Utilization of Hypervalent Iodine in Organic Synthesis: A Novel and Facile Two-Step Protocol for the Synthesis of New Derivatives of 1*H*-Imidazo[1,2-b]Pyrazole by the Cyclocondensation involving α-Tosyloxyacetophenones

Ming Li*†‡, Guilong Zhao†, Lirong Wen†, Wei Cao†,
Shusheng Zhang†, Huazheng Yang‡

†College of Chemistry and Molecular Engineering, Qingdao University of Science and Technology, Qingdao, 266042, P. R. China
‡State Key Laboratory of Elemental Organic Chemistry, Nankai University, Tianjin, 300071, P. R. China
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A series of new 2-aryl-7-cyano/ethoxycarbonyl-6-methylthio-1*H*-imidazo[1,2-*b*]pyrazoles (**5**) have been synthesized in moderate to good yields, *via* a two-step cyclocondensation procedure of 5-amino-4-cyano/ethoxycarbonyl-3-methylthio-1*H*-pyrazole (**1**) and α-bromoacetophenones (**3**) or α-tosyloxyacetophenones (**2**), which were prepared by the reactions of acetophenones with [hydroxy(tosyloxy)iodo]benzene (HTIB). The intermediates, 5-amino-1-(aroylmethyl)-4- cyano/ethoxycarbonyl-3-methylthio-1*H*-pyrazoles (**4**), have been isolated, serving as evidence for the regioselectivity. When utilizing α-tosyloxy-acetophenones, the reactions were more eco-friendly, the reaction time was significantly reduced and the synthetic procedure was more convenient and easier to manipulate. Surprisingly, using potassium carbonate to displace sodium carbonate in the synthesis of **4**, in the case of **1** (R= CN), two novel cyclocondensation products have been isolated and fully characterized, followed by the proposal of a plausible mechanism.

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Imidazo[1,2-*b*]pyrazole derivatives have rarely been reported; they, however, exhibit various bioactivities [1-7]. Inspired by these observations, we are interested in investigating the synthetic methods and bioactivities of these fused heterocyclic compounds.

There have been a variety of methods for the synthesis of imidazo[1,2-*b*]pyrazoles [1,5-13], among which, however, many involved tedious and time-consuming multistep procedures. Consequently, we would like to herein report a novel and facile two-step protocol for this heterocyclic nucleus.

The α-haloketones are useful and versatile reagents in organic synthesis, which are, nevertheless, difficult to obtain and highly lachrymatory, toxic, and not readily available. In this work they have been replaced by eco-friendly reagents such as α-tosyloxyketones (α-tosyloxyacetophenones in these cases). The α-tosyloxyacetophenones were prepared by the α-tosyloxylation of acetophenones with a extensively employed and versatile hypervalent iodine reagent, [hydroxy(tosyloxy)iodo]benzene (HTIB) in refluxing acetonitrile [14-17]. Encouraged by all these observations, we now would like to report an eco-friendly and easily manipulated protocol for the synthesis of a series of new and potentially bioactive derivatives of 1*H*-imidazo[1,2-*b*]pyrazole (**5**) by a two-step cyclocondensation reaction of 5-amino-4-cyano/ethoxycarbonyl-3-methylthio-1*H*-pyrazole (**1**) and α-bromoacetophenones (**3**) or α-tosyloxyacetophenones (**2**). The syntheses of all compounds involved **2**, some randomly selected compounds (**4a**, **4b** and **4c**) involved **3**, which was used in comparison with **2**, to ensure that the properties of leaving groups would not affect the regioselectivity between the nucleophilic substitution of **1** to **3**.

Results and Discussion.

Compounds **4**, **5**, **6** and **7** were synthesized through the procedure involving **2**. The randomly selected compounds **4a**, **4b** and **4c** have been through the procedure involving **3**. Both procedures gave identical compounds as proven through melting points, IR, and ^{1}H NMR. However, employing **2** rather than **3** showed such advantages as reduced reaction time, enhanced isolated yields and a more eco-friendly procedure.

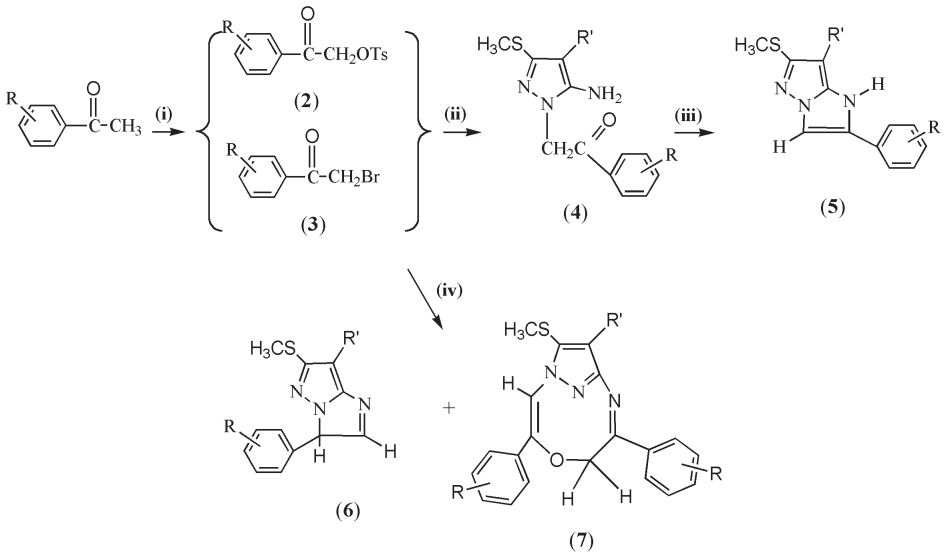
Theoretically, the reaction of **1** with **2** or **3** may not generate the compounds **5** under a single reaction condition. The reason is that the first step, a nucleophilic substitution (Scheme 1), usually requires alkaline conditions to remove the proton of **1** in order to improve the nucleophilicity of the endocyclic nitrogen, while the second step often requires an acidic one to improve the electrophilicity of the carbonyl group. The acidic conditions in the second step may be required because the electron-withdrawing effect of the pyrazole ring significantly reduces the nucleophilicity of the exocyclic amino group, and electron-withdrawing conjugate effect of benzene ring also reduces electrophilicity of the carbonyl group. We have substantiated the aforementioned acidic reaction conditions by providing an acidic atmosphere through the addition of several drops of concentrated hydrochloric acid in absolute ethanol. This improved the electrophilicity of the carbonyl group of **4**, allowing the cyclocondensation reaction of **4** to furnish **5** after several hours at reflux.

In theory, the reaction of **1** with **2** or **3** may produce **4** or its regioisomer **4-1** because of the possibility that both the endocyclic and exocyclic nitrogen atoms can attack the

carbon atom at the α-position of **2** or **3** under alkaline conditions. The cyclocondensation of **4** or **4-1** would produce **5** or its tautomer **5-1**, and **5-2** or its tautomer **5-3**, respectively. This is based on the principle that equilibrium usually exists between the imine and enamine structures (Scheme 2). The isolation of intermediates **4**, as pure compounds whose structures have been unambiguously characterized, provide strong evidence for the proposed mechanism that **1** with **2** or **3** react highly regioselectively. The reason for this observation is that the endocyclic nitrogen atom is more nucleophilic than that of the exocyclic nitrogen atom due to the electron-withdrawing effect of the pyrazole ring. Under acidic conditions the cyclocondensation reaction of intermediates **4** yields products **5**. The overall thermodynamic stability of **5** is greater than that of **5-1**, because structure **5** is fully conjugated while that of **5-1** is not. In structure **5-1** the CH_2 group disrupts the conjugation system compared with that of **5**, which cannot be compensated for by the more stable imine sub-structure.

An interesting phenomenon was observed when **1** (R'=CN) reacted with **2** or **3**. When **1** (R'=CN) reacted with **2** or **3** in the presence of sodium carbonate, the reaction generated **4** followed by the cyclocondensation under an acidic condition to give **5**, as described above. However, when the reaction was carried out in the presence of potassium carbonate, two novel compounds, **6** and **7**, were isolated and identified unexpectedly (Scheme 1). When **1** (R'=COOEt) was used, the above phenomenon was not observed. That is, the reaction of **1** (R'=COOEt) with **2** or **3** generated **4**, with neither **6** nor **7** being detectable.

Scheme 1

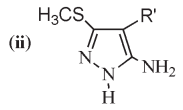


4a R'=COOEt, R=*p*-CH_3
4b R'=COOEt, R=*p*-Cl
4c R'=CN, R=*p*-F
4d R'=CN, R=*p*-CH_3

5a R'=COOEt, R=*p*-CH_3
5b R'=COOEt, R=*p*-Cl
5c R'=COOEt, R=2,5-dichloro
5d R'=COOEt, R=*p*-F
5e R'=COOEt, R=H
5f R'=CN, R=*p*-F
5g R'=CN, R=*p*-CH_3

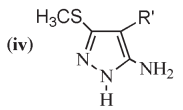
6 R'=CN, R=*p*-F
7 R'=CN, R=*p*-F

(i) HTIB, MeCN, reflux for **2** and Br_2, Et_2O for **3**

(ii)  , Na_2CO_3, MeCN, reflux

(**1**)

(iii) HCl, EtOH, reflux

(iv)  , K_2CO_3, MeCN, reflux

(**1**)

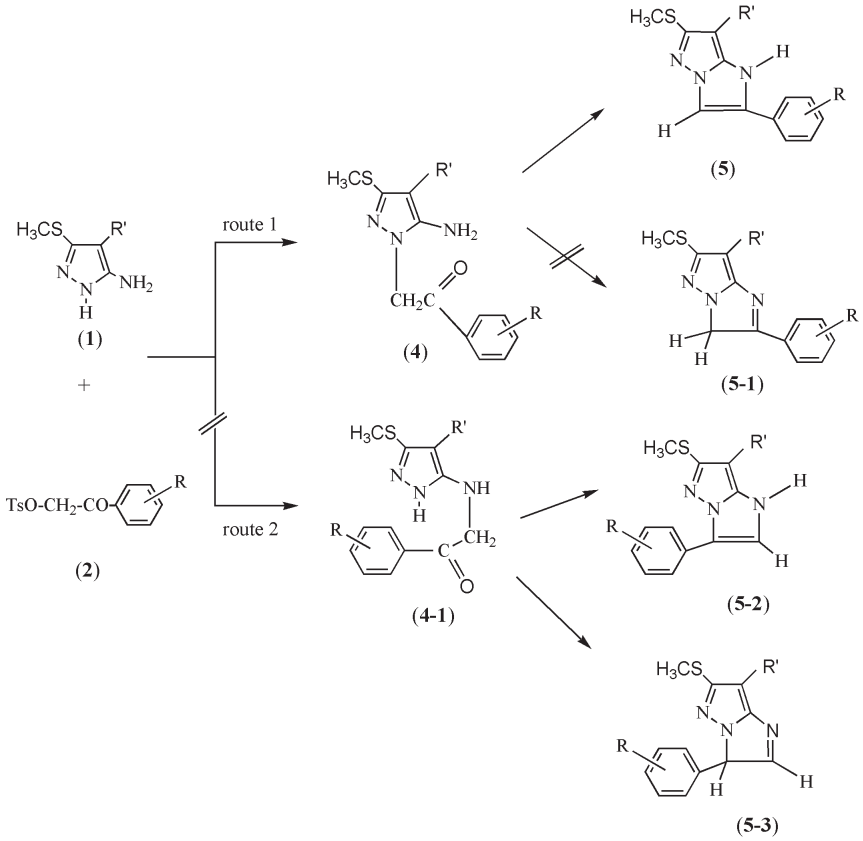
Synthetic route for the synthesis of compounds **4**, **5**, **6** and **7**.

A plausible mechanism for the formations of **6** and **7** is proposed in Scheme 3. X. L. Ren *et al* [18] recently reported a regioselective reaction occurring in the case of methylation of **1** (R'= COOEt or CN) in presence of potassium carbonate in acetone (Scheme 3 section one), where the regioselectivity methylated products are formed through anion intermediates. When R'=COOEt, the methylation occurred almost exclusively at the N-position near the amino group to afford the product **B**III, which agrees with our result (the highly regioselective formation of **4a-b**). However when R'=CN, the reported methylated ratio of **A**II to **A**III is 83:100. This also also agrees well with our results, where the amounts of **6** and **7** were comparable (Scheme 3, section two). A detailed mechanism is shown for the formation of **6** and **7** is shown in Scheme 4. The formation of **6** seems to be inconsistent with formation of **5** rather than its tautomer **5-1**. Perhaps, the role played by potassium ion can be reasonably stated as follows: the potassium ion stabilizes the generated anion thus diminishing the nucleophilic character of the endocyclic nitrogen atom. On the other hand, concerning the function of R', we believe that an intramolecular hydrogen bond can be formed between COOEt and the amino group at C-4 position in the case of R'= COOEt, but it can not in the case of R'= CN. However, further investigation into the reason is under way in our laboratory.

The novel structures of **6** and **7**, as well as the reaction procedure have great potential for applications in the synthesis of bioactive analogues. Great care has been taken in the determination of the novel structure of compound **7**, which was based on IR, ^{1}H NMR, MS, and elemental analysis. As summarized in the experimental section, the IR, ^{1}H NMR, and elemental analysis are all in good accordance with the proposed structure; nevertheless, the MS spectrum showed no molecular ion peak even employing electrospray ionization technique (ESI), but only several reasonable fragment ion peaks which were in good agreement with the above structure (Scheme 5).

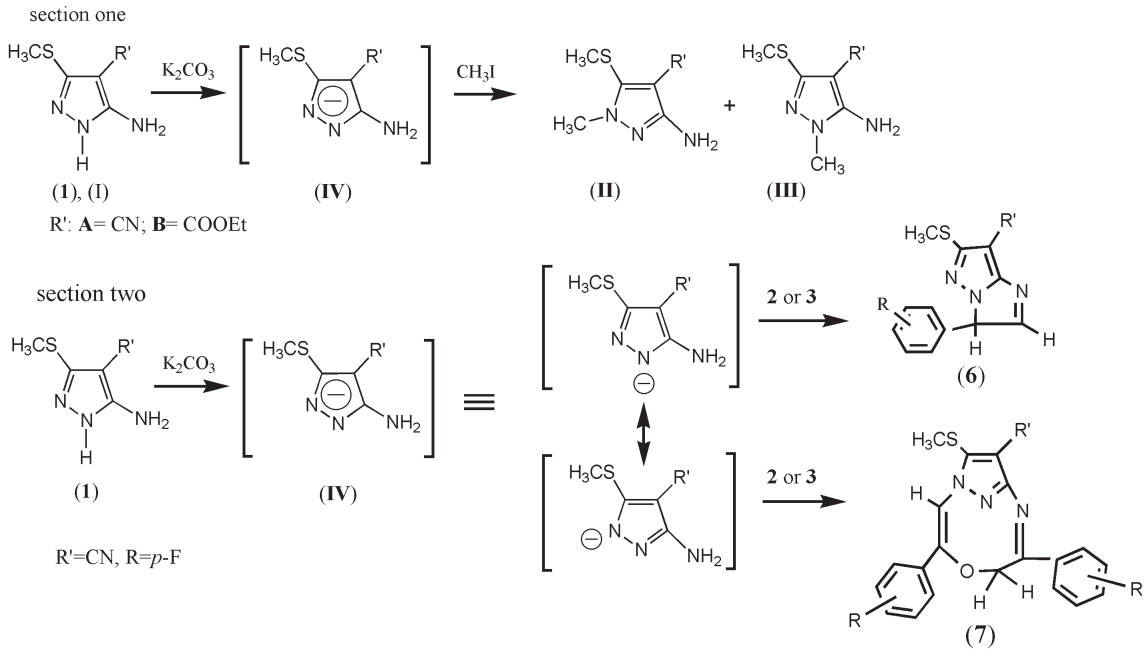
The imidazo[1,2-*b*]pyrazole derivatives, have been mainly reported to be anti-cancer reagents[3-6]. We herein would like to report their fungicidal activity, with the result that both the intermediates and the title compounds exhibited certain inhibitory activities (at 50 ppm) against *Gibberella zeae* (**4a**), *Alternaria solani* (**4d** and **5e**) and *Phoma asparagi* (**5e**) [19]. Further studies on other bioactivities are also under investigation.

Scheme 2



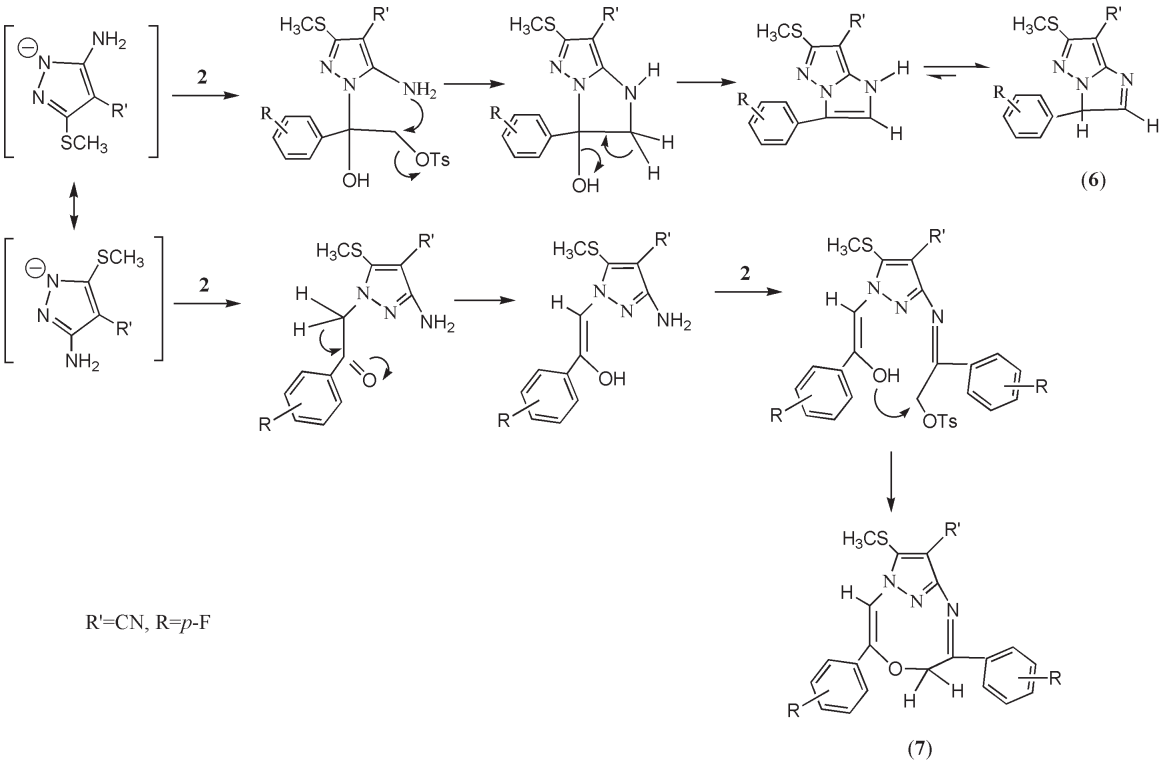
The proposed reaction pathway for cyclocondensation.

Scheme 3



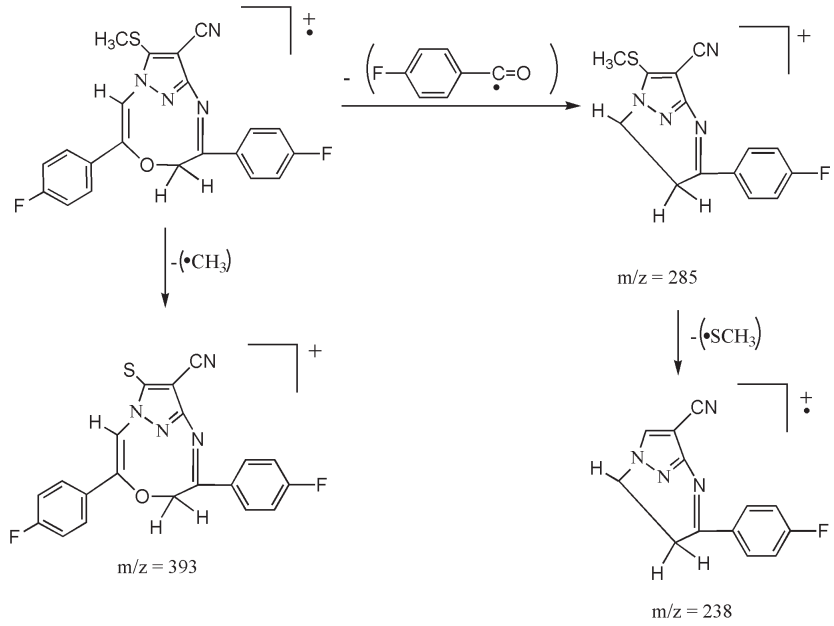
The proposed reaction mechanism for the formation of **6** and **7**.

Scheme 4



Detailed mechanism for the formation of **6** and **7**.

Scheme 5



Proposed structures for fragment ions observed in the ESI-MS spectrum of compound **7**.

EXPERIMENTAL

Melting points were determined with RY-1 apparatus in capillaries and are uncorrected. IR spectra were obtained on a Nicolet 501P FT-IR spectrophotometer as KBr plates. ^{1}H NMR spectra were recorded on a Jeol JNM-ECP 600M or on a Bruker AC-300 spectrometer in DMSO-d_6, and the chemical shifts were expressed in ppm with reference to TMS as internal standard. The elemental analyses were performed with a Yanaco MT-3 CHN analyzer or Vario EL III analyzer. Mass specta was obtained on a Thermo Finnigan LCQ Advantage instrument employing the technique of electrospray ionization (ESI). Column chromatography was carried out using Silica Gel H-60 (Qingdao Haiyang Co. Ltd., 60-100 mesh). Thin layer chromatography (Whatman K6F) was used to control the course of reactions and ascertain the purity of the reported compounds, and detection of the components was made by exposure to ultraviolet light. Compound **1** was prepared according to the literature procedure [20].

General Procedure for the Synthesis of **4** *via* α-Bromoacetophenones (**3**).

In a typical procedure, a suspended solution of 5 mmol of **1**, 5 mmol of *p*-methyl-α-bromoacetophenone (**3a**), which was prepared from *p*-methylacetophenone and bromine according to the literature [21], and 0.5 g of sodium carbonate in 30 mL of acetonitrile was refluxed for around 10 hours until the starting material was consumed completely, as indicated by tlc. On cooling, the solid was removed through filtration, and the filtrate was evaporated to give crude **4a**, which was purified by column chromatography using ethyl acetate/petroleum ether (1:4) as eluent.

General Procedure for the Intermediate (**4**) *via* α-Tosyloxyacetophenones (**2**).

In a typical procedure, 1.961 g (5 mmol) of [hydroxy(tosyloxy)iodo]benzene (HTIB) and 5 mmol of *p*-methylacetophenone were dissolved in 30 mL of acetonitrile, and the solution was refluxed for about 45 minutes until the starting materials disappeared, as indicated by tlc, to obtain a solution of **2a** in acetonotrile [14-17]. After cooling, 5 mmol of **1** and 0.5 g of sodium carbonate were added to the above solution, and the suspended solution was then refluxed for another 3 hours until completion of the reaction, as indicated by tlc. A similar workup to the procedure through α-bromoacetophenones **3a** gave the pure intermediate **4a**.

5-Amino-1-(*p*-methylbenzoylmethyl)-4-ethoxycarbonyl-3-methylthio-1*H*-pyrazole (**4a**).

This compound was obtained as white needle, yield 77%; mp 162.5-163.5°; ir: 1695 (C=O, of ester), 1687 (C=O, of ketone), 3242, 3324(N-H) cm^{-1}. ^{1}H nmr: δ 1.26 (t, 3H, J = 7Hz, CH_2CH_3), 4.18 (q, 2H, J = 7Hz; CH_2CH_3), 2.30 (s, 3H, SCH_3), 5.55 (s, 2H, NCH_2), 6.35 (s, 2H, NH_2), 7.39, 7.93 (dd, 4H, J= 8.7 Hz Ph-H), 2.41 (s, 3H, Ph-CH_3).

Anal. Calcd. for $C_{16}H_{19}N_3O_3S$: C, 57.64; H, 5.75; N, 12.61. Found: C, 57.66; H, 5.74; N, 12.63.

5-Amino-1-(*p*-chlorobenzoylmethyl)-4-ethoxycarbonyl-3-methylthio-1*H*-pyrazole (**4b**).

This compound was obtained as white needle, yield 69%; mp 174-175°; ir: 1698 (C=O, of ester), 1670 (C=O, of ketone), 3240, 3325(N-H) cm^{-1}. ^{1}H nmr: δ 1.27 (t, 3H, J = 7Hz, CH_2CH_3), 4.17 (q, 2H, J = 7Hz, CH_2CH_3), 2.30 (s, 3H, SCH_3), 5.58 (s, 2H, NCH_2), 6.37 (s, 2H, NH_2), 7.67, 8.04 (dd, 4H, J= 8.7 Hz, Ph-H).

Anal. Calcd. for $C_{15}H_{16}ClN_3O_3S$: C, 50.98; H, 4.57; N, 11.90. Found: C, 50.96; H, 4.56; N, 11.88.

5-Amino-1-(*p*-fluorobenzoylmethyl)-4-cyano-3-methylthio-1*H*-pyrazole (**4c**).

This compound was obtained as white prism, yield 79%; mp 148-149°; ir: 2207 (CN), 1701 (C=O, of ketone), 3251, 3363 (N-H) cm^{-1}. ^1H nmr: δ 2.42 (s, 3H, SCH_3), 5.58 (s, 2H, CH_2), 6.77 (s, 2H, NH_2), 7.40~7.46, 8.08~8.13 (t+q, 2H+2H, $^3J_{H-H} = {}^3J_{H-F}$ = 8.7 Hz, $^4J_{H-F}$ = 5.7Hz, Ph-H).

Anal. Calcd. for $C_{13}H_{11}FN_4OS$: C, 53.78; H, 3.82; N, 19.31. Found: C, 53.79; H, 3.81; N, 19.33.

5-Amino-1-(*p*-methylbenzoylmethyl)-4-cyano-3-methylthio-1*H*-pyrazole (**4d**).

This compound was obtained as white prism, yield 72%; mp 148-149°; ir: 2215 (CN), 1694 (C=O, of ketone), 3220, 3327 (N-H) cm^{-1}. ^1H nmr: δ 2.41 (s, 3H, SCH_3), 2.43 (s, 3H, Ph-CH_3), 5.68 (s, 2H, CH_2), 6.71 (s, 2H, NH_2), 7.39~7.41, 7.93~7.96 (dd, 2H+2H, J 8.2 Hz, Ph-H).

Anal. Calcd. for $C_{14}H_{14}N_4OS$: C, 58.72; H, 4.93; N, 19.58. Found: C, 58.74; H, 4.94; N, 19.56.

General Procedure for the Cyclocondensation of **4**.

In a typical procedure, crude **4a**, which was obtained from either α-bromoacetophenone **3a** or α-tosyloxyacetophenone **2a**, was dissolved in 30 mL of absolute ethanol, followed by the addition of several drops of concentrated hydrochloric acid. The resulting solution was then refluxed for around 3 hours, and cooled to room temperature. The solution was then evaporated *in vacuo* to afford crude **5a**, which was crystallized from absolute ethanol to afford pure final product **5a**.

2-(*p*-Methylphenyl)-7-ethoxycarbonyl-6-methylthio-1*H*-imidazo[1,2-*b*]pyrazole (**5a**).

This compound was obtained as white needle, yield 65%; mp 175-176°; ir: 1670 (C=O, of ester), 3133 (=C-H), 3236, 3338 (N-H) cm^{-1}. ^1H nmr: δ 1.31 (t, 3H, J = 7 Hz, CH_2CH_3), 4.24 (q, 2H, J = 7 Hz, CH_2CH_3), 2.47 (s, 3H, SCH_3), 8.30 (s, 1H, =CH), 12.26, (s, 1H, NH), 7.50, 7.85 (dd, 4H, J = 8.8 Hz, Ph-H), 2.21 (s, 3H, Ph-CH_3).

Anal. Calcd. for $C_{16}H_{17}N_3O_2S$: C, 60.93; H, 5.44; N, 13.33. Found: C, 60.95; H, 5.44; N, 13.35.

2-(*p*-Chlorophenyl)-7-ethoxycarbonyl-6-methylthio-1*H*-imidazo[1,2-*b*]pyrazole (**5b**).

This compound was obtained as white needle, yield 40%; mp 214-215°; ir: 1674 (C=O, of ester), 3116 (=C-H), 3221(N-H) cm^{-1}. ^1H nmr: δ 1.31 (t, 3H, J = 7 Hz, CH_2CH_3), 4.25 (q, 2H, J = 7 Hz, CH_2CH_3), 2.48 (s, 3H, SCH_3), 8.30 (s, 1H, =CH), 12.29, (s, 1H, NH), 7.54, 7.88 (dd, 4H, J = 8.8 Hz, Ph-H).

Anal. Calcd. for $C_{15}H_{14}ClN_3O_2S$: C, 53.72; H, 4.21; N, 12.54. Found: C, 53.74; H, 4.22; N, 12.56.

2-(2,5-Dichlorophenyl)-7-ethoxycarbonyl-6-methylthio-1*H*-imidazo[1,2-*b*]pyrazole (**5c**).

This compound was obtained as white prism, yield 65%; mp 189-190.5°; ir: 1674 (C=O, of ester), 3125 (=C-H), 3237, 3345 (N-H) cm^{-1}. ^1H nmr: δ 1.31 (t, 3H, J = 7 Hz, CH_2CH_3), 4.25 (q, 2H, J = 7 Hz, CH_2CH_3), 2.48 (s, 3H, SCH_3), 8.32 (s, 1H, =CH), 12.80, (s, 1H, NH), 7.74-7.98 (m, 3H, Ph-H).

Anal. Calcd. for $C_{15}H_{13}Cl_2N_3O_2S$: C, 48.78; H, 3.55; N, 11.38. Found: C, 48.76; H, 3.56; N, 11.36.

2-(*p*-Fluorophenyl)-7-ethoxycarbonyl-6-methylthio-1*H*-imidazo[1,2-*b*]pyrazole (**5d**).

This compound was obtained as white needle, yield 58%; mp 168-169°; ir: 1658 (C=O, of ester), 3159 (=C-H), 3269 (N-H) cm^{-1}. ^1H nmr: δ 1.31 (t, 3H, J = 7 Hz; CH_2CH_3), 4.24 (q, 2H, J = 7 Hz; CH_2CH_3), 2.48 (s, 3H, SCH_3), 8.22 (s, 1H, =CH), 12.24 (s, 1H, NH), 7.33, 7.89 (mm, 4H, J= 8.8 Hz, Ph-H) [22].

Anal. Calcd. for $C_{15}H_{14}FN_3O_2S$: C, 56.41; H, 4.42; N, 13.17. Found: C, 56.43; H, 4.41; N, 13.15.

2-Phenyl-7-ethoxycarbonyl-6-methylthio-1*H*-imidazo[1,2-*b*]-pyrazole (**5e**).

This compound was obtained as white needle, yield 60%; mp 166-167°; ir: 3346, 3251, (N-H), 3127 (=C-H), 1680 (C=O, of ester) cm^{-1}. ^1H nmr: δ 1.33 (t, 3H, J = 7Hz, CH_2CH_3), 4.26 (q, 2H, J = 7Hz, CH_2CH_3), 2.48 (s, 3H, SCH_3), 8.25 (s, 1H, =CH), 12.24 (s, 1H, NH) 7.47-7.85 (m, 5H, Ph-H).

Anal. Calcd. for $C_{15}H_{15}N_3O_2S$: C, 59.78; H, 5.02; N, 13.95. Found: C, 59.76; H, 5.02; N, 13.97.

2-(*p*-Fluorophenyl)-7-cyano-6-methylthio-1*H*-imidazo[1,2-*b*]-pyrazole (**5f**).

This compound was obtained as white needle, yield 88%; mp 278° (dec); ir: 2218 (CN), 3012 (=C-H), 3183 (N-H) cm^{-1}. ^1H nmr: δ 2.59 (s, 3H, SCH_3), 8.35 (s, 1H, =CH), 7.33~7.39, 7.77~7.82 (t+q, 2H+2H, $^3J_{H-H} = {}^3J_{H-F}$ = 8.7 Hz, $^4J_{H-F}$ = 5.7 Hz, Ph-H), 12.93 (s, 1H, NH).

Anal. Calcd. for $C_{13}H_9FN_4S$: C, 57.34; H, 3.33; N, 20.59. Found: C, 57.36; H, 3.34; N, 20.57.

2-(*p*-Methylphenyl)-7-cyano-6-methylthio-1*H*-imidazo[1,2-*b*]-pyrazole (**5g**).

This compound was obtained as white needle, yield 83%; mp 260° (dec); ir: 2222 (CN), 3096 (=C-H), 3236 (N-H) cm^{-1}. ^1H nmr: δ 2.58 (s, 3H, SCH_3), 2.34 (s, 3H, Ph-CH_3), 8.30 (s, 1H, =CH), 7.28~7.31, 7.63~7.65 (dd, 2H+2H, J =8.2 Hz, Ph-H), 12.94 (s, 1H, NH).

Anal. Calcd. for $C_{14}H_{12}N_4S$: C, 62.67; H, 4.51; N, 20.89. Found: C, 62.69; H, 4.52; N, 20.87.

The Synthesis of Compounds **6** and **7**.

In the synthetic procedure of compound **4c** as described above, the sodium carbonate was replace by potassium carbonate. A similar workup gave **6** and **7** from one pot.

7-Cyano-3-(*p*-fluorophenyl)-6-methylthioimidazo[1,2-*b*]-3*H*-pyrazole (**6**).

This compound was obtained as white needle, yield 39%; mp 206-207°; ir: 2229 (CN), 1619 (C=N), 3111(=C-H) cm^{-1}. ^1H nmr: δ 2.71 (s, 3H, SCH_3), 9.34 (d, 1H, J = 7 Hz, N=CH), 7.91 (d, 1H, J = 7Hz, N-CH), 7.43, 8.36 (mm, 2H+2H, Ph-H) [22].

Anal. Calcd. for $C_{13}H_9FN_4S$: C, 57.34; H, 3.33; N, 20.59. Found: C, 57.34; H, 3.35; N, 20.62.

6-Cyano-2,9-di(*p*-fluorophenyl)-5-methylthio-(4,5,7-triazo-1-oxa-2,5,7-cyclononatrieno)[4,5,6-*a*,*b*]pyrazole (**7**).

This compound was obtained as white prism, yield 50%; mp 252-253°; ir: 2221 (CN), 1234 (C-O),1622 (C=N), 3084 (=C-H) cm^{-1}. ^1H nmr: 2.72 (s, 3H, SCH_3), 7.91 (s, 1H, =CH), 4.52 (s, 2H, CH_2), 7.18, 7.44 (mm,2H+2H, Ph-H), 7.55, 8.29 (mm,2H+2H,Ph-H)[22]; ESI-ms: m/z 393 ($[M-CH_3]^+$), 285 ($[M-A]^+$, A = *p*- fluorobenzoyl free radical), 238 ($[M-A-SCH_3]^{\cdot+}$).

Anal. Calcd. for $C_{21}H_{14}F_2N_4OS$: C, 61.75; H, 3.46; N, 13.73; S, 7.83. Found: C, 61.79; H, 3.48; N, 13.76; S, 7.84.

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REFERENCES AND NOTES

* Correspondence: Li Ming, College of Chemistry and Molecular Engineering, Qingdao University of Science and Technology, Qingdao, 266042, P. R. China; Fax: +86-532-4023927; E-mail: liming928@263.net.

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[22] *p*-Fluorophenyl group exists in compounds **6** and **7**, resulting in complication of the spectra due to the coupling between the fluorine and hydrogen atoms in the proton nuclear magnetic resonance spectra (300 MHz). As a result, the signals corresponding to the protons of benzene ring are not observed as dd-shaped peaks, but rather as mm-shaped peaks. When the spectra were obtained on a Jeol JNM-ECP 600M instrument (600 MHz), the aforementioned couplings were observed clearly and the coupling constants (**4c** and **5f**) were also reported.