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SYNTHESIS OF 4-AROYL-5-ARYLPYRAZOLES AND 4-AROYL-3-ARYLPYRAZOLES VIA THE REACTION OF ENAMINODIKETONES WITH SUBSTITUTED HYDRAZINES

Rika Kotouge,^a Takashi Nishiyama,^a Akira Yamauchi,^b Kanako Ono,^a Noriyuki Hatae,^c Tsutomu Oikawa,^c Satoshi Hibino,^a and Tominari Choshi^{a*}

^aGraduate School of Pharmacy Pharmaceutical Sciences, Faculty of Pharmacy and Pharmaceutical Sciences, Fukuyama University, Fukuyama, Hiroshima 729-0292, Japan. ^bDepartment of Biochemistry, Kawasaki Medical School, Kurashiki, Okayama, 701-0192, Japan. ^cFaculty of Pharmaceutical Sciences, Yokohama University of Pharmacy, 601 Matano, Totsuka-ku, Yokohama 245-0066, Japan. ^dFaculty of Health and Social Work, Kanagawa University of Human Services, 1-10-1 Heiseicho, Yokosuka, Kanagawa 238-8522, Japan. E-mail: choshi@fupharm.fukuyama-u.ac.jp

Abstract — Pyrazole is a five-membered heterocyclic compound and is one of the important heterocycles in the fields of medicine and pharmacology. Here, we demonstrate the reactivity of symmetrical enaminodiketones **8–14** with substituted hydrazines. When using alkylhydrazines, if the substituent size of the alkyl group is small, it is possible to selectively synthesize 1-substituted 4-aryl-5-arylpyrazoles and their regioisomers, 1-substituted 4-aryl-3-arylpyrazoles, by choosing the solvent (EtOH or toluene). When they react with bulky substituted hydrazines (e.g., cyclohexyl, phenyl, or pyridyl), only 1-substituted 4-aryl-5-arylpyrazoles are selectively obtained.

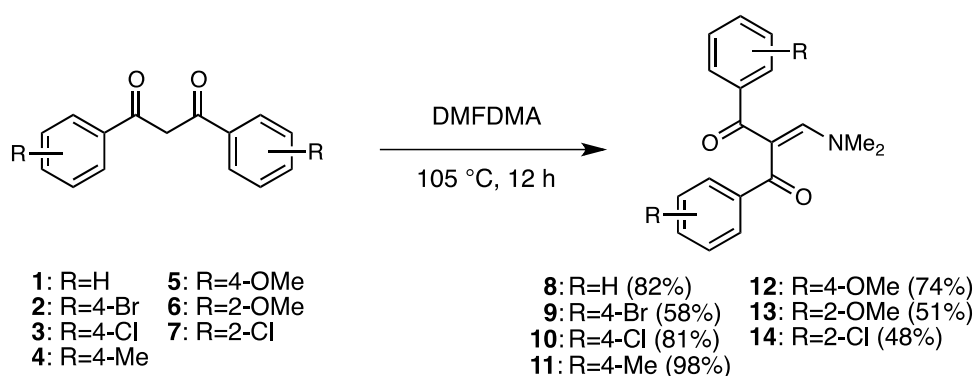
INTRODUCTION

Pyrazole, as well as other five-membered heterocyclic compounds, is an important heterocycle in the medicinal field. In fact, pyrazole and its derivatives appear in many pharmacological agents from diverse therapeutic categories, such as antibacterial,¹ antifungal,² anticancer,³ anti-inflammatory,⁴ and antiviral⁵ agents. Owing to this diversity of biological activities, pyrazole and its derivatives have attracted much attention from medicinal chemists.⁶ Many efforts for synthesis have been reported in review articles thus far concerning pyrazole and its derivatives.⁷ Among these, many synthetic approaches for a pyrazole ring

included the reaction of either 1,3-dicarbonyl compounds or their synthetic equivalents with hydrazine derivatives.⁸ Recently, (β -keto- β -sulfonyl)enamines⁹ and (β -keto- β -alkoxycarbonyl)enamines¹⁰ have been utilized as useful synthons for the synthesis of five- and six-membered heterocyclic compounds, such as pyrazoles, isoxazoles, pyrimidines, and pyridines. In these enamines, the generally used ones were easily prepared from active methylene compounds with dimethylformamide dimethyl acetal (DMFDMA). We previously reported the synthesis of symmetrical 1,3-dicarbonyl compounds, which are dibenzoylmethane derivatives, for the assay of antimutagenicity.¹¹ In addition, we are currently exploring the other biological activities of dibenzoylmethanes.¹² We planned a new way to utilize these symmetrical 1,3-dicarbonyl compounds, dibenzoylmethanes, and found that the enaminodiketone derived from dibenzoylmethanes with DMFDMA is of interest as a precursor for a new mode of substituents of five-membered pyrazole derivatives.

RESULTS AND DISCUSSION

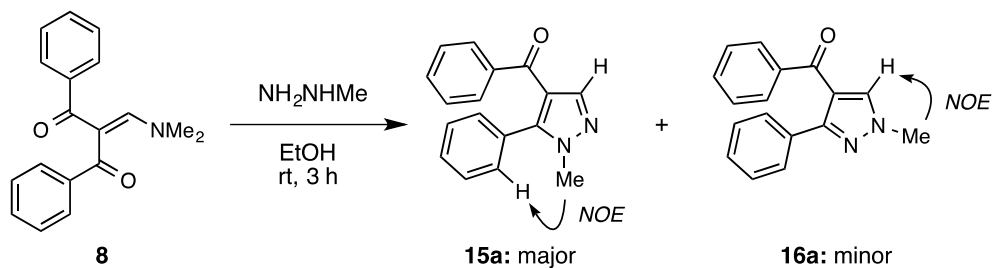
The aim of our research is to synthesize novel pyrazoles via the reaction of symmetrical enaminodiketones with substituted hydrazines and to search for pharmaceutical lead compounds that use them. In this paper, we report the regioselective synthesis of two isomers, 4-aryl-5-arylpyrazoles and 4-aryl-3-arylpyrazoles, which are provided by the reaction of symmetrical enaminodiketones with substituted hydrazines. Substituted enaminodiketones **8–14** were prepared by the reaction of dibenzoylmethanes **1–7** with DMFDMA at 105 °C for 12 h in 48–98% yields (Scheme 1).



Scheme 1

Next, the reaction of the enaminodiketone **8** with methylhydrazine was conducted in EtOH at rt for 3 h under ambient conditions (Scheme 2) to produce a mixture of two pyrazoles **15a** and **16a** (72 : 28).¹³ the evaporation of the solvent and purification of the crude products via silica gel column pyrazoles **15a** and **16a** were obtained in 52% and 14% yields, respectively (Table 1, entry 1). The structures of these pyrazoles were determined by ¹H-NMR spectral data and NOE experiments. In the NOE experiment of the major pyrazole **15a**, the selective irradiation of the *N*-methyl

group singlet (3.82 ppm) resulted in an enhancement of the *ortho* protons of the phenyl group on pyrazole C-5. Therefore, **15a** was assigned as 4-benzoyl-1-methyl-5-phenylpyrazole. Similarly, the selective irradiation of the *N*-methyl group singlet (3.99 ppm) of the minor pyrazole **16a**, resulted in an enhancement of the protons of pyrazole C-5. Therefore, **16a** was assigned as 4-benzoyl-1-methyl-3-phenylpyrazole.



Scheme 2

Table 1. Synthesis of Substituted 1-Methylpyrazoles from Enaminodiketones **8-14** and Methylhydrazine

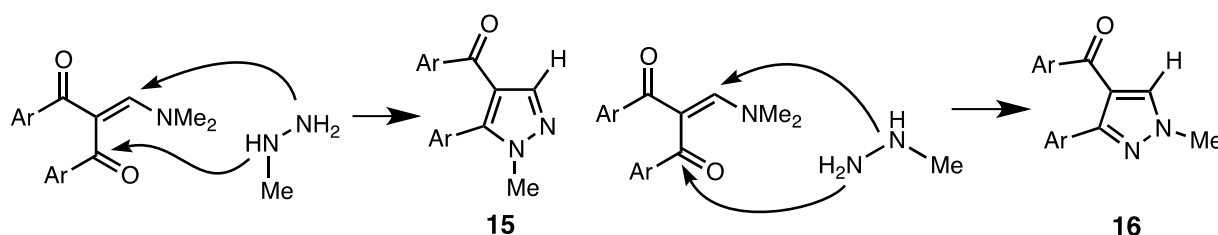
entry	SM	R	Solvent	Temp.	Time (h)	Yield (%) ¹⁾	15 : 16 ²⁾	Yield (%) ³⁾
1	8	H	EtOH	rt	3	72	72 : 28	15a (52), 16a (14)
2	8	H	EtOH	reflux	1	88	85 : 15	15a (75), 16a (13)
3	8	H	MeCN	rt	3	100	40 : 60	15a (33), 16a (56)
4	8	H	DMF	rt	3	69	45 : 55	15a (24), 16a (30)
5	8	H	benzene	rt	3	62	20 : 80	15a (15), 16a (35)
6	8	H	toluene	rt	3	72	14 : 86	15a (22), 16a (50)
7	9	4-Br	EtOH	rt	12	89	63 : 37	15b (63), 16b (16)
8	9	4-Br	toluene	rt	3	82	23 : 77	15b (24), 16b (52)
9	10	4-Cl	EtOH	rt	3	80	72 : 28	15c (42), 16c (21)
10	10	4-Cl	toluene	rt	3	44	23 : 77	15c (13), 16c (21)
11	11	4-Me	EtOH	rt	3	81	71 : 29	15d (56), 16d (25)
12	11	4-Me	toluene	rt	3	75	27 : 73	15d (19), 16d (56)
13	12	4-OMe	EtOH	rt	12	73	75 : 25	15e (39), 16e (31)
14	12	4-OMe	toluene	rt	3	60	38 : 62	15e (20), 16e (33)
15	13	2-OMe	EtOH	rt	3	80	77 : 23	15f (53), 16f (7)
16	13	2-OMe	toluene	rt	3	73	83 : 17	15f (60), 16f (7)
17	14	2-Cl	EtOH	rt	3	79	73 : 27	15g (43), 16g (29)
18	14	2-Cl	toluene	rt	3	79	86 : 14	15g (57), 16g (14)

1) Yield (%) of mixture **15** and **16**; 2) Integration ratio of *N*-Me group **15** and **16**;
3) Isolation yield (%).

However, Okada and co-workers reported that the reaction of *N,N*-dimethylaminomethylene-1,1,1,5,5,5-hexafluoropentane-2,4-dione with methylhydrazine in MeCN produces 1-methyl-4-trifluoroacetyl-3-trifluoromethylpyrazole.¹⁴ It was considered that the selectivity of this reaction is dependent on the solvent because the pyrazole has the same substituted form as that of the obtained regioisomer **16a**. Similarly, when the reaction of enaminodiketone **8** with methylhydrazine was conducted in MeCN, the ratio of product **15a** to **16a** provided the reverse ratio of 40 : 60 (Table 1, entry 3).

Therefore, we attempted various reaction conditions to investigate the regioselectivity of pyrazole formation. As shown in Table 1, when the reaction of **8** with methylhydrazine was refluxed in EtOH, the ratio of product **15a** to **16a** was 85 : 15 (entry 2). The selectivity of 4-aryl-5-arylpyrazole **15a** increased. Upon heating, this reaction formed 4-aryl-5-arylpyrazole preferentially. Sequentially, the reaction of **8** with methylhydrazine was conducted in dimethylformamide (DMF), benzene, and toluene to determine the relative reactivity of the primary amine and the secondary amine in substituted hydrazine in order to obtain information on the solvent dependence for the regioselective formation of the pyrazole.

When the same reaction was conducted in DMF, benzene, and toluene as the solvent, the ratio of the products **15a** and **16a** became opposite (entries 4–6). The regioisomer, 4-aryl-3-arylpyrazole **16a** was obtained as the main product. In particular, the selectivity in toluene was remarkable.



Scheme 3

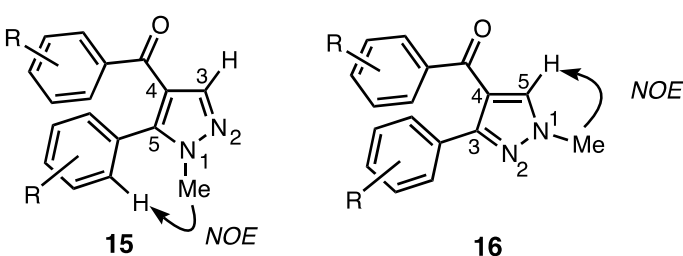
As shown in Scheme 3, the difference in regioselectivity observed using methylhydrazine produced 4-aryl-5-arylpyrazole **15** because the Michael addition of the primary amine on the conjugated double bond of enaminodiketone followed by heterocyclization takes precedence in EtOH. However, for the same reaction in toluene as the aprotic solvent, the attack of the primary amine on the carbonyl group or the Michael addition of the secondary amine on the conjugated double bond took precedence, and the 4-aryl-3-arylpyrazole **16** was obtained as the main product.

Next, the reactivities of other enaminodiketones **9–14** with methylhydrazine were investigated when EtOH and toluene were used as solvents. The formation ratio of the two obtained pyrazoles exhibited the same trend as for the above result (entries 7–18). In the case of enaminodiketones **13** and **14**, 4-aryl-5-arylpyrazoles **15f** and **15g** were obtained as the main products, regardless of the reaction in toluene (entries 16 and 18). Because the substituent (OMe, Cl) at the *ortho* position of the phenyl group

on enaminodiketones **13** and **14** has steric hindrance, pyrazoles **15f** and **15g** were obtained as the main products because the primary amine of methylhydrazine cannot attack the carbonyl group; thus, it reacted with the conjugated double bond.

The structural features of 4-aryl-5-aryl-1-methylpyrazoles **15a–15g** and 4-aryl-3-aryl-1-methylpyrazoles **16a–16g** that were obtained are summarized in Table 2. In the $^1\text{H-NMR}$ spectra, the chemical shift of the *N*-methyl group of **15** was located slightly upfield that of **16**. However, the chemical shift of the $\text{C}_3\text{-H}$ of **15** was located slightly downfield that of $\text{C}_5\text{-H}$ of **16**.

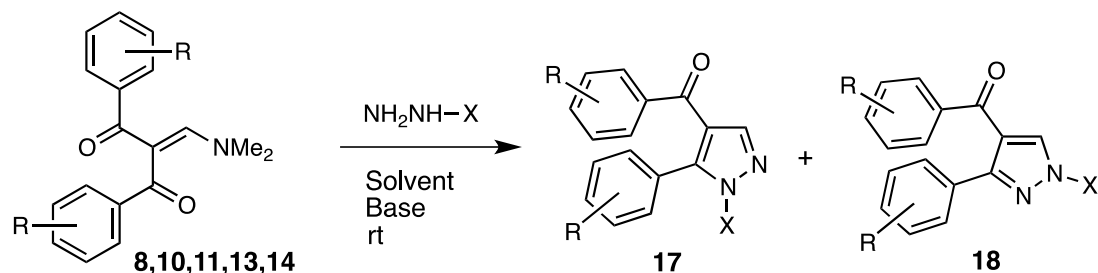
Table 2. Characterization of Substituted 4-Aryloyl-5-aryl-1-methylpyrazoles **15** and Its Isomer **16**



		$^1\text{H-NMR}$ (ppm)		$^1\text{H-NMR}$ (ppm)		
		<i>N</i> -Me	$\text{C}_3\text{-H}$	<i>N</i> -Me	$\text{C}_5\text{-H}$	
H	15a	3.82	7.87	16a	3.99	7.76
4-Br	15b	3.81	7.82	16b	3.99	7.73
4-Cl	15c	3.82	7.83	16c	3.99	7.73
4-Me	15d	3.82	7.83	16d	4.00	7.71
4-OMe	15e	3.82	7.83	16e	3.97	7.71
2-OMe	15f	3.73	7.94	16f	3.95	7.87
2-Cl	15g	3.68	7.92	16g	3.98	7.80

Subsequently, we investigated the regioselectivity of the pyrazoles obtained by the reaction of the enaminodiketones with various alkylhydrazines (ethyl, 2-hydroxyethyl, cyclohexyl, and benzyl) and arylhydrazines (phenyl, 2-pyridyl).

First, the reaction of enaminodiketone **8** with alkylhydrazines in EtOH or toluene as the solvent produced the pyrazole and its regioisomer (entries 1–8). The bulky alkyl group of the alkylhydrazines increased the regioselectivity of pyrazole **17** in EtOH. In toluene, the formation ratio of the regioisomer pyrazole **18** increased. Regarding cyclohexylhydrazine, the cyclohexyl group is bulky and nucleophilic attack of the secondary amine to the conjugated double bond of the enaminodiketone during the reaction is difficult; thus, only pyrazole **17c** was obtained in both solvents (entries 5 and 6). Next, the reaction of various enaminodiketones with benzylhydrazine was investigated (entries 7–16). Specifically, the reaction of any enaminodiketone with benzylhydrazine in EtOH selectively provided pyrazole **17**.

Table 3. Synthesis of Substituted Pyrazoles **17** and **18** from Enaminodiketones and Various Substituted Hydrazines

entry	SM ¹⁾	R	X	Solvent	Base	Time (h)	Yield (%) ²⁾	17 : 18 ³⁾	Yield (%) ⁴⁾
1	8	H	Et	EtOH	K ₂ CO ₃	12	67	96 : 4	17a (67)
2	8	H	Et	toluene	K ₂ CO ₃	12	50	21 : 79	17a (6), 18a (22)
3	8	H	CH ₂ CH ₂ OH	EtOH	K ₂ CO ₃	12	78	100 : 0	17b (78)
4	8	H	CH ₂ CH ₂ OH	toluene	K ₂ CO ₃	12	83	60 : 40	17b (36), 18b (15)
5	8	H	cyclohexyl	EtOH	K ₂ CO ₃	12	83	100 : 0	17c (83)
6	8	H	cyclohexyl	toluene	K ₂ CO ₃	12	78	100 : 0	17c (78)
7	8	H	Bn	EtOH	K ₂ CO ₃	12	67	100 : 0	17d (67)
8	8	H	Bn	toluene	K ₂ CO ₃	12	72	27 : 73	– ⁵⁾
9	10	4-Cl	Bn	EtOH	K ₂ CO ₃	2	93	100 : 0	17e (93)
10	10	4-Cl	Bn	toluene	Et ₃ N	2	74	54 : 46	17e (58), 18e (10)
11	11	4-Me	Bn	EtOH	K ₂ CO ₃	12	77	91 : 9	17f (77)
12	11	4-Me	Bn	toluene	Et ₃ N	2	87	25 : 75	17f (9), 18f (20) ⁶⁾
13	13	2-OMe	Bn	EtOH	Et ₃ N	12	75	96 : 4	17g (75)
14	13	2-OMe	Bn	toluene	Et ₃ N	2	83	52 : 48	17g (26), 18g (13) ⁶⁾
15	14	2-Cl	Bn	EtOH	Et ₃ N	2	78	95 : 5	17h (78)
16	14	2-Cl	Bn	toluene	Et ₃ N	3	82	74 : 26	17h (68), 18h (14)
17	8	H	Ph	EtOH	–	12	33	100 : 0	17i (33)
18	8	H	Ph	toluene	–	12	89	100 : 0	17i (89)
19	8	H	2-pyridyl	EtOH	K ₂ CO ₃	12	67	100 : 0	17j (67)
20	8	H	2-pyridyl	toluene	K ₂ CO ₃	12	78	100 : 0	17j (78)
21	10	4-Cl	Ph	EtOH	–	1	98	100 : 0	17k (98)
22	10	4-Cl	Ph	toluene	–	12	67	88 : 12	17k (67)
23	11	4-Me	Ph	EtOH	–	2	75	100 : 0	17l (75)
24	11	4-Me	Ph	toluene	–	3	70	93 : 7	17l (70)
25	13	2-OMe	Ph	EtOH	–	2	60	100 : 0	17m (60)
26	13	2-OMe	Ph	toluene	–	2	49	100 : 0	17m (49)
27	14	2-Cl	Ph	EtOH	–	1	69	100 : 0	17n (69)
28	14	2-Cl	Ph	toluene	–	12	64	100 : 0	17n (64)

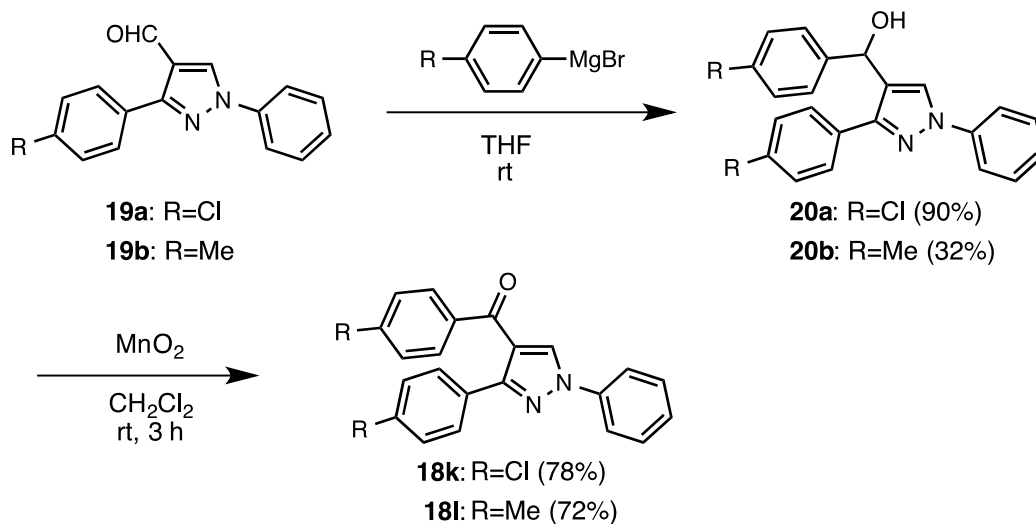
The reaction was carried out at rt.

1) SM: starting material; 2) Yield (%) of mixture **17** and **18**; 3) Integration ratio of C₃-H of pyrazole **17** and C₅-H of pyrazole **18**; 4) Isolation yield (%); 5) Can not separate; 6) Separated by preparative TLC.

In toluene, the reaction of enaminodiketones **8**, **10**, and **11** with benzylhydrazine increased the formation of regioisomer pyrazole **18** (entries 8, 10, and 12). In contrast, enaminodiketones **13** and **14** produced

pyrazoles **17g** and **17h**, respectively, as the main products via the influence of the substituent at the *ortho* position of the phenyl group, as described in Table 1 (entries 14 and 16).

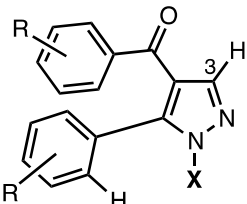
In 2004, the synthesis of 1-aryl-4-benzoyl-5-phenylpyrazoles via the reaction of *N,N*-dimethylaminomethylene-1,3-diphenylpropane-1,3-dione (**8**) with arylhydrazines was reported by Giulia and co-workers.¹⁵ In their studies, the formation of their regioisomers was not mentioned. Therefore, we attempted to assess the reactivity of enaminodiketones with arylhydrazines (phenylhydrazine and 2-pyridylhydrazine). Even if the reaction was conducted in either EtOH or toluene, only pyrazole **17i–17n** were obtained (entries 17–28). In the case of entries 22 and 24, trace amounts of regioisomers **18k** and **18l** were detected via ¹H-NMR spectra, respectively; however, they were difficult to separate via chromatography. The structures of pyrazoles **17i–17n** were determined by ¹H-NMR spectral data and NOE experiments. In the NOE experiment of pyrazole **17i**, the selective irradiation of the protons of pyrazole C-3 (3.82 ppm) resulted in an enhancement of the *ortho* protons of the benzoyl group of its C-4. Thereafter, the regioisomer **18i** of **17i** was reported by Oida and co-workers.¹⁶ However, it was confirmed that the ¹H-NMR data of **17i** and **18i** do not agree with each other. In addition, regioisomers **18k** and **18l** of **17k** and **17l** were synthesized via the route shown in Scheme 4. The pyrazole-4-carbaldehydes **19a** and **19b** were synthesized according to the method reported by Kumar and co-workers.¹⁷ Treatment of **19a** and **19b** with a Grignard reagent yielded alcohols **20a** and **20b**, respectively, and the sequential oxidation of **20a** and **20b** with MnO₂ provided pyrazoles **18k** and **18l** in 78% and 72% yields, respectively. The ¹H-NMR spectra of the synthesized pyrazoles, **18k** and **18l**, did not agree with those of pyrazoles **17k** and **17l**. With these results, in the case of arylhydrazines, it is possible that pyrazoles **17i–17n** were obtained via the nucleophilic attack of the primary amine on the conjugated double bond, followed by heterocyclization because the nucleophilicity of the secondary amine was weak and the aryl group was bulky.



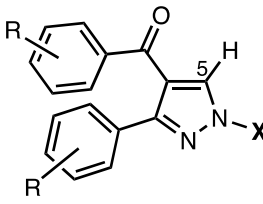
Scheme 4

The structural features of the 1-alkyl-4-aryl-5-arylpyrazoles **17a–17h** and 1-alkyl-4-aryl-3-arylpyrazoles **18a–18h** that were obtained are summarized in Table 4. The chemical shifts of the C₃-H of pyrazoles **17a–17h** and that of C₅-H of regioisomers **18a–18h** showed the same trend as that of substituted 1-methylpyrazole. In contrast, the chemical shifts of C₃-H of 4-aryl-5-aryl-1-phenylpyrazoles **17i–17n** and those of C₅-H of the 4-aryl-3-aryl-1-phenylpyrazoles **18i, 18k, and 18l** showed reverse data. Consequently, we found that it could be used as an index to distinguish between the pyrazole and its regioisomer.

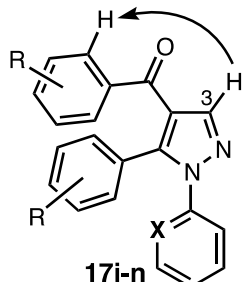
Table 4. Characterization of Substituted 4-Aryloyl-5-aryl-1-methylpyrazoles **17** and Its Isomer **18**



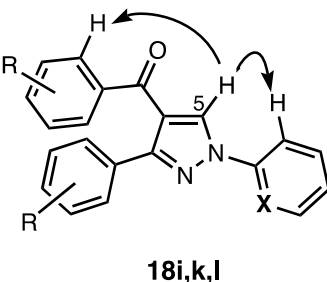
17a-h



18a,b,d-h



17i-n



18i,k,l

		¹ H-NMR (ppm)					¹ H-NMR (ppm)		
R	X		C ₃ -H of 17	C ₅ -H of 18	R	X	C ₃ -H of 17	C ₅ -H of 18	
H	Et	a	7.89	7.80	H	CH	i	8.05	8.24 ¹⁾
H	CH ₂ CH ₂ OH	b	7.92	7.85	H	N	j	8.08	–
H	cyclohexyl	c	7.89	–	4-Cl	CH	k	8.00	8.24
H	Bn	d	7.94	7.70	4-Me	CH	l	8.00	8.23
4-Cl	Bn	e	7.90	7.71	2-OMe	CH	m	8.13	–
4-Me	Bn	f	7.90	7.67	2-Cl	CH	n	8.03	–
2-OMe	Bn	g	8.02	7.83					
2-Cl	Bn	h	7.98	7.82					

1) ref.15

CONCLUSION

Herein, we demonstrated the reactivity of symmetrical enaminodiketones **8–14** with substituted hydrazines. When using alkylhydrazines, if the substituents on alkylhydrazines are of a small size, it is possible to selectively synthesize 1-substituted 4-aryl-5-arylpyrazoles and their regioisomers, 1-substituted 4-aryl-3-arylpyrazoles, by choosing the solvent (EtOH or toluene). In addition, when they react with bulky substituted hydrazines (e.g., cyclohexyl, phenyl, or pyridyl), only 1-substituted 4-aryl-5-arylpyrazoles are selectively obtained. Currently, various bioactivity screenings for synthesized pyrazoles are in progress. Moreover, we plan to use the enaminodiketones as a precursor for the synthesis of other heterocyclic compounds, such as pyrimidine derivatives, to search for pharmaceutical lead

compounds.

EXPERIMENTAL

General Methods: All non-aqueous reactions were carried out under an atmosphere of nitrogen in dried glassware unless otherwise noted. Solvents were dried and distilled according to standard protocols. Analytical thin-layer chromatography was performed with Silica gel 60PF₂₅₄ (Merck). Silica gel column chromatography was performed with Silica gel 60 (70–230 mesh, Kanto Co. Lit.). All melting points were determined on Yanagimoto micro melting point apparatus and are uncorrected. Proton nuclear magnetic resonance (¹H-NMR) spectra were recorded on a JEOL AL-300 at 300 MHz. Chemical shifts are reported relative to Me₄Si (δ 0.00). NMR spectra were measured with CDCl₃ unless otherwise noted. Multiplicity is indicated by one or more of the following: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); br (broad). Carbon nuclear magnetic resonance (¹³C-NMR) spectra were recorded on a JEOL AL-300 at 75 MHz. Chemical shifts are reported relative to CDCl₃ (δ 77.0) and DMSO-*d*₆ (δ 39.7). Infrared spectra were recorded with ATR method using a Shimadzu FTIR-8000 spectrophotometer and Technologies DuraScop. Low and high-resolution mass spectra were recorded on JEOL JMS-700 spectrometers by direct inlet system.

General procedure for *N,N*-dimethylaminomethylene-1,3-diphenylpropane-1,3-dione: A mixture of dibenzoylmethane (1.5 mmol) and dimethylformamide dimethyl acetal (DMFDMA) (15 mL) was heated at 105 °C for 12 h. After cooling to an ambient temperature, the reaction mixture was quenched with water, and then was extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, and evaporated *in vacuo*. The residue was purified by column chromatography (silica gel, 30 g) using EtOAc-hexane (3:97, v/v) as an eluent to give the enaminediketone.

N,N-Dimethylaminomethylene-1,3-diphenylpropane-1,3-dione (**8**)

The same procedure as above was carried out using dibenzoylmethane (**1**) (500 mg, 2.23 mmol) to give enaminediketone **8** (510 mg, 82%) as yellow solid. mp 81–83 °C (EtOAc-hexane). IR (ATR) ν = 3024, 1651, 1577 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃) δ : 2.81 (3H, br s), 3.27 (3H, br s), 7.16–7.29 (6H, m), 7.50–7.65 (4H, m), 7.67 (1H, s). ¹³C NMR (75 MHz, CDCl₃) δ : 42.3, 47.4, 111.4, 127.8, 128.9, 131.0, 140.9, 158.1, 194.8. MS *m/z*: 279 (M⁺). HRMS (EI): calcd for C₁₈H₁₇NO₂ 279.1259; found 279.1232.

N,N-Dimethylaminomethylene-1,3-di(4-bromophenyl)propane-1,3-dione (**9**)

The same procedure as above was carried out using di(4-bromobenzoyl)methane (**2**) (500 mg, 1.32 mmol) to give the enaminediketone **9** (332 mg, 58%) as orange solid. mp 156–158 °C (EtOAc-hexane). IR (ATR) ν = 2962, 1651, 1574 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃) δ : 2.76 (3H, br s), 3.31 (3H, br s), 7.18–7.27 (4H, m), 7.50–7.52 (4H, m), 7.64 (1H, s). ¹³C NMR (75 MHz, CDCl₃) δ : 42.3, 47.6, 110.6, 126.0,

130.4, 131.2, 139.4, 158.3, 193.1. MS m/z : 435 (M^+), 437 (M^+2), 439 (M^+4). HRMS (EI): calcd for $C_{18}H_{15}Br_2NO_2$ 434.9470; found 434.9484.

***N,N*-Dimethylaminomethylene-1,3-di(4-chlorophenyl)propane-1,3-dione (10)**

The same procedure as above was carried out using di(4-chlorobenzoyl)methane (**3**) (500 mg, 1.71 mmol) to give the enaminodiketone **10** (481 mg, 81%) as yellow solid. mp 155–157 °C (EtOAc-hexane). IR (ATR) $\nu = 2970, 1651, 1570\text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.77 (3H, br s), 3.32 (3H, br s), 7.20 (4H, d, $J = 8.6\text{ Hz}$), 7.45–7.60 (4H, m), 7.64 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 42.3, 47.6, 110.7, 128.2, 130.2, 137.4, 139.0, 158.3, 193.0. MS m/z : 347 (M^+), 349 (M^+2), 351 (M^+4). HRMS (EI): calcd for $C_{18}H_{15}Cl_2NO_2$ 347.0480; found 347.0484.

***N,N*-Dimethylaminomethylene-1,3-di(4-methylphenyl)propane-1,3-dione (11)**

The same procedure as above was carried out using di(4-methylbenzoyl)methane (**4**) (500 mg, 1.98 mmol) to give the enaminodiketone **11** (596 mg, 98%) as yellow solid. mp 115–116 °C (EtOAc-hexane). IR (ATR) $\nu = 2962, 1604, 1554\text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.27 (6H, s), 2.80–3.20 (6H, br s), 7.03 (4H, d, $J = 8.2\text{ Hz}$), 7.53 (4H, d, $J = 8.2\text{ Hz}$), 7.67 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 21.3, 42.3, 47.0, 111.5, 129.1, 138.0, 142.2, 157.5, 194.5. MS m/z : 307 (M^+). HRMS (EI): calcd for $C_{20}H_{21}NO_2$ 307.1572; found 307.1562.

***N,N*-Dimethylaminomethylene-1,3-di(4-methoxyphenyl)propane-1,3-dione (12)**

The same procedure as above was carried out using di(4-methoxybenzoyl)methane (**5**) (500 mg, 176 mmol) to give the enaminodiketone **12** (442 mg, 74%) as orange oil. IR (ATR) $\nu = 3001, 1639, 1598\text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.80–3.20 (6H, br s), 3.76 (6H, s), 6.71 (4H, d, $J = 8.8\text{ Hz}$), 7.50–7.60 (4H, m), 7.59 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 42.5, 47.4, 55.2, 111.4, 113.1, 129.0, 130.8, 133.7, 157.2, 193.6. MS m/z : 339 (M^+). HRMS (EI): calcd for $C_{20}H_{21}NO_4$ 339.1471; found 339.1479.

***N,N*-Dimethylaminomethylene-1,3-di(2-methoxyphenyl)propane-1,3-dione (13)**

The same procedure as above was carried out using di(2-methoxybenzoyl)methane (**6**) (500 mg, 1.76 mmol) to give the enaminodiketone **13** (304 mg, 51%) as orange solid. mp 154–156 °C (EtOAc-hexane). IR (ATR) $\nu = 2935, 1593, 1566\text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.86 (3H, br s), 3.33 (3H, br s), 3.64 (6H, s), 6.47 (2H, d, $J = 8.5\text{ Hz}$), 6.70 (2H, t, $J = 8.5\text{ Hz}$), 7.07 (2H, t, $J = 8.5\text{ Hz}$), 7.25 (2H, d, $J = 8.5\text{ Hz}$), 7.80 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 43.0, 47.7, 54.9, 110.0, 115.3, 119.3, 129.5, 130.9, 131.2, 156.3, 158.3, 192.5. MS m/z : 339 (M^+). HRMS (EI): calcd for $C_{20}H_{21}NO_4$ 339.1471; found 339.1461.

***N,N*-Dimethylaminomethylene-1,3-di(2-chlorophenyl)propane-1,3-dione (14)**

The same procedure as above was carried out using di(2-chlorobenzoyl)methane (**7**) (320 mg, 1.09 mmol) to give the enaminodiketone **14** (182 mg, 48%) as orange solid. mp 129–131 °C (EtOAc-hexane). IR

(ATR) $\nu = 2927, 1610, 1574 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.96 (3H, br s), 3.39 (3H, br s), 7.06–7.08 (6H, m), 7.28–7.31 (2H, m), 7.85 (1H, s). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ : 43.4, 48.3, 113.5, 126.3, 129.5, 129.5, 130.3, 131.0, 140.6, 160.7, 191.4. MS m/z : 347 (M^+), 349 ($\text{M}^+ + 2$), 351 ($\text{M}^+ + 4$). HRMS (EI): calcd for $\text{C}_{18}\text{H}_{15}\text{Cl}_2\text{NO}_2$ 347.0480; found 347.0491.

General procedure for 1-substituted 4-aryl-5-arylpyrazoles and 1-substituted 4-aryl-3-arylpyrazoles: Method 1: A mixture of enaminodiketone (0.10 mmol) and substituted hydrazine (0.12 mmol) in solvent (1.5 mL) was stirred at rt. After evaporating *in vacuo*, the residue was purified by column chromatography (silica gel, 30 g) using EtOAc-hexane as an eluent to give the pyrazole.

Method 2: A suspension of enaminodiketone (0.10 mmol), substituted hydrazine (0.12 mmol), and K_2CO_3 or Et_3N (0.30 mmol) in solvent (1.5 mL) was stirred at rt. The reaction mixture was quenched with water, and then was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 , and evaporated *in vacuo*. The residue was purified by column chromatography (silica gel, 30 g) using EtOAc-hexane as an eluent to give the pyrazole.

4-Benzoyl-1-methyl-5-phenylpyrazole (15a)

The same procedure (Method 1) as above was carried out using enaminodiketone **8** (50 mg, 0.18 mmol) to give the pyrazole **15a** (14 mg, 28%) as yellow oil and the regioisomer **16a** (3 mg, 6%) as yellow oil. IR (ATR) $\nu = 1647 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.82 (3H, s), 7.30–7.52 (8H, m), 7.75 (2H, d, $J = 8.5 \text{ Hz}$), 7.87 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 37.3, 120.2, 128.1, 128.4, 129.0, 129.2, 129.3, 129.9, 132.0, 138.9, 141.9, 146.3, 189.5. MS m/z : 262 (M^+). HRMS (EI): calcd for $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}$ 262.1106; found 262.1111.

4-Benzoyl-1-methyl-3-phenylpyrazole (16a)

IR (ATR) $\nu = 1643 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.99 (3H, s), 7.28–7.35 (3H, m), 7.38 (2H, d, $J = 8.0 \text{ Hz}$), 7.46–7.52 (1H, m), 7.61–7.64 (2H, m), 7.75–7.78 (2H, m), 7.76 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 39.3, 119.5, 128.1, 128.2, 128.3, 128.8, 129.3, 132.27, 132.33, 136.1, 139.1, 153.2, 189.9. MS m/z : 262 (M^+). HRMS (EI): calcd for $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}$ 262.1106; found 262.1123.

4-(4-Bromobenzoyl)-5-(4-bromophenyl)-1-methylpyrazole (15b)

The same procedure (Method 1) as above was carried out using enaminodiketone **9** (50 mg, 0.11 mmol) to give the pyrazole **15b** (34 mg, 63%) as yellow solid and the regioisomer **16b** (7 mg, 16%) as yellow solid. mp 117–119 °C (EtOAc-hexane). IR (ATR) $\nu = 1645 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.81 (3H, s), 7.27 (2H, d, $J = 8.5 \text{ Hz}$), 7.57 (2H, d, $J = 8.5 \text{ Hz}$), 7.61 (2H, d, $J = 8.5 \text{ Hz}$), 7.65 (2H, d, $J = 8.5 \text{ Hz}$), 7.82 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 37.4, 119.9, 124.1, 127.2, 127.6, 130.7, 131.4, 131.6, 131.8, 137.5, 141.7, 145.3, 188.0. MS m/z : 418 (M^+), 420 ($\text{M}^+ + 2$), 422 ($\text{M}^+ + 4$). HRMS (EI): calcd for $\text{C}_{17}\text{H}_{12}\text{Br}_2\text{N}_2\text{O}$ 417.9316; found 417.9331.

4-(4-Bromobenzoyl)-3-(4-bromophenyl)-1-methylpyrazole (16b)

mp 137–138 °C (EtOAc-hexane). IR (ATR) $\nu = 1635 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.99 (3H, s), 7.47 (2H, d, $J = 8.8 \text{ Hz}$), 7.55 (4H, d, $J = 8.8 \text{ Hz}$), 7.64 (2H, d, $J = 8.8 \text{ Hz}$), 7.73 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 39.4, 119.0, 122.7, 127.4, 130.3, 130.7, 131.1, 131.2, 131.6, 136.2, 137.8, 152.0, 188.4. MS m/z : (M^+) MS m/z : 418 (M^+), 420 ($\text{M}^+ + 2$), 422 ($\text{M}^+ + 4$). HRMS (EI): calcd for $\text{C}_{17}\text{H}_{12}\text{Br}_2\text{N}_2\text{O}$ 417.9316; found 417.9327.

4-(4-Chlorobenzoyl)-5-(4-chlorophenyl)-1-methylpyrazole (15c)

The same procedure (Method 1) as above was carried out using enaminodiketone **10** (50 mg, 0.14 mmol) to give the pyrazole **15c** (19 mg, 42%) as yellow solid and the regioisomer **16c** (10 mg, 21%) as yellow solid. mp 103–105 °C (EtOAc-hexane). IR (ATR) $\nu = 1643 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.82 (3H, s), 7.33 (2H, d, $J = 8.5 \text{ Hz}$), 7.39 (2H, d, $J = 8.5 \text{ Hz}$), 7.44 (2H, d, $J = 8.5 \text{ Hz}$), 7.61 (2H, d, $J = 8.5 \text{ Hz}$), 7.83 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 37.4, 119.9, 127.1, 128.6, 128.9, 130.6, 131.2, 135.8, 137.1, 138.6, 141.7, 145.3, 187.9. MS m/z : 330 (M^+), 332 ($\text{M}^+ + 2$), 334 ($\text{M}^+ + 4$). HRMS (EI): calcd for $\text{C}_{17}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}$ 330.0327; found 330.0314.

4-(4-Chlorobenzoyl)-3-(4-chlorophenyl)-1-methylpyrazole (16c)

mp 130–132 °C (EtOAc-hexane). IR (ATR) $\nu = 1643 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.99 (3H, s), 7.31 (2H, d, $J = 8.7 \text{ Hz}$), 7.38 (2H, d, $J = 8.7 \text{ Hz}$), 7.60 (2H, d, $J = 8.7 \text{ Hz}$), 7.72 (2H, d, $J = 8.7 \text{ Hz}$), 7.73 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 39.4, 119.1, 128.3, 128.6, 130.0, 130.6, 134.4, 136.1, 137.3, 138.8, 152.0, 188.3 (a pair of peak at the aromatic region is overlapped). MS m/z : 330 (M^+), 332 ($\text{M}^+ + 2$), 334 ($\text{M}^+ + 4$). HRMS (EI): calcd for $\text{C}_{17}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}$ 330.0327; found 330.0330.

1-Methyl-4-(4-methylbenzoyl)-5-(4-methylphenyl)pyrazole (15d)

The same procedure (Method 1) as above was carried out using enaminodiketone **11** (50 mg, 0.16 mmol) to give the pyrazole **15d** (25 mg, 56%) as yellow solid and the regioisomer **16d** (12 mg, 25%) as yellow solid. mp 92–93 °C (EtOAc-hexane). IR (ATR) $\nu = 1643 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.39 (6H, s), 3.82 (3H, s), 7.20 (2H, d, $J = 8.8 \text{ Hz}$), 7.23–7.29 (4H, m), 7.69 (2H, d, $J = 8.8 \text{ Hz}$), 7.83 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 21.3, 21.5, 37.2, 120.1, 126.0, 128.8, 129.1, 129.4, 129.7, 136.4, 139.2, 141.7, 142.7, 146.3, 189.1. MS m/z : 290 (M^+). HRMS (EI): calcd for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}$ 290.1419; found 290.1423.

1-Methyl-4-(4-methylbenzoyl)-3-(4-methylphenyl)pyrazole (16d)

mp 117–118 °C (EtOAc-hexane). IR (ATR) $\nu = 1645 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.33 (3H, s), 2.39 (3H, s), 4.00 (3H, s), 7.12 (2H, d, $J = 8.8 \text{ Hz}$), 7.18 (2H, d, $J = 8.8 \text{ Hz}$), 7.54 (2H, d, $J = 8.8 \text{ Hz}$), 7.69 (2H, d, $J = 8.8 \text{ Hz}$), 7.71 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 21.2, 21.5, 39.2, 119.3, 128.5, 128.7, 128.8, 129.5, 135.8, 136.5, 137.9, 142.9, 153.0, 189.5 (a pair of peak at the aromatic region is overlapped).

MS m/z : 290 (M^+). HRMS (EI): calcd for $C_{19}H_{18}N_2O$ 290.1419; found 290.1419.

4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-1-methylpyrazole (15e)

The same procedure (Method 1) as above was carried out using enaminediketone **12** (50 mg, 0.15 mmol) to give the pyrazole **15e** (19 mg, 39%) as orange solid and the regioisomer **16e** (15 mg, 31%) as yellow oil. mp 107–109 °C (EtOAc-hexane). IR (ATR) $\nu = 1639\text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.82 (3H, s), 3.84 (3H, s), 3.85 (3H, s), 6.88 (2H, d, $J = 8.6$ Hz), 6.96 (2H, d, $J = 8.6$ Hz), 7.32 (2H, d, $J = 8.6$ Hz), 7.79 (2H, d, $J = 8.6$ Hz), 7.83 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 37.2, 55.2, 55.3, 113.3, 113.8, 120.0, 121.0, 131.2, 131.5, 131.6, 141.4, 145.8, 160.1, 162.7, 188.2. MS m/z : 322 (M^+). HRMS (EI): calcd for $C_{19}H_{18}N_2O_3$ 322.1317; found 322.1302.

4-(4-Methoxybenzoyl)-3-(4-methoxyphenyl)-1-methylpyrazole (16e)

IR (ATR) $\nu = 1631\text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.80 (3H, s), 3.85 (3H, s), 3.97 (3H, s), 6.85 (2H, d, $J = 8.6$ Hz), 6.87 (2H, d, $J = 8.6$ Hz), 7.59 (2H, d, $J = 8.6$ Hz), 7.71 (1H, s), 7.79 (2H, d, $J = 8.6$ Hz). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 37.1, 55.1, 55.2, 113.2, 113.7, 119.9, 120.8, 131.1, 131.4, 131.5, 141.3, 145.7, 160.0, 162.6, 188.1. MS m/z : 322 (M^+). HRMS (EI): calcd for $C_{19}H_{18}N_2O_3$ 322.1317; found 322.1324.

4-(2-Methoxybenzoyl)-5-(2-methoxyphenyl)-1-methylpyrazole (15f)

The same procedure (Method 1) as above was carried out using enaminediketone **13** (50 mg, 0.15 mmol) to give the pyrazole **15f** (26 mg, 53%) as yellow solid and the regioisomer **16f** (3 mg, 7%) as yellow oil. mp 99–100 °C (EtOAc-hexane). IR (ATR) $\nu = 1628\text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.66 (3H, s), 3.67 (3H, s), 3.73 (3H, s), 6.64 (1H, d, $J = 8.6$ Hz), 6.77–6.88 (3H, m), 7.07 (1H, dd, $J = 8.6$ Hz), 7.16–7.31 (3H, m), 7.94 (1H, br s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 37.0, 55.2($\times 2$), 110.4, 117.5, 119.7, 120.0, 122.4, 128.8, 130.0, 130.9, 131.1, 131.6, 141.7, 141.7, 142.9, 156.4, 156.7, 189.6 (a pair of peak at the aromatic region is overlapped). MS m/z : 322 (M^+). HRMS (EI): calcd for $C_{19}H_{18}N_2O_3$ 322.1317; found 322.1319.

4-(2-Methoxybenzoyl)-3-(2-methoxyphenyl)-1-methylpyrazole (16f)

IR (ATR) $\nu = 1635\text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.54 (3H, s), 3.62 (3H, s), 3.95 (3H, s), 6.55 (2H, t, $J = 8.8$ Hz), 6.58 (2H, t, $J = 8.8$ Hz), 6.58 (2H, t, $J = 8.8$ Hz), 6.80 (1H, dt, $J = 7.7, 1.0$ Hz), 6.88 (1H, dt, $J = 7.7, 1.0$ Hz), 7.15 (1H, dt, $J = 7.7, 1.8$ Hz), 7.18 (1H, dt, $J = 7.7, 1.8$ Hz), 7.27–7.32 (2H, m), 7.87 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 39.2, 54.8, 55.2, 109.8, 110.3, 119.4, 119.9, 120.0, 122.0, 123.2, 129.5, 129.6, 130.4, 131.5, 134.8, 150.0, 156.7, 156.8, 189.5. MS m/z : 322 (M^+). HRMS (EI): calcd for $C_{19}H_{18}N_2O_3$ 322.1317; found 322.1322.

4-(2-Chlorobenzoyl)-5-(2-chlorophenyl)-1-methylpyrazole (15g)

The same procedure (Method 1) as above was carried out using enaminediketone **14** (50 mg, 0.14 mmol) to give the pyrazole **15g** (21 mg, 43%) as white solid and the regioisomer **16g** (12 mg, 29%) as yellow oil.

mp 75–77 °C (EtOAc-hexane). IR (ATR) $\nu = 1647 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.68 (3H, s), 7.11–7.39 (8H, m), 7.92 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 37.1, 121.9, 126.3, 126.8, 128.0, 128.3, 129.6, 129.7, 130.6, 130.7, 131.0, 131.6, 134.1, 139.2, 141.9, 143.3, 188.2. MS m/z : 330 (M^+), 332 ($\text{M}^+ + 2$), 334 ($\text{M}^+ + 4$). HRMS (EI): calcd for $\text{C}_{17}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}$ 322.1317; found 322.1303.

4-(2-Chlorobenzoyl)-3-(2-chlorophenyl)-1-methylpyrazole (16g)

IR (ATR) $\nu = 1651 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.98 (3H, s), 7.12–7.28 (5H, m), 7.32–7.39 (3H, m), 7.80 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 39.5, 122.0, 126.2, 126.3, 129.0, 129.1, 129.7, 129.7, 130.9, 131.0, 131.3, 131.7, 133.9, 135.6, 138.9, 187.7 (a pair of peak at the aromatic region is overlapped). MS m/z : 330 (M^+), 332 ($\text{M}^+ + 2$), 334 ($\text{M}^+ + 4$). HRMS (EI): calcd for $\text{C}_{17}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}$ 498.1825; found 322.1317.

4-Benzoyl-1-ethyl-5-phenylpyrazole (17a)

The same procedure (Method 2) as above was carried out using enaminodiketone **8** (50 mg, 0.18 mmol) to give the pyrazole **17a** (34 mg, 67%) as orange oil. IR (ATR) $\nu = 1647 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 1.41 (3H, t, $J = 7.2 \text{ Hz}$), 4.10 (2H, q, $J = 7.2 \text{ Hz}$), 7.34–7.50 (8H, m), 7.76 (2H, d, $J = 7.7 \text{ Hz}$), 7.89 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 15.5, 44.6, 120.1, 128.1, 128.4, 129.2, 129.2, 129.7, 131.9, 139.0, 141.9, 145.8, 189.5 (a pair of peak at the aromatic region is overlapped). MS m/z : 276 (M^+). HRMS (EI): calcd for $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}$ 276.1263; found 276.1252.

4-Benzoyl-1-ethyl-3-phenylpyrazole (18a)

The same procedure (Method 2) as above was carried out using enaminodiketone **8** (50 mg, 0.18 mmol) to give the pyrazole **17a** (2.8 mg, 6%) and the regioisomer **18a** (11 mg, 22%) as yellow oil. IR (ATR) $\nu = 1643 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 1.58 (3H, t, $J = 7.4 \text{ Hz}$), 4.26 (2H, q, $J = 7.4 \text{ Hz}$), 7.28–7.34 (3H, m), 7.37 (2H, d, $J = 8.1 \text{ Hz}$), 7.46–7.51 (1H, m), 7.61–7.64 (2H, m), 7.75–7.78 (2H, m), 7.80 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 15.4, 47.5, 119.3, 128.1, 128.2, 128.2, 128.8, 129.3, 132.2, 132.5, 134.4, 139.2, 153.0, 190.0. MS m/z : 276 (M^+). HRMS (EI): calcd for $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}$ 276.1263; found 276.1251.

4-Benzoyl-1-(2-hydroxyethyl)-5-phenylpyrazole (17b)

The same procedure (Method 2) as above was carried out using enaminodiketone **8** (50 mg, 0.18 mmol) to give the pyrazole **17b** (42 mg, 78%) as yellow oil. IR (ATR) $\nu = 1643 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.28 (1H, t, $J = 6.1 \text{ Hz}$), 4.00–4.05 (2H, m), 4.16–4.19 (2H, m), 7.35–7.52 (8H, m), 7.74–7.77 (2H, m), 7.92 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 51.0, 61.4, 100.5, 120.1, 128.1, 128.4, 139.1, 129.4, 130.0, 132.1, 138.6, 142.1, 146.9, 189.5. MS m/z : 292 (M^+). HRMS (EI): calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}_2$ 292.1212; found 292.1236.

4-Benzoyl-1-(2-hydroxyethyl)-3-phenylpyrazole (18b)

The same procedure (Method 2) as above was carried out using enaminodiketone **8** (50 mg, 0.18 mmol)

to give the pyrazole **17b** (17 mg, 36%) and the regioisomer **18b** (8 mg, 15%) as yellow oil. IR (ATR) $\nu = 3498, 1635 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 4.09–4.12 (2H, m), 4.31–4.34 (2H, m), 7.29–7.40 (3H, m), 7.48–7.55 (1H, m), 7.61–7.65 (2H, m), 7.76–7.79 (2H, m), 7.85 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 54.3, 61.5, 119.3, 128.1, 128.2, 128.4, 128.8, 129.4, 132.4, 136.2, 138.9, 153.4, 189.9 (a pair of peak at the aromatic region is overlapped). MS m/z : 292 (M^+). HRMS (EI): calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}_2$ 292.1212; found 292.1207.

4-Benzoyl-1-cyclohexyl-5-phenylpyrazole (17c)

The same procedure (Method 2) as above was carried out using enaminodiketone **8** (50 mg, 0.18 mmol) to give the pyrazole **17c** (48 mg, 83%) as white solid. mp 105–107 °C (EtOAc-hexane). IR (ATR) $\nu = 1639 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 1.19–1.30 (3H, m), 1.83–2.11 (7H, m), 3.94–4.08 (1H, m), 7.29–7.50 (8H, m), 7.74–7.77 (2H, m), 7.89 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 24.9, 25.3, 33.0, 57.9, 119.7, 128.0, 128.4, 129.1, 129.2, 129.3, 129.7, 131.9, 139.0, 141.7, 145.3, 189.6. MS m/z : 330 (M^+). HRMS (EI): calcd for $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}$ 330.1732; found 330.1748.

4-Benzoyl-1-benzyl-5-phenylpyrazole (17d)

The same procedure (Method 2) as above was carried out using enaminodiketone **8** (50 mg, 0.18 mmol) to give the pyrazole **17d** (42 mg, 67%) as orange oil. IR (ATR) $\nu = 1647 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 5.26 (2H, s), 7.05–7.10 (2H, m), 7.27–7.40 (10H, m), 7.45–7.51 (1H, m), 7.74–7.77 (2H, m), 7.94 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 53.2, 120.4, 127.2, 127.8, 128.1, 128.4, 128.6, 128.9, 129.2, 129.3, 129.9, 132.0, 136.2, 138.8, 142.3, 146.6, 189.5. MS m/z : 338 (M^+). HRMS (EI): calcd for $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}$ 338.1419; found 338.1425.

1-Benzyl-4-(4-chlorobenzoyl)-5-(4-chlorophenyl)pyrazole (17e)

The same procedure (Method 2) as above was carried out using enaminodiketone **10** (50 mg, 0.14 mmol) to give the pyrazole **17e** (54 mg, 93%) as white solid. IR (ATR) $\nu = 1639 \text{ cm}^{-1}$. mp 138–139 °C (EtOAc-hexane). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 5.25 (2H, s), 7.05–7.10 (2H, m), 7.22 (2H, d, $J = 8.5$ Hz), 7.26–7.34 (3H, m), 7.38 (2H, d, $J = 8.5$ Hz), 7.39 (2H, d, $J = 8.5$ Hz), 7.72 (2H, d, $J = 8.5$ Hz), 7.90 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 53.5, 120.3, 127.16, 127.19, 128.1, 128.6, 128.8, 130.6, 131.3, 132.8, 135.86, 135.93, 137.1, 138.7, 142.1, 145.6, 187.9. MS m/z : 406 (M^+), 408 (M^++2), 410 (M^++4). HRMS (EI): calcd for $\text{C}_{23}\text{H}_{16}\text{Cl}_2\text{N}_2\text{O}$ 406.0640; found 406.0652.

1-Benzyl-4-(4-chlorobenzoyl)-3-(4-chlorophenyl)pyrazole (18e)

The same procedure (Method 2) as above was carried out using enaminodiketone **10** (50 mg, 0.14 mmol) to give the pyrazole **17e** (33 mg, 58%) as yellow solid and the regioisomer **18e** (6 mg, 10%) as orange solid. mp 115–117 °C (EtOAc-hexane). IR (ATR) $\nu = 1643 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 5.33 (2H, s), 7.24–7.38 (9H, m), 7.60 (2H, d, $J = 8.9$ Hz), 7.69 (2H, d, $J = 8.9$ Hz), 7.71 (1H, s). $^{13}\text{C-NMR}$ (75

MHz, CDCl₃) δ : 55.8, 119.6, 128.4, 128.7, 129.3, 129.3, 130.1, 130.5, 130.7, 133.4, 134.6, 134.7, 135.1, 137.1, 139.0, 152.1, 188.4. m/z : 406 (M⁺), 408 (M⁺+2), 410 (M⁺+4). HRMS (EI): calcd for C₂₃H₁₆Cl₂N₂O 406.0640; found 406.0626.

1-Benzyl-4-(4-methylbenzoyl)-5-(4-methylphenyl)pyrazole (17f)

The same procedure (Method 2) as above was carried out using enaminodiketone **11** (100 mg, 0.33 mmol) to give the pyrazole **17f** (92 mg, 77%) as orange oil. IR (ATR) ν = 1643 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃) δ : 2.36 (3H, s), 2.37 (3H, s), 5.25 (2H, s), 7.08–7.11 (2H, m), 7.18–7.21 (6H, m), 7.29–7.32 (3H, m), 7.70 (2H, d, J = 8.6 Hz), 7.90 (1H, s). ¹³C-NMR (75 MHz, CDCl₃) δ : 21.3, 21.5, 53.0, 120.3, 125.9, 127.2, 127.8, 128.6, 128.8, 129.1, 129.4, 129.7, 136.2, 136.4, 139.3, 142.2, 142.7, 146.7, 189.1. MS m/z : 366 (M⁺). HRMS (EI): calcd for C₂₅H₂₂N₂O 366.1715; found 366.1732.

1-Benzyl-4-(4-methylbenzoyl)-3-(4-methylphenyl)pyrazole (18f)

The same procedure (Method 2) as above was carried out using enaminodiketone **11** (50 mg, 0.16 mmol) to give the pyrazole **17f** (5 mg, 9%) as orange oil and the regioisomer **18f** (12 mg, 20%) as yellow solid. mp 85–86 °C (EtOAc-hexane). IR (ATR) ν = 1651 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃) δ : 2.33 (3H, s), 2.37 (3H, s), 5.37 (2H, s), 7.13 (2H, d, J = 8.2 Hz), 7.16 (2H, d, J = 8.2 Hz), 7.27–7.40 (5H, m), 7.56 (2H, d, J = 8.2 Hz), 7.66 (2H, d, J = 8.2 Hz), 7.67 (1H, s). ¹³C-NMR (75 MHz, CDCl₃) δ : 21.3, 21.6, 56.4, 119.7, 127.3, 128.0, 128.5, 128.6, 128.8, 128.9, 129.0, 129.6, 134.9, 135.4, 136.5, 138.1, 143.1, 153.0, 189.7. MS m/z : 366 (M⁺). HRMS (EI): calcd for C₂₅H₂₂N₂O 366.1732; found 366.1736.

1-Benzyl-4-(2-methoxybenzoyl)-5-(2-methoxyphenyl)pyrazole (17g)

The same procedure (Method 2) as above was carried out using enaminodiketone **13** (100 mg, 0.29 mmol) to give the pyrazole **17g** (88 mg, 75%) as yellow oil. IR (ATR) ν = 1631 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃) δ : 3.57 (3H, s), 3.64 (3H, s), 5.06 (1H, d, J = 15.1 Hz), 5.16 (1H, d, J = 15.1 Hz), 6.59 (1H, d, J = 8.5 Hz), 6.68 (1H, d, J = 8.5 Hz), 6.77 (1H, t, J = 7.5 Hz), 6.80 (1H, t, J = 7.5 Hz), 6.95–7.02 (3H, m), 7.13–7.24 (6H, m), 8.02 (1H, s). ¹³C-NMR (75 MHz, CDCl₃) δ : 53.4, 54.9, 55.1, 110.4, 117.4, 119.6, 120.0, 122.8, 127.5, 127.6, 128.3, 128.4, 128.8, 129.8, 131.0, 131.2, 131.5, 136.1, 141.7, 143.2, 156.3, 156.7, 189.7. MS m/z : 398 (M⁺). HRMS (EI): calcd for C₂₅H₂₂N₂O₃ 398.1630; found 398.1651.

1-Benzyl-4-(2-methoxybenzoyl)-3-(2-methoxyphenyl)pyrazole (18g)

The same procedure (Method 2) as above was carried out using enaminodiketone **13** (50 mg, 0.15 mmol) to give the pyrazole **17g** (16 mg, 26%) as yellow oil and the regioisomer **18g** (8 mg, 13%) as yellow oil. IR (ATR) ν = 1635 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃) δ : 3.53 (3H, s), 3.59 (3H, s), 5.35 (2H, s), 6.55 (2H, t, J = 7.9 Hz), 6.78 (1H, t, J = 7.3 Hz), 6.88 (1H, t, J = 7.5 Hz), 7.12–7.20 (2H, m), 7.27–7.44 (7H, m), 7.83 (1H, s). ¹³C-NMR (75 MHz, CDCl₃) δ : 54.8, 55.1, 56.4, 109.8, 110.3, 119.5, 119.9, 121.9, 123.4, 128.3, 128.4, 128.9, 129.3, 129.7, 129.8, 130.5, 131.7, 133.8, 135.3, 149.9, 156.7, 156.9, 189.5. MS m/z : 398 (M⁺). HRMS (EI): calcd for C₂₅H₂₂N₂O₃ 398.1630; found 398.1619.

1-Benzyl-4-(2-chlorobenzoyl)-5-(2-chlorophenyl)pyrazole (17h)

The same procedure (Method 2) as above was carried out using enaminodiketone **14** (50 mg, 0.14 mmol) to give the pyrazole **17h** (44 mg, 78%) as orange solid. mp 73–75 °C (EtOAc-hexane). IR (ATR) $\nu = 1651 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 5.00 (1H, d, $J = 15.2 \text{ Hz}$), 5.22 (1H, d, $J = 15.2 \text{ Hz}$), 6.94–7.00 (2H, m), 7.07–7.40 (13H, m), 7.98 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 53.8, 122.1, 126.2, 126.6, 127.6, 127.8, 128.0, 128.4, 128.6, 129.5, 129.6, 130.7, 131.0, 131.7, 134.1, 135.4, 139.0, 142.1, 143.1, 188.2 (a pair of peak at the aromatic region is overlapped). MS m/z : 398 (M^+). HRMS (EI): calcd for $\text{C}_{23}\text{H}_{16}\text{Cl}_2\text{N}_2\text{O}_3$ 406.0640; found 406.0648.

1-Benzyl-4-(2-chlorobenzoyl)-3-(2-chlorophenyl)pyrazole (18h)

The same procedure (Method 2) as above was carried out using enaminodiketone **14** (50 mg, 0.14 mmol) to give the pyrazole **17h** (40 mg, 68%) as orange solid and the regioisomer **18h** (8 mg, 14%) as orange oil. IR (ATR) $\nu = 1651 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 5.38 (2H, s), 7.09–7.42 (13H, m), 7.82 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 56.6, 122.3, 126.17, 126.24, 128.0, 128.6, 129.1, 129.2, 129.70, 129.73, 130.9, 131.1, 131.4, 131.6, 133.9, 134.7, 134.9, 138.8, 150.8, 187.9 (a pair of peak at the aromatic region is overlapped). MS m/z : 406 (M^+), 408 (M^{+2}), 410 (M^{+4}). HRMS (EI): calcd for $\text{C}_{23}\text{H}_{16}\text{Cl}_2\text{N}_2\text{O}_3$ 406.0640; found 406.0636.

4-Benzoyl-1,5-diphenylpyrazole (17i)

The same procedure (Method 1) as above was carried out using enaminodiketone **8** (50 mg, 0.18 mmol) to give the pyrazole **17i** (53 mg, 89%) as yellow solid. mp 132–134 °C (EtOAc-hexane). IR (ATR) $\nu = 1647 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 7.24–7.33 (10H, m), 7.41 (2H, d, $J = 8.4 \text{ Hz}$), 7.51 (1H, t, $J = 8.4 \text{ Hz}$), 7.81 (2H, d, $J = 8.4 \text{ Hz}$), 8.05 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 121.2, 125.4, 128.1, 128.2, 128.8, 128.9, 129.0, 129.4, 130.3, 132.3, 138.7, 139.1, 142.9, 145.5, 189.8 (a pair of peak at the aromatic region is overlapped). m/z : 324 (M^+). HRMS (EI): calcd for $\text{C}_{22}\text{H}_{16}\text{N}_2\text{O}$ 324.1263; found 324.1279.

4-Benzoyl-5-phenyl-1-(2-pyridyl)pyrazole (17j)

The same procedure (Method 2) as above was carried out using enaminodiketone **8** (50 mg, 0.18 mmol) to give the pyrazole **17j** (53 mg, 78%) as white solid. mp 156–158 °C (EtOAc-hexane). IR (ATR) $\nu = 1655 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 7.24–7.33 (5H, m), 7.38 (2H, t, $J = 7.8 \text{ Hz}$), 7.47–7.53 (1H, m), 7.75–7.82 (1H, m), 7.80 (2H, d, $J = 7.2 \text{ Hz}$), 8.08 (1H, s), 8.42 (1H, dd, $J = 4.8, 0.9 \text{ Hz}$). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 119.6, 121.7, 123.2, 128.0, 128.2, 128.9, 129.3, 130.1, 132.3, 138.1, 138.5, 143.2, 145.8, 148.8, 151.6, 190.0 (a pair of peak at the aromatic region is overlapped). MS m/z : 393 (M^+). HRMS (EI): calcd for $\text{C}_{21}\text{H}_{13}\text{Cl}_2\text{N}_3\text{O}$ 393.0436; found 393.0423.

4-(4-Chlorobenzoyl)-5-(4-chlorophenyl)-1-phenylpyrazole (17k)

The same procedure (Method 1) as above was carried out using enaminodiketone **10** (50 mg, 0.14 mmol) to give the pyrazole **17k** (54 mg, 98%) as white solid. mp 185–186 °C (EtOAc-hexane). IR (ATR) ν = 1651 cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 7.07 (2H, d, J = 8.6 Hz), 7.22–7.29 (4H, m), 7.31–7.39 (3H, m), 7.42 (2H, d, J = 8.6 Hz), 7.78 (2H, d, J = 8.6 Hz), 8.00 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 120.9, 125.4, 127.0, 128.4, 128.6, 128.7, 129.1, 130.7, 131.7, 135.5, 137.0, 138.8, 138.9, 142.8, 144.4, 188.3. MS m/z : 392 (M^+), 394 ($\text{M}^+ + 2$), 396 ($\text{M}^+ + 4$). HRMS (EI): calcd for $\text{C}_{22}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}$ 392.0483; found 392.0477.

4-(4-Methylbenzoyl)-5-(4-methylphenyl)-1-phenylpyrazole (**17l**)

The same procedure (Method 1) as above was carried out using enaminodiketone **11** (50 mg, 0.16 mmol) to give the pyrazole **17l** (41 mg, 75%) as yellow solid. mp 165–167 °C (EtOAc-hexane). IR (ATR) ν = 1639 cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.31 (3H, s), 2.40 (3H, s), 7.07 (2H, d, J = 8.3 Hz), 7.14 (2H, d, J = 8.3 Hz), 7.22–7.34 (7H, m), 7.76 (2H, d, J = 8.5 Hz), 8.00 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 21.4, 21.6, 121.2, 125.4, 125.8, 127.9, 128.87, 128.92, 129.0, 129.6, 130.2, 136.2, 139.0, 139.2, 142.8, 143.0, 145.6, 189.4. MS m/z : 352 (M^+). HRMS (EI): calcd for $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}$ 352.1576; found 352.1592.

4-(2-Methoxybenzoyl)-5-(2-methoxyphenyl)-1-phenylpyrazole (**17m**)

The same procedure (Method 1) as above was carried out using enaminodiketone **13** (50 mg, 0.15 mmol) to give the pyrazole **17m** (35 mg, 60%) as white solid. mp 86–87 °C (EtOAc-hexane). IR (ATR) ν = 1635 cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.41 (3H, s), 3.63 (3H, s), 6.60 (1H, d, J = 8.4 Hz), 6.61 (1H, d, J = 8.2 Hz), 6.73 (1H, t, J = 7.3 Hz), 6.83 (1H, t, J = 7.5 Hz), 7.00 (1H, dd, J = 7.5, 1.7 Hz), 7.11–7.30 (8H, m), 8.13 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 54.8, 55.1, 110.4, 118.0, 119.7, 119.9, 123.4, 124.4, 127.6, 128.5, 129.0, 129.8, 130.8, 131.4, 131.7, 139.7, 142.2, 142.7, 156.48, 156.53, 189.9 (a pair of peak at the aromatic region is overlapped). MS m/z : 384 (M^+). HRMS (EI): calcd for $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}_3$ 384.1474; found 384.1459.

4-(2-Chlorobenzoyl)-5-(2-chlorophenyl)-1-phenylpyrazole (**17n**)

The same procedure (Method 1) as above was carried out using enaminodiketone **14** (50 mg, 0.14 mmol) to give the pyrazole **17n** (39 mg, 69%) as orange solid. mp 120–122 °C (EtOAc-hexane). IR (ATR) ν = 1658 cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 7.10–7.36 (13H, m), 8.03 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 122.9, 124.7, 126.3, 126.5, 128.3, 128.6, 128.8, 129.4, 129.7, 130.7, 130.80, 130.83, 131.9, 134.2, 138.8, 139.0, 142.6, 142.9, 188.3 (a pair of peak at the aromatic region is overlapped). MS m/z : 392 (M^+), 394 ($\text{M}^+ + 2$), 396 ($\text{M}^+ + 4$). HRMS (EI): calcd for $\text{C}_{22}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}$ 392.0483; found 392.0496.

4-Chlorophenyl-[3-(4-chlorophenyl)-1-phenylpyrazol-4-yl]methanol (**20a**)

4-Chlorophenylmagnesium bromide (1 M in Et_2O solution, 1.1 mL, 1.1 mmol) was added dropwise to an ice/water-cooled solution of pyrazole-4-carbaldehyde **19a** (282 mg, 1.0 mmol) in THF (10 mL). After

stirring at rt for 4 h, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution and was extracted with EtOAc. The organic layer was washed with brine, dried with Na_2SO_4 , and evaporated *in vacuo*. The residue was purified by column chromatography (EtOAc/hexane 2:8, v/v) to give the alcohol **20a** (354 mg, 90%). mp 135–137 °C (EtOAc-hexane). IR (ATR) $\nu = 3344 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.57 (1H, d, $J = 4.4 \text{ Hz}$), 5.89 (1H, d, $J = 4.4 \text{ Hz}$), 7.25–7.34 (5H, m), 7.38 (2H, d, $J = 8.7 \text{ Hz}$), 7.42 (2H, t, $J = 7.4 \text{ Hz}$), 7.57 (1H, s), 7.62–7.65 (2H, m), 7.74 (2H, d, $J = 8.7 \text{ Hz}$). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 67.6, 116.6, 119.0, 124.3, 126.8, 127.6, 128.7, 128.8, 129.38, 129.43, 131.1, 133.5, 134.2, 139.5, 141.4, 150.2. MS m/z : 394 (M^+). HRMS (EI): calcd for $\text{C}_{22}\text{H}_{16}\text{Cl}_2\text{N}_2\text{O}$ 394.0640; found 394.0656.

4-Methylphenyl-[3-(4-methylphenyl)-1-phenylpyrazol-4-yl]methanol (20b)

A solution of 4-bromotoluene (308 mL, 2.5 mmol) in THF (2 mL) was added dropwise to a mixture of magnesium (73 mg, 3.0 mmol), a small piece of iodine in THF (3 mL) at rt. After stirring at same temperature for 30 min, Grignard reagent was prepared by heating the reaction mixture at 50 °C for 1 h. The Grignard reagent was added dropwise to a solution of pyrazole-4-carbaldehyde **19b** (262 mg, 1.0 mmol) in THF (5 mL) at rt, and then stirred at same temperature for 12 h. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution and was extracted with EtOAc. The organic layer was washed with brine, dried with Na_2SO_4 , and evaporated *in vacuo*. The residue was purified by column chromatography (EtOAc/hexane 1:9, v/v) to give the alcohol **20b** (113 mg, 32 %) as an oil. IR (ATR) $\nu = 3737 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.34 (3H, s), 2.38 (3H, s), 5.93 (1H, s), 7.15 (2H, d, $J = 8.2 \text{ Hz}$), 7.20–7.27 (3H, m), 7.32 (2H, d, $J = 8.2 \text{ Hz}$), 7.39 (2H, t, $J = 8.2 \text{ Hz}$), 7.62–7.68 (2H, m), 7.64 (1H, s), 7.70 (2H, d, $J = 8.4 \text{ Hz}$). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 21.1, 21.3, 66.2, 118.2, 124.8, 126.3, 127.4, 128.1, 129.15, 129.22, 129.3, 130.1, 137.3, 137.9, 139.9, 140.4, 151.3 (a pair of peak at the aromatic region is overlapped). MS m/z : 354 (M^+). HRMS (EI): calcd for $\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}$ 354.1732; found 354.1747.

4-(4-Chlorobenzoyl)-3-(4-chlorophenyl)-1-phenylpyrazole (18k)

A suspension of alcohol **20a** (100 mg, 0.25 mmol) and MnO_2 (220 mg, 2.53 mmol) in CH_2Cl_2 (5 mL) was stirred at rt for 3 h. The reaction mixture was filtrated through a Celite pad. The filtrate was evaporated *in vacuo*, and the residue was purified by column chromatography (silica gel, 30 g) using EtOAc-hexane (3:97, v/v) as an eluent to give the pyrazole **18k** (78 mg, 78%) as yellow solid. mp 129–130 °C (EtOAc-hexane). IR (ATR) $\nu = 1639 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 7.33 (2H, d, $J = 8.6 \text{ Hz}$), 7.35–7.14 (1H, m), 7.40 (2H, d, $J = 8.6 \text{ Hz}$), 7.50 (2H, t, $J = 7.5 \text{ Hz}$), 7.70 (2H, d, $J = 8.6 \text{ Hz}$), 7.76 (2H, d, $J = 7.6 \text{ Hz}$), 7.78 (2H, d, $J = 8.6 \text{ Hz}$), 8.24 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 119.5, 120.7, 127.8, 128.4, 128.8, 129.7, 130.1, 130.3, 130.8, 132.4, 134.8, 137.1, 139.0, 139.2, 152.7, 188.4. MS m/z : 392 (M^+) 394 (M^++2), 396 (M^++4). HRMS (EI): calcd for $\text{C}_{22}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}$ 392.0483; found 392.0498.

4-(4-Methylbenzoyl)-3-(4-methylphenyl)-1-phenylpyrazole (18l)

The same procedure as above was carried out using the alcohol **20b** (60 mg, 0.17 mmol) to give the pyrazole **18l** (43 mg, 72%) as a yellow solid. mp 161–163 °C (EtOAc-hexane). IR (ATR) $\nu = 1631 \text{ cm}^{-1}$. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 2.35 (3H, s), 2.41 (3H, s), 7.16 (2H, d, $J = 8.1 \text{ Hz}$), 7.22 (2H, d, $J = 8.4 \text{ Hz}$), 7.35 (1H, t, $J = 7.5 \text{ Hz}$), 7.49 (2H, t, $J = 7.5 \text{ Hz}$), 7.65 (2H, d, $J = 8.1 \text{ Hz}$), 7.78 (4H, d, $J = 8.4 \text{ Hz}$), 8.23 (1H, s). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 21.3, 21.6, 119.5, 121.1, 127.3, 128.6, 128.9, 129.0, 129.2, 129.6, 129.7, 132.0, 136.3, 138.4, 139.3, 143.4, 153.9, 189.7. MS m/z : 352 (M^+). HRMS (EI): calcd for $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}$ 352.1576; found 352.1588.

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