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

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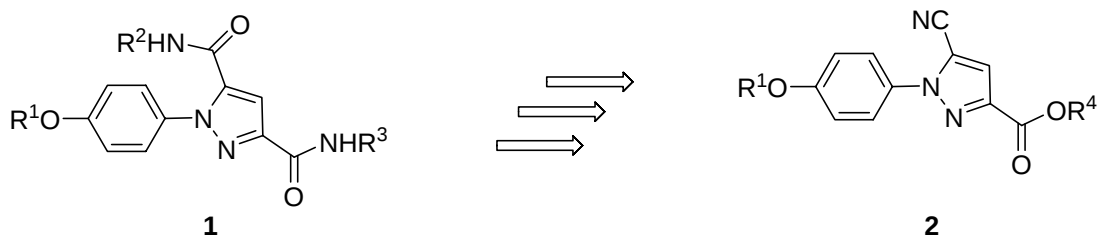
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Abstract – A regioselective 1,3-dipolar cycloaddition of 3-(4-ethoxyphenyl)-4-cyanosydnone with propargylic esters having a bulky alkyl group was developed. This new reaction provided alkyl 5-cyano-1-aryl-1*H*-pyrazole-3-carboxylate as a major product.

INTRODUCTION

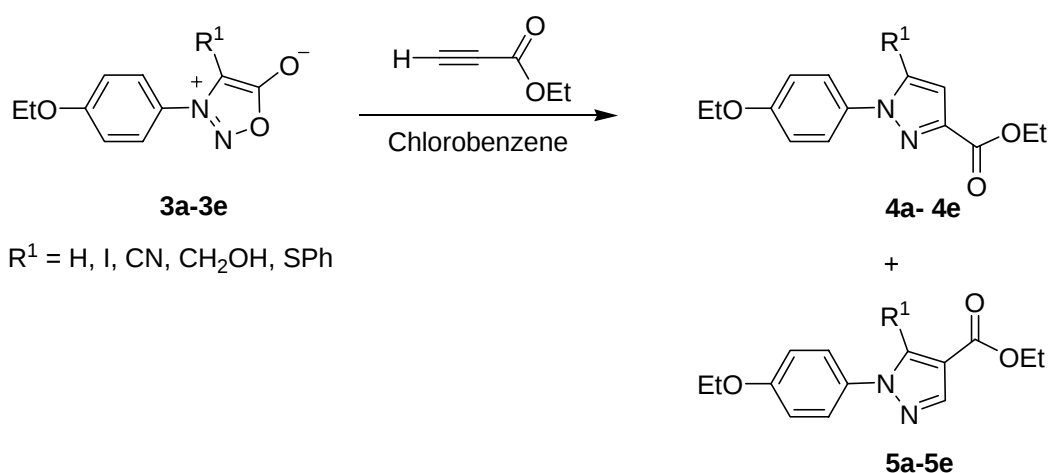
Pyrazole compounds (**1**) were demonstrated as potent inhibitors of *H. pylori* dihydroorotate dehydrogenase (DHODase).^{1,2} They can be conveniently synthesized from alkoxy 5-cyano-1-aryl-1*H*-pyrazole-3-carboxylate (**2**) by use of amination and Ritter reaction.³



Sydnones attract attention due to their widely useful properties, including biological and pharmaceutical usage,⁴ synthetic application,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-substituted 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 ¹H 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 interaction of dipoles LUMO of 3-(4-ethoxyphenyl)-4-substituted sydnones (**3a–3e**) with acetylene dipolarophile HOMO was suggested to be the controlling term.¹²



Scheme 1

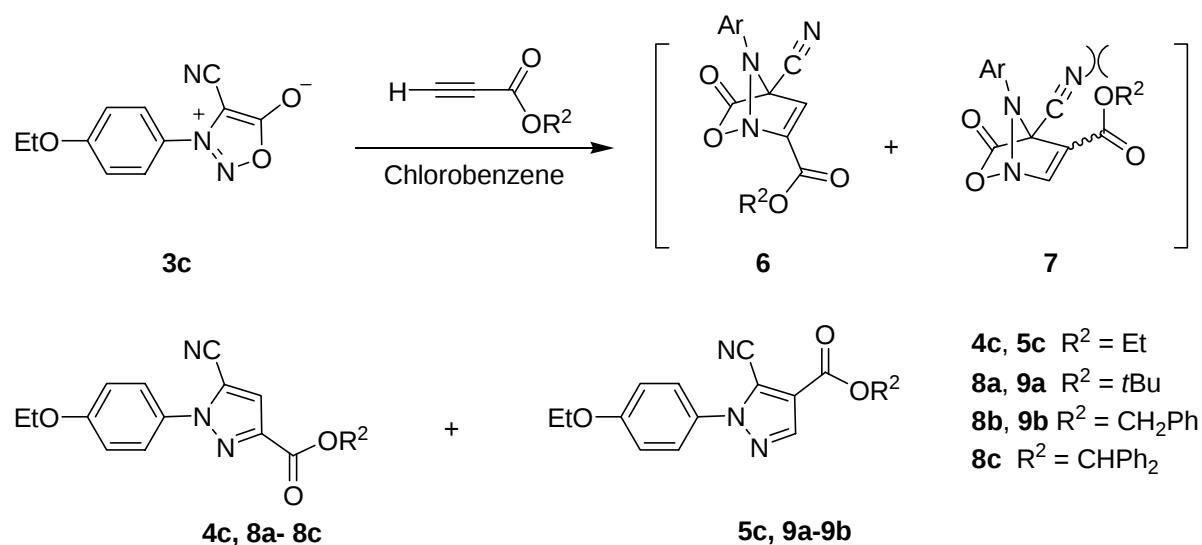
Table 1. The 1,3-dipolar addition between 3-(4-ethoxyphenyl)-4-substituted sydnone (**3a–3e**) and ethyl propiolate.

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 ₂ OH	63 (4d)	37 (5d)	71
3e	SPh	52 (4e)	48 (5e)	71

^aThe ratios of **4/5** (3-carboethoxy-substituted isomer/4-carboethoxy-substituted isomer) were determined by ¹H 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-dichlorobenzene (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-cyanosydnone¹⁴ (**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 substituent R² of acetylene with 4-cyano group of sydnone (**3c**). As the bulky group substituent R² in acetylene was increased (Et, *t*-Bu,¹⁵ and CH₂Ph¹⁶), 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 (R² = CHPh₂), 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	<i>t</i> -Bu	78 (8a)	22 (9a)	79
3	CH_2Ph	57 (8b)	43 (9b)	76
4	CHPh_2	~ 100 (8c)	<i>b</i>	85 ^c

^aThe ratios of **4c/5c** and **8/9** were determined by ¹H NMR. ^bNo detectable. ^cOnly **8c** was isolated.

In summary, we developed an efficient method to control the regioselectivity of 1,3-dipolar cycloaddition for propargylic ester having a bulky alkyl group ($R^2 = \text{CHPh}_2$) 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: Sydnone 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} absorption. 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 $\text{DMSO}-d_6$ as solvent. ^{13}C NMR spectra were obtained on a Bruker (75 MHz) spectrometer by use 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)-1H-pyrazole-3-carboxylate (4a): mp 92–93 °C (MeOH); ^1H NMR (CDCl_3 , 300 MHz) δ 1.31–1.37 (m, 6 H, $2 \times \text{CH}_3$), 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 $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3$; C: 64.60, H: 6.20, N: 10.76. Found: C: 64.45, H: 6.32, N: 10.63.

Ethyl 1-(4-ethoxyphenyl)-1H-pyrazole-4-carboxylate (5a): mp 103–105 °C (MeOH); ^1H NMR (CDCl_3 , 300 MHz) δ 1.28–1.39 (m, 6 H, $2 \times \text{CH}_3$), 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 $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3$; 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-1H-pyrazole-3-carboxylate (4b): mp 70–71 °C (MeOH); ^1H NMR (CDCl_3 , 300 MHz) δ 1.29–1.39 (m, 6 H, $2 \times \text{CH}_3$), 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 $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_3$; 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-1H-pyrazole-4-carboxylate (5b): mp 109–110 °C (MeOH); ^1H NMR (CDCl_3 , 300 MHz) δ 1.28–1.40 (m, 6 H, $2 \times \text{CH}_3$), 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 $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_3$; 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)-1H-pyrazole-3-carboxylate (4c): mp 72–73 °C (MeOH); ^1H NMR (CDCl_3 , 300 MHz) δ 1.31–1.39 (m, 6 H, $2 \times \text{CH}_3$), 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 $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_3$; 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)-1H-pyrazole-4-carboxylate (5c): mp 110–112 °C (MeOH); ^1H NMR (CDCl_3 , 300 MHz) δ 1.31–1.40 (m, 6 H, $2 \times \text{CH}_3$), 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 $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_3$; C: 69.15, H: 5.30, N: 16.82. Found: C: 69.05, H: 5.42, N: 16.77.

Ethyl 1-(4-ethoxyphenyl)-5-(hydroxymethyl)-1H-pyrazole-3-carboxylate (4d): mp 108–109 °C (MeOH); ^1H NMR (CDCl_3 , 300 MHz) δ 1.27–1.38 (m, 6 H, $2 \times \text{CH}_3$), 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, $\text{CH}_2\text{-OH}$), 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 C₁₅H₁₈N₂O₄; 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)-1H-pyrazole-4-carboxylate (5d): mp 79–80 °C (MeOH); ¹H NMR (CDCl₃, 300 MHz) δ 1.24–1.36 (m, 6 H, 2 × CH₃), 4.08 (q, *J* = 10.0 Hz, 2H, CH₂), 4.26 (q, *J* = 10.4 Hz, 2H, CH₂), 4.65 (d, *J* = 3.8 Hz, 2H, CH₂-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); ¹³C NMR (CDCl₃, 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 C₁₅H₁₈N₂O₄; 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)-1H-pyrazole-3-carboxylate (4e): mp 68–69 °C (MeOH); ¹H NMR (CDCl₃, 300 MHz) δ 1.29–1.36 (m, 6 H, 2 × CH₃), 3.96 (q, *J* = 10.4 Hz, 2H, CH₂), 4.34 (q, *J* = 10.6 Hz, 2H, CH₂), 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); ¹³C NMR (CDCl₃, 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 C₂₀H₂₀N₂O₃S; 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)-1H-pyrazole-4-carboxylate (5e): mp 91–92 °C (MeOH); ¹H NMR (CDCl₃, 300 MHz) δ 1.18 (t, *J* = 6.9 Hz, 3H, CH₃), 1.33 (t, *J* = 6.8 Hz, 3H, CH₃), 3.96 (q, *J* = 10.4 Hz, 2H, CH₂), 4.19 (q, *J* = 10.2 Hz, 2H, CH₂), 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); ¹³C NMR (CDCl₃, 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 C₂₀H₂₀N₂O₃S; 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)-1H-pyrazole-3-carboxylate (8a):** ¹H NMR (CDCl₃, 300 MHz) δ 1.18–1.26 (m, 9 H, CH₃), 1.37 (t, *J* = 10.5 Hz, 3 H, CH₃), 4.01 (q, *J* = 10.5 Hz, 2 H, CH₂), 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); ¹³C NMR (CDCl₃, 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 C₁₇H₁₉N₃O₃; 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)-1H-pyrazole-4-carboxylate (9a):** ¹H NMR (CDCl₃, 300 MHz) δ

1.15–1.23 (m, 9 H, CH₃), 1.38 (t, $J = 10.7$ Hz, 3 H, CH₃), 4.07 (q, $J = 10.7$ Hz, 2 H, CH₂), 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); ¹³C NMR (CDCl₃, 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 C₁₇H₁₉N₃O₃; 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)-1H-pyrazole-3-carboxylate (8b): ¹H NMR (CDCl₃, 300 MHz) δ 1.37 (t, $J = 10.4$ Hz, 3 H, CH₃), 4.01 (q, $J = 10.4$ Hz, 2 H, CH₂), 5.33 (s, 2 H, PhCH₂), 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); ¹³C NMR (CDCl₃, 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 C₂₀H₁₇N₃O₃; 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)-1H-pyrazole-4-carboxylate (9b): ¹H NMR (CDCl₃, 300 MHz) δ 1.37 (t, $J = 10.4$ Hz, 3 H, CH₃), 4.01 (q, $J = 10.4$ Hz, 2 H, CH₂), 5.32 (s, 2 H, PhCH₂), 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); ¹³C NMR (CDCl₃, 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 C₂₀H₁₇N₃O₃; 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)-1H-pyrazole-3-carboxylate (8c): ¹H NMR (CDCl₃, 300 MHz) δ 1.35 (t, $J = 10.4$ Hz, 3 H, CH₃), 3.98 (q, $J = 10.4$ Hz, 2 H, CH₂), 6.92 (d, $J = 7.7$ Hz, 2 H, ArH), 7.08 (s, 1 H, Ph₂CH), 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); ¹³C NMR (CDCl₃, 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 C₂₆H₂₁N₃O₃; C: 73.74, H: 5.00, N: 9.92. Found: C: 73.65, H: 5.12, N: 9.96.

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