

**SCOPE AND LIMITATIONS IN THE REGIOSELECTIVE SYNTHESIS OF 1,3,5-TRISUBSTITUTED PYRAZOLES FROM  $\beta$ -AMINO ENONES AND HYDRAZINE DERIVATIVES.  $^{13}\text{C}$ -CHEMICAL SHIFT PREDICTION RULES FOR 1,3,5-TRISUBSTITUTED PYRAZOLES**

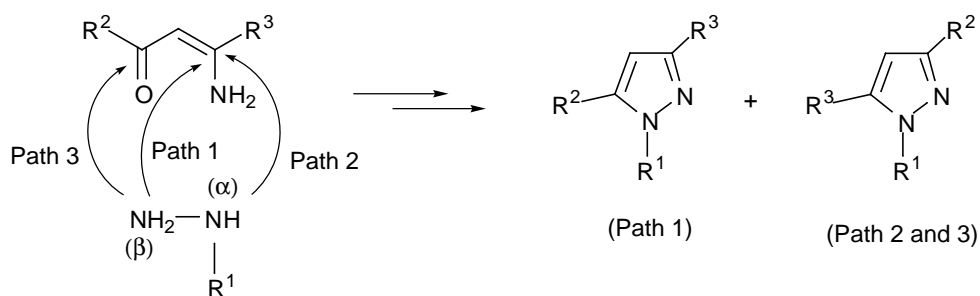
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**Abstract** -  $\beta$ -Amino enones react with hydrazine derivatives to give regioselectively 1,3,5-trisubstituted pyrazoles. The synthetic method only presents limitations when the  $\beta$ -substituent of the enone and the hydrazine substituent are bulky or possess an electron withdrawing character. Comparison of the  $^{13}\text{C}$ -NMR spectra of the seventy pyrazoles allowed us to estimate a  $^{13}\text{C}$ -chemical shift prediction rule for 1,3,5-trisubstituted pyrazoles, with deviations of less than  $\pm 1$  ppm.

## SYNTHESIS

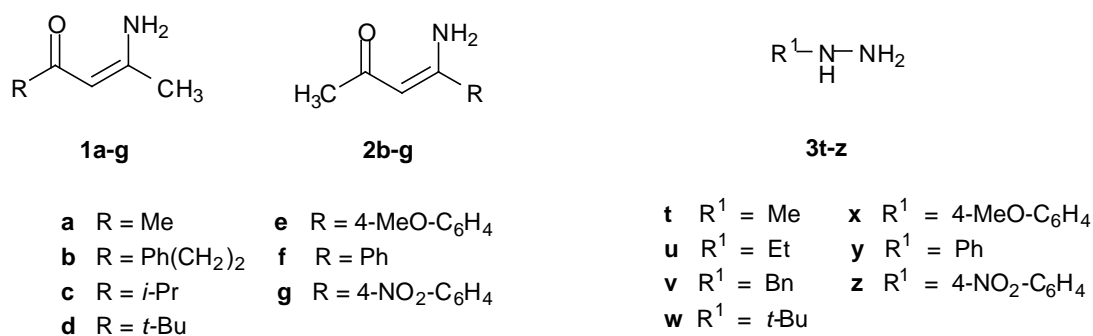
In a previous paper<sup>1</sup> on the regioselective synthesis of pyrazoles, starting from alkyl  $\beta$ -amino enones and alkyhydrazines, we described the competition between the predictable mechanisms which lead to mixtures of regioisomer pyrazoles (Scheme 1). We confirmed that the process evolved preferably by an initial conjugated addition of hydrazine nitrogen N $\beta$  to the enone and subsequent cyclization to pyrazole (Path 1).



**Scheme 1**

We have now widened and complemented our study with more varied and numerous substrates, summarising the empirical observations concerning reactivity and regioselectivity in a straightforward way. From the information obtained, general experimental procedures are suggested for obtaining the maximum chemical yield of the expected pyrazole. We also outline the limitations of the synthetic method.

The  $\beta$ -amino enones studied have been ordered and tabulated in two regioisomer series (Series 1 and 2, Scheme 2). Both reacted toward alkyl substituted hydrazines with different steric hindrance ( $R^1 = \text{Me, Et, Bn, } i\text{-Pr and } t\text{-Bu}$ ), or aryl substituents bearing different electron withdrawing groups ( $R^1 = 4\text{-MeO-C}_6\text{H}_4, \text{Ph, } 4\text{-NO}_2\text{-C}_6\text{H}_4$ ). The series 2, with the aryl group or the more bulky alkyl substituent in  $C\beta$ , was the most interesting, given that it led in the majority of cases to those pyrazoles which can not be obtained starting from their  $\beta$ -dicarbonylic equivalent.<sup>2-4</sup> The results outlined in Tables 1 and 2 show only the optimum experimental conditions.

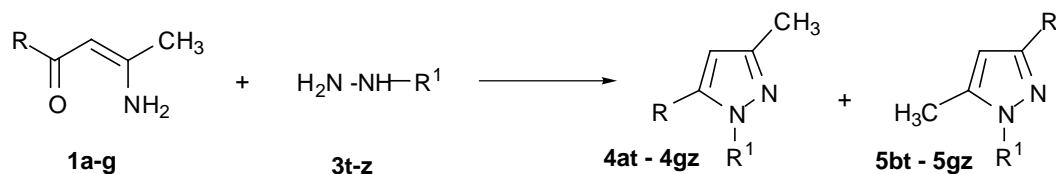


### Scheme 2

The success of the synthetic method was dependent upon various factors. Among the most relevant were the solvent utilised, the acid catalysis and the nature of the  $R^1$  and R substituents.

Dimethyl sulfoxide was the most appropriate solvent in the reactions of alkyl  $\beta$ -amino enones with alkyldiazines while in the remaining cases ethanol led to similar or better results.

The catalysis with acetic or hydrochloric acid, which is normally employed to accelerate the reaction,<sup>1,5</sup> conditioned the regioselectivity of the process. The methylhydrazine, which inverted its regiochemistry depending on the acid used, was the reagent which best allowed us to formulate a hypothesis concerning the influence of the acidity on the reaction mechanism. In acetic acid/ethanol the protonation of the hydrazine nitrogens<sup>6,7</sup> is not produced and the  $N\alpha$  atom would act as an initial nucleophile (Path 2, Scheme 1) which possesses a reduced steric hindrance. In hydrochloric acid/ethanol, the more basic  $N\alpha$  is protonated and  $N\beta$  would act as a nucleophile in the initial conjugated addition (Path 1, Scheme 1). The participation of path 2 in acetic acid medium decreased rapidly with the size and withdrawing character of

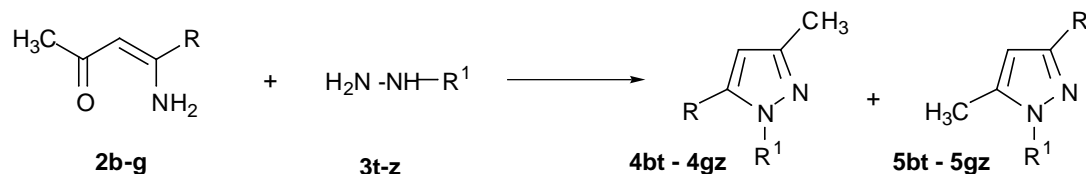
**Table 1.** Preparation of pyrazoles (**4**) from  $\beta$ -amino enones (**1a-g**) (Series 1) and hydrazine derivatives.

Entry	Starting	R	R <sup>1</sup>	<b>1</b> : <b>3</b>	Solvent	Catalyst	T/°C	t/h	<b>4</b> : <b>5</b> (%) <sup>a</sup>	Pyrazole (%) <sup>b</sup>
1	<b>1a + 3t</b>	Me	Me	1 : 1.1	EtOH	AcOH	20	24	- <sup>f</sup>	<b>4at</b> (71)
2	<b>1a + 3u</b>	Me	Et <sup>c</sup>	1 : 1.1	EtOH	AcOH	20	24	- <sup>f</sup>	<b>4au</b> (70)
3	<b>1a + 3v</b>	Me	Bn <sup>c</sup>	1 : 1.1	EtOH	AcOH	20	24	- <sup>f</sup>	<b>4av</b> (78)
4	<b>1a + 3w</b>	Me	<i>t</i> -Bu <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	24	- <sup>f</sup>	<b>4aw</b> (80)
5	<b>1a + 3x</b>	Me	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.2	EtOH	-	78	1	- <sup>f</sup>	<b>4ax</b> (90)
6	<b>1a + 3y</b>	Me	Ph <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	1	- <sup>f</sup>	<b>4ay</b> (91)
7	<b>1a + 3z</b>	Me	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 1.2	EtOH	AcOH	20	24	- <sup>f</sup>	<b>4az</b> (92)
8	<b>1b + 3t</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	Me	1 : 1.2	DMSO	-	80	12	1 : - <sup>e</sup> (93)	<b>4bt</b> (81)
9	<b>1b + 3u</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	Et <sup>c</sup>	1 : 1.2	EtOH	HCl	20	24	8 : 1 (95)	<b>4bu</b> (78)
10	<b>1b + 3v</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	Bn <sup>c</sup>	1 : 1.2	DMSO	-	20	2	1 : - <sup>e</sup> (95)	<b>4bv</b> (83)
11	<b>1b + 3w</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	<i>t</i> -Bu <sup>d</sup>	1 : 1.2	DMSO	-	37	72	1 : - <sup>e</sup> (93)	<b>4bw</b> (78)
12	<b>1b + 3x</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	48	1 : - <sup>e</sup> (72)	<b>4bx</b> (62)
13	<b>1b + 3y</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	Ph <sup>d</sup>	1 : 1.4	DMSO	-	20	48	1 : - <sup>e</sup> (95)	<b>4by</b> (79)
14	<b>1c + 3t</b>	<i>i</i> -Pr	Me	1 : 1.2	DMSO	-	80	16	1 : - <sup>e</sup> (92)	<b>4ct</b> (84)
15	<b>1c + 3v</b>	<i>i</i> -Pr	Bn <sup>c</sup>	1 : 1.2	DMSO	-	20	2	1 : - <sup>e</sup> (97)	<b>4cv</b> (83)
16	<b>1c + 3w</b>	<i>i</i> -Pr	<i>t</i> -Bu <sup>d</sup>	1 : 1.2	DMSO	-	60	48	1 : - <sup>e</sup> (95)	<b>4cw</b> (86)
17	<b>1c + 3x</b>	<i>i</i> -Pr	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	48	1 : - <sup>e</sup> (95)	<b>4cx</b> (83)
18	<b>1c + 3y</b>	<i>i</i> -Pr	Ph <sup>d</sup>	1 : 1.2	EtOH	HCl	20	24	1 : - <sup>e</sup> (90)	<b>4cy</b> (78)
19	<b>1c + 3z</b>	<i>i</i> -Pr	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 1.2	EtOH	HCl	20	24	1 : - <sup>e</sup> (88)	<b>4cz</b> (72)
20	<b>1d + 3t</b>	<i>t</i> -Bu	Me	1 : 1.2	DMSO	-	80	16	1 : - <sup>e</sup> (86)	<b>4dt</b> (72)
21	<b>1d + 3v</b>	<i>t</i> -Bu	Bn <sup>c</sup>	1 : 1.2	DMSO	-	20	2	1 : - <sup>e</sup> (98)	<b>4dv</b> (86)
22	<b>1d + 3w</b>	<i>t</i> -Bu	<i>t</i> -Bu <sup>d</sup>	1 : 1.2	DMSO	-	37	150	1 : - <sup>e</sup> (78)	<b>4dw</b> (86)
23	<b>1d + 3x</b>	<i>t</i> -Bu	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	48	1 : - <sup>e</sup> (98)	<b>4dx</b> (87)
24	<b>1d + 3y</b>	<i>t</i> -Bu	Ph <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	8	1 : - <sup>e</sup> (92)	<b>4dy</b> (79)
25	<b>1d + 3z</b>	<i>t</i> -Bu	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 1.2	EtOH	AcOH	20	48	1 : - <sup>e</sup> (98)	<b>4dz</b> (85)
26	<b>1e + 3t</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	Me	1 : 1.2	EtOH	AcOH	20	24	1 : 2.2 (96)	<b>5et</b> (51)
27	<b>1e + 3u</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	Me	1 : 1.2	EtOH	HCl	20	24	4 : 1 (94)	<b>4et</b> (61)
28	<b>1e + 3v</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	Bn <sup>c</sup>	1 : 1.1	EtOH	HCl	20	24	1 : - <sup>e</sup> (99)	<b>4ev</b> (96)
29	<b>1e + 3w</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	<i>t</i> -Bu <sup>d</sup>	1 : 1.1	EtOH	AcOH	20	48	1 : - <sup>e</sup> (98)	<b>4ew</b> (92)
30	<b>1e + 3x</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.1	EtOH	AcOH	20	24	1 : - <sup>e</sup> (97)	<b>4ex</b> (89)
31	<b>1e + 3y</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	Ph <sup>d</sup>	1 : 1.1	EtOH	AcOH	20	24	1 : - <sup>e</sup> (98)	<b>4ey</b> (91)
32	<b>1e + 3z</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 1.1	EtOH	AcOH	20	24	1 : - <sup>e</sup> (96)	<b>4ez</b> (90)
33	<b>1f + 3t</b>	Ph	Me	1 : 1.2	EtOH	AcOH	20	48	1 : 4 (93)	<b>5ft</b> (57)
34	<b>1f + 3u</b>	Ph	Me	1 : 1.2	EtOH	HCl	20	48	1 : - <sup>e</sup> (91)	<b>4ft</b> (82)
35	<b>1f + 3v</b>	Ph	Bn <sup>c</sup>	1 : 1.2	EtOH	HCl	20	48	1 : - <sup>e</sup> (90)	<b>4fv</b> (81)
36	<b>1f + 3w</b>	Ph	<i>t</i> -Bu <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	48	1 : - <sup>e</sup> (95)	<b>4fw</b> (87)
37	<b>1f + 3x</b>	Ph	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	24	1 : - <sup>e</sup> (98)	<b>4fx</b> (89)
38	<b>1f + 3y</b>	Ph	Ph <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	24	1 : - <sup>e</sup> (99)	<b>4fy</b> (93)
39	<b>1f + 3z</b>	Ph	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 1.2	EtOH	AcOH	20	48	1 : - <sup>e</sup> (97)	<b>4fz</b> (90)
40	<b>1g + 3t</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	1 : 1.1	EtOH	AcOH	20	48	1 : 5.5 (96)	<b>5gt</b> (70)
41	<b>1g + 3u</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	1 : 1.2	EtOH	HCl	20	48	2.5 : 1 (92)	<b>4gt</b> (49)
42	<b>1g + 3v</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Bn <sup>c</sup>	1 : 1.2	EtOH	HCl	20	50	18 : 1 (96)	<b>4gv</b> (76)
43	<b>1g + 3w</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	<i>t</i> -Bu <sup>d</sup>	1 : 2.0	EtOH	AcOH	20	120	1 : - <sup>e</sup> (97)	<b>4gw</b> (95)
44	<b>1g + 3x</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	48	1 : - <sup>e</sup> (96)	<b>4gx</b> (88)
45	<b>1g + 3y</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Ph <sup>d</sup>	1 : 1.2	EtOH	AcOH	20	30	1 : - <sup>e</sup> (93)	<b>4gy</b> (86)
46	<b>1g + 3z</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 1.2	EtOH	AcOH	20	72	1 : - <sup>e</sup> (95)	<b>4gz</b> (90)

<sup>a</sup> Estimated from <sup>1</sup>H-NMR spectra of the crude product. <sup>b</sup> Isolated yield. <sup>c</sup> Oxalate derivative. <sup>d</sup> Hydrochloride derivative. <sup>e</sup> In some cases 0-4% of the regioisomer (**5**) can be detected by <sup>1</sup>H-NMR of the crude product. <sup>f</sup> Pyrazoles (**4at-4az**), without regioisomerism, were prepared exclusively for the elaboration of the <sup>13</sup>C Prediction Rules

R<sup>1</sup>. Thus, it was only observed in low proportion when R<sup>1</sup> = Et or Bn and it was inexistent in bulky alkylhydrazines (*e.g.* R<sup>1</sup> = *t*-Bu) or arylhydrazines (R<sup>1</sup> = aryl) which evolved preferably *via* Path 1 (Scheme 1) in hydrochloric or acetic acid medium.

**Table 2.** Preparation of pyrazoles (**5**) from  $\beta$ -amino enones (**2b-g**) (Series 2) and hydrazine derivatives.



Entry	Starting	R	R <sup>1</sup>	<b>2</b> : <b>3</b>	Solvent	Catalyst	T/°C	t/h	<b>4</b> : <b>5</b> (%) <sup>a</sup>	Pyrazole(%) <sup>b</sup>
47	<b>2b</b> + <b>3t</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	Me	1 : 1.2	DMSO	-	80	16	- <sup>e</sup> : 1 (92)	<b>5bt</b> (81)
48	<b>2b</b> + <b>3u</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	Et <sup>c</sup>	1 : 1.5	EtOH	HCl	20	64	1 : 4.2 (93)	<b>5bu</b> (58)
49	<b>2b</b> + <b>3v</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	Bn <sup>c</sup>	1 : 1.2	DMSO	-	20	20	1 : 6 (91)	<b>5bv</b> (69)
50	<b>2b</b> + <b>3w</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	<i>t</i> -Bu <sup>d</sup>	1 : 3.0	EtOH	AcOH	80	40	- <sup>e</sup> : 1 (86)	<b>5bw</b> (71)
51	<b>2b</b> + <b>3x</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.3	DMSO	AcOH	20	40	1 : 18 (88)	<b>5bx</b> (72)
52	<b>2b</b> + <b>3y</b>	(CH <sub>2</sub> ) <sub>2</sub> Ph	Ph <sup>d</sup>	1 : 1.3	DMSO	AcOH	20	48	1 : 20 (93)	<b>5by</b> (83)
53	<b>2c</b> + <b>3t</b>	<i>i</i> -Pr	Me	1 : 1.2	DMSO	-	80	40	- <sup>e</sup> : 1 (86)	<b>5ct</b> (71)
54	<b>2c</b> + <b>3v</b>	<i>i</i> -Pr	Bn <sup>c</sup>	1 : 1.2	DMSO	-	20	24	1 : 8 (92)	<b>5cv</b> (73)
55	<b>2c</b> + <b>3w</b>	<i>i</i> -Pr	<i>t</i> -Bu <sup>d</sup>	1 : 1.2	DMSO	AcOH	80	48	1 : 6 (89)	<b>5cw</b> (63)
56	<b>2c</b> + <b>3x</b>	<i>i</i> -Pr	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.5	EtOH	AcOH	20	76	1 : 19 (85)	<b>5cx</b> (68)
57	<b>2c</b> + <b>3y</b>	<i>i</i> -Pr	Ph <sup>d</sup>	1 : 1.5	EtOH	AcOH	20	72	1 : 8 (93)	<b>5cy</b> (71)
58	<b>2c</b> + <b>3z</b>	<i>i</i> -Pr	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 1.5	EtOH	AcOH	30	72	-	<b>5cz</b> (0)
59	<b>2d</b> + <b>3t</b>	<i>t</i> -Bu	Me	1 : 1.2	DMSO	-	80	20	1 : 11 (83)	<b>5dt</b> (65)
60	<b>2d</b> + <b>3v</b>	<i>t</i> -Bu	Bn <sup>c</sup>	1 : 1.2	DMSO	-	80	30	1 : 2.4 (85)	<b>5dv</b> (49)
61	<b>2d</b> + <b>3w</b>	<i>t</i> -Bu	<i>t</i> -Bu <sup>d</sup>	1 : 3.0	DMSO	AcOH	60	72	1 : 0 (30)	<b>5dw</b> (0)
62	<b>2d</b> + <b>3x</b>	<i>t</i> -Bu	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 2.0	DMSO	AcOH	50	96	3.4 : 1 (96)	<b>5dx</b> (16)
63	<b>2d</b> + <b>3z</b>	<i>t</i> -Bu	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 2.0	EtOH	AcOH	60	96	1 : 0 (33)	<b>5dz</b> (0)
64	<b>2e</b> + <b>3t</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	Me	1 : 1.1	EtOH	AcOH	20	135	1.5 : 1 (69)	<b>5et</b> (15)
65	<b>2e</b> + <b>3t</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	Me	1 : 1.5	EtOH	HCl	20	135	1 : 5 (60)	<b>5et</b> (38) <sup>f</sup>
66	<b>2e</b> + <b>3v</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	Bn <sup>c</sup>	1 : 1.5	EtOH	AcOH	20	168	1 : 3.3 (93)	<b>5ev</b> (54)
67	<b>2e</b> + <b>3w</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	<i>t</i> -Bu <sup>d</sup>	1 : 2.0	EtOH	AcOH	20	96	-	<b>5ew</b> (0)
68	<b>2e</b> + <b>3x</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	4-MeO-C <sub>6</sub> H <sub>4</sub>	1 : 2.0	EtOH	AcOH	20	72	1 : 5 (91)	<b>5ex</b> (70)
69	<b>2e</b> + <b>3y</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	Ph	1 : 2.0	EtOH	AcOH	20	36	1 : 9 (93)	<b>5ey</b> (81)
70	<b>2e</b> + <b>3z</b>	4-MeO-C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 2.0	EtOH	AcOH	20	48	- <sup>e</sup> : 1 (96)	<b>5ez</b> (89)
71	<b>2f</b> + <b>3t</b>	Ph	Me	1 : 1.2	EtOH	AcOH	20	48	9 : 1 (86)	<b>5ft</b> (-)
72	<b>2f</b> + <b>3t</b>	Ph	Me	1 : 1.2	EtOH	HCl	78	4	1 : 4 (70)	<b>5ft</b> (40) <sup>g</sup>
73	<b>2f</b> + <b>3v</b>	Ph	Bn <sup>c</sup>	1 : 1.5	EtOH	AcOH	20	144	1 : 4 (85)	<b>5fv</b> (57)
74	<b>2f</b> + <b>3w</b>	Ph	<i>t</i> -Bu <sup>d</sup>	1 : 2.0	EtOH	AcOH	20	120	1 : 1 (92)	<b>5fw</b> (35)
75	<b>2f</b> + <b>3x</b>	Ph	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.5	EtOH	AcOH	20	48	1 : 9 (97)	<b>5fx</b> (83)
76	<b>2f</b> + <b>3y</b>	Ph	Ph <sup>d</sup>	1 : 1.5	EtOH	AcOH	20	24	- <sup>e</sup> : 1 (96)	<b>5fy</b> (89)
77	<b>2f</b> + <b>3z</b>	Ph	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 1.5	EtOH	AcOH	20	48	- <sup>e</sup> : 1 (95)	<b>5fz</b> (91)
78	<b>2g</b> + <b>3t</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	1 : 1.5	EtOH	AcOH	20	94	5 : 1 (91)	<b>5gt</b> (-)
79	<b>2g</b> + <b>3t</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	1 : 1.5	EtOH	HCl	20	166	1 : 2.6 (80)	<b>5gt</b> (44) <sup>h</sup>
80	<b>2g</b> + <b>3v</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Bn <sup>c</sup>	1 : 1.5	EtOH	HCl	20	137	1 : 10 (80)	<b>5gv</b> (63)
81	<b>2g</b> + <b>3w</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	<i>t</i> -Bu <sup>d</sup>	1 : 1.5	EtOH	AcOH	20	120	-	<b>5gw</b> (0)
82	<b>2g</b> + <b>3x</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4-MeO-C <sub>6</sub> H <sub>4</sub> <sup>d</sup>	1 : 1.5	EtOH	AcOH	20	53	1 : 20 (95)	<b>5gx</b> (83)
83	<b>2g</b> + <b>3y</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Ph <sup>d</sup>	1 : 2.0	EtOH	AcOH	20	144	1 : 15 (98)	<b>5gy</b> (81)
84	<b>2g</b> + <b>3z</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1 : 2.0	EtOH	AcOH	20	144	1 : 12 (62)	<b>5gz</b> (49)

<sup>a</sup> Estimated from <sup>1</sup>H-NMR spectra of the crude product. <sup>b</sup> Isolated yield. <sup>c</sup> Oxalate derivative. <sup>d</sup> Hydrochloride derivative. <sup>e</sup> In some cases 0-4% of the regioisomer (**4**) can be detected by <sup>1</sup>H-NMR of the crude product. <sup>f</sup> 51% of pyrazole (**5et**) was obtained from **1e**, see entry 26 in Table 1. <sup>g</sup> 57% of pyrazole (**5ft**) was obtained from **1f**, see entry 33 in Table 1. <sup>h</sup> 70% of pyrazole (**5gt**) was obtained from **1g**, see entry 40 in Table 1.

Although theoretically the catalysis with hydrochloric acid should favour the formation of pyrazole (4) from 1 or (5) from 2, there were few instances in which it coincided with the optimum conditions of the synthetic method (See entries 9, 18, 19, 27, 28, 34, 35, 41, 42, 48 and 80 in Tables 1 and 2). The hydrochloric acid partially hydrolysed the  $\beta$ -amino enones to  $\beta$ -diketones and these evolved to the corresponding pyrazoles with less regioselectivity. With the exception of the methylhydrazine, the catalysis with the acetic acid was of more general application than that of the hydrochloric acid.

On the other hand, we observed a large similarity between the reactivity of the substrates and the regiochemistry of the process. Thus, the  $\beta$ -amino enones of series 1, more reactive than their regioisomers, led almost exclusively to the expected pyrazole. In series 2, the rate of reaction and selectivity decreased at the same time as the size of the R and R<sup>1</sup> substituents increased or the steric hindrance of one of them was combined with the withdrawing character of the other. Examples of extreme situations, without synthetic interest due to their low reactivity or lack of regioselectivity, were the experiments corresponding to the entries 58, 61-63, 67, 74 and 81 in Table 2 (R<sup>1</sup> = R-3 = *t*-Bu; R<sup>1</sup> = *t*-Bu, R-3 = Aryl; R<sup>1</sup> = 4-NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>, R-3 = *i*-Pr; R<sup>1</sup> = Aryl, R-3 = *t*-Bu).

### *Synthetic conclusions*

In conclusion, we suggest the following general experimental procedures for the synthesis of 1,3,5-trisubstituted pyrazoles starting from  $\beta$ -amino enones and hydrazine derivatives:

- (a) When all the substituents are alkylic, the most appropriate solvent is dimethyl sulfoxide. If the process is slow, it can be accelerated by gentle heating or by catalysis with acetic acid.
- (b) The dimethyl sulfoxide can be changed for ethanol/acetic acid (5:1) at room temperature when one of the substituents is aromatic (R<sup>1</sup> or R).
- (c) In the reaction of less bulky alkylhydrazines (*e.g.* R<sup>1</sup> = Me, Et) with aromatic  $\beta$ -amino enones the recommended medium is ethanol/hydrochloric acid (5 mL : 50  $\mu$ L) at room temperature.
- (d) In the reactions of  $\beta$ -amino enones which possess the more bulky alkyl or aryl group at C $\beta$  (series 2) - less regioselective than their regioisomers - it is advisable to increase the proportion of hydrazine derivative (1 : 1.2 to 1 : 2 or 1 : 3).
- (e) In the reactions of the previous  $\beta$ -amino enones in section (d), the free hydrazines frequently yield better results than their hydrochloride derivatives.
- (f) The greatest limitations have been presented by the  $\beta$ -amino enones of the series 2. In these cases, the method may not be viable when: (f.1) the R( $\beta$ ) group is very bulky (*e.g.* R = *t*-Bu) and R<sup>1</sup> is also bulky or aromatic; (f.2) the R( $\beta$ ) group is medium size (*e.g.* R = *i*-Pr) and R<sup>1</sup> is a withdrawing aromatic group; (f.3) the R( $\beta$ ) group is aromatic and R<sup>1</sup> is very bulky (*e.g.* R<sup>1</sup> = *t*-Bu).

## <sup>13</sup>C CHEMICAL SHIFT PREDICTION RULES

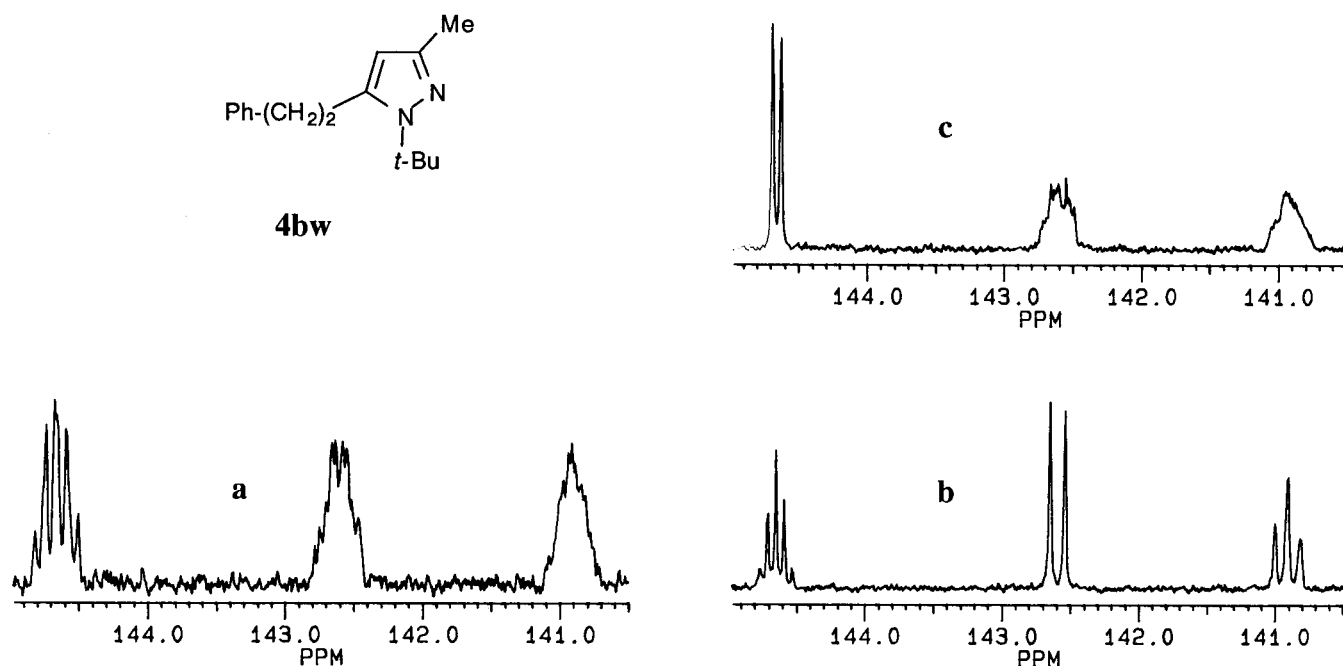
The absence in the literature of <sup>13</sup>C chemical shift prediction rules for substituted pyrazoles is due, fundamentally, to the intense disturbances and modifications provoked by other additional substituents which makes it difficult to quantify and extrapolate the influence ( $Z_{ij}$ ) of a given substituent. However, the high number of pyrazoles synthesized by us, together with the adequate combination of substituents in comparable positions, allowed us to formulate some prediction rules for 1,3,5-trisubstituted pyrazoles (Table 5). In these rules we took as the base the 1,3,5-trimethylpyrazole and not 1-methylpyrazole by cause the substituents  $R_i = \text{Me}$  and not  $R_i = \text{H}$  were the reference available in our collection of seventy compounds.

Firstly, we proceeded to the correct identification of the signal corresponding to <sup>13</sup>C-3 and <sup>13</sup>C-5, which frequently inverted their position in the spectra or they were mistaken for signals of other aromatic substituents. This was carried out by means of <sup>1</sup>H Low-Power Decoupling of <sup>13</sup>C-NMR experiments<sup>8</sup> which correlated an unequivocal <sup>1</sup>H signal with <sup>13</sup>C signal of the nuclei separated by two, three or more bonds. Figure 1 shows the spectra without (**a**) and with (**b**, **c**) decoupling for the 1-*tert*-butyl-3-methyl-5-(2-phenylethyl)pyrazole (**4bw**): **a** is the expanded C-3, C-5 region of the <sup>1</sup>H-coupled <sup>13</sup>C-NMR spectrum. In **b** the protons of the ethylene group at C-5 were irradiated and C-5 was transformed into a doublet with  $^2J_{\text{C}5\text{-H}4} = 7.9$  Hz. In **c** the CH<sub>3</sub>-3 protons were irradiated and in this case C-3 was a doublet with  $^2J_{\text{C}3\text{-H}4} = 4.5$  Hz. The decoupling experiments, together with the NOE experiments, were used for the unequivocal distinction of the pairs of regioisomer pyrazoles.

Starting from the unequivocal  $\delta_{\text{C}3}$ ,  $\delta_{\text{C}4}$  and  $\delta_{\text{C}5}$  (Table 3) the  $Z_{ij}$  were estimated as an average of various comparable situations. Below we give a summary of the methodology employed, taking an initial example the preliminary estimation of  $Z_{55}$ .

For each  $R^5 \neq \text{Me}$  we calculated the difference of the chemical shift ( $\Delta\delta_{55}$ ) of its <sup>13</sup>C-5 with respect to that of a reference pyrazole with  $R^5 = \text{Me}$  and the same  $R^1$  and  $R^3$  (Table 4). The  $\Delta\delta_{55}$  obtained in different compounds were tabulated in rows, the last value corresponding to the average of them. When the experimental data deviated considerably they were not taken into account as regards calculating the average and we incorporated for this situation a final correction. Thus, for example, in the case of  $R^1 = \text{Bu}^t$  the entire column needed a correction of + 2 ppm.

Following a methodology similar to that described for  $\Delta\delta_{55}$ , the remaining  $\Delta\delta_{ij}$ , were estimated with their corresponding corrections. Preliminary prediction rules were formulated which were, later, repeatedly refined until we obtained the minimum deviations between the calculated and experimental values. Of the two hundred and ten shifts calculated with the definitive rules (Table 5), one hundred and ninety seven showed a deviation lower than  $\pm 0.5$  ppm and in only one was it greater than  $\pm 1$  ppm (Table 3). By the

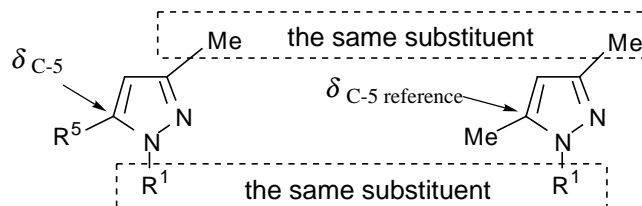


**Figure 1.**  $^1\text{H}$  Low-Power Decoupling of  $^{13}\text{C}$ -NMR spectra through two or more bonds for the 1-*tert*-butyl-3-methyl-5-(2-phenylethyl)pyrazole (**4bw**): (a) without decoupling; (b) with decoupling by irradiation at C5-( $\text{CH}_2$ ) $_2$ ; (c) with decoupling by irradiation at C3- $\text{CH}_3$ .

**Table 3.**  $^{13}\text{C}$ -Chemical shift data ( $\text{CDCl}_3$ ) for C-3, C-4 and C-5 of 1,3,5-trisubstituted pyrazoles (**4at-5gz**).

Pyrazole	Experimental C-3 (Calculated C-3)	Experimental C-4 (Calculated C-4)	Experimental C-5 (Calculated C-5)	Pyrazole	Experimental C-3 (Calculated C-3)	Experimental C-4 (Calculated C-4)	Experimental C-5 (Calculated C-5)
<b>4at</b>	146.82 (146.82)	104.58 (104.58)	138.87 (138.87)	<b>4gt</b>	147.86 (148.14)	106.61 (106.80)	141.86 (141.65)
<b>4av</b>	147.14 (147.34)	105.24 (105.25)	138.82 (139.24)	<b>4gv</b>	148.71 (148.66)	107.29 (107.44)	142.43 (142.02)
<b>4aw</b>	143.22 (143.19)	106.78 (107.21)	136.53 (136.54)	<b>4gw</b>	145.65 (145.91)	109.35 (110.63)	140.80 (141.12)
<b>4ax</b>	147.48 (147.83)	105.67 (105.89)	138.44 (139.33)	<b>4gx</b>	149.45 (149.15)	108.22 (108.11)	141.18 (141.01)
<b>4ay</b>	148.01 (148.41)	106.38 (106.59)	139.41 (139.46)	<b>4gy</b>	149.51 (149.73)	108.65 (108.81)	140.93 (141.14)
<b>4az</b>	150.52 (150.18)	109.13 (108.81)	139.70 (139.89)	<b>4gz</b>	151.53 (151.50)	111.00 (111.03)	141.73 (141.57)
<b>4bt</b>	147.04 (147.21)	103.78 (103.63)	142.85 (143.13)	<b>5bt</b>	150.80 (151.07)	103.80 (104.11)	138.67 (138.75)
<b>4bv</b>	147.52 (147.73)	104.46 (104.30)	143.11 (143.52)	<b>5bv</b>	151.30 (151.59)	104.65 (104.78)	138.90 (139.12)
<b>4bw</b>	144.83 (144.98)	105.88 (106.26)	142.75 (142.62)	<b>5bw</b>	148.97 (148.84)	106.75 (106.74)	138.22 (138.22)
<b>4bx</b>	148.11 (148.22)	104.70 (104.94)	143.32 (143.61)	<b>5bx</b>	152.01 (152.08)	105.12 (105.42)	138.94 (139.21)
<b>4by</b>	148.73 (148.80)	105.41 (105.64)	143.47 (143.74)	<b>5by</b>	152.75 (152.66)	105.99 (106.12)	139.13 (139.34)
<b>4ct</b>	146.98 (146.98)	101.16 (101.12)	149.87 (150.41)	<b>5ct</b>	157.19 (157.73)	101.27 (101.81)	138.00 (138.41)
<b>4cv</b>	147.57 (147.50)	101.82 (101.79)	150.45 (150.78)	<b>5cv</b>	158.25 (158.25)	102.41 (102.48)	138.79 (138.78)
<b>4cw</b>	144.96 (144.75)	103.59 (103.75)	150.95 (150.98)	<b>5cw</b>	155.50 (155.50)	104.30 (104.38)	137.80 (137.88)
<b>4cx</b>	148.10 (147.99)	101.95 (101.93)	151.00 (150.87)	<b>5cx</b>	158.70 (158.74)	103.16 (103.06)	139.04 (138.87)
<b>4cy</b>	148.33 (148.57)	102.36 (102.63)	150.69 (151.00)	<b>5cy</b>	159.35 (159.32)	103.67 (103.76)	138.93 (139.00)
<b>4cz</b>	150.56 (150.34)	104.94 (104.85)	151.53 (151.43)	<b>5dt</b>	160.52 (160.58)	101.45 (101.64)	138.35 (138.44)
<b>4dt</b>	146.08 (145.96)	103.03 (102.94)	151.69 (151.94)	<b>5dv</b>	160.86 (161.10)	102.28 (102.31)	138.47 (138.81)
<b>4dv</b>	147.07 (146.48)	103.33 (103.61)	152.49 (152.31)	<b>5dx</b>	161.66 (161.59)	102.90 (102.95)	138.78 (138.90)
<b>4dw</b>	143.67 (143.73)	106.89 (106.77)	152.86 (152.81)	<b>5et</b>	149.72 (149.86)	101.93 (102.02)	139.60 (139.61)
<b>4dx</b>	146.70 (146.97)	103.06 (102.75)	153.51 (153.60)	<b>5ev</b>	150.13 (150.38)	102.75 (102.69)	139.68 (139.98)
<b>4dy</b>	147.38 (147.55)	103.62 (103.45)	153.86 (153.73)	<b>5ex</b>	150.95 (150.87)	103.33 (103.33)	140.16 (140.07)
<b>4dz</b>	148.41 (149.32)	104.69 (105.67)	154.10 (154.16)	<b>5ey</b>	151.19 (151.45)	103.87 (104.03)	139.95 (140.20)
<b>4et</b>	147.26 (147.62)	105.02 (105.10)	143.98 (143.91)	<b>5ez</b>	152.76 (152.52)	106.32 (106.25)	140.51 (140.63)
<b>4ev</b>	148.05 (148.14)	105.61 (105.77)	144.55 (144.28)	<b>5ft</b>	149.75 (149.99)	102.28 (102.48)	139.45 (139.41)
<b>4ew</b>	145.06 (145.39)	109.09 (108.93)	143.15 (143.38)	<b>5fv</b>	150.19 (150.51)	103.18 (103.15)	139.64 (139.78)
<b>4ex</b>	148.88 (148.63)	106.52 (106.41)	143.40 (143.27)	<b>5fw</b>	147.51 (147.76)	105.25 (105.11)	138.97 (138.88)
<b>4ey</b>	149.23 (149.21)	107.11 (107.11)	143.43 (143.40)	<b>5fx</b>	150.89 (151.00)	103.61 (103.79)	140.08 (139.87)
<b>4ez</b>	151.05 (150.98)	109.40 (109.33)	144.11 (143.83)	<b>5fy</b>	151.48 (151.58)	104.35 (104.49)	140.06 (140.00)
<b>4ft</b>	147.14 (147.54)	105.27 (105.49)	144.00 (144.00)	<b>5fz</b>	152.49 (152.65)	106.35 (106.71)	140.47 (140.43)
<b>4fv</b>	148.03 (148.06)	105.86 (106.16)	144.66 (144.37)	<b>5gt</b>	147.47 (147.67)	103.50 (103.29)	140.47 (140.50)
<b>4fw</b>	145.15 (145.31)	108.94 (109.32)	143.38 (143.47)	<b>5gv</b>	147.86 (148.19)	104.17 (103.96)	140.59 (140.87)
<b>4fx</b>	148.88 (148.55)	107.11 (106.80)	143.56 (143.36)	<b>5gx</b>	148.76 (148.68)	104.60 (104.60)	141.09 (140.96)
<b>4fy</b>	149.31 (149.13)	107.67 (107.50)	143.58 (143.49)	<b>5gy</b>	149.14 (149.26)	105.13 (105.30)	141.00 (141.09)
<b>4fz</b>	150.71 (150.90)	109.59 (109.72)	143.86 (143.92)	<b>5gz</b>	150.43 (150.33)	106.95 (107.52)	141.27 (141.52)

**Table 4.** Estimation of the  $\Delta\delta_{55}$  (preliminary  $Z_{55}$ ).



$\Delta\delta_{55} = \delta_{C-5} - \delta_{C-5 \text{ reference}}$							
$R^5$	$R^1 = \text{Me}$	$R^1 = \text{Bn}$	$R^1 = 4\text{-MeO-C}_6\text{H}_4$	$R^1 = \text{Ph}$	$R^1 = 4\text{-NO}_2\text{-C}_6\text{H}_4$	$\Delta\delta_{55}$	$R^1 = t\text{-Bu}$
Me	0.00	0.00	0.00	0.00	0.00	<b>0.00</b>	0.00
$\text{C}_6\text{H}_5(\text{CH}_2)_2$	3.88	4.29	4.88	4.06	-	<b>4.28</b>	6.22
<i>i</i> -Pr	11.10	11.63	11.87	11.28	11.83	<b>11.54</b>	14.42
<i>t</i> -Bu	12.82	13.67	15.07	14.45	14.40	<b>14.07</b>	16.37
4-MeO-C <sub>6</sub> H <sub>4</sub>	5.11	5.73	4.96	4.02	4.41	<b>4.84</b>	6.62
Ph	5.13	5.84	5.12	4.17	4.16	<b>4.88</b>	6.85
4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	2.99	3.61	2.74	1.52	2.03	<b>2.58</b>	4.27
							Correction + 2.00

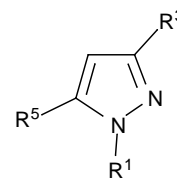
**Table 5.** <sup>13</sup>C Chemical shift prediction rules for 1,3,5-trisubstituted pyrazoles.

General Equation:  $\delta_{C-j} = \text{base} + \sum Z_{ij} + C$

$$\delta_{C-3} = 146.82 + \sum Z_{i3} + C$$

$$\delta_{C-4} = 104.58 + \sum Z_{i4} + C$$

$$\delta_{C-5} = 138.87 + \sum Z_{i5} + C$$



base:  $\delta_{C-3}$ ,  $\delta_{C-4}$  and  $\delta_{C-5}$  for the 1,3,5-trimethylpyrazole

$Z_{ij}$ : Influence on  $\delta_{C-j}$  chemical shift of the substituent  $R^i$

C: Corrections

$Z_{1j}$				$Z_{3j}$			
$R^1$ ( $i=1$ )	$Z_{13}$	$Z_{14}$	$Z_{15}$	$R^3$ ( $i=3$ )	$Z_{33}$	$Z_{34}$	$Z_{35}$
Me	0.00	0.00	0.00	Me	0.00	0.00	0.00
Bn	0.52	0.67	0.37	Ph(CH <sub>2</sub> ) <sub>2</sub>	4.25	-0.47	-0.12
<i>t</i> -Bu	-2.23	2.63	-0.53	<i>i</i> -Pr	10.91	-2.77	-0.46
4-MeO-C <sub>6</sub> H <sub>4</sub>	1.01	1.31	0.46	<i>t</i> -Bu	13.76	-2.94	-0.43
Ph	1.59	2.01	0.59	4-MeO-C <sub>6</sub> H <sub>4</sub>	3.04	-2.56	0.74
4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	3.36	4.23	1.02	Ph	3.17	-2.10	0.54
				4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	0.85	-1.29	1.63

$Z_{5j}$				$C$			
$R^5$ ( $i=5$ )	$Z_{53}$	$Z_{54}$	$Z_{55}$	Corrections		$C$	
Me	0.00	0.00	0.00	$R^1$	$\Delta\delta_{C-3}$	$\Delta\delta_{C-4}$	$\Delta\delta_{C-5}$
Ph(CH <sub>2</sub> ) <sub>2</sub>	0.39	-0.95	4.28	<i>t</i> -Bu	-1.4 ( $R^3 = R^5 = \text{Me}$ )	1.2 ( $R^5 = t\text{-Bu, Ar}$ )	1.4 ( $R^5 = t\text{-Bu}$ ) 1.1 ( $R^5 = i\text{-Pr}$ ) -1.8 ( $R^3 = R^5 = \text{Me}$ )
<i>i</i> -Pr	0.16	-3.46	11.54	Ar		-0.5 ( $R^5 = i\text{-Pr}$ ) -1.5 ( $R^5 = t\text{-Bu}$ )	-1.1 ( $R^5 = \text{Ar}$ ) 1.2 ( $R^5 = t\text{-Bu}$ )
<i>t</i> -Bu	-0.86	-1.64	13.07	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	-0.7 ( $R^3 = \text{Ar}$ )		
4-MeO-C <sub>6</sub> H <sub>4</sub>	0.80	0.52	5.04				
Ph	0.72	0.91	5.13				
4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	1.32	2.22	2.78				



methodology which the  $Z_{ij}$  were estimated these can not be directly extrapolated to mono- or disubstituted pyrazoles, although they can serve as a starting point for wider research with greater variety as regards the nature and position of the substituents.

Apart from our objective with respect to prediction rules, we should point out that the provisional tables (e.g. Table 4) and the definitive Table 5 can provide interesting and abundant information concerning the paramagnetic and diamagnetic effects of the substituents and, as a consequence, a systematic empirical data base for theoretical calculations.

## EXPERIMENTAL

Melting points were measured on a Reichert-Jung Thermo Galen and are uncorrected. Boiling points correspond to the oven temperature in a Kugelrohr GKR-51.  $^1\text{H-NMR}$  spectra were recorded on a Bruker AC300 spectrometer, and chemical shifts are given downfield from  $\text{SiMe}_4$  as an internal standard;  $^{13}\text{C-NMR}$  spectra were carried out with complete  $^1\text{H}$  decoupling and the assignments were made by additional DEPT experiments. MS spectra were measured on a Hewlett-Packard 5988A mass spectrometer.

Starting compounds were prepared as previously described. Synthesis of **1a**, **1f**, and **1g** involves the condensation of ammonia with  $\beta$ -diketones.<sup>9</sup>  $\beta$ -Amino enones (**1b-e**, **2b-f**) were obtained by catalytic hydrogenation<sup>10-12</sup> of 3,5-disubstituted isoxazoles: these were prepared regioselectively by the procedure of Nitz *et al.*<sup>13</sup> from oximes and *N*-methoxy-*N*-methylalkylamides. Nitration of the 5-methyl-3-phenylisoxazole to the 5-methyl-3-(4-nitrophenyl)isoxazole and subsequent opening with  $\text{Mo}(\text{CO})_6$ <sup>14</sup> yielded the  $\beta$ -amino enone (**2g**).

### Reaction of $\beta$ -amino enones with hydrazine derivatives. Synthesis of 1,3,5-trisubstituted pyrazoles.

A mixture of  $\beta$ -amino enone (2.8 mmol) and hydrazine derivative (3.4 mmol) in 5 mL of the solvent, were stirred in the conditions given in Tables 1 and 2 (50  $\mu\text{L}$  of  $\text{HCl}$  or 1 mL of  $\text{AcOH}$ , is added when an acid is employed as catalyst). The solution was poured into water (20 mL) and extracted with methylene dichloride (3 x 20 mL). The organic layer was dried over anhydrous magnesium sulfate and the solvent was removed *in vacuo*. The residue was purified by recrystallization from hexane-toluene (**4at**, **4bt**, **4bw**, **4cy**, **4cz**, **4ex**, **4ey**, **4fv**, **4fy**, **5bt**), recrystallization from methanol (**4az**, **4dx**, **4dy**, **4dz**, **4ew**, **4ez**, **4fx**, **4fz**, **4gw**, **4gx**, **4gy**, **4gz**, **5ez**, **5fy**, **5fz**, **5gx**), distillation (**4au**, **4av**, **4aw**, **4ax**, **4ay**, **4ct**, **4cv**, **4cw**, **4cx**, **4dv**, **4ev**) or chromatographed on silica gel with methylene dichloride or methylene dichloride-diethyl ether (20 : 1) as eluents (**4bu**, **4bv**, **4bx**, **4by**, **4dt**, **4dw**, **4et**, **4ft**, **4fw**, **4gt**, **4gv**, **5bu-5by**, **5ct-5cy**, **5dt-5dx**,

**5et-5ey, 5ft-5fx, 5gt, 5gv, 5gy, 5gz).**

**1,3,5-Trimethylpyrazole (4at).** Yield 71% (Table 1), mp 36 °C (lit.,<sup>15</sup> mp 36-37 °C);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.16 (6H, s), 3.65 (3H, s) and 5.74 (1H, s);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 10.9 (CH<sub>3</sub>), 13.2 (CH<sub>3</sub>), 35.4 (CH<sub>3</sub>), 104.6 (CH), 138.9 (C) and 146.8 (C);  $m/z$  110 (M<sup>+</sup>, 100%).

**3,5-Dimethyl-1-ethylpyrazole (4au).** Yield 70% (Table 1), bp 75 °C at 30 mmHg (lit.,<sup>16</sup> bp 72 °C at 20 mmHg);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 1.36 (3H, t,  $J$  7.2), 2.21 (6H, s), 4.00 (2H, q,  $J$  7.2) and 5.77 (1H, s);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 10.6 (CH<sub>3</sub>), 13.2 (CH<sub>3</sub>), 15.3 (CH<sub>3</sub>), 43.2 (CH<sub>2</sub>), 104.6 (CH), 137.8 (C) and 146.8 (C);  $m/z$  124 (M<sup>+</sup>, 100%).

**1-Benzyl-3,5-dimethylpyrazole (4av).** Yield 78% (Table 1), bp 140-142 °C at 10 mmHg (lit.,<sup>17</sup> bp 154-156 °C at 18 mmHg);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.11 (3H, s), 2.25 (3H, s), 5.19 (2H, s), 5.84 (1H, s) and 7.05-7.30 (5H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 10.8 (CH<sub>3</sub>), 13.3 (CH<sub>3</sub>), 52.3 (CH<sub>2</sub>), 105.3 (CH), 126.2 (2CH), 127.1 (CH), 128.4 (2CH), 137.1 (C), 138.8 (C) and 147.1 (C);  $m/z$  186 (M<sup>+</sup>, 42%) and 91 (100).

**1-tert-Butyl-3,5-dimethylpyrazole (4aw).** Yield 80% (Table 1), bp 66-68 °C at 11 mmHg;  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 1.30 (9H, s), 1.88 (3H, s), 2.06 (3H, s) and 5.44 (1H, s);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 12.4 (CH<sub>3</sub>), 13.3 (CH<sub>3</sub>), 29.0 (3CH<sub>3</sub>), 57.7 (C), 106.8 (CH), 136.5 (C) and 143.2 (C);  $m/z$  152 (M<sup>+</sup>, 42%) and 96 (100). Anal. Calcd for C<sub>9</sub>H<sub>16</sub>N<sub>2</sub>: C, 71.01; H, 10.59; N, 18.40. Found: C, 70.83; H, 10.65; N, 18.52.

**3,5-Dimethyl-1-(4-methoxyphenyl)pyrazole (4ax).** Yield 90% (Table 1), bp 108-110 °C at 0.1 mmHg (lit.,<sup>18</sup> hydrochloride derivative mp 131-136 °C);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.18 (3H, s), 2.25 (3H, s), 3.72 (3H, s), 5.89 (1H, s), 6.87 (2H, d,  $J$  8.8) and 7.26 (2H, d,  $J$  8.8);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 11.4 (CH<sub>3</sub>), 12.8 (CH<sub>3</sub>), 54.6 (CH<sub>3</sub>), 105.7 (CH), 113.3 (2CH), 125.5 (2CH), 132.5 (C), 138.4 (C), 147.5 (C) and 158.0 (C);  $m/z$  202 (M<sup>+</sup>, 100%). Anal. Calcd for C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>O: C, 71.26; H, 6.98; N, 13.85. Found: C, 71.31; H, 6.95; N, 13.79.

**3,5-Dimethyl-1-phenylpyrazole (4ay).** Yield 91% (Table 1), bp 76-78 °C at 0.1 mmHg (lit.,<sup>19</sup> bp 114-118 °C at 1.2 mmHg);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.28 (3H, s), 2.29 (3H, s), 5.99 (1H, s) and 7.37-7.43 (5H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 11.7 (CH<sub>3</sub>), 12.8 (CH<sub>3</sub>), 106.4 (CH), 123.9 (2CH), 126.4 (CH), 128.2 (2CH), 138.4 (C), 139.4 (C) and 148.0 (C);  $m/z$  172 (M<sup>+</sup>, 100%).

**3,5-Dimethyl-1-(4-nitrophenyl)pyrazole (4az).** Yield 92% (Table 1), mp 101-103 °C (lit.,<sup>20</sup> mp 101-102.5 °C);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.26 (3H, s), 2.40 (3H, s), 6.05 (1H, s), 7.6 (2H, m) and 8.28 (2H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 12.9 (CH<sub>3</sub>), 13.2 (CH<sub>3</sub>), 109.1 (CH), 123.1 (2CH), 124.4 (2CH), 139.7 (C), 144.7 (C), 145.2 (C) and 150.5 (C);  $m/z$  217 (M<sup>+</sup>, 100%).

**1,3-Dimethyl-5-(2-phenylethyl)pyrazole (4bt).** Yield 81% (Table 1), mp 81-82 °C (lit.,<sup>1</sup> mp 81-82 °C);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.22 (3H, s), 2.88 (4H, m, A<sub>2</sub>B<sub>2</sub>), 3.58 (3H, s), 5.83 (1H, s) and 7.15-7.32 (5H, m);

$\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 13.5 (CH<sub>3</sub>), 27.7 (CH<sub>2</sub>), 35.1 (CH<sub>2</sub>), 35.5 (CH<sub>3</sub>), 103.8 (CH), 126.3 (CH), 128.3 (2CH), 128.5 (2CH), 140.7 (C), 142.8 (C) and 147.0 (C);  $m/z$  200 (M<sup>+</sup>, 23%) and 109 (100).

**1-Ethyl-3-methyl-5-(2-phenylethyl)pyrazole (4bu).** Yield 78% (Table 1), bp 155 °C at 2 mmHg;  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 1.29 (3H, t,  $J$  7.1), 2.22 (3H, s), 2.83 (4H, m, A<sub>2</sub>B<sub>2</sub>), 3.88 (2H, q,  $J$  7.1), 5.80 (1H, s) and 7.13-7.28 (5H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 13.1 (CH<sub>3</sub>), 15.2 (CH<sub>3</sub>), 27.0 (CH<sub>2</sub>), 34.7 (CH<sub>2</sub>), 42.8 (CH<sub>2</sub>), 103.2 (CH), 125.8 (CH), 127.8 (2CH), 128.1 (2CH), 140.3 (C), 141.6 (C) and 146.6 (C);  $m/z$  214 (M<sup>+</sup>, 15%) and 123 (100). Anal. Calcd for C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>: C, 78.46; H, 8.47; N, 13.07. Found: C, 78.48; H, 8.51; N, 13.01.

**1-Benzyl-3-methyl-5-(2-phenylethyl)pyrazole (4bv).** Yield 83% (Table 1), bp 160-163 °C at 0.4 mmHg (lit.,<sup>1</sup> bp 160-163 °C at 0.4 mmHg);  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 2.27 (3H, s), 2.77 (4H, m, A<sub>2</sub>B<sub>2</sub>), 5.14 (2H, s), 5.90 (1H, s) and 7.01-7.30 (10H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 13.5 (CH<sub>3</sub>), 27.4 (CH<sub>2</sub>), 34.8 (CH<sub>2</sub>), 52.5 (CH<sub>2</sub>), 104.5 (CH), 126.2 (CH), 126.4 (2CH), 127.4 (CH), 128.2 (2CH), 128.4 (2CH), 128.6 (2CH), 137.4 (C), 140.6 (C), 143.1 (C) and 147.5 (C);  $m/z$  276 (M<sup>+</sup>, 7%) and 91 (100).

**1-tert-Butyl-3-methyl-5-(2-phenylethyl)pyrazole (4bw).** Yield 78% (Table 1), mp 87-89 °C (lit.,<sup>1</sup> mp 87-89 °C);  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 1.61 (9H, s), 2.23 (3H, s), 3.01 (4H, m, A<sub>2</sub>B<sub>2</sub>), 5.95 (1H, s) and 7.22-7.34 (5H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 13.6 (CH<sub>3</sub>), 30.2 (CH<sub>2</sub>), 30.4 (3CH<sub>3</sub>), 35.6 (CH<sub>2</sub>), 59.1 (C), 105.9 (CH), 126.2 (CH), 128.2 (2CH), 128.5 (2CH), 141.1 (C), 142.7 (C) and 144.8 (C);  $m/z$  242 (M<sup>+</sup>, 6%) and 95 (100).

**1-(4-Methoxyphenyl)-3-methyl-5-(2-phenylethyl)pyrazole (4bx).** Yield 62% (Table 1), bp 230-232 °C at 1 mmHg;  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 2.29 (3H, s), 2.83 (4H, s), 3.74 (3H, s), 6.00 (1H, s) and 6.88-7.22 (9H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 13.3 (CH<sub>3</sub>), 27.8 (CH<sub>2</sub>), 34.8 (CH<sub>2</sub>), 55.1 (CH<sub>3</sub>), 104.7 (CH), 113.8 (2CH), 125.9 (CH), 126.6 (2CH), 128.0 (2CH), 128.1 (2CH), 132.6 (C), 140.5 (C), 143.3 (C) 148.1 (C) and 158.7 (C);  $m/z$  292 (M<sup>+</sup>, 47%) and 201 (100). Anal. Calcd for C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O: C, 78.06; H, 6.89; N, 9.58. Found: C, 77.99; H, 6.94; N, 9.62.

**3-Methyl-1-phenyl-5-(2-phenylethyl)pyrazole (4by).** Yield 79% (Table 1), bp 248-249 °C at 10 mmHg;  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 2.31 (3H, s), 2.87 (4H, m, A<sub>2</sub>B<sub>2</sub>), 6.04 (1H, s) and 7.05-7.41 (10H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 13.4 (CH<sub>3</sub>), 28.1 (CH<sub>2</sub>), 35.0 (CH<sub>2</sub>), 105.4 (CH), 125.2 (2CH), 126.1 (CH), 127.5 (CH), 128.1 (2CH), 128.3 (2CH), 128.9 (2CH), 139.6 (C), 140.5 (C) 143.5 (C) and 148.7 (C);  $m/z$  262 (M<sup>+</sup>, 39%) and 171 (100). Anal. Calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>: C, 82.40; H, 6.92; N, 10.68. Found: C, 82.41; H, 6.88; N, 10.71.

**1,3-Dimethyl-5-isopropylpyrazole (4ct).** Yield 84% (Table 1), bp 75-78 °C at 5.5 mmHg (lit.,<sup>1</sup> bp 75-78 °C at 5.5 mmHg);  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 1.23 (6H, d,  $J$  6.9), 2.22 (3H, s), 2.88 (1H, m,  $J$  6.9), 3.74 (3H, s) and 5.80 (1H, s);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 13.4 (CH<sub>3</sub>), 22.3 (2CH<sub>3</sub>), 25.4 (CH), 35.6 (CH<sub>3</sub>), 101.2 (CH),

147.0 (C) and 150.0 (C);  $m/z$  138 ( $M^+$ , 26%) and 123 (100).

**1-Benzyl-5-isopropyl-3-methylpyrazole (4cv).** Yield 83% (Table 1), bp 105-110 °C at 0.3 mmHg (lit.,<sup>1</sup> bp 105-110 °C at 0.3 mmHg);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.12 (6H, d,  $J$  6.8), 2.26 (3H, s), 2.80 (1H, m,  $J$  6.8), 5.25 (2H, s), 5.87 (1H, s) and 7.02-7.30 (5H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.6 ( $CH_3$ ), 22.9 (2 $CH_3$ ), 25.3 (CH), 52.3 ( $CH_2$ ), 101.8 (CH), 126.3 (2CH), 127.3 (CH), 128.6 (2CH), 137.9 (C), 147.6 (C) and 150.5 (C);  $m/z$  214 ( $M^+$ , 11%) and 91 (100).

**1-tert-Butyl-5-isopropyl-3-methylpyrazole (4cw).** Yield 86% (Table 1), bp 90-92 °C at 2 mmHg (lit.,<sup>1</sup> bp 90-92 °C at 2 mmHg);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.25 (6H, d,  $J$  6.8), 1.63 (9H, s), 2.21 (3H, s), 3.32 (1H, m,  $J$  6.8) and 5.91 (1H, s);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.6 ( $CH_3$ ), 24.5 (2 $CH_3$ ), 26.9 (CH), 30.7 (3 $CH_3$ ), 59.0 (C), 103.6 (CH), 145.0 (C) and 150.9 (C);  $m/z$  180 ( $M^+$ , 11%) and 109 (100).

**5-Isopropyl-1-(4-methoxyphenyl)-3-methylpyrazole (4cx).** Yield 83% (Table 1), bp 130-132 °C at 1 mmHg;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.11 (6H, d,  $J$  6.9), 2.26 (3H, s), 2.88 (1H, m,  $J$  6.9) 3.78 (3H, s), 5.94 (1H, s), 6.91 (2H, d,  $J$  8.9) and 7.26 (2H, d,  $J$  8.9);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.4 ( $CH_3$ ), 22.7 (2 $CH_3$ ), 25.2 (CH), 55.2 ( $CH_3$ ), 101.9 (CH), 113.9 (2CH), 127.1 (2CH), 132.9 (C), 148.1 (C), 151.0 (C) and 158.9 (C);  $m/z$  230 ( $M^+$ , 73%) and 215 (100). Anal. Calcd for  $C_{14}H_{18}N_2O$ : C, 73.01; H, 7.88; N, 12.16. Found: C, 73.06; H, 7.83; N, 12.19.

**5-Isopropyl-3-methyl-1-phenylpyrazole (4cy).** Yield 78% (Table 1), mp 66-68 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.15 (6H, d,  $J$  6.7), 2.29 (3H, s), 3.00 (1H, m,  $J$  6.7), 5.98 (1H, s) and 7.28-7.43 (5H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.2 ( $CH_3$ ), 22.6 (2 $CH_3$ ), 25.1 (CH), 102.4 (CH), 125.5 (2CH), 127.4 (CH), 128.7 (2CH), 139.8 (C), 148.3 (C) and 150.7 (C);  $m/z$  200 ( $M^+$ , 61%) and 185 (100). Anal. Calcd for  $C_{13}H_{16}N_2$ : C, 77.96; H, 8.05; N, 13.99. Found: C, 77.84; H, 8.09; N, 14.07.

**5-Isopropyl-3-methyl-1-(4-nitrophenyl)pyrazole (4cz).** Yield 72% (Table 1), mp 58-60 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.23 (6H, d,  $J$  6.7), 2.31 (3H, s), 3.12 (1H, m,  $J$  6.7) 6.11 (1H, s), 7.64 (2H, d,  $J$  9.1) and 8.33 (2H, d,  $J$  9.1);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 23.0 (2 $CH_3$ ), 25.6 (CH), 104.9 (CH), 124.6 (2CH), 125.0 (2CH), 145.3 (C) 146.0 (C), 150.6 (C) and 151.5 (C);  $m/z$  245 ( $M^+$ , 100%). Anal. Calcd for  $C_{13}H_{15}N_3O_2$ : C, 63.66; H, 6.16; N, 17.13. Found: C, 63.62; H, 6.14; N, 17.22.

**5-tert-Butyl-1,3-dimethylpyrazole (4dt).** Yield 72% (Table 1), bp 80-83 °C at 0.8 mmHg (lit.,<sup>1</sup> bp 80-83 °C at 0.8 mmHg);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.31 (9H, s), 2.16 (3H, s), 3.86 (3H, s) and 5.77 (1H, s);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.2 ( $CH_3$ ), 29.5 (3 $CH_3$ ), 31.0 (C), 38.8 ( $CH_3$ ), 103.0 (CH), 146.1 (C) and 151.7 (C);  $m/z$  152 ( $M^+$ , 23%) and 137 (100).

**1-Benzyl-5-tert-butyl-3-methylpyrazole (4dv).** Yield 86% (Table 1), bp 150-152 °C at 2 mmHg (lit.,<sup>1</sup> bp 150-152 °C at 2 mmHg);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.19 (9H, s), 2.16 (3H, s), 5.36 (2H, s), 5.80 (1H, s) and 6.83-7.21 (5H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 30.2 (3 $CH_3$ ), 31.2 (C), 53.9 ( $CH_2$ ), 103.3 (CH),

125.8 (2CH), 126.9 (CH), 128.3 (2CH), 138.5 (C), 147.1 (C) and 152.5 (C);  $m/z$  228 ( $M^+$ , 4%) and 91 (100).

**1,5-Di-*tert*-butyl-3-methylpyrazole (4dw).** Yield 86% (Table 1), bp 110-115 °C at 3 mmHg (lit.,<sup>1</sup> bp 110-115 °C at 3 mmHg);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.45 (9H, s), 1.69 (9H, s), 2.19 (3H, s) and 5.96 (1H, s);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.4 ( $CH_3$ ), 31.9 (3 $CH_3$ ), 32.5 (3 $CH_3$ ), 32.7 (C), 60.9 (C), 106.9 (CH), 143.7 (C) and 152.9 (C);  $m/z$  194 ( $M^+$ , 9%) and 123 (100).

**5-*tert*-Butyl-1-(4-methoxyphenyl)-3-methylpyrazole (4dx).** Yield 87% (Table 1), mp 123 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.16 (9H, s), 2.26 (3H, s), 3.84 (3H, s), 5.96 (1H, s), 6.92 (2H, d,  $J$  8.7) and 7.28 (2H, d,  $J$  8.7);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.1 ( $CH_3$ ), 30.4 (3 $CH_3$ ), 31.5 (C), 55.0 ( $CH_3$ ), 103.1 (CH), 113.2 (2CH), 129.6 (2CH), 134.7 (C), 146.7 (C), 153.5 (C) and 159.4 (C);  $m/z$  244 ( $M^+$ , 27%) and 229 (100). Anal. Calcd for  $C_{15}H_{20}N_2O$ : C, 73.74; H, 8.25; N, 11.46. Found: C, 73.65; H, 8.28; N, 11.53.

**5-*tert*-Butyl-3-methyl-1-phenylpyrazole (4dy).** Yield 79% (Table 1), mp 78-79 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.17 (9H, s), 2.27 (3H, s), 5.98 (1H, s) and 7.27-7.43 (5H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.4 ( $CH_3$ ), 30.8 (3 $CH_3$ ), 31.9 (C), 103.6 (CH), 128.6 (2CH), 128.8 (2CH), 128.9 (CH), 142.3 (C), 147.4 (C) and 153.9 (C);  $m/z$  214 ( $M^+$ , 27%) and 199 (100). Anal. Calcd for  $C_{14}H_{18}N_2$ : C, 78.46; H, 8.47; N, 13.07. Found: C, 78.52; H, 8.42; N, 13.06.

**5-*tert*-Butyl-3-methyl-1-(4-nitrophenyl)pyrazole (4dz).** Yield 85% (Table 1), mp 138 °C (lit.,<sup>21</sup> mp 135-136 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.19 (9H, s), 2.27 (3H, s), 6.05 (1H, s), 7.58 (2H, m) and 8.32 (2H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.1 ( $CH_3$ ), 30.7 (3 $CH_3$ ), 31.7 (C), 104.7 (CH), 123.7 (2CH), 129.5 (2CH), 147.4 (C), 147.6 (C), 148.4 (C) and 154.1 (C);  $m/z$  259 ( $M^+$ , 51%) and 244 (100).

**1,3-Dimethyl-5-(4-methoxyphenyl)pyrazole (4et).** Yield 61% (Table 1), mp 74-75 °C (lit.,<sup>22</sup> mp 73 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.26 (3H, s), 3.76 (3H, s), 3.80 (3H, s), 6.00 (1H, s), 6.93 (2H, d,  $J$  8.6) and 7.28 (2H, d,  $J$  8.6);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.3 ( $CH_3$ ), 36.8 ( $CH_3$ ), 55.1 ( $CH_3$ ), 105.0 (CH), 113.8 (2CH), 123.1 (C), 129.7 (2CH), 144.0 (C), 147.3 (C) and 159.4 (C);  $m/z$  202 ( $M^+$ , 100%).

**1-Benzyl-5-(4-methoxyphenyl)-3-methylpyrazole (4ev).** Yield 96% (Table 1), bp 160 °C at 0.4 mmHg;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.35 (3H, s), 3.80 (3H, s), 5.28 (2H, s), 6.11 (1H, s) and 6.89-7.31 (9H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 52.5 ( $CH_2$ ), 55.1 ( $CH_3$ ), 105.6 (CH), 113.9 (2CH), 123.1 (C), 126.4 (2CH), 127.1 (CH), 128.4 (2CH), 129.9 (2CH), 137.9 (C), 144.5 (C), 148.1 (C) and 159.6 (C);  $m/z$  278 ( $M^+$ , 75%) and 91 (100). Anal. Calcd for  $C_{18}H_{18}N_2O$ : C, 77.67; H, 6.52; N, 10.06. Found: C, 77.62; H, 6.49; N, 10.10.

**1-*tert*-Butyl-5-(4-methoxyphenyl)-3-methylpyrazole (4ew).** Yield 92% (Table 1), mp 151-153 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.36 (9H, s), 2.21 (3H, s), 3.77 (3H, s), 5.83 (1H, s), 6.82 (2H, d,  $J$  8.6) and 7.16 (2H, d,  $J$  8.6);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 31.2 (3 $CH_3$ ), 55.2 ( $CH_3$ ), 60.4 (C), 109.1 (CH), 113.1

(2CH), 126.6 (C), 131.5 (2CH), 143.2 (C), 145.1 (C) and 159.4 (C);  $m/z$  244 ( $M^+$ , 22%) and 188 (100). Anal. Calcd for  $C_{15}H_{20}N_2O$ : C, 73.74; H, 8.25; N, 11.46. Found: C, 73.77; H, 8.20; N, 11.53.

**1,5-Di-(4-methoxyphenyl)-3-methylpyrazole (4ex).** Yield 89% (Table 1), mp 87-88 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.36 (3H, s), 3.77 (3H, s), 3.78 (3H, s), 6.23 (1H, s) and 6.78-7.26 (8H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 55.2 ( $CH_3$ ), 55.4 ( $CH_3$ ), 106.5 (CH), 113.7 (2CH), 113.9 (2CH), 123.1 (C), 126.5 (2CH), 129.8 (2CH), 133.5 (C), 143.4 (C), 148.9 (C), 158.5 (C) and 159.2 (C);  $m/z$  294 ( $M^+$ , 100%). Anal. Calcd for  $C_{18}H_{18}N_2O_2$ : C, 73.45; H, 6.16; N, 9.52. Found: C, 73.37; H, 6.14; N, 9.56.

**5-(4-Methoxyphenyl)-3-methyl-1-phenylpyrazole (4ey).** Yield 91% (Table 1), mp 82-84 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.37 (3H, s), 3.77 (3H, s), 6.25 (1H, s), 6.80 (2H, d,  $J$  8.9), 7.13 (2H, d,  $J$  8.9) and 7.22-7.30 (5H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 55.1 ( $CH_3$ ), 107.1 (CH), 113.7 (2CH), 123.0 (C), 125.0 (2CH), 126.9 (CH), 128.7 (2CH), 129.8 (2CH), 140.1 (C), 143.4 (C), 149.2 (C) and 159.3 (C);  $m/z$  264 ( $M^+$ , 92%) and 77 (100). Anal. Calcd for  $C_{17}H_{16}N_2O$  requires C, 77.25; H, 6.10; N, 10.60. Found: C, 77.15; H, 6.13; N, 10.65.

**5-(4-Methoxyphenyl)-3-methyl-1-(4-nitrophenyl)pyrazole (4ez).** Yield 90% (Table 1), mp 150-154 °C (lit.,<sup>3</sup> mp 147-149 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.37 (3H, s), 3.82 (3H, s), 6.28 (1H, s), 6.87 (2H, d,  $J$  8.8), 7.14 (2H, d,  $J$  8.8), 7.44 (2H, d,  $J$  9.1) and 8.15 (2H, d,  $J$  9.1);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 55.3 ( $CH_3$ ), 109.4 (CH), 114.2 (2CH), 122.4 (C), 124.1 (2CH), 124.3 (2CH), 130.0 (2CH), 144.1 (C), 145.0 (C), 145.4 (C), 151.1 (C) and 160.0 (C);  $m/z$  309 ( $M^+$ , 100%).

**1,3-Dimethyl-5-phenylpyrazole (4ft).** Yield 82% (Table 1), bp 100-103 °C at 1 mmHg (lit.,<sup>23</sup> bp 146 °C at 12 mmHg, mp 22 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.28 (3H, s), 3.77 (3H, s), 6.05 (1H, s) and 7.36 (5H, s);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.1 ( $CH_3$ ), 36.7 ( $CH_3$ ), 105.3 (CH), 128.0 (CH), 128.3 (4CH), 130.7 (C), 144.0 (C) and 147.1 (C);  $m/z$  172 ( $M^+$ , 100%).

**1-Benzyl-3-methyl-5-phenylpyrazole (4fv).** Yield 81% (Table 1), mp 78-79 °C (lit.,<sup>24</sup> mp 79-80 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.39 (3H, s), 5.32 (2H, s), 6.18 (1H, s) and 7.08-7.39 (10H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 52.6 ( $CH_2$ ), 105.9 (CH), 126.4 (2CH), 127.1 (CH), 128.2 (CH), 128.4 (4CH), 128.5 (2CH), 130.7 (C), 137.8 (C), 144.7 (C) and 148.0 (C);  $m/z$  248 ( $M^+$ , 37%) and 91 (100).

**1-tert-Butyl-3-methyl-5-phenylpyrazole (4fw).** Yield 87% (Table 1), mp 99-101 °C (lit.,<sup>25</sup> mp 98 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.43 (9H, s), 2.29 (3H, s), 5.92 (1H, s) and 7.26-7.38 (5H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 31.2 (3 $CH_3$ ), 60.5 (C), 108.9 (CH), 127.6 (2CH), 128.1 (CH), 130.3 (2CH), 134.6 (C), 143.4 (C) and 145.1 (C);  $m/z$  214 ( $M^+$ , 10%) and 158 (100).

**1-(4-Methoxyphenyl)-3-methyl-5-phenylpyrazole (4fx).** Yield 89% (Table 1), mp 119-121 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.36 (3H, s), 3.76 (3H, s), 6.26 (1H, s) and 6.73-7.22 (9H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 55.3 ( $CH_3$ ), 107.1 (CH), 114.0 (2CH), 126.5 (2CH), 127.9 (CH), 128.3 (2CH), 128.5 (2CH), 130.8

(C), 133.5 (C), 143.6 (C), 148.9 (C) and 158.6 (C);  $m/z$  264 ( $M^+$ , 100%). Anal. Calcd for  $C_{17}H_{16}N_2O$ : C, 77.25; H, 6.10; N, 10.60. Found: C, 77.19; H, 6.12; N, 10.66.

**3-Methyl-1,5-diphenylpyrazole (4fy).** Yield 93% (Table 1), mp 67-69 °C (lit.,<sup>23</sup> mp 63 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.38 (3H, s), 6.29 (1H, s) and 7.23-7.27 (10H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 107.7 (CH), 125.0 (2CH), 127.0 (CH), 128.0 (CH), 128.3 (2CH), 128.6 (2CH), 128.7 (2CH), 130.7 (C), 140.1 (C), 143.6 (C) and 149.3 (C);  $m/z$  234 ( $M^+$ , 100%).

**3-Methyl-1-(4-nitrophenyl)-5-phenylpyrazole (4fz).** Yield 90% (Table 1), mp 100-101 °C (lit.,<sup>3</sup> mp 102-103 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.32 (3H, s), 6.29 (1H, s) and 7.16-8.06 (9H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.2 ( $CH_3$ ), 109.6 (CH), 123.8 (2CH), 124.0 (2CH), 128.3 (2CH), 128.5 (3CH), 129.9 (C), 143.8 (C), 144.5 (C), 145.0 (C) and 150.7 (C);  $m/z$  279 ( $M^+$ , 100%).

**1,3-Dimethyl-5-(4-nitrophenyl)pyrazole (4gt).** Yield 49% (Table 1), mp 163-165 °C (lit.,<sup>22</sup> mp 166 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.25 (3H, s), 3.83 (3H, s), 6.17 (1H, s), 7.53-7.56 (2H, m) and 8.23-8.26 (2H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.2 ( $CH_3$ ), 37.3 ( $CH_3$ ), 106.6 (CH), 123.8 (2CH), 129.0 (2CH), 136.9 (C), 141.9 (C), 147.2 (C) and 147.9 (C);  $m/z$  217 ( $M^+$ , 100%).

**1-Benzyl-3-methyl-5-(4-nitrophenyl)pyrazole (4gv).** Yield 76% (Table 1), mp 117-118 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.35 (3H, s), 5.32 (2H, s), 6.26 (1H, s) and 7.01-8.22 (9H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 53.3 ( $CH_2$ ), 107.3 (CH), 123.9 (2CH), 126.3 (2CH), 127.6 (CH), 128.8 (2CH), 129.2 (2CH), 137.1 (C), 137.2 (C), 142.4 (C), 147.4 (C) and 148.7 (C);  $m/z$  293 ( $M^+$ , 57%) and 292 (100). Anal. Calcd for  $C_{17}H_{15}N_3O_2$ : C, 69.61; H, 5.15; N, 14.33. Found: C, 69.72; H, 5.18; N, 14.25.

**1-tert-Butyl-3-methyl-5-(4-nitrophenyl)pyrazole (4gw).** Yield 95% (Table 1), mp 175-176 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.44 (9H, s), 2.29 (3H, s), 5.95 (1H, s), 7.26-7.54 (2H, m) and 8.23-8.26 (2H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.4 ( $CH_3$ ), 31.3 (3 $CH_3$ ), 60.9 (C), 109.3 (CH), 122.9 (2CH), 131.2 (2CH), 140.8 (C), 141.7 (C), 145.7 (C) and 147.6 (C);  $m/z$  259 ( $M^+$ , 25%) and 203 (100). Anal. Calcd for  $C_{14}H_{17}N_3O_2$ : C, 64.85; H, 6.61; N, 16.20. Found: C, 64.70; H, 6.63; N, 16.27.

**1-(4-Methoxyphenyl)-3-methyl-5-(4-nitrophenyl)pyrazole (4gx).** Yield 88% (Table 1), mp 155-156 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.37 (3H, s), 3.80 (3H, s), 6.41 (1H, s), 6.84-6.87 (2H, m), 7.14-7.17 (2H, m), 7.33-7.36 (2H, m) and 8.10-8.13 (2H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.4 ( $CH_3$ ), 55.4 ( $CH_3$ ), 108.2 (CH), 114.3 (2CH), 123.7 (2CH), 126.7 (2CH), 128.9 (2CH), 132.7 (C), 136.9 (C), 141.2 (C), 146.9 (C), 149.5 (C) and 159.1 (C);  $m/z$  309 ( $M^+$ , 100%). Anal. Calcd for  $C_{17}H_{15}N_3O_3$ : C, 66.01; H, 4.89; N, 13.58. Found: C, 66.15; H, 4.90; N, 13.52.

**2-Methyl-5-(4-nitrophenyl)-1-phenylpyrazole (4gy).** Yield 86% (Table 1), mp 99-100 °C (lit.,<sup>26</sup> mp 105-106 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.40 (3H, s), 6.45 (1H, s) and 7.24-8.15 (9H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.2 ( $CH_3$ ), 108.6 (CH), 123.4 (2CH), 124.9 (2CH), 127.5 (CH), 128.8 (2CH), 128.9 (2CH),

136.5 (C), 139.3 (C), 140.9 (C), 146.7 (C) and 149.5 (C);  $m/z$  279 ( $M^+$ , 100%).

**3-Methyl-1,5-di(4-nitrophenyl)pyrazole (4gz).** Yield 90% (Table 1), mp 187-188 °C;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.40 (3H, s), 6.48 (1H, s), 7.41-7.43 (4H, m) and 8.20-8.22 (4H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 13.5 ( $CH_3$ ), 111.0 (CH), 124.1 (2CH), 124.6 (2CH), 124.7 (2CH), 129.3 (2CH), 136.3 (C), 141.7 (C), 144.3 (C), 146.0 (C), 147.6 (C) and 151.5 (C);  $m/z$  324 ( $M^+$ , 100%). Anal. Calcd for  $C_{16}H_{12}N_4O_4$ : C, 59.26; H, 3.73; N, 17.28. Found: C, 59.11; H, 3.72; N, 17.33.

**1,5-Dimethyl-3-(2-phenylethyl)pyrazole (5bt).** Yield 81% (Table 2), mp 85-86 °C (lit.,<sup>1</sup> mp 85-86 °C);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.18 (3H, s), 2.89 (4H, m,  $A_2B_2$ ), 3.68 (3H, s), 5.78 (1H, s) and 7.14-7.29 (5H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 11.0 ( $CH_3$ ), 30.0 ( $CH_2$ ), 35.4 ( $CH_3$ ), 36.0 ( $CH_2$ ), 103.8 (CH), 125.7 (CH), 128.1 (2CH), 128.2 (2CH), 138.7 (C), 141.8 (C) and 150.8 (C);  $m/z$  200 ( $M^+$ , 31%) and 109 (100).

**1-Ethyl-5-methyl-3-(2-phenylethyl)pyrazole (5bu).** Yield 58% (Table 2), bp 165 °C at 5 mmHg;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.30 (3H, t,  $J$  7.2), 2.12 (3H, s), 2.89 (4H, m), 3.93 (2H, q,  $J$  7.2), 5.74 (1H, s) and 7.12-7.22 (5H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 10.3 ( $CH_3$ ), 15.0 ( $CH_3$ ), 29.8 ( $CH_2$ ), 35.7 ( $CH_2$ ), 42.9 ( $CH_2$ ), 103.4 (CH), 125.3 (CH), 127.7 (2CH), 127.9 (2CH), 137.3 (C), 141.5 (C) and 150.4 (C);  $m/z$  214 ( $M^+$ , 25%) and 123 (100). Anal. Calcd for  $C_{14}H_{18}N_2$ : C, 78.46; H, 8.47; N, 13.07. Found: C, 78.44; H, 8.43; N, 13.13.

**1-Benzyl-5-methyl-3-(2-phenylethyl)pyrazole (5bv).** Yield 69% (Table 2), bp 155-157 °C at 0.6 mmHg (lit.,<sup>1</sup> bp 155-157 °C at 0.6 mmHg);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.11 (3H, s), 2.93 (4H, m,  $A_2B_2$ ), 5.21 (2H, s), 5.84 (1H, s) and 6.99-7.30 (10H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 11.1 ( $CH_3$ ), 30.1 ( $CH_2$ ), 36.0 ( $CH_2$ ), 52.6 ( $CH_2$ ), 104.6 (CH), 125.7 (CH), 126.4 (2CH), 127.3 (CH), 128.2 (2CH), 128.4 (2CH), 128.6 (2CH), 137.3 (C), 138.9 (C), 141.8 (C) and 151.3 (C);  $m/z$  276 ( $M^+$ , 12%) and 277 (100).

**1-tert-Butyl-5-methyl-3-(2-phenylethyl)pyrazole (5bw).** Yield 71% (Table 2), bp 228-230 °C at 1 mmHg (lit.,<sup>1</sup> bp 228-230 °C at 1 mmHg);  $\delta_H$ (300 MHz;  $CDCl_3$ ) 1.53 (9H, s), 2.30 (3H, s), 2.80 (4H, m,  $A_2B_2$ ), 5.71 (1H, s) and 7.08-7.18 (5H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 14.7 ( $CH_3$ ), 30.0 ( $CH_2$ ), 30.1 (3 $CH_3$ ), 35.9 ( $CH_2$ ), 59.2 (C), 106.7 (CH), 125.7 (CH), 128.2 (2CH), 128.4 (2CH), 138.2 (C), 142.2 (C) and 149.0 (C);  $m/z$  242 ( $M^+$ , 43%) and 95 (100).

**1-(4-Methoxyphenyl)-5-methyl-3-(2-phenylethyl)pyrazole (5bx).** Yield 72% (Table 2), bp 225-228 °C at 0.9 mmHg;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.27 (3H, s), 3.04 (4H, m), 3.83 (3H, s), 6.01 (1H, s) and 6.96-7.38 (9H, m);  $\delta_C$ (75.4 MHz;  $CDCl_3$ ) 11.9 ( $CH_3$ ), 30.0 ( $CH_2$ ), 35.8 ( $CH_2$ ), 55.1 ( $CH_3$ ), 105.1 (CH), 113.8 (2CH), 125.6 (CH), 126.1 (2CH), 128.1 (2CH), 128.2 (2CH), 132.8 (C), 138.9 (C), 141.7 (C), 152.0 (C) and 158.5 (C);  $m/z$  292 ( $M^+$ , 84%) and 201 (100). Anal. Calcd for  $C_{19}H_{20}N_2O$ : C, 78.06; H, 6.89; N, 9.58. Found: C, 78.14; H, 6.89; N, 9.53.

**5-Methyl-1-phenyl-3-(2-phenylethyl)pyrazole (5by).** Yield 83% (Table 2), bp 248-249 °C at 10 mmHg;  $\delta_H$ (300 MHz;  $CDCl_3$ ) 2.33 (3H, s), 3.02 (4H, m), 6.03 (1H, s) and 7.20-7.52 (10H, m);  $\delta_C$ (75.4 MHz;



CDCl<sub>3</sub>) 12.5 (CH<sub>3</sub>), 30.2 (CH<sub>2</sub>), 36.0 (CH<sub>2</sub>), 106.0 (CH), 124.8 (2CH), 125.8 (CH), 127.3 (CH), 128.3 (2CH), 128.4 (2CH), 129.0 (2CH), 139.1 (C), 139.9 (C), 141.9 (C) and 152.7 (C); *m/z* 262 (M<sup>+</sup>, 60%) and 171 (100). Anal. Calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>: C, 82.40; H, 6.92; N, 10.68. Found: C, 82.34; H, 6.93; N, 10.73.

**1,5-Dimethyl-3-isopropylpyrazole (5ct).** Yield 71% (Table 2), bp 65-67 °C at 5 mmHg (lit.,<sup>1</sup> bp 65-67 °C at 5 mmHg); δ<sub>H</sub>(300 MHz; CDCl<sub>3</sub>) 1.23 (6H, d, *J* 7.0), 2.19 (3H, s), 2.90 (1H, m, *J* 7.0), 3.67 (3H, s) and 5.79 (1H, s); δ<sub>C</sub>(75.4 MHz; CDCl<sub>3</sub>) 10.6 (CH<sub>3</sub>), 22.6 (2CH<sub>3</sub>), 27.3 (CH), 35.1 (CH<sub>3</sub>), 101.3 (CH), 138.0 (C) and 157.2 (C); *m/z* 138 (M<sup>+</sup>, 29%) and 123 (100).

**1-Benzyl-3-isopropyl-5-methylpyrazole (5cv).** Yield 73% (Table 2), bp 100-105 °C at 0.4 mmHg (lit.,<sup>1</sup> bp 100-105 °C at 0.4 mmHg); δ<sub>H</sub>(300 MHz; CDCl<sub>3</sub>) 1.26 (6H, d, *J* 6.9), 2.12 (3H, s), 2.97 (1H, m, *J* 6.9), 5.22 (2H, s), 5.88 (1H, s) and 7.02-7.30 (5H, m); δ<sub>C</sub>(75.4 MHz; CDCl<sub>3</sub>) 11.2 (CH<sub>3</sub>), 23.1 (2CH<sub>3</sub>), 27.8 (CH), 52.6 (CH<sub>2</sub>), 102.4 (CH), 126.5 (2CH), 127.3 (CH), 128.6 (2CH), 137.5 (C), 138.8 (C) and 158.3 (C); *m/z* 214 (M<sup>+</sup>, 28%) and 91 (100).

**1-tert-Butyl-3-isopropyl-5-methylpyrazole (5cw).** Yield 63% (Table 2), bp 95-96 °C at 3 mmHg (lit.,<sup>1</sup> bp 95-96 °C at 3 mmHg); δ<sub>H</sub>(300 MHz; CDCl<sub>3</sub>) 1.22 (6H, d, *J* 6.9), 1.61 (9H, s), 2.40 (3H, s), 2.91 (1H, m, *J* 6.9) and 5.82 (1H, s); δ<sub>C</sub>(75.4 MHz; CDCl<sub>3</sub>) 14.7 (CH<sub>3</sub>), 23.1 (2CH<sub>3</sub>), 27.8 (CH), 30.1 (3CH<sub>3</sub>), 59.0 (C), 104.3 (CH), 137.8 (C) and 155.5 (C); *m/z* 180 (M<sup>+</sup>, 21%) and 109 (100).

**3-Isopropyl-1-(4-methoxyphenyl)-5-methylpyrazole (5cx).** Yield 68% (Table 2), bp 125-130 °C at 0.5 mmHg; δ<sub>H</sub>(300 MHz; CDCl<sub>3</sub>) 1.19 (6H, d, *J* 7.0), 2.15 (3H, s), 2.91 (1H, m, *J* 7.0), 3.72 (3H, s), 5.90 (1H, s) 6.82-6.87 (2H, m) and 7.18-7.26 (2H, m); δ<sub>C</sub>(75.4 MHz; CDCl<sub>3</sub>) 12.2 (CH<sub>3</sub>), 23.0 (2CH<sub>3</sub>), 27.9 (CH), 55.4 (CH<sub>3</sub>), 103.2 (CH), 114.1 (2CH), 126.3 (2CH), 133.2 (C), 139.0 (C), 158.7 (C) and 159.0 (C); *m/z* 230 (M<sup>+</sup>, 62%) and 215 (100). Anal. Calcd for C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>O: C, 73.01; H, 7.88; N, 12.16. Found: C, 73.11; H, 7.84; N, 12.14.

**3-Isopropyl-5-methyl-1-phenylpyrazole (5cy).** Yield 71% (Table 2), bp 160 °C at 9 mmHg; δ<sub>H</sub>(300 MHz; CDCl<sub>3</sub>) 1.29 (6H, d, *J* 7.0), 2.29 (3H, s), 3.02 (1H, m, *J* 7.0), 6.02 (1H, s) and 7.29-7.42 (5H, m); δ<sub>C</sub>(75.4 MHz; CDCl<sub>3</sub>) 12.4 (CH<sub>3</sub>), 22.8 (2CH<sub>3</sub>), 27.7 (CH), 103.7 (CH), 124.7 (2CH), 127.0 (CH), 128.8 (2CH), 138.9 (C), 141.1 (C) and 159.4 (C); *m/z* 200 (M<sup>+</sup>, 40%) and 185 (100). Anal. Calcd for C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>: C, 77.96; H, 8.05; N, 13.99. Found: C, 78.02; H, 8.01; N, 13.97.

**3-tert-Butyl-1,5-dimethylpyrazole (5dt).** Yield 65% (Table 2), bp 70-73 °C at 0.7 mmHg (lit.,<sup>1</sup> bp 70-73 °C at 0.7 mmHg); δ<sub>H</sub>(300 MHz; CDCl<sub>3</sub>) 1.28 (9H, s), 2.22 (3H, s), 3.71 (3H, s) and 5.85 (1H, s); δ<sub>C</sub>(75.4 MHz; CDCl<sub>3</sub>) 11.1 (CH<sub>3</sub>), 30.6 (3CH<sub>3</sub>), 31.8 (C), 35.7 (CH<sub>3</sub>), 101.4 (CH), 138.4 (C) and 160.5 (C); *m/z* 152 (M<sup>+</sup>, 24%) and 137 (100).

**1-Benzyl-3-tert-butyl-5-methylpyrazole (5dv).** Yield 49% (Table 2), bp 70-73 °C at 0.7 mmHg (lit.,<sup>1</sup> bp 70-73 °C at 0.7 mmHg); δ<sub>H</sub>(300 MHz; CDCl<sub>3</sub>) 1.32 (9H, s), 2.10 (3H, s), 5.24 (2H, s), 5.91 (1H, s) and

6.99-7.30 (5H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 11.2 (CH<sub>3</sub>), 30.6 (3CH<sub>3</sub>), 31.9 (C), 52.7 (CH<sub>2</sub>), 102.3 (CH), 126.4 (2CH), 127.2 (CH), 128.5 (2CH), 137.6 (C), 138.5 (C) and 160.9 (C);  $m/z$  228 (M<sup>+</sup>, 7%) and 91 (100).

**3-*tert*-Butyl-1-(4-methoxyphenyl)-5-methylpyrazole (5dx).** Yield 16% (Table 2), oil;  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 1.33 (9H, s), 2.25 (3H, s), 3.83 (3H, s), 6.04 (1H, s) 6.93-6.96 (2H, m) and 7.33-7.36 (2H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 12.3 (CH<sub>3</sub>), 30.5 (3CH<sub>3</sub>), 32.0 (C), 55.5 (CH<sub>3</sub>), 102.9 (CH), 114.0 (2CH), 126.4 (2CH), 133.3 (C), 138.8 (C), 158.6 (C) and 161.7 (C);  $m/z$  244 (M<sup>+</sup>, 50%) and 229 (100).

**1,5-Dimethyl-3-(4-methoxyphenyl)pyrazole (5et).** Yield 51% (Table 1), mp 92-93 °C (lit.,<sup>22</sup> mp 91 °C);  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 2.27 (3H, s), 3.78 (3H, s), 3.81 (3H, s), 6.24 (1H, s), 6.89-6.92 (2H, m) and 7.66-7.69 (2H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 11.2 (CH<sub>3</sub>), 35.9 (CH<sub>3</sub>), 55.2 (CH<sub>3</sub>), 101.9 (CH), 113.8 (2CH), 126.5 (2CH), 126.6 (C), 139.6 (C), 149.7 (C) and 159.0 (C);  $m/z$  202 (M<sup>+</sup>, 100%) and 187 (92).

**1-Benzyl-3-(4-methoxyphenyl)-5-methylpyrazole (5ev).** Yield 54% (Table 2), mp 82-83 °C;  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 2.20 (3H, s), 3.82 (3H, s), 5.32 (2H, s), 6.30 (1H, s) and 6.90-7.74 (9H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 11.3 (CH<sub>3</sub>), 53.0 (CH<sub>2</sub>), 55.2 (CH<sub>3</sub>), 102.7 (CH), 113.9 (2CH), 123.2 (C), 126.7 (2CH), 127.4 (CH), 128.6 (2CH), 130.0 (2CH), 137.2 (C), 139.7 (C), 150.1 (C) and 159.1 (C);  $m/z$  278 (M<sup>+</sup>, 6%) and 91 (100). Anal. Calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.60; H, 6.53; N, 10.11.

**1,3-Di(4-methoxyphenyl)-5-methylpyrazole (5ex).** Yield 70% (Table 2), mp 106-107 °C;  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 2.30 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 6.42 (1H, s) and 6.91-7.79 (8H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 12.3 (CH<sub>3</sub>), 55.3 (CH<sub>3</sub>), 55.5 (CH<sub>3</sub>), 103.3 (CH), 113.9 (2CH), 114.2 (2CH), 126.2 (C), 126.6 (2CH), 126.9 (2CH), 133.1 (C), 140.2 (C), 151.0 (C), 159.0 (C) and 159.3 (C);  $m/z$  294 (M<sup>+</sup>, 100%). Anal. Calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.43; H, 6.14; N, 9.49.

**3-(4-Methoxyphenyl)-5-methyl-1-phenylpyrazole (5ey).** Yield 81% (Table 2), mp 101-102 °C;  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 2.32 (3H, s), 3.79 (3H, s), 6.43 (1H, s) and 6.89-7.80 (9H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 12.4 (CH<sub>3</sub>), 55.1 (CH<sub>3</sub>), 103.9 (CH), 113.8 (2CH), 124.8 (2CH), 126.0 (C), 126.8 (2CH), 127.4 (CH), 129.0 (2CH), 139.8 (C), 140.0 (C), 151.2 (C) and 159.3 (C);  $m/z$  264 (M<sup>+</sup>, 100%). Anal. Calcd for C<sub>17</sub>H<sub>16</sub>N<sub>2</sub>O: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.27; H, 6.13; N, 10.57.

**3-(4-Methoxyphenyl)-5-methyl-1-(4-nitrophenyl)pyrazole (5ez).** Yield 89% (Table 2), mp 154-155 °C;  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 2.51 (3H, s), 3.85 (3H, s), 6.54 (1H, s) and 6.94-8.36 (8H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 13.4 (CH<sub>3</sub>), 55.3 (CH<sub>3</sub>), 106.3 (CH), 114.1 (2CH), 123.7 (2CH), 124.8 (2CH), 125.2 (C), 127.1 (2CH), 140.5 (C), 145.1 (C), 145.7 (C), 152.8 (C) and 159.9 (C);  $m/z$  309 (M<sup>+</sup>, 100%). Anal. Calcd for C<sub>17</sub>H<sub>15</sub>N<sub>3</sub>O<sub>3</sub>: C, 66.01; H, 4.89; N, 13.58. Found: C, 66.12; H, 4.91; N, 13.51.

**1,5-Dimethyl-3-phenylpyrazole (5ft).** Yield 57% (Table 1), mp 40-41 °C (lit.,<sup>23</sup> mp 36 °C);  $\delta_H$ (300 MHz; CDCl<sub>3</sub>) 2.21 (3H, s), 3.73 (3H, s), 6.27 (1H, s) and 7.25-7.81 (5H, m);  $\delta_c$ (75.4 MHz; CDCl<sub>3</sub>) 11.0

(CH<sub>3</sub>), 35.9 (CH<sub>3</sub>), 102.3 (CH), 125.2 (2CH), 127.1 (CH), 128.3 (2CH), 133.6 (C), 139.5 (C) and 149.8 (C); *m/z* 172 (M<sup>+</sup>, 100%).

**1-Benzyl-5-methyl-3-phenylpyrazole (5fv).** Yield 57% (Table 2), mp 87-88 °C (lit.,<sup>24</sup> mp 87.5-88 °C);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.24 (3H, s), 5.37 (2H, s), 6.42 (1H, s) and 7.15-7.88 (10H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 11.2 (CH<sub>3</sub>), 53.0 (CH<sub>2</sub>), 103.2 (CH), 125.4 (2CH), 126.5 (2CH), 127.3 (CH), 127.4 (CH), 128.5 (2CH), 128.6 (2CH), 133.7 (C), 137.0 (C), 139.6 (C) and 150.2 (C); *m/z* 248 (M<sup>+</sup>, 5%) and 91 (100).

**1-tert-Butyl-5-methyl-3-phenylpyrazole (5fw).** Yield 35% (Table 2), bp 160-165 °C at 1 mmHg;  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 1.66 (9H, s), 2.44 (3H, s), 6.31 (1H, s) and 7.20-7.79 (5H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 14.7 (CH<sub>3</sub>), 30.0 (3CH<sub>3</sub>), 59.8 (C), 105.3 (CH), 125.3 (2CH), 126.9 (CH), 128.4 (2CH), 134.1 (C), 139.0 (C) and 147.5 (C); *m/z* 214 (M<sup>+</sup>, 22%) and 158 (100). Anal. Calcd for C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>: C, 78.46; H, 8.47; N, 13.07. Found: C, 78.40; H, 8.50; N, 13.10.

**1-(4-Methoxyphenyl)-5-methyl-3-phenylpyrazole (5fx).** Yield 83% (Table 2), mp 98-100 °C;  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.32 (3H, s), 3.85 (3H, s), 6.49 (1H, s) and 6.97-7.86 (9H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 12.2 (CH<sub>3</sub>), 55.3 (CH<sub>3</sub>), 103.6 (CH), 114.0 (2CH), 125.5 (2CH), 126.3 (2CH), 127.5 (CH), 128.4 (2CH), 132.8 (C), 133.3 (C), 140.1 (C), 150.9 (C) and 158.8 (C); *m/z* 264 (M<sup>+</sup>, 100%). Anal. Calcd for C<sub>17</sub>H<sub>16</sub>N<sub>2</sub>O: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.17; H, 6.10; N, 10.65.

**1,3-Diphenyl-5-methylpyrazole (5fy).** Yield 89% (Table 2), mp 49-50 °C (lit.,<sup>27</sup> mp 44-46 °C);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.39 (3H, s), 6.52 (1H, s) and 7.27-7.86 (10H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 12.6 (CH<sub>3</sub>), 104.4 (CH), 125.0 (2CH), 125.7 (2CH), 127.6 (CH), 127.7 (CH), 128.5 (2CH), 129.1 (2CH), 133.3 (C), 139.9 (C) 140.1 (C) and 151.5 (C); *m/z* 234 (M<sup>+</sup>, 100%).

**5-Methyl-1-(4-nitrophenyl)-3-phenylpyrazole (5fz).** Yield 91% (Table 2), mp 125-126 °C;  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.49 (3H, s), 6.59 (1H, s) and 7.35-8.33 (9H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 13.0 (CH<sub>3</sub>), 106.3 (CH), 123.4 (2CH), 124.4 (2CH), 125.5 (2CH), 128.1 (CH), 128.5 (2CH), 132.3 (C), 140.5 (C), 144.7 (C), 145.4 (C) and 152.5 (C); *m/z* 279 (M<sup>+</sup>, 75%) and 77 (100). Anal. Calcd for C<sub>16</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>: C, 68.81; H, 4.69; N, 15.04. Found: C, 68.82; H, 4.67; N, 15.01.

**1,5-Dimethyl-3-(4-nitrophenyl)pyrazole (5gt).** Yield 70% (Table 1), mp 194-196 °C (lit.,<sup>22</sup> mp 166 °C);  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.31 (3H, s), 3.83 (3H, s), 6.39 (1H, s), 7.85-7.88 (2H, m) and 8.18-8.21 (2H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 11.2 (CH<sub>3</sub>), 36.4 (CH<sub>3</sub>), 103.5 (CH), 124.0 (2CH), 125.5 (2CH), 140.0 (C), 140.5 (C), 146.6 (C) and 147.5 (C); *m/z* 217 (M<sup>+</sup>, 100%).

**1-Benzyl-5-methyl-3-(4-nitrophenyl)pyrazole (5gv).** Yield 63% (Table 2), mp 144-145 °C;  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.26 (3H, s), 5.36 (2H, s), 6.48 (1H, s) and 7.13-8.26 (9H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 11.3 (CH<sub>3</sub>), 53.4 (CH<sub>2</sub>), 104.2 (CH), 124.0 (2CH), 125.8 (2CH), 126.7 (2CH), 127.8 (CH), 128.8 (2CH), 136.4 (C), 140.0 (C), 140.5 (C), 146.7 (C) and 147.9 (C); *m/z* 293 (M<sup>+</sup>, 66%) and 91 (100). Anal. Calcd for

C<sub>17</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.53; H, 5.13; N, 14.37.

**1-(4-Methoxyphenyl)-5-methyl-3-(4-nitrophenyl)pyrazole (5gx).** Yield 83% (Table 2), mp 146-147 °C;  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.35 (3H, s), 3.87 (3H, s), 6.59 (1H, s) and 7.00-8.26 (8H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 12.3 (CH<sub>3</sub>), 55.6 (CH<sub>3</sub>), 104.6 (CH), 114.4 (2CH), 124.1 (2CH), 126.0 (2CH), 126.5 (2CH), 132.5 (C), 139.8 (C), 141.1 (C), 147.0 (C), 148.8 (C) and 159.4 (C);  $m/z$  309 (M<sup>+</sup>, 100%). Anal. Calcd for C<sub>17</sub>H<sub>15</sub>N<sub>3</sub>O<sub>3</sub>: C, 66.01; H, 4.89; N, 13.58. Found: C, 65.98; H, 4.91; N, 13.52.

**5-Methyl-3-(4-nitrophenyl)-1-phenylpyrazole (5gy).** Yield 81% (Table 2), mp 161-163 °C;  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.40 (3H, s), 6.62 (1H, s), 7.42-7.53 (5H, m), 7.99-8.03 (2H, m) and 8.24-8.28 (2H, m);  $\delta_{\text{C}}$ (75.4 MHz; CDCl<sub>3</sub>) 12.5 (CH<sub>3</sub>), 105.1 (CH), 124.1 (2CH), 125.0 (2CH), 126.0 (2CH), 128.2 (CH), 129.3 (2CH), 139.5 (C), 139.7 (C), 141.0 (C), 147.1 (C) and 149.1 (C);  $m/z$  279 (M<sup>+</sup>, 100%). Anal. Calcd for C<sub>16</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>: C, 68.81; H, 4.69; N, 15.04. Found: C, 68.83; H, 4.68; N, 14.97.

**1,3-Di(4-nitrophenyl)-5-methylpyrazole (5gz).** Yield 49% (Table 2), mp 210-211 °C;  $\delta_{\text{H}}$ (300 MHz; CDCl<sub>3</sub>) 2.54 (3H, s), 6.70 (1H, s), 7.78-7.81 (2H, m), 8.00-8.03 (2H, m), 8.27-8.30 (2H, m) and 8.39-8.42 (2H, m);  $\delta_{\text{C}}$ (75.4 MHz; DMSO-*d*<sub>6</sub>) 12.8 (CH<sub>3</sub>), 107.4 (CH), 124.2 (2CH), 124.4 (2CH), 124.9 (2CH), 126.3 (2CH), 138.7 (C), 142.2 (C), 144.2(C), 145.9 (C), 146.9 (C) and 149.7 (C);  $m/z$  324 (M<sup>+</sup>, 100%). Anal. Calcd for C<sub>16</sub>H<sub>12</sub>N<sub>4</sub>O<sub>4</sub>: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.31; H, 3.74; N, 17.30.

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