$; C, 68.34; H, 6.37; N, 11.81. Found: C, 68.35; H, 6.33; N, 11.80.

(4*Z*)-2,4-Dihydro-4-[[5-hydroxy-1-(3-methylphenyl)-3-propyl-1*H*-pyrazol-4-yl]methylene]-2-(3-methylphenyl)-5-propyl-3*H*-pyrazol-3-one (2m) Yellow solid; Mp 123-125 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 17.86 (s, 1H), 7.71-7.70 (d, *J* = 7.6 Hz, 4H), 7.34-7.32 (m, 2H), 7.30 (s, 1H), 7.10-7.09 (d, *J* = 8.0 Hz, 2H), 2.71-2.67 (m, 4H), 2.41 (s, 6H), 1.82-1.78 (m, 4H), 1.09-1.06 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.2, 156.1, 138.8, 137.9, 137.5, 128.6, 127.3, 121.8, 118.4, 108.7, 29.1, 22.1, 21.5, 14.1; MS (FAB): *m/z* = 442.24 $[M+H]^+$; IR (KBr): 3443, 2960, 2929, 1611, 1535, 1491, 1457, 1358, 1323,

1240, 1221, 1113, 898, 779, 683 cm^{-1}. Anal. Calcd for $C_{27}H_{30}N_4O_2$; C, 73.28; H, 6.83; N, 12.66. Found: C, 73.30; H, 6.82; N, 12.62.

(4*Z*)-2-(3-Bromophenyl)-4-[[1-(3-bromophenyl)-5-hydroxy-3-propyl-1*H*-pyrazol-4-yl]methylene]-2-4-dihydro-5-propyl-3*H*-pyrazol-3-one (2n) Yellow solid; Mp 171-172 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 17.88 (s, 1H), 8.15-8,14 (m, 2H), 7.94-7.92 (d, *J* = 7.2 Hz, 2H), 7.41-7.39 (d, *J* = 6.4 Hz, 2H), 7.32 (s, 1H), 7.30-7.28 (m, 2H), 2.68-2.65 (m, 4H), 1.81-1.76 (m, 4H), 1.09-1.05 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.5, 156.4, 138.8, 138.0, 130.1, 129.3, 123.7, 122.5, 119.2, 108.8, 29.1, 21.8, 14.0; MS (FAB): *m/z* = 572.02 $[M+H]^+$; IR (KBr): 3445, 2959, 2922, 1618, 1586, 1541, 1477, 1443, 1356, 1188, 1085, 1013, 876, 778, 679 cm^{-1}. Anal. Calcd for $C_{25}H_{24}Br_2N_4O_2$; C, 52.47; H, 4.23; Br, 27.92; N, 9.79. Found: C, 52.50; H, 4.21; Br, 27.94; N, 9.76.

(4*Z*)-2-(3-Chlorophenyl)-4-[[1-(3-chlorophenyl)-5-hydroxy-3-propyl-1*H*-pyrazol-4-yl]methylene]-2-4-dihydro-5-propyl-3*H*-pyrazol-3-one (2o) Yellow solid; Mp 168-170 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 17.87 (s, 1H), 8.01-8,00 (m, 2H), 7.90-7.88 (d, *J* = 8.4 Hz, 2H), 7.39-7.35 (m, 2H), 7.33 (s, 1H), 7.26-7.24 (d, *J* = 8.4 Hz, 2H), 2.70-2.67 (m, 4H), 1.82-1.77 (m, 4H), 1.10-1.05 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.3, 156.6, 138.6, 137.9, 135.0, 130.9, 122.6, 116.4, 116.0, 113.8, 29.2, 21.5, 14.0; MS (FAB): *m/z* = 482.13 $[M+H]^+$; IR (KBr): 3447, 2964, 2925, 1622, 1588, 1546, 1481, 1412, 1359, 1217, 1088, 1014, 872, 777, 670 cm^{-1}. Anal. Calcd for $C_{25}H_{24}Cl_2N_4O_2$; C, 62.12; H, 5.00; Cl, 14.67; N, 11.59. Found: C, 62.10; H, 5.01; Cl, 14.64; N, 11.56.

(4*Z*)-2,4-Dihydro-4-[[5-hydroxy-1-(3,5-dimethylphenyl)-3-propyl-1*H*-pyrazol-4-yl]methylene]-2-(3-5-dimethylphenyl)-5-propyl-3*H*-pyrazol-3-one (2p) Yellow solid; Mp 194-196 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 17.85 (s, 1H), 7.51 (s, 4H), 7.33 (s, 1H), 6.93 (s, 2H), 2.71-2.67 (m, 4H), 2.37 (s, 12H), 1.83-1.74 (m, 4H), 1.09-1.05 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.1, 153.7, 139.0, 138.4, 137.6, 129.6, 118.9, 109.7, 29.1, 22.1, 21.4, 14.1; MS (FAB): *m/z* = 470.27 $[M+H]^+$; IR (KBr): 3445, 2959, 2924, 1622, 1591, 1546, 1472, 1366, 1331, 1297, 1242, 1159, 1105, 847, 683 cm^{-1}. Anal. Calcd for $C_{29}H_{34}N_4O_2$; C, 74.01; H, 7.28; N, 11.91. Found: C, 74.02; H, 7.30; N, 11.90.

(4*Z*)-2-(3-Bromophenyl)-4-[[1-(3-bromophenyl)-5-hydroxy-3-isopropyl-1*H*-pyrazol-4-yl]methylene]-2,4-dihydro-5-isopropyl-3*H*-pyrazol-3-one (2q) Yellow solid; Mp 219-221 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 17.74 (s, 1H), 8.17-8,16 (m, 2H), 7.98-7.95 (d, *J* = 8.2 Hz, 2H), 7.44 (s, 1H), 7.41-7.38 (d, *J* = 8.0 Hz, 2H), 7.33-7.28 (m, 2H), 3.13-3.06 (m, 2H), 1.40-1.39 (d, *J* = 6.8 Hz, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.7, 160.7, 138.9, 137.5, 130.1, 129.2, 123.7, 122.5, 119.3, 107.9, 26.9, 21.5; MS (FAB): *m/z* = 572.02 $[M+H]^+$; IR (KBr): 3441, 2965, 2926, 1622, 1586, 1541, 1480, 1381, 1358, 1261, 1111,

1000, 862, 777, 692 cm^{-1}. Anal. Calcd for $C_{25}H_{24}Br_2N_4O_2$; C, 52.47; H, 4.23; Br, 27.92; N, 9.79. Found: C, 52.50; H, 4.21; Br, 27.94; N, 9.80.

(4*Z*)-2-(3-Chlorophenyl)-4-[[1-(3-chlorophenyl)-5-hydroxy-3-isopropyl-1*H*-pyrazol-4-yl]methylene]-2,4-dihydro-5-isopropyl-3*H*-pyrazol-3-one (2r) Yellow solid; Mp 212-214 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 17.74 (s, 1H), 8.03-8,02 (m, 2H), 7.93-7.81 (d, *J* = 8.0 Hz, 2H), 7.45 (s, 1H), 7.39-7.35 (m, 2H), 7.25-7.23 (d, *J* = 7.6 Hz, 2H), 3.11-3.08 (m, 2H), 1.41-1.39 (d, *J* = 7.6 Hz, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.8, 160.8, 138.8, 137.5, 134.6, 129.9, 126.3, 120.9, 118.8, 107.9, 26.9, 21.5; MS (FAB): *m/z* = 482.13 $[M+H]^+$; IR (KBr): 3449, 2963, 2922, 1624, 1559, 1541, 1482, 1381, 1357, 1259, 1094, 859, 775, 745, 682 cm^{-1}. Anal. Calcd for $C_{25}H_{24}Cl_2N_4O_2$; C, 62.12; H, 5.00; Cl, 14.67; N, 11.59. Found: C, 62.11; H, 5.02; Cl, 14.66; N, 11.58.

(4*Z*)-2,4-Dihydro-4-[[5-hydroxy-3-isopropyl-1-(3,5-dimethylphenyl)-1*H*-pyrazol-4-yl]methylene]-5-isopropyl-2-(3,5-dimethylphenyl)-3*H*-pyrazol-3-one (2s) Yellow solid; Mp 184-186 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ = 17.74 (s, 1H), 7.52 (s, 4H), 7.46 (s, 1H), 6.92 (s, 2H), 3.14-3.07 (m, 2H), 2.37 (s, 12H), 1.41-1.39 (d, *J* = 6.8 Hz, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.2, 160.3, 138.6, 138.0, 137.2, 129.9, 118.8, 109.7, 26.9, 21.6, 21.4; MS (FAB): *m/z* = 470.27 $[M+H]^+$; IR (KBr): 3441, 2963, 2922, 1613, 1585, 1536, 1472, 1379, 1357, 1257, 1156, 1089, 926, 847, 686 cm^{-1}. Anal. Calcd for $C_{29}H_{34}N_4O_2$; C, 74.01; H, 7.28; N, 11.91. Found: C, 74.03; H, 7.31; N, 11.89.

ACKNOWLEDGEMENTS

We are grateful for the financial support of the National Natural Science Foundation of China (No. 21202133) and Young Teacher Research Foundation of Northwest Normal University (NWNU-LKQN-08-8, NWNU-kjcxgc-03-73, kjcxgc-03-63). We also thank Key Laboratory of Eco-Environment-Related Polymer Materials (Northwest Normal University), Ministry of Education, for financial support. We also thank Dr. Hanfeng Ding (zhejiang university) for fruitful discussions.

REFERENCES AND NOTES

1. (a) Y. A. Azev, S. V. Shorshnev, and B. V. Golomolzin, *Tetrahedron Lett.*, 2009, **50**, 2899; (b) Y. A. Azev and S. V. Shorshnev, *Chem. Heterocycl. Compds.*, 2009, **45**, 115; (c) J. Wanga, W. F. Caoa, J. H. Sua, H. Tian, Y. H. Huangb, and Z. R. Sun, *Dyes Pigm.*, 2003, **57**, 171; (d) Y. G. Shermolovich and S. V. Yemets, *J. Fluorine Chem.*, 2000, **101**, 111.
2. M. Radi, V. Bernardo, B. Bechi, D. Castagnolo, M. Pagano, and M. Botta, *Tetrahedron Lett.*, 2009, **50**, 6572.
3. Y. A. Azev, H. Neunhoeffer, S. Foro, H. J. Lindner, and S. V. Shorshnev, *Mendeleev Commun.*,

1995, **5**, 229.

4. Y. A. Azev, E. A. Oparina, I. S. Kovalev, P. A. Slepuhin, and R. K. Novikova, *Mendeleev Commun.*, 2012, **22**, 37.
5. F. F. Wong and Y. Y. Huang, *Tetrahedron*, 2011, **67**, 3863.
6. (a) K. Omura, A. K. Sharma, and D. Swern, *J. Org. Chem.*, 1976, **41**, 957; (b) A. J. Mancuso, S.-L. Huang, and D. Swern, *J. Org. Chem.*, 1978, **43**, 2480.
7. H. Fei, J. Yu, Y. Jiang, H. Guo, and J. Cheng, *Org. Biomol. Chem.*, 2013, **11**, 7092.
8. J. Liu, X. Wang, H. Guo, X. Shi, X. Ren, and G. Huang, *Tetrahedron*, 2012, **68**, 1560.
9. G. Cerchiaro, A. M. D. C. Ferreira, A. B. Teixeira, H. M. Magalhães, A. C. Cunha, V. F. Ferreira, L. S. Santos, M. N. Eberlin, J. M. S. Skakle, S. M. S. V. Wardell, and J. L. Wardell, *Polyhedron*, 2006, **25**, 2055.
10. A. C. Olivieri, D. Sanz, R. M. Claramunt, and J. Elguero, *J. Chem. Soc., Perkin Trans. 2,* 1993, 1597.
11. W. Hänsel, *Liebigs Ann. Chem.*, 1976, 1680.
12. CCDC 850167 contains supplementary crystallographic data for compound **2f**; data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
13. U. Drück and W. Litke, *Acta Cryst.*, 1980, **B36**, 3002.
14. W. Hänsel, *Liebigs Ann. Chem.*, 1976, 1380.
15. P. Gilli, V. Ferretti, V. Bertolasi, and G. Gilli, 'Advances in Molecular Structure Research: A Novel Approach to Hydrogen Bonding Theory, 'Vol. 2, ed. by M. Hargittai, JAI Press Ltd., Greenwich Conneticut, USA, 1996, pp. 67-102.
16. (a) F. Lehmann, M. Holm, and S. Laufer, *J. Comb. Chem.*, 2008, **10**, 364; (b) X, J. Wang, J. Tan, and K. Grozinger, *Tetrahedron Lett.*, 2000, **50**, 4713.