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REGIOSELECTIVITY IN 1,3-DIPOLAR CYCLOADDITION OF 3-(4-ETHOXYPHENYL)-4-CYANOSYDNONE WITH PROPARGYLIC ESTERS

En-Ming Chang,[b] Fung Fuh Wong,[*,a] Tse-Hsin Chen,[b] Kuo-Chen Chiang,[a] and Mou-Yung Yeh[*,b,c]

[a]Sustainable Environment Research Center, National Cheng Kung University, No. 500, Sec. 3, An-ming Rd., Tainan City, Taiwan 709, R.O.C.

[b]Department of Chemistry, National Cheng Kung University, No. 1, Ta Hsueh Rd., Tainan, Taiwan 70101, R.O.C.

[c]Nan Jeon Institute of Technology, No.178, Chaocin Rd., Yanshuei Township, Tainan County 737, Taiwan R. O. C.

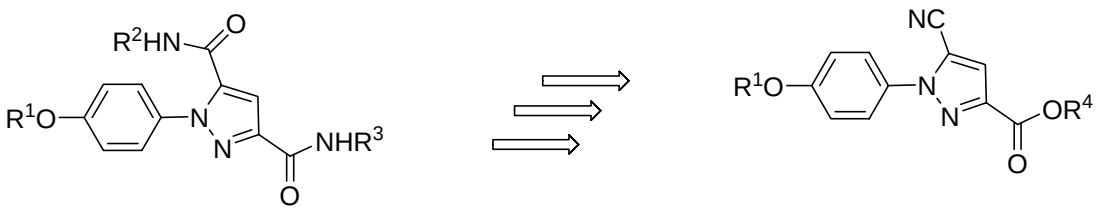
*Corresponding Author. Tel.: +886 6 384 0136 ext. 212; Fax.: +886 6 384 0960.

E-mail address: wongungfuh@yahoo.com.tw (F. F. Wong).

Abstract – A regioselective 1,3-dipolar cycloaddition of 3-(4-ethoxyphenyl)-4-cyanosydnone with propargylic esters having a bulky alkyl group was developed. This new reaction provided alkyl 5-cyano-1-aryl-1*H*-pyrazole-3-carboxylate as a major product.

INTRODUCTION

Pyrazole compounds (**1**) were demonstrated as potent inhibitors of H. pylori dihydroorotate dehydrogenase (DHODase).[1,2] They can be conveniently synthesized from alkoxy 5-cyano-1-aryl-1*H*-pyrazole-3-carboxylate (**2**) by use of amination and Ritter reaction.[3]

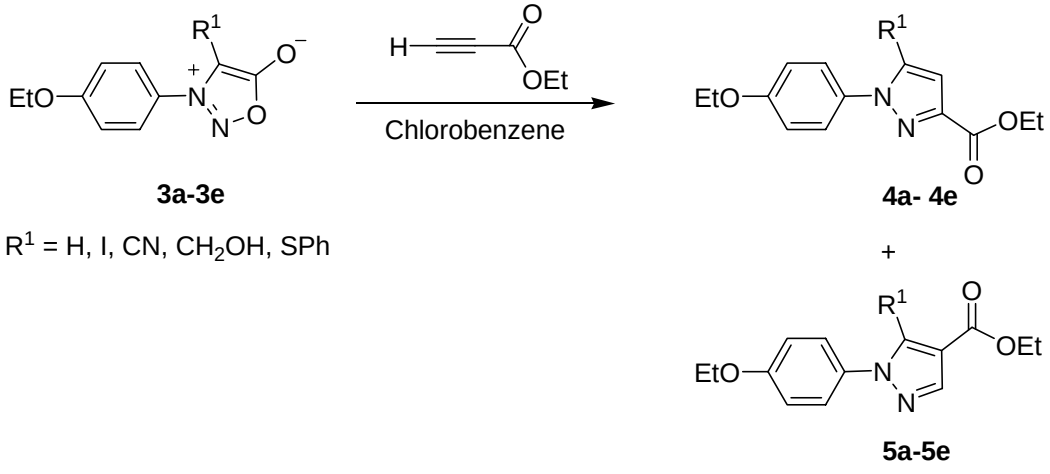


1 **2**

Sydnones attract attention dues to their wildly useful properties, including biological and pharmaceutical usage,[4] synthetic appilcation,[5] photochromic properties,[6] and preparation of electroluminescent materials.[7] Sydnones undergo smooth cycloaddition with acetylene to give pyrazoles.[8–12] The reaction involves a 1,3-dipolar cycloaddition of the sydnones in its cyclic azomethine imine form. The initially formed cycloadducts readily extrude carbon dioxide to produce a mixture of regioisomeric pyrazoles. In this paper, we developed a regioselective cycloaddition of 3-(4-ethoxyphenyl)-4-cyanosydnone with bulky substituted propargylic ester to give pyrazoles as a single isomeric product.

RESULTS AND DISCUSSION

3-(4-Ethoxyphenyl)-4-substitited sydnones (**3a**–**3e**) were treated with ethyl propiolate in chlorobenzene at ~130 °C and the progress of the reaction was monitored by carbon dioxide evolution without isolating the intermediate cycloadducts. The synthetic pathway was shown in Scheme 1 and the ratios of regioisomers were tabulated in Table 1. Identification of each was made on the basis of its characteristic ^{1}H NMR spectrum. Particular attention was given to the chemical shift of pyrazole proton. The ring proton (4-H) in the 3-carboethoxy-substituted isomer (**4a**–**4e**) appeared 1.2–1.3 ppm upfield relative to the 3-H in the 4-carboethoxy-substituted isomer (**5a**–**5e**). In all cases, a mixture of regioisomers (**4** and **5**) were obtained in 51%–90% yields and the ratio of **4**/**5** were provided from 76/24 to 52/48 (see Table 1). According to the frontier molecular orbital theory, sydnones are used as 1,3-dipoles, The interation of dipoles LUMO of 3-(4-ethoxyphenyl)-4-substitited sydnones (**3a**–**3e**) with acetylene dipolarophile HOMO was suggested to be the controlling term.[12]



3a-3e

R^1 = H, I, CN, CH_2OH, SPh

Scheme 1

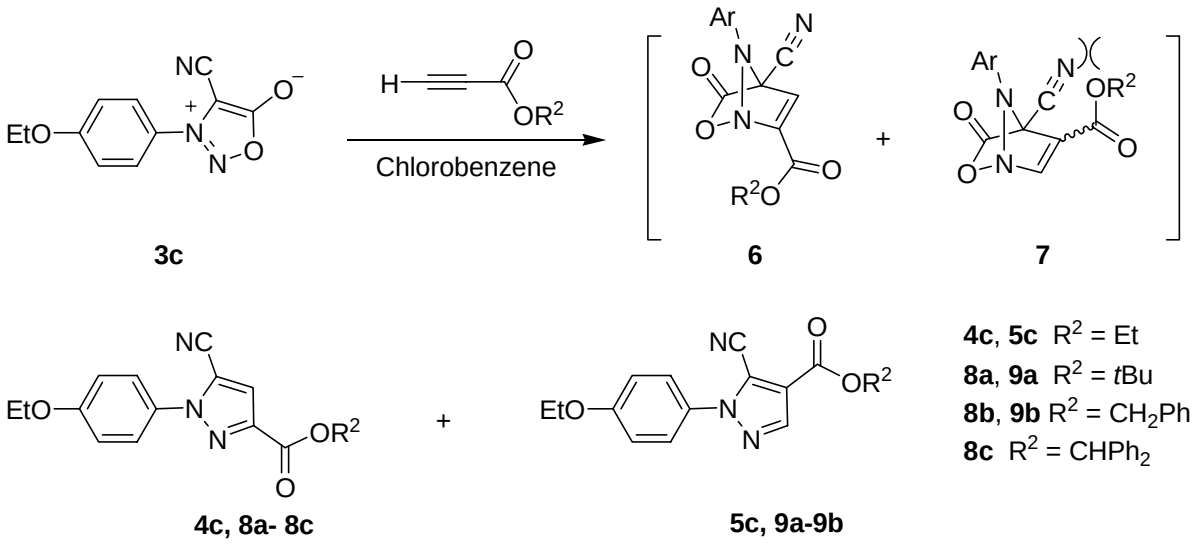
Table 1. The 1,3-dipolar addition between 3-(4-ethoxyphenyl)-4-substitited sydnones (**3a**–**3e**) and ethyl propiolate.

Sydnone	R^1	The ratios of regioisomers[a]		Total isolated yield of **4** and **5**
		4a–**4e**	**5a**–**5e**	
3a	H	76 (**4a**)	24 (**5a**)	90
3b	I	56 (**4b**)	44 (**5b**)	81
3c	CN	58 (**4c**)	42 (**5c**)	80
3d	CH_2OH	63 (**4d**)	37 (**5d**)	71
3e	SPh	52 (**4e**)	48 (**5e**)	71

[a]The ratios of **4**/**5** (3-carboethoxy-substituted isomer/4-carboethoxy-substituted isomer) were determined by ^{1}H NMR.

In control experiments, the 1,3-dipolar cycloaddition of the 3-(4-ethoxyphenyl)-4-cyanosydnone (**3c**) with ethyl propiolate was investigated in 1,2-dichlorobezene (bp 180 °C), 1,2-dichloroethene (bp 85 °C), isobutyl alcohol (bp 180 °C), toluene (bp 110 °C), and *p*-xylene (bp 138 °C) under refluxing conditions for 48 h. The ratios of regioisomers were not changed significantly (**4c**/**5c** = 55/45). When the 1,3-dipolar cycloaddition was performed in DMF at reflux, the ratio of regioisomers (**4c**/**5c**) was inverted from 55/45 to 40/60.

For the optimization of ratio of the regioisomers (**4c**/**5c**), 3-(*p*-ethoxyphenyl)-4-cyanosydnone[14] (**3c**) was treated with the unsymmetrically substituted acetylenes in chlorobenzene at reflux (see Scheme 2). The reaction gave two *N*-bridged **6** and **7** as the intermediates. The regiochemistry of cycloaddition was controlled by the steric effect of bulk substitutent R^2 of acetylene with 4-cyano group of sydnone (**3c**). As the bulky group substitutent R^2 in acetylene was increased (Et, *t*-Bu,[15] and CH_2Ph[16]), the ratio of regioisomers (**8**/**9**) was improved from 57/43 to 75/25 (see Table 2). When 3-(4-ethoxyphenyl)-4-cyanosydnone (**3c**) was reacted with bulky propargylic ester ($R^2 = CHPh_2$), this reaction gave diphenylmethy 5-cyano-1-(*p*-ethoxyphenyl)-1*H*-pyrazole-3-carboxylate (**8c)** as single isomeric product in 85% yield. The reaction was consistent with the cycloaddition reaction of munchnones with unsymmetrically substituted acetylene, which also gave single isomeric cycloadduct.[17,18]



Scheme 2

Table 2. The 1,3-dipolar addition between 3-(4-ethoxyphenyl)-4-cyanosydnone (**3c**) and the unsymmetrically substituted propiolate.

Entry	R^2	The ratios of regioisomers[a]		Total isolated yields of isomers (**4c**, **5c**, **8**, and **9**)
		4c, and **8a**–**8c**	**5c, 9a**–**9b**	
1	Et	58 (**4c**)	42 (**5c**)	80
2	*t*-Bu	78 (**8a**)	22 (**9a**)	79
3	CH_2Ph	57 (**8b**)	43 (**9b**)	76
4	$CHPh_2$	~ 100 (**8c**)	-[b]	85[c]

[a]The ratios of **4c**/**5c** and **8**/**9** were determined by ^{1}H NMR. [b]No detectable. [c]Only **8c** was isolated.

In summery, we developed a efficient method to control the regioselectivity of 1,3-dipolar cycloaddition for propargylic ester having a bulky alkyl group ($R^2 = CHPh_2$) with 3-(*p*-ethoxyphenyl)-4-cyanosydnone This reaction gave **8c** as a single isomer. 5-Cyano-1-aryl-1*H*-pyrazole-3-carboxylate (**8c**) could be applied in the synthesis of pyrazole DHOHase inhibitors.

EXPERIMENTAL

General Procedure: Sydnones were synthesized according to literature procedures.[5] All chemicals were reagent grade and used as purchased. All reactions were carried out under nitrogen atmosphere and

monitored by TLC analysis. Analytical thin-layer chromatography (TLC) was performed on precoated plates (silica gel 60 F-254), purchased from Merck Inc. Purification by gravity column chromatography was carried out by use of Merck Reagents silica gel 60 (particle size 0.063–0.200 mm, 70–230 mesh ASTM). Infrared (IR) spectra were measured on a Bomem Michelson Series FT-IR spectrophotometer. The wavenumbers reported are referenced to the polystyrene 1601 cm^{-1} absortion. Absorption intensities are recorded by the following abbreviations: s, strong; m, medium; w, weak. ^1H NMR spectra were obtained on a Bruker (300 MHz) spectrometer by use of $CDCl_3$ and DMSO- *d6* as solvent. ^{13}C NMR spectra were obtained on a Bruker (75 MHz) spectrometer by used of $CDCl_3$ as solvent. Carbon-13 chemical shifts are referenced to the center of the $CDCl_3$ triplet (δ 77.0 ppm). Multiplicities are recorded by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; *J*, coupling constant (hertz). Elemental analyses were carried out on a Heraeus CHN–O RAPID element analyzer.

General Procedure for the 1,3-Dipolar Cycloaddition: A solution of 3-(*p*-ethoxyphenyl)-4-cyanosydnone (**3c**, 0.23 g, 1.0 equiv) in 10 mL of THF solution was added diphenylmethoxy propiolate (0.25 g, 2.0 equiv) and heated to reflux for 48 h under N_2. After the reaction was completed, the reaction mixture was concentrated under reduced pressure to remove chlorobenzene. The residue was dissolved in 2.0 mL of CH_2Cl_2 and purified by silica gel open column chromatography to provide the corresponding products (**4a**–**4e**, **5a**–**5e**, **8a**–**8c** and **9a**–**9b**).

Ethyl 1-(4-ethoxyphenyl)-1*H*-pyrazole-3-carboxylate (4a): mp 92–93 °C (MeOH); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.31–1.37 (m, 6 H, 2 × CH_3), 3.98 (q, *J* = 10.4 Hz, 2H, CH_2), 4.35 (q, *J* = 10.6 Hz, 2H, CH_2), 6.87 (d, *J* = 7.2 Hz, 2H, ArH), 6.89 (d, J = 2.6 Hz, 1H, pyrazole-H), 7.54 (d, *J* = 7.2 Hz, 2H, ArH), 7.74 (d, *J* = 2.6 Hz, 1H, pyrazole-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.80, 15.16, 61.47, 64.24, 110.51, 115.42, 122.15, 128.84, 133.59, 145.14, 158.84, 162.81; IR (KBr) 2980 (s), 2933 (s), 1718 (m, C=O), 1261 (w) cm^{-1}; FABMS *m/z* (relative intensity) 262 (M+2 , 19), 261 (M+1, 100), 260 (M, 81); Anal. Calcd for $C_{14}H_{16}N_2O_3$;C: 64.60 ,H: 6.20, N: 10.76. Found: C: 64.45, H: 6.32, N: 10.63.

Ethyl 1-(4-ethoxyphenyl)-1*H*-pyrazole-4-carboxylate (5a): mp 103–105 °C (MeOH); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.28–1.39 (m, 6 H, 2 × CH_3), 4.00 (q, *J* = 10.4 Hz, 2H, CH_2), 4.26 (q, *J* = 10.6 Hz, 2H, CH_2), 6.90 (d, *J* = 8.8 Hz, 2H, ArH), 7.52 (d, *J* = 8.8 Hz, 2H, ArH), 7.99 (s, 1H, pyrazole-H), 8.23 (s, 1H, pyrazole-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.34, 14.69, 60.30, 63.81, 115.11, 116.45, 121.18, 129.89, 132.87, 141.78, 158.32, 162.90; IR (KBr) 2969 (s), 2930 (s), 1706 (m, C=O), 1268 (w) cm^{-1}; FABMS *m/z* (relative intensity) 262 (M+2 , 8), 261 (M+1, 46), 260 (M, 28); Anal. Calcd for $C_{14}H_{16}N_2O_3$; C: 64.60, H: 6.20, N: 10.76. Found: C: 64.72, H: 6.28, N: 10.59.

Ethyl 1-(4-ethoxyphenyl)-5-iodo-1*H*-pyrazole-3-carboxylate (4b): mp 70–71 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.29–1.39 (m, 6 H, 2 × CH_3), 4.00 (q, *J* = 10.4 Hz, 2H, CH_2), 4.33 (q, *J* = 10.6 Hz, 2H, CH_2), 6.88 (d, *J* = 8.9 Hz, 2H, ArH), 7.04 (s, 1H, pyrazole-H), 7.31 (d, *J* = 8.9 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.30, 14.67, 61.20, 63.78, 83.43, 114.40, 119.12, 127.93, 132.53, 146.20, 159.53, 161.43; IR (KBr) 2979 (s), 2931 (s), 1721 (m, C=O), 576 (w) cm^{-1}; FABMS *m/z* (relative intensity) 388 (M+2 , 2), 387 (M+1, 11), 386 (M, 4); Anal. Calcd for $C_{14}H_{15}N_2O_3$; C: 43.54, H: 3.91, N: 7.25. Found: C: 43.41, H: 4.02, N: 7.09.

Ethyl 1-(4-ethoxyphenyl)-5-iodo-1*H*-pyrazole-4-carboxylate (5b): mp 109–110 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.28–1.40 (m, 6 H, 2 × CH_3), 4.01 (q, *J* = 10.4 Hz, 2H, CH_2), 4.29 (q, *J* = 10.6 Hz, 2H, CH_2), 6.91 (d, *J* = 9.0 Hz, 2H, ArH), 7.28 (d, *J* = 9.0 Hz, 2H, ArH), 8.06 (s, 1H, pyrazole-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.28, 14.69, 60.45, 63.81, 89.35, 114.52, 119.15, 128.13, 132.71, 143.45, 159.55, 162.02; IR (KBr) 2980 (s), 2931 (s), 1710 (m, C=O), 578 (w) cm^{-1}; FABMS *m/z* (relative intensity) 388 (M+2 , 2), 387 (M+1, 10), 386 (M, 3); Anal. Calcd for $C_{14}H_{15}N_2O_3$; C: 43.54, H: 3.91, N: 7.25. Found: C: 43.62, H: 3.98, N: 7.11.

Ethyl 5-cyano-1-(4-ethoxyphenyl)-1*H*-pyrazole-3-carboxylate (4c): mp 72–73 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31–1.39 (m, 6 H, 2 × CH_3), 4.01 (q, *J* = 10.4 Hz, 2 H, CH_2), 4.37 (q, *J* = 10.6 Hz, 2 H, CH_2), 6.93 (d, *J* = 8.8 Hz, 2 H, ArH), 7.39 (s, 1 H, pyrazole-H), 7.53 (d, *J* = 8.8 Hz, 2 H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.71, 15.09, 62.17, 64.39, 110.56, 115.55, 116.15, 118.08, 125.47, 131.34, 144.95, 160.42, 161.05; IR (KBr) 2984 (s), 2916 (s), 2239 (m, C=N), 1727 (m, C=O) cm^{-1}; FABMS *m/z* (relative intensity) 287 (M+2 , 30), 286 (M+1, 6), 285 (M, 4); Anal. Calcd for $C_{15}H_{15}N_3O_3$; C: 69.15, H: 5.30, N: 16.82. Found: C: 69.32, H: 5.23, N: 16.72.

Ethyl 5-cyano-1-(4-ethoxyphenyl)-1*H*-pyrazole-4-carboxylate (5c): mp 110–112 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31–1.40 (m, 6 H, 2 × CH_3), 4.02 (q, *J* = 10.3 Hz, 2 H, CH_2), 4.34 (q, *J* = 10.6 Hz, 2 H, CH_2), 6.95 (d, *J* = 8.8 Hz, 2 H, ArH), 7.51 (d, *J* = 8.8 Hz, 2 H, ArH), 8.06 (s, 1 H, pyrazole-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.09, 14.64, 61.48, 63.93, 109.63, 115.15, 115.94, 121.89, 124.87, 130.84, 141.64, 159.91, 160.44; IR (KBr) 2991 (s), 2228 (m, C=N), 1718 (m, C=O) cm^{-1}; FABMS *m/z* (relative intensity) 287 (M+2 , 20), 286 (M+1, 100), 285 (M, 85); Anal. Calcd for $C_{15}H_{15}N_3O_3$; C: 69.15 ,H: 5.30, N: 16.82. Found: C: 69.05, H: 5.42, N: 166.77.

Ethyl 1-(4-ethoxyphenyl)-5-(hydroxymethyl)-1*H*-pyrazole-3-carboxylate (4d): mp 108–109 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27–1.38 (m, 6 H, 2 × CH_3), 4.09 (q, *J* = 10.3 Hz, 2H, CH_2), 4.29 (q, *J* = 10.3 Hz, 2H, CH_2), 4.45 (d, *J* = 5.3 Hz, 2H, CH_2-OH), 5.51 (t, *J* = 5.5 Hz, 1H, OH), 6.86 (s, 1H, pyrazole-H), 7.07 (d, *J* = 8.7 Hz, 2H, ArH), 7.54 (d, *J* = 8.7 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.08, 15.45, 54.92, 61.16, 64.34, 109.86, 115.60, 126.79, 132.63, 143.36, 146.04, 159.33, 162.56; IR (KBr) 3440 (br, OH), 2980 (s), 2879 (s), 1698 (m, C=O), 576 (w) cm^{-1}; FABMS *m/z* (relative

intensity) 292 (M+2 , 4), 291 (M+1, 20), 290 (M, 10); Anal. Calcd for $C_{15}H_{18}N_2O_4$; C: 62.06, H: 6.25, N: 9.65. Found: C: 62.15, H: 6.07, N: 9.71.

Ethyl 1-(4-ethoxyphenyl)-5-(hydroxymethyl)-1*H*-pyrazole-4-carboxylate (5d): mp 79–80 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.24–1.36 (m, 6 H, 2 × CH_3), 4.08 (q, *J* = 10.0 Hz, 2H, CH_2), 4.26 (q, *J* = 10.4 Hz, 2H, CH_2), 4.65 (d, *J* = 3.8 Hz, 2H, CH_2-OH), 5.39 (t, *J* = 5.3 Hz, 1H, OH), 7.06 (d, *J* = 8.6 Hz, 2H, ArH), 7.55 (d, *J* = 8.6 Hz, 2H, ArH), 7.99 (s, 1H, pyrazole-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.64, 14.98, 52.04, 60.17, 63.86, 113.04, 115.05, 126.58, 131.98, 141.27, 145.59, 158.87, 163.00; IR (KBr) 3474 (br, OH), 2923 (s), 2875 (s), 1690 (m, C=O) cm^{-1}; FABMS *m/z* (relative intensity) 292 (M+2 , 2), 291 (M+1, 9), 290 (M, 2); Anal. Calcd for $C_{15}H_{18}N_2O_4$; C: 62.06, H: 6.25, N: 9.65. Found: C: 61.98, H: 6.37, N: 9.61.

Ethyl 1-(4-ethoxyphenyl)-5-(phenylthio)-1*H*-pyrazole-3-carboxylate (4e): mp 68–69 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.29–1.36 (m, 6 H, 2 × CH_3), 3.96 (q, *J* = 10.4 Hz, 2H, CH_2), 4.34 (q, *J* = 10.6 Hz, 2H, CH_2), 6.79 (d, *J* = 9.0 Hz, 2H, ArH), 6.96 (s, 1H, pyrazole-H), 7.04 (d, *J* = 9.0 Hz, 2H, ArH), 7.12–7.18 (m, 3H, ArH), 7.23 (d, *J* = 6.9 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.33, 14.66, 61.16, 63.71, 114.31, 115.73, 127.12, 127.39, 129.29, 129.45, 131.55, 133.86, 135.86, 143.99, 159.21, 161.93; IR (KBr) 2979 (s), 2934 (s), 1719 (m, C=O), 1609 (w) cm^{-1}; FABMS *m/z* (relative intensity) 370 (M+2 , 5), 369 (M+1, 18), 368 (M, 6); Anal. Calcd for $C_{20}H_{20}N_2O_3S$; C: 65.20, H: 5.47, N: 7.60. Found: C: 65.38, H: 5.54, N: 7.53.

Ethyl 1-(4-ethoxyphenyl)-5-(phenylthio)-1*H*-pyrazole-4-carboxylate (5e): mp 91–92 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (t, *J* = 6.9 Hz, 3H, CH_3), 1.33 (t, *J* = 6.8 Hz, 3H, CH_3), 3.96 (q, *J* = 10.4 Hz, 2H, CH_2), 4.19 (q, *J* = 10.2 Hz, 2H, CH_2), 6.78 (d, *J* = 8.9 Hz, 2H, ArH), 6.94 (d, *J* = 8.9 Hz, 2H, ArH), 7.04–7.10 (m, 3H, ArH), 7.17 (d, *J* = 8.9 Hz, 2H, ArH), 8.10 (s, 1H, pyrazole-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.15, 14.66, 60.39, 63.73, 114.34, 118.65, 126.66, 127.30, 128.44, 128.99, 131.58, 134.56, 135.91, 142.52, 159.16, 162.23; IR (KBr) 2979 (s), 2933 (s), 1718 (m, C=O), 1608 (m) cm^{-1}; FABMS *m/z* (relative intensity) 370 (M+2 , 2), 369 (M+1, 6), 368 (M, 2); Anal. Calcd for $C_{20}H_{20}N_2O_3S$; C: 65.20, H: 5.47, N: 7.60. Found: C: 65.13, H: 5.60, N: 7.67.

***tert*-Butyl 5-cyano-1-(4-ethoxyphenyl)-1*H*-pyrazole-3-carboxylate (8a)**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18–1.26 (m, 9 H, CH_3), 1.37 (t, *J* = 10.5 Hz, 3 H, CH_3), 4.01 (q, *J* = 10.5 Hz, 2 H, CH_2), 6.68 (s, 1 H, pyrazole-H), 6.92 (d, *J* = 8.9 Hz, 2 H, ArH), 7.48 (d, *J* = 8.9 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.71, 28.75, 61.94, 83.42, 111.43, 114.35, 116.83, 118.79, 124.39, 132.79, 144.12, 160.38, 160.75; IR (KBr) 2983 (s), 2917(s), 2228 (m, C=N), 1730 (m, C=O) cm^{-1}; Anal. Calcd for $C_{17}H_{19}N_3O_3$; C: 65.16, H: 6.11, N: 13.41. Found: C: 65.12, H: 6.15, N: 13.45.

***tert*-Butyl 5-cyano-1-(4-ethoxyphenyl)-1*H*-pyrazole-4-carboxylate (9a)**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ

1.15–1.23 (m, 9 H, CH_3), 1.38 (t, J = 10.7 Hz, 3 H, CH_3), 4.07 (q, J = 10.7 Hz, 2 H, CH_2), 7.04 (d, J = 8.7 Hz, 2 H, ArH), 7.51 (d, J = 8.7 Hz, 2 H, ArH), 7.89 (s, 1 H, pyrazole-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 114.33, 28.15, 61.68, 82.64, 109.97, 115.84, 116.48, 121.73, 123.99, 131.09, 141.27, 159.63, 161.12; IR (KBr) 2955 (s), 2870(s), 2236 (m, C=N), 1726 (m, C=O) cm^{-1}; Anal. Calcd for $C_{17}H_{19}N_3O_3$; C: 65.16, H: 6.11, N: 13.41. Found: C: 65.14, H: 6.09, N: 13.36.

Benzyl 5-cyano-1-(4-ethoxyphenyl)-1*H*-pyrazole-3-carboxylate (8b): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.37 (t, J = 10.4 Hz, 3 H, CH_3), 4.01 (q, J = 10.4 Hz, 2 H, CH_2), 5.33 (s, 2 H, $PhCH_2$), 6.93 (d, J = 9.0 Hz, 2 H, ArH), 7.26–7.32 (m, 3 H, ArH), 7.36 (s, 1 H, pyrazole-H), 7.38 (d, J = 9.0 Hz, 2 H, ArH), 7.52 (d, J = 9.0 Hz, 2 H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.63, 63.94, 67.22, 110.04, 115.11, 115.70, 117.76, 124.96, 128.40, 128.52, 128.61, 130.86, 135.23, 144.16, 159.99, 160.42; IR (KBr) 3139 (s), 2980 (s), 2924 (m, C=N), 1734 (m, C=O) cm^{-1}; Anal. Calcd for $C_{20}H_{17}N_3O_3$; C: 69.15, H: 4.93, N: 12.10. Found: C: 69.32, H: 5.01, N: 12.02.

Benzyl 5-cyano-1-(4-ethoxyphenyl)-1*H*-pyrazole-4-carboxylate (9b): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.37 (t, J = 10.4 Hz, 3 H, CH_3), 4.01 (q, J = 10.4 Hz, 2 H, CH_2), 5.32 (s, 2 H, $PhCH_2$), 6.94 (d, J = 8.9 Hz, 2 H, ArH), 7.25–7.34 (m, 3 H, ArH), 7.40 (d, J = 8.9 Hz, 2 H, ArH), 7.50 (d, J = 8.9 Hz, 2 H, ArH), 8.07 (s, 1 H, pyrazole-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.63, 63.94, 67.03, 109.61, 115.16, 116.09, 121.56, 124.89, 128.40, 128.48, 128.61, 130.79, 135.18, 141.75, 159.96, 160.25; IR (KBr) 3118 (s), 2980 (s), 2934 (m, C=N), 1726 (m, C=O) cm^{-1}; Anal. Calcd for $C_{20}H_{17}N_3O_3$; C: 69.15, H: 4.93, N: 12.10. Found: C: 69.08, H: 4.90, N: 12.25.

Benzhydry 5-cyano-1-(4-ethoxyphenyl)-1*H*-pyrazole-3-carboxylate (8c): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.35 (t, J = 10.4 Hz, 3 H, CH_3), 3.98 (q, J = 10.4 Hz, 2 H, CH_2), 6.92 (d, J = 7.7 Hz, 2 H, ArH), 7.08 (s, 1 H, Ph_2CH), 7.15 (s, 1 H, pyrazole-H), 7.20–7.35 (m, 8 H, ArH), 7.41 (d, J = 7.7 Hz, 2 H, ArH), 7.47–7.54 (m, 2 H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.66, 63.95, 77.92, 110.11, 115.15, 115.65, 117.82, 124.92, 124.97, 127.22, 128.15, 128.57, 128.62, 130.95, 139.53, 139.59, 144.21, 159.65, 159.99; IR (KBr) 3031 (s), 2980 (s), 2929 (m, C=N), 1726 (m, C=O) cm^{-1}; Anal. Calcd for $C_{26}H_{21}N_3O_3$; C: 73.74, H: 5.00, N: 9.92. Found: C: 73.65, H: 5.12, N: 9.96.

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