A Novel Route to 4-Oxy/thio substituted-1*H*-pyrazol-5(4*H*)-ones *via* Efficient Cross-Claisen Condensation

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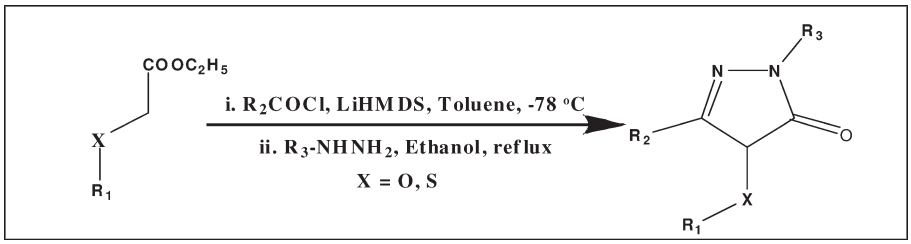

α-Oxy/thio substituted β-keto esters were synthesized through an efficient cross-Claisen condensation of oxy/thio substituted acetic acid ethyl esters with acid chlorides, which in turn converted *in situ* into 4-oxy/thio substituted-1*H*-pyrazol-5(4*H*)-ones by the addition of hydrazine and its derivatives. This method has been found to be extremely fast, general, and useful toward the synthesis of inaccessible pyrazolones and synthetically demanding 4-oxy/thio substituted pyrazolones.

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INTRODUCTION

A considerable interest has been shown to develop new methods for the synthesis of heterocyclic systems. Particularly, 2,3-pyrazol-1(5*H*)-ones have been reported as pharmaceuticals and useful intermediates in the synthesis of heterocycles [1,2]. Some of the aryloxy pyrazolone derivatives are in clinical practice for the treatment of a variety of disorders caused by human immunodeficiency virus and other genetic ailments caused by retroviruses such as acquired immune deficiency syndrome [3]. To date, synthesis of these compounds have been somewhat limited by the available chemistry. The reaction of β-keto esters with hydrazine and its derivatives is a general and most prevalent method to obtain pyrazolones [4], other synthetic methods which do not require β-keto esters have also been reported [5], but these methods tend to have serious drawbacks such as step intensive, usage of sensitive palladium catalysts, and carbon monoxide. So these factors confer that usage of β-keto esters as an intermediate is the broadest and most efficient way to synthesize pyrazolones. To synthesize 4-oxy/thio substituted pyrazolones indeed, α-oxy/thio substituted β-keto esters are still in need. The reported methods to synthesize α-oxy/thio substituted β-keto esters have serious drawbacks such as step intensive, time consuming, and usage of imidazoles [6]. There is a single-step reaction protocol for the self-Claisen condensation [7], which has main limitation in varying the substituents. Hence, there is a need to develop an efficient procedure for cross-Claisen condensation.

RESULTS AND DISCUSSION

This work focused on the cross-Claisen condensation between oxy/thio substituted acetic acid ethyl ester and acid chlorides. We hypothesized that an ester enolate might react in a smooth manner with strong electrophile acid chloride, if proper conditions have maintained to slow down the side reactions such as, self-Claisen condensation and *O*-alkylation. However, there have been very few reports on the application of cross-Claisen condensation between different esters [8] or between esters and acid chlorides, and some successful results were also been reported in the reactions using hydroxyl esters [9]. A nucleophilic reaction of an ester enolate with acid imidazolide has been widely used to synthesis β-keto esters [10], but it would rather be expensive to use imidazolide or active ester in an industrial setting.

Recently, Tanabe and coworkers [11] reported an efficient Ti-crossed Claisen esters and acid chlorides to provide a variety of β-keto esters; this method also suffers by the usage of imidazoles and costlier $TiCl_4$. Hence, we indent to improve the efficiency of traditional cross-Claisen condensation by changing the equivalence of base, acid chloride, reaction time, sequence of addition of reactants, temperature, and solvents choosing compound **1** as representative example. The results of every

Table 1

Yield of the reaction optimized with different equivalent of reactants.

Method	Cross condensed product (%)[a]	Self-condensed product (%)[a]
A	05	81
B	13	68
C	10	54
D	23	35
E	47	22
F	64	09

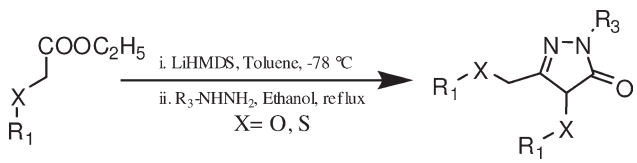
[a] Isolated yield.

change accomplished have been represented as different methods A–I (detailed procedure given in Experimental Section). The yield of cross- and self-condensed products were given in Table 1.

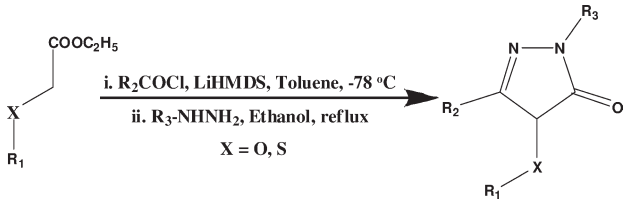
Our initial attempt to synthesize pyrazolone by method A resulted in undesirable self-condensed pyrazolone as major product (Scheme 1) and the desired cross-condensed pyrazolone (Scheme 2) as a minor product (5%). Then the yield of cross-condensed product was optimized with reference to the compound **1** by changing the equivalence of base, acid chloride, time, and order of addition of reactants (methods A–F), and the results were given in Table 1. After finding the suitable composition of equivalence of base, acid chloride, and the order of additions (method F), the reaction condition was optimized by carrying out the experiment at different temperatures (Table 2) and then with different bases and solvents (Table 3).

As expected, the yield of self-condensed product was increased with increasing the temperature. The results shown in Table 3 clearly revealed that the lithium enolate was reacting smoothly with stronger electrophilic acid chloride compared with other enolates (sodium and potassium). The reaction between lithium enolate and the acid chloride was favored in toluene than in tetrahyrofuran (THF). The side reactions were slowed down in a hydrocarbon solvent like toluene which disfavored the possible formation of the intermediates with charges and hence the ester enolate react with the acid chloride. The attempt to improve the yield by carrying out the experiment in two steps was failed, as we could not isolate the β-keto esters as very pure [only 70–80% of purity was recorded using liquid chromatography-mass spectroscopy (LC-MS)] in step 1, and the overall yield of the condensation of β-keto esters with hydrazine hydrate also observed as moderate (∼ 60%). Finally, in method F, we could achieve the maximum yield.

Scheme 1



Scheme 2



The above experiments clearly revealed that the usage of more than 3 equiv. of base avoided the self-condensation. The highly active oxyacetic acid ethyl ester undergoes self-Claisen condensation quickly than the other bulky, sterically hindered esters such as *t*-butyl, benzyl, and *iso*-propyl in the solution phase (solvated) [12], and hence to avoid the self-condensation, the time lag should be avoided between the addition of base and acid chloride (not more than 2 min). Hence, the attention toward rapid addition of base and acid chloride was indeed. Various new derivatives of pyrazolones from β-keto ester intermediates were synthesized to test the generality of this method and their results are given in Table 4. It revealed that yields were generally good, although conditions are not optimized for each of the reactions.

In few cases, the hydrazides of corresponding acetic acid ethyl esters were observed in crude LCMS. Many functional groups were tolerated with less or no side products. Mainly, electrophile-containing enolizable α-protons were successfully coupled with the ester enolates to form β-keto esters. Particularly, cyano functionality was retained in compound **5**. Steric effect could be observed in case of compound **8**, pyrazolone formation was affected sterically by the presence of tetrazole ring (β-keto ester and the corresponding hydrazide was observed in LCMS). Among the substituted hydrazines, highly nucleophilic methyl hydrazine worked well under these conditions and phenyl hydrazine did not react with β-keto esters in the same conditions due to its less nucleophilicity. However, the conditions of less

Table 2

Yield of the reaction optimized at different temperatures.

Method	Temperature (°C)	Cross-condensed product (%)[a]	Self-condensed product (%)[a]
G	−50	62	13
H	−20	57	15
I	0	48	21

[a] Isolated yield.

Table 3

Effect of solvent and base on the yield.

Base	Solvent	Yield (%)[a]
LiHMDS (1.0*M* THF)	Toluene	64
NaHMDS (1.0*M* THF)	Toluene	47
KHMDS (1.0*M* THF)	Toluene	38
LDA (1.0*M* THF)	Toluene	31
NaOMe	THF	14
KO^{t}Bu	THF	07
LiHMDS (1.0*M* THF)	THF	38

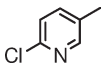
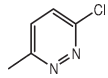
[a] Isolated yield.

nucleophilic phenyl hydrazines with the β-keto esters were successful when we do the reaction in two steps (see general procedure, method J).

In summary, an efficient, extremely rapid method that is hitherto unreported to synthesize α-oxy/thio substituted β-keto esters from oxy/thio substituted acetic acid esters and acid chlorides through efficient cross-Claisen condensation has been developed. The β-keto esters were treated with hydrazine *in situ* to get new derivatives of 4-oxy/thio substituted pyrazolones in good yield. As this method is successful with different oxy/thio acetic acid ethyl esters and acid chlorides, it can be

Table 4

List of 4-oxy/thio substituted-1*H*-pyrazol-5(4*H*)-ones prepared by method F.

Product	X	R_1	R_2	R_3	Yield (%)[a]
1	O	—Ph	—CH_3	—H	64
2	O	—CH_3	—4Cl—Ph	—H	57
3	O	—CH_2—3Br—Ph	—CH_2CH_3	—H	60
4	O	—4OCH_3—Ph	—CH_2CH_3	—H	57
5	O	—4CN—Ph	—CH_3	—H	48
6	S	—Ph	—$(CH_2)_4CH_3$	—H	74
7	S	—CH_2Ph	—Cylopropyl	—H	54
8	O	—Ph	—2—Tetrazolo5—clorophenyl	—H	0[b]
9	O	—4Cl—Ph	—Ph	—H	52
10	S	—Ph		—H	51
11	O	—Ph	—CH_2CH_3	—H	57
12	O	—Ph	—CH_2OCH_3	—H	54
13	O	—CH_2—3Br—Ph	—CH_3	—H	58
14	O	—4OCH_3—Ph	—CH_3	—H	62
15	S	—Ph	—CH_3	—H	67
16	S	—Ph	—Isobutyl	—H	74
17	S	—Ph	—CH $(CH_3)_2$	—H	71
18	S	—CH_2Ph	—CH_2CH_3	—H	61
19	S	—CH_2Ph	—CH_2OCH_3	—H	58
20	S	—4Cl—Ph	—Isobutyl	—H	78
21	O	—Ph	—4Cl—Ph	—H	59
22	O	—Ph	—CH $(CH_3)_3$	—H	58
23	O	—Ph	—Isobutyl	—CH_3	64
24	O	—Ph	—CH_3	—Ph	0[c]
25	O	—Ph	—CH_3	—4F—Ph	0[c]
26	S	—Ph	—CH_3	—CH_3	60
27	O	—Ph	—CH_2CH_3	—CH_3	77[c]
28	O	—Ph	—Isobutyl	—4F—Ph	52[d]
29	S	—Ph	—CH_3	—4F—Ph	58[d]
30	O	—Ph	—CH_2CH_3	—CH_2CF_3	49[d]
31	O	—Ph	—CH_3	—4F—Ph	60[d]
32	S	—Ph	—Isobutyl	—4F—Ph	51[d]
33	O	—Ph	—CH_2CH_3	—4F—Ph	61[d]
34	S	—Ph	— $(CH_2)_4CH_3$		29[c],[d]
35	S	—Ph	—CH_2CH_3	—4F—Ph	40[c],[d]

[a] Isolated yield.
[b] Only β-keto ester and the corresponding hydrazide was observed in crude LCMS.
[c] Percentage of product in crude LCMS.
[d] Prepared by method J.

regarded as useful method for the synthesis of previously inaccessible pyrazolones as well as pharmaceutically demanding pyrazolones. At present, we are adopting this method to synthesize other heterocycles, which originate from β-keto esters.

EXPERIMENTAL

All the reagents were purchased from Aldrich and used as received. Lithium hexamethyl disilylamide (LiHMDS) solutions were kept under nitrogen atmosphere after opening. Acid chlorides were freshly prepared and used. Dry toluene, AcOH, and EtOH were supplied by Spectrochem. All chemistry was performed under a nitrogen atmosphere using standard techniques. Melting points were determined by Buchi B-545 apparatus. All the NMR spectra were recorded using Bruker AMX 400 or Bruker DPX 300 Instrument with 5-mm PABBO BB-1H tubes. ^{1}H-NMR spectra recorded using $\sim$ 0.03*M* solutions in d_6-DMSO at 300 or 400 MHz with tetramethyl silane (TMS) as internal reference. ^{13}C-NMR spectra were recorded using $\sim$ 0.05*M* solutions in d_6-DMSO at 75 or 100 MHz with TMS as internal reference. In many cases, pyrazolones were recorded in the enol form whenever d_6-DMSO was used as solvent. IR spectra were recorded using NICOLET 6700 FTIR (Thermo scientific). MALDI experiment was carried out using laser beam (intensity, 350 nm) in Bruker autoflex III smart beam. LCMS were obtained using Agilent 1200 series LC and Micromass zQ spectrometer. Column chromatography was performed using a silica gel (230–400 mesh).

General procedure to synthesis pyrazolones (method F). LiHMDS (19.4 mL, 1.0*M* in THF, 19.4 mmol) was added quickly to the solution of phenoxyacetic acid ethyl ester (1 g, 5.5 mmol) in toluene (15 mL) using syringe at −78°C with agitation and the formed anion is allowed to stand for $\sim$ 2 min. Then, acetyl chloride (1 mL, 13.8 mmol) was added in a lot with stirring. The reaction mixture was removed from acetone-dry ice bath and stirred for 10 min, then 2 mL of AcOH was added with stirring. EtOH (15 mL) and hydrazine hydrate (1.5 mL, 44 mmol) were added to the reaction mixture, refluxed for 10 min. Then, the reaction mixture was concentrated to dryness under reduced pressure and redissolved in EtOAc, the organic layer was washed with saturated brine solution, dried over Na_2SO_4, and evaporated under reduced pressure. Crude product was purified by column chromatography using MeOH:EtOAc (1:99). Yield of the product was 676 mg (64%). Yield of the unwanted self-condensed product was 140 mg (9%).

Method A. LiHMDS (5.5 mL, 1.0*M* in THF, 5.5 mmol) was added slowly to the solution of phenoxy acetic acid ethyl ester (1 g, 5.5 mmol) in toluene (15 mL) at −78°C with stirring (30 min), followed by acetyl chloride (0.39 mL, 5.5 mmol) in dropwise at the same temperature. Resulting solution was slowly (10 min) warmed to −20°C, then quenched with AcOH (2 mL) and EtOH (15 mL). Hydrazine hydrate (1.5 mL, 4.4 mmol) was added and refluxed for 10 min. The resulting light brown solution was concentrated directly and the obtained residue was redissolved in EtOAc, washed with brine solution, dried over Na_2SO_4, and evaporated under reduced pressure. Crude product was purified by column chromatography using MeOH:EtOAc (1:99). Yield of the product was 90 mg (8%). Yield of the unwanted self-condensed product was 1.26 g (81%).

Method B. The LiHMDS in THF was taken as 11.1 mmol and other additions, conditions were followed as such in method A. Yield of the product was 144 mg (13%). Yield of the unwanted self-condensed product was 1.12 g (72%).

Method C. Phenoxy acetic acid ethyl ester (1 g, 5.5 mmol) in toluene was added slowly to the solution of LiHMDS (5.5 mL, 1.0*M* in THF, 5.5 mmol) in toluene (10 mL) at −78°C over a period of 10 min and the mixture stirred at this temperature for 30 min, then acetyl chloride (0.39 mL, 5.5 mmol) was added slowly to reaction mixture over a period of 5 min at the same temperature. The resulting solution was slowly (10 min) warmed to −20°C, then quenched with AcOH (2 mL) and EtOH (15 mL). Hydrazine hydrate (1.5 mL, 44 mmol) was added and refluxed for 10 min. The resulting light brown solution was concentrated to dryness and redissolved in EtOAc, the separated organic layer was washed with brine solution, dried over Na_2SO_4, and evaporated under reduced pressure. Crude product was purified by column chromatography using MeOH:EtOAc (1:99). Yield of the product was 105 mg (10%). Yield of the unwanted self-condensed product was 1.06 g (68%).

Method D. LiHMDS (5.5 mL, 1.0*M* in THF, 5.5 mmol) was added quickly to the solution of phenoxy acetic acid ethyl ester (1 g, 5.5 mmol) in toluene (15 mL) using syringe at −78°C with stirring, and the formed anion is allowed to stand for $\sim$1 min, then acetyl chloride (0.39 mL, 5.5 mmol) was added in a lot with stirring. Reaction mixture was removed from acetone-dry ice bath, stirred for 10 min, and then added 2 mL of AcOH with stirring. EtOH (15 mL) and hydrazine hydrate (1.5 mL, 44 mmol) were added and refluxed for 10 min. Reaction mixture was concentrated to dryness under reduced pressure and redissolved in EtOAC, the organic layer washed with brine solution, dried over Na_2SO_4, and evaporated under reduced pressure. Crude product was purified by column chromatography using MeOH:EtOAc (1:99). Yield of the product was 242 mg (23%). Yield of the unwanted self-condensed product was 548 mg (35%).

Method E. LiHMDS (11.1 mL, 1.0*M* in THF, 11.1 mmol) was added quickly using syringe to the solution of phenoxy acetic acid ethyl ester (1 g, 5.5 mmol) in toluene (15 mL) at −78°C with stirring, and the formed anion is allowed to stand for $\sim$ 1 min, then acetyl chloride (0.8 mL, 11.1 mmol) added in a lot with stirring. Reaction mixture was removed from acetone-dry ice bath and stirred for 10 min, then 2 mL of AcOH was added with stirring. EtOH (15 mL) and hydrazine hydrate (1.5 mL, 44 mmol) were added and refluxed for 10 min. Reaction mixture was concentrated to dryness under reduced pressure and redissolved in EtOAc, then organic layer washed with brine solution, dried over Na_2SO_4, and evaporated under reduced pressure. Crude product was purified by column chromatography using MeOH:EtOAc (1:99). Yield of the product was 496 mg (47%). Yield of the unwanted self-condensed product was 344 mg (22%).

In methods G, H, and I, the reaction was carried out at −50, −20, and 0°C, respectively. The additions and other conditions were followed as such given in method F.

General procedure to synthesize *N*-substituted pyrazolones: (Method J). LiHMDS (19.4 mmol, 1*M* solution in THF) was added quickly using syringe to the solution of an ester (5.5 mmol) in toluene (15 mL) at −30°C with stirring, the formed anion is allowed to stand for $\sim$ 2 min, then acid chloride (13.8 mmol) was added in one portion with stirring. Reaction mixture was removed from acetone-dry ice bath and continues the stirring for 10 min, then quenched with water,

and extracted with EtOAc (2 × 100 mL). Then, combined organic layer was dried over Na_2SO_4, concentrated at rotary evaporator. The obtained crude product was taken in the mixture of EtOH (20 mL) and AcOH (2 mL), to this substituted hydrazine (10 mmol) was added and refluxed overnight. Reaction was monitored by thin layer chromatography (TLC); reaction mixture was concentrated to dryness. See specific compounds for purification details.

3-Methyl-4-phenoxy-1H-pyrazol-5(4H)-one (1) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), white solid. m.p. 221.7–222.8°C; IR (KBr): ν 3738, 2571, 2296, 1588 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.12 (brs, 1H), 7.27 (t, J = 7.4 Hz, 2H), 6.96 (t, J = 7.3 Hz, 1H), 6.85 (d, J = 7.8 Hz, 2H), 1.96 (s, 3H), 1.36 (brs, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 159.1, 152.9, 130.8, 129.3, 121.9, 120.5, 115.1, 9.27; LC-MS: *m/z* 190.3 (M+); Anal. Calcd. for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.02; H, 5.18; N, 14.63.

3-(4-Chlorophenyl)-4-methoxy-1H-pyrazol-5(4H)-one (2) This compound was obtained according to above general procedure of method F. Purified by preparative high performance liquid chromatography (HPLC) [MeCN: trifluoro acetic acid (TFA)], pale brown solid. m.p. 147.8–148.9°C; IR (KBr): ν 3292, 2944, 2360, 1736, 1656 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.90 (brs, 2H), 7.73 (d, J = 6.8 Hz, 2H), 7.49 (d, J = 7.0 Hz, 2H), 3.70 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 152.7, 131.1, 129.5, 128.8, 128.3, 126.7, 126.2, 60.4; LC-MS: *m/z* 224.8 (M+); Anal. Calcd. for $C_{10}H_9ClN_2O_2$: C, 53.47; H, 4.04; N, 12.47. Found: C, 53.55; H, 4.24; N, 12.50.

3-Ethyl-4-(3-bromophenylmethoxy)-1H-pyrazol-5(4H)-one (3) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), pale yellow solid. m.p. 220.1–221.7°C; IR (KBr): ν 2969, 2927, 2722, 2130, 1783, 1715 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.90 (brs, 1H), 9.70 (brs, 1H), 7.56 (s, 1H), 7.49 (d, J = 6.7 Hz, 1H), 7.36 (t, J = 7.3 Hz, 1H), 7.30 (d, J = 7.5 Hz, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 152.8, 141.1, 135.0, 131.0, 130.9, 130.8, 127.4, 124.3, 121.9, 73.9, 17.2, 13.3; LC-MS: *m/z* 297.1 (M+), Anal. Calcd. for $C_{12}H_{13}BrN_2O_2$: C, 48.50; H, 4.41; N, 9.43. Found: C, 48.62; H, 4.32; N, 9.39.

3-Ethyl-4-(4-methoxyphenyoxy)-1H-pyrazol-5(4H)-one (4) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), white solid, m.p. 256.3–257.5°C; IR (KBr): ν 2937, 2833, 2702, 1621, 1536 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.30 (brs, 1H), 9.70 (brs, 1H), 6.83 (d, J = 9.1 Hz, 2H), 6.78 (d, J = 9.3 Hz, 2H), 3.68 (s, 3H), 2.35 (q, J = 7.6 Hz, 2H), 1.03 (t, J = 7.6 Hz, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 154.3, 153.3, 153.0, 136.1, 120.6, 115.9, 114.9, 55.8, 17.4, 13.0; LC-MS: *m/z* 234.9 (M+); Anal. Calcd. for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.38; H, 5.94; N, 12.09.

3-Methyl-4-(4-cyanophenyoxy)-1H-pyrazol-5(4H)-one (5) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), pale yellow solid. m.p. 281.3–282.8°C; IR (KBr); ν 2677, 2221, 1596, 1497 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.50 (brs, 1H), 9.80 (brs, 1H), 7.76 (d, J = 4.8 Hz, 2H), 7.01 (d, J = 9.6 Hz, 2H), 1.97 (s, 3H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 162.5, 152.4, 134.7, 134.6, 119.3, 116.8, 116.3, 104.4, 9.21; LC-MS: *m/z* 215.9 (M+); Anal. Calcd. for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22; N, 19.53. Found: C, 61.44; H, 4.35; N, 19.64.

3-Pentyl-4-(phenylthio)-1H-pyrazol-5(4H)-one (6) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), white solid. m.p. 182.1–183.5°C; IR (KBr) ν 3061, 2953, 2923, 2854, 1587 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 12.00 (brs, 1H), 10.00 (brs, 1H), 7.21 (t, J = 7.7 Hz, 2H), 7.05 (t, J = 7.3 Hz, 1H), 6.97 (d, J = 7.3 Hz, 2H), 2.48 (t, J = 7.7 Hz, 2H), 1.46 (m, 2H), 1.21 (m, 4H), 1.13 (t, J = 5.0 Hz, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 162.8, 149.0, 139.8, 129.2, 125.3, 125.0, 87.0, 31.1, 28.2, 25.0, 22.1, 14.2. LC-MS: *m/z* 263.0 (M+); Anal. Calcd. for $C_{14}H_{18}N_2OS$: C, 64.09; H, 6.91; N, 10.68. Found: C, 64.00; H, 6.98; N, 10.55.

3-Cyclopropyl-4-(phenylmethylthio)-1H-pyrazol-5(4H)-one (7) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), pale yellow solid. m.p. 231.0–231.9°C; IR (KBr) ν 3066, 2955, 2923, 2868, 1583 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.20 (brs, 1H), 9.77 (brs, 1H), 7.24–7.17 (m, 3H), 7.11 (d, J = 6.7 Hz, 2H), 3.69 (s, 2H), 1.58–1.51 (m, 1H), 0.66 (t, J = 2.2 Hz, 2H), 0.58 (t, J = 5.0 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 162.4, 149.3, 139.0, 129.3, 128.5, 127.0, 90.5, 7.2, 7.1; LC-MS: *m/z* 246.9 (M+); Anal. Calcd. for $C_{13}H_{14}N_2OS$: C, 63.39; H, 5.73; N, 11.37. Found: C, 63.53; H, 5.65; N, 11.49.

4-(4-Chlorophenoxy)-3-phenyl-1H-pyrazol-5(4H)-one (9) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), pale yellow solid. m.p. 226.7–227.8°C; IR (KBr) ν 3447, 3203, 2281, 1614, 1525 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD): δ 7.66 (m, 2H), 7.40–7.38 (m, 3H), 7.22 (d, J = 8.6 Hz, 2H), 7.05 (d, J = 8.6 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 164.6, 149.2, 139.3, 133.4, 131.7, 130.8, 129.9, 128.8, 128.5, 127.8, 88.7; LC-MS: *m/z* 300.9 (M+); Anal. Calcd. for $C_{15}H_{11}ClN_2O_2$: C, 62.80; H, 3.87; N, 9.77. Found: C, 62.85; H, 3.69; N, 9.77.

3-(6-Chloropyridine-2-yl)-4-(phenylthio)-1H-pyrazol-5 (4H)-one (10) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), off white semisolid. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.00 (brs, 1H), 10.50 (brs, 1H), 8.70 (s, 1H), 8.28 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.27 (t, J = 8.0 Hz, 2H), 7.11 (t, J = 7.2 Hz, 1H), 7.04 (d, J = 7.6 Hz, 2H); LC-MS: *m/z* 303.0 (M+).

3-Ethyl-4-phenoxy-1H-pyrazol-5(4H)-one (11) This compound was obtained according to above general procedure of method F. Purified by column chromatography (acetone:EtOAc, 1:4), white solid. m.p. 196.2–197.3°C; IR (KBr): ν 3787, 2977, 2698, 1620 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.30 (s, 1H), 9.70 (s, 1H), 7.27 (t, J = 7.6 Hz, 2H), 6.96 (t, J = 7.4 Hz, 1H), 6.84 (d, J = 7.9 Hz, 2H), 2.35 (q, J = 7.6 Hz, 2H), 1.03 (t, J = 7.6 Hz, 3H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 159.3, 152.9, 136.2, 130.2, 121.8, 119.9, 115.1, 17.4, 13.0; LC-MS: *m/z* 204.3 (M+); Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.09; H, 5.92; N, 13.72. Found: C, 64.17; H, 5.88; N, 13.64.

3-Methoxymethyl-4-phenoxy-1H-pyrazol-5(4H)-one (12) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), pale yellow solid. m.p. 146.4–147.2°C; IR (KBr):

ν 3206, 2930, 2550, 2361, 1587 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.70 (s, 1H), 9.80 (s, 1H), 7.27 (t, J = 7.4 Hz, 2H), 6.97 (t, J = 7.3 Hz, 1H), 6.87 (d, J = 8.6 Hz, 2H), 4.16 (s, 2H), 3.15 (s, 3H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 159.1, 152.3, 131.3, 129.7, 122.0, 121.3, 115.2, 62.8, 57.76; LC-MS: m/z 220.1 (M+); Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.08; H, 5.319; N, 12.68.

3-Methyl-4-(3-bromophenylmethoxy)-1H-pyrazol-5(4H)-one (13) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), white solid. m.p. 183.6–184.7°C; IR (KBr): ν 2966, 2923, 2871, 2557, 2361, 1588 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.80 (brs, 1H), 9.60 (brs, 1H), 7.57 (s, 1H), 7.50 (d, J = 5.9 Hz, 1H), 7.37 (d, J = 5.8 Hz, 1H), 7.31 (t, J = 7.7 Hz, 1H), 4.81 (s, 2H), 1.90 (s, 3H); ^{13}C-NMR (75 MHz. DMSO-d_6): δ 152.8, 141.2, 131.0, 130.9, 130.85, 129.4, 127.4, 125.12, 121.9, 73.9, 9.2; LC-MS: m/z 283.8 (M+); Anal. Calcd. for $C_{11}H_{11}BrN_2O_2$: C, 46.66; H, 3.92; N, 9.89. Found: C, 46.54; H, 3.84; N, 9.82.

3-Methyl-4-(4-methoxyphenyoxy)-1H-pyrazol-5(4H)-one (14) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), white solid. m.p. 201.0–202.7°C; IR (KBr): ν 2833, 2701, 1621, 1572 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 11.20 (brs, 1H), 9.70 (brs, 1H), 6.25 (d, J = 7.2 Hz, 2H), 6.80 (d, J = 6.7 Hz, 2H), 3.67 (s, 3H), 1.90 (s, 3H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 154.4, 153.1, 152.9, 130.7, 121.4, 116.0, 114.9, 55.8, 9.26; LC-MS: m/z 220.9 (M+); Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.07; H, 5.55; N, 12.68.

3-Methyl-4-phenylthio-1H-pyrazol-5(4H)-one (15) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), pale yellow solid. m.p. 292.3–294.1°C; IR (KBr): ν 3007, 2656, 1575, 1478 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 10.00 (brs, 1H), 7.22 (t, J = 7.7 Hz, 2H), 7.06 (t, J = 7.5 Hz, 1H), 6.96 (d, J = 8.3 Hz, 2H), 2.08 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 162.7, 145.0, 139.5, 129.3, 125.2, 125.1, 87.3, 10.7; LC-MS: m/z 206.9 (M+); Anal. Calcd. for $C_{10}H_{10}N_2OS$: C, 58.23; H, 4.89; N, 13.58. Found: C, 58.18; H, 4.76; N, 13.45.

3-Isobutyl-4-(phenylthio)-1H-pyrazol-5(4H)-one (16) This compound was obtained according to above general procedure of method F. Purified by column chromatography (Pet. ether:-EtOAc, 1:1), pale yellow solid. m.p. 198.1–198.4°C; IR (KBr) ν 3061, 2954, 2866, 2591, 1590 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.00 (brs, 1H), 10.00 (brs, 1H), 7.22 (t, J = 7.6 Hz, 2H), 7.07 (t, J = 7.2 Hz, 1H), 6.97 (d, J = 7.6 Hz, 2H), 2.36 (d, J = 7.6 Hz, 2H), 1.85 (m, 1H), 0.90 (d, J = 4.4 Hz, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 162.8, 147.9, 139.7, 129.1, 125.2, 124.9, 87.5, 34.2, 28.2, 22.6; LC-MS: m/z 248.9 (M+); Anal. Calcd. for $C_{13}H_{16}N_2OS$: C, 62.87; H, 6.49; N, 11.28. Found: C, 62.80; H, 6.41; N, 11.20.

3-Isopropyl-4-(phenylthio)-1H-pyrazol-5(4H)-one (17) This compound was obtained according to above general procedure of method F. Purified by column chromatography (Pet. ether:-EtOAc, 1:1), white solid. m.p. 216.1–217.2°C; IR (KBr): ν 3054, 2970, 2735, 1604 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.00 (brs, 1H), 10.00 (brs, 1H), 7.23 (t, J = 7.6 Hz, 2H), 7.07 (t, J = 7.2 Hz, 1H), 6.97 (d, J = 7.6 Hz, 2H), 2.96 (m, 1H), 1.15 (d, J = 9.6 Hz, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 162.8, 154.0, 139.8, 129.2, 125.1, 125.0, 85.6, 25.8, 21.9; LC-MS: m/z 233.8 (M+); Anal. Calcd. for $C_{12}H_{14}N_2OS$: C, 61.51; H; 6.02; N, 11.96. Found: C, 61.44; H; 5.98; N, 12.06.

3-Ethyl-4-(benzylthio)-1H-pyrazol-5(4H)-one (18) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:9), white solid. m.p. 226.9–227.8°C; IR (KBr): ν 3061, 3024, 2930, 1576 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.50 (brs, 1H), 9.80 (brs, 1H), 7.25–7.08 (m, 3H), 7.07 (d, J = 6.6 Hz, 2H), 3.66 (s, 2H), 2.10 (q, J = 8.0 Hz, 2H), 0.84 (t, J = 7.6 Hz, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 162.5, 149.4, 139.1, 129.2, 128.4, 126.9, 89.4, 18.1, 13.3; LC-MS: m/z 234.9 (M+); Anal. Calcd. for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02; N, 11.96. Found: C, 61.50; H, 6.06; N, 11.88.

3-Methoxymetyl-4-(benzylthio)-1H-pyrazol-5(4H)-one (19) This compound was obtained according to above general procedure of method F. Purified by column chromatography (Pet. ether:-EtOAc, 1:1), white solid. m.p. 226.6–227.9°C; IR (KBr): ν 3058, 2982, 2817, 2362, 1577 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.31–7.17 (m, 3H), 7.07 (d, J = 7.6 Hz, 2H), 3.79 (s, 2H), 3.69 (s, 2H), 3.13 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD): δ 164.3, 148.3, 140.7, 130.7, 129.7, 128.3, 93.1, 65.7, 59.0, 41.3; LC-MS: m/z 251.0 (M+); Anal. Calcd. for $C_{12}H_{14}N_2O_2S$: C, 57.51; H, 5.68; N, 11.04. Found: C, 57.51; H, 5.68; N, 11.04.

3-Isobutyl-4-(4-chlorophenylthio)-1H-pyrazol-5(4H)-one (20) This compound was obtained according to above general procedure of method F. Purified by column chromatography (Pet. ether:-EtOAc, 1:1), off white solid. m.p. 227–228°C; IR (KBr): ν 2956, 2869, 1701, 1603 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.00 (brs, 1H), 10.00 (brs, 1H), 7.29 (d, J = 8.4 Hz, 2H), 6.98 (d, J = 6.8 Hz, 2H), 2.36 (d, J = 6.8 Hz, 2H), 1.85 (m, 1H), 0.78 (d, J = 6.4 Hz, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 162.7, 147.9, 138.9, 129.5, 129.1, 126.8, 87.1, 34.2, 28.2, 22.6; LC-MS: m/z 282.6 (M+); Anal. Calcd. for $C_{13}H_{15}ClN_2OS$: C, 55.21; H, 5.35; N, 9.91. Found: C, 55.11; H, 5.24; N, 9.84.

3-(4-Chlorophenyl)-4-phenoxy-1H-pyrazol-5(4H)-one (21) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:EtOAc, 1:99), pale yellow solid. m.p. 208.2–209.9°C; IR (KBr): ν 3915, 3787, 3661, 2740, 1589 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 12.20 (brs, 1H), 10.10 (brs, 1H), 7.63 (d, J = 8.3 Hz, 2H), 7.45 (d, J = 10.7 Hz, 2H), 7.28 (t, J = 8.0 Hz, 2H), 6.98 (t, J = 7.5 Hz, 1H), 6.91 (d, J = 7.7 Hz, 2H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 158.3, 132.8, 130.1, 129.4, 126.8, 122.4; LC-MS: m/z 287.2 (M+); Anal. Calcd. for $C_{15}H_{11}ClN_2O_2$: C, 62.84; H, 3.87; N, 9.77. Found: C, 62.87; H, 3.78; N, 9.66.

3-Tert-butyl-4-phenoxy-1H-pyrazol-5(4H)-one (22) This compound was obtained according to above general procedure of method F. Purified by preparative HPLC, brown semisolid. IR (KBr): ν 2964, 2868, 2716, 1599, 1562 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 10.00 (brs, 2H), 7.26 (t, J = 7.4 Hz, 2H), 6.94 (t, J = 7.0 Hz, 1H), 6.83 (d, J = 7.5 Hz, 2H), 1.16 (s, 9H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 159.0, 153.1, 142.7, 129.8, 121.8, 119.0, 115.1, 31.7, 29.2; LC-MS: m/z 232.3 (M+); Anal. Calcd. for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.09; H, 6.89; N, 12.186.

3-Isobutyl-1-methyl-4-phenoxy-1H-pyrazol-5(4H)-one (23) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH: CH_2Cl_2, 2:98), pale brown solid. m.p. 141.4–142.7°C; IR

(KBr): ν 3188, 2956, 2870, 1693, 1588 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD): δ 7.27 (t, J = 7.5 Hz, 2H), 6.97 (t, J = 7.3 Hz, 1H), 6.92 (d, J = 7.6 Hz, 2H), 3.48 (s, 3H), 2.31 (d, J = 7.3 Hz, 2H), 1.89 (m, 1H), 0.96 (d, J = 6.3 Hz, 6H); ^{13}C-NMR (100 MHz, CD_3OD): δ 160.2, 142.7, 130.8, 123.4, 116.3, 34.9, 32.0, 29.2, 22.0; LC-MS: *m/z* 247.0 (M+); Anal. Calcd. for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37; O, 12.29. Found: C, 68.15; H, 7.26; N, 11.297.

1,3-Dimethyl-4-(phenylthio)-1H-pyrazol-5(4H)-one (26) This compound was obtained according to above general procedure of method F. Purified by column chromatography (MeOH:CH_2Cl_2, 2:98), pale brown solid. m.p. 170.5–171.8°C; IR (KBr): ν 3065, 2918, 2359, 1583 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.30 (brs, 1H), 7.25 (t, J = 8.0 Hz, 3H), 7.09 (t, J = 7.2 Hz, 1H), 6.98 (d, J = 7.6 Hz, 1H), 3.15 (brs, 3H), 1.98 (brs, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 155.6, 149.8, 139.6, 129.4, 125.1, 125.1, 49.1, 33.9, 12.6; LC-MS: *m/z* 220.2 (M+); Anal. Calcd. for $C_{11}H_{12}N_2OS$: C, 59.97; H, 5.49; N, 12.72; Found: C, 60.07; H, 5.41; N, 12.68.

1-(4-Flurophenyl)-3-isobutyl-4-phenoxy-1H-pyrazol-5(4H)-one (28) This compound was obtained according to above general procedure of method J. Purified by column chromatography (MeOH:EtOAc, 1:9), white solid. m.p. 198–199.4°C; IR (KBr): ν 3077, 2954, 2922, 2867, 1590 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.69 (m, 2H), 7.27 (m, 4H), 7.01 (m, 3H), 2.39 (d, J = 7.1 Hz, 2H), 1.98 (m, 1H), 0.94 (d, J = 6.6 Hz, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 158.8, 144.4, 144.1, 135.9, 130.0, 123.0, 122.3, 121.5, 116.0, 115.3, 35.5, 27.5, 22.8; LC-MS: *m/z* 325.5 (M+); Anal. Calcd. for $C_{19}H_{19}FN_2O_2$: C, 69.92; H, 5.87; N, 8.58. Found: C, 69.81; H, 5.82; N, 8.47.

1-(4-Flurophenyl)-3-methyl-4-(phenylthio)-1H-pyrazol-5 (4H)-one (29) This compound was obtained according to above general procedure method of J. Purified by column chromatography (MeOH:EtOAc, 1:99), pale yellow solid. m.p. 202.1–202.6°C; IR (KBr): ν 3067, 2447, 1583 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.57 (brs, 1H), 7.74 (m, 2H), 7.30 (m, 4H), 7.01 (t, J = 7.2 Hz, 1H), 6.95 (d, J = 8.4 Hz, 2H), 1.98 (brs, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 161.5, 159.1, 152.4, 138.8, 135.1, 129.5, 125.4, 123.4, 116.3, 116.4, 12.8; LC-MS: *m/z* 299.7 (M+); Anal. Calcd. for $C_{16}H_{13}FN_2OS$: C, 63.98; H, 4.36; N, 9.33. Found: C, 64.07; H, 4.25; N, 9.26.

3-Ethyl-1-(4-(2,2,2-trifluoroethyl)phenyl)-4-phenoxy-1H-pyrazol-5(4H)-one (30) This compound was obtained according to above general procedure of method J. Purified by column chromatography (MeOH:EtOAc, 1:99), white solid. m.p. 189.7–190.4°C; IR (KBr): ν 2976, 2500, 1583, 1489 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.37 (brs, 1H), 7.30 (t, J = 8.3 Hz, 3H), 6.99 (t, J = 7.3 Hz, 1H), 6.86 (d, J = 8.0 Hz, 2H), 4.69 (brs, 2H), 2.25 (q, J = 7.4 Hz, 2H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 158.5, 145.6, 144.4, 129.6, 129.3, 128.0, 125.2, 122.4, 121.8, 119.6, 117.0, 114.9, 114.7, 47.5, 19.2; LC-MS: *m/z* 285.9 (M+); Anal. Calcd. for $C_{13}H_{13}F_3N_2O_2$: C, 54.55; H, 4.58; N, 9.79; Found: C, 54.46; H, 4.51; N, 9.88.

1-(4-Flurophenyl)-3-methyl-4-phenoxy-1H-pyrazol-5(4H)-one (31) This compound was obtained according to above general procedure of method J. Purified by column chromatography (MeOH:EtOAc, 1:99), pale yellow solid. m.p. 190.2–191.7°C; IR (KBr): ν 3084, 2922, 2687, 1721, 1632 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.75 (d, J = 4.5 Hz, 2H), 7.30 (d, J = 7.5 Hz, 4H), 7.01(t, J = 6.9 Hz, 1H), 6.94 (d, J = 8.3 Hz, 2H), 2.48 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 160.7, 158.2, 140.9, 129.6, 129.4, 21.9, 115.8, 115.5, 114.8, 10.9; LC-MS: *m/z* 284.5 (M+); Anal. Calcd. for $C_{16}H_{13}FN_2O_2$: C, 67.60; H, 4.61; N, 9.85. Found: C, 67.55; H, 4.76; N, 9.735.

1-(4-Fluorophenyl)-3-isobutyl-4-(phenylthio)-1H-pyrazol-5(4H)-one (32) This compound was obtained according to above general procedure of method J. Purified by column chromatography (30% EtOAc in Pet. ether), white solid. m.p. 219.4–220.6°C, IR (KBr): ν 3061, 3026, 2652, 1736, 1577 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.20 (brs, 1H), 7.75 (d, J = 8.5 Hz, 2H), 7.28 (m, 4H), 7.08 (m, 3H), 2.35 (d, J = 3.1 Hz, 2H), 1.92 (m, 1H), 0.84 (d, J = 6.6 Hz, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 161.5, 159.1, 155.0, 139.0, 135.2, 129.4, 125.4, 125.3, 123.5, 116.3, 116.1, 55.4, 36.1, 27.8, 22.8; LC-MS: *m/z* 320.8 (M+); Anal. Calcd. for $C_{19}H_{19}FN_2OS$: C, 66.64; H, 5.59; N, 8.18. Found: C, 66.57; H, 5.51; N, 8.22.

3-Ethyl-1-(4-fluorophenyl)-4-phenoxy-1H-pyrazol-5(4H)-one (33) This compound was obtained according to above general procedure of method J. Purified by column chromatography (30% EtOAc in Pet. ether), white solid. m.p. 168.3–169.5°C; IR (KBr): ν 3066, 2980, 2880, 2777, 2702, 2627, 1623 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.58 (brs, 1H), 7.75 (d, J = 8.8 Hz, 2H), 7.32 (t, J = 7.2 Hz, 3H), 7.00 (m, 3H), 2.34 (brs, 2H), 1.60 (brs, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 158.8, 146.3, 135.9, 130.1, 123.1, 122.3, 119.2, 166.2, 116.0, 115.5, 115.2, 19.8, 12.5; LC-MS: *m/z* 298.6 (M+); Anal. Calcd. for $C_{17}H_{15}FN_2O$: C, 68.45; H, 5.07; N, 9.39. Found: C, 68.33; H, 5.15; N, 9.21.

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