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# A convenient synthesis of 1,5-diarylpyrazoles from Baylis-Hillman adducts using HY-zeolite

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### Abstract

A facile and convenient protocol was developed for the synthesis of 1,5-diarylpyrazoles using Baylis-Hillman adducts in the presence of HY-zeolite as an efficient recyclable heterogeneous catalyst in reasonable reaction times (1.5–2.5 h) and high yields (78–90%).

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Baylis-Hillman adducts containing chemospecific functional groups in close proximity are versatile building blocks for the synthesis of several important group of compounds [1–4] which among them are naturally occurring products such as mycestericin E [5], necic acids [6], terpenoids [7], insect pheromones [8], oxygen- and nitrogen-containing heterocycles [9–11] and many other biologically active compounds.

An interesting application of Baylis-Hillman adducts has been found in the synthesis of 1,5-diaryl pyrazoles [12]. Aryl pyrazoles are key substructures in a large variety of compounds of important medicinal and pesticidal properties [13]. Therefore extensive studies have been devoted to the synthesis of these compounds [12]. Arylpyrazoles are normally prepared from appropriately substituted 1,3-dicarbonyl compounds which suffer from multistep synthesis and low yields [12,14].

On the other hand, zeolites are used as catalysts for wide range of processes, from simple drying to complicated catalytic reactions. Acidic zeolites such as HY-zeolite is unique acid catalyst that has become popular over the last two decades. Zeolite HY contains a framework system of supercages, which are connected by a three-dimensional array of large diameter channels and this array enables a much easier diffusion of reactants and products [15]. This heterogeneous catalyst has been used in various chemical transformations [16–20].

Thus the remarkable catalytic activity together with easy availability, operational simplicity of HY-zeolites and our continued interests for the development of efficient and environmentally friendly procedures for the synthesis of heterocyclic compounds [21], encouraged us to study the conversion of Baylis-Hillman adducts into 1,5-diarylpyrazoles in the presence of HY-zeolite.

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Table 1 Synthesis of 1,5-diarylpyrazoles over HY-zeolite catalyst (2a-i).

Entry	Ar	Ar'	Time (h)	Yield (%) <sup>a,b</sup>
a	p-FC <sub>6</sub> H <sub>4</sub>	Ph	$2.5(5.5)^{c}$	85 (63) <sup>c</sup>
b	p-FC <sub>6</sub> H <sub>4</sub>	$p-MeC_6H_4$	2.0	87
c	m-BrC <sub>6</sub> H <sub>4</sub>	Ph	1.75	83
d	p-BrC <sub>6</sub> H <sub>4</sub>	Ph	1.75	80
e	$2,4-Cl_2C_6H_3$	Ph	2.50	78
f	2-Furyl	Ph	1.75	86
g	5-NO <sub>2</sub> -2-furyl	Ph	1.5	85
h	2-Thienyl	Ph	1.5	90
i	m-ClC <sub>6</sub> H <sub>4</sub>	Ph	1.75	84

<sup>a</sup> Isolated yield.

<sup>b</sup> Identified by spectroscopic (IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR) and elemental analyses.

<sup>c</sup> Classical reaction was carried out using 1a (0.45 mmol), phenylhydrazine hydrochloride (0.57 mmol) in 1,2-dichloroethane (4 mL) under reflux condition which provided the pyrazole 2a in 63% yield after 5.5 h.

The Baylis-Hillman adducts (1a-i) were synthesized and converted to the related 1,5-diarylpyrazoles in ClCH<sub>2</sub>CH<sub>2</sub>Cl as solvent, in the presence of HY-zeolite (Si/Al: 2.54) (Scheme 1). The results are summarized in Table 1.

The characteristic features of the product (2a-i) formation are the appearance of two separate singlets (2.0-2.62 ppm) for the methyl groups attached to the pyrazole ring. In this protocol the catalytic activity of the catalyst was remained almost unchanged after fourth reuse of the catalyst which offers very attractive feature to this heterogeneous catalytic reaction. This reaction was also examined in the absence of the catalyst, by using substrate **1a**, which gave the product (**2a**) in much longer reaction time and lower yield (Table 1).

Finally we developed a convenient and facile protocol for the synthesis of 1,5-diarylpyrazoles using HY-zeolite, in low reaction times (1.5–2.5 h) and excellent yields (78–90%).

## 1. Experimental

Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were determined on a Shimadzo IR-470 spectrometer. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a 500 MHz Bruker DRX-500 in CDCl<sub>3</sub> as solvent and TMS as internal standard. Elemental analyses were done on a Carlo-Erba EA1110CNNO-S analyzer and agreed with the calculated values. Preparative thin layer chromatography was prepared from Merck Kieselgel 60 H, F<sub>254</sub>, Art No. 7730. For column chromatography Merck Kieselgel 60, Art No. 107733 was employed.

A mixture of Baylis-Hillman adduct (1) (0.45 mmol), aryl hydrazine (0.57 mmol) and HY-zeolite (0.1 g) in 1,2dichloroethane (4 mL) was refluxed for the required reaction time (Table 1). The mixture diluted with  $CH_2Cl_2$  and washed with water and the organic layer was dried (MgSO<sub>4</sub>). Evaporation of the solvent under vacuum provided a residue which was purified by column chromatography (petroleum ether/ethyl acetate: 3/1) to furnish the desired pyrazole in 78–90% yields (Table 1).

**2a**: Orange oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.06 (s, 3H), 2.37 (s, 3H), 7.03 (m, 2H), 7.17 (m, 5H), 7.29 (m, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  162.8 (d, <sup>1</sup>*J*<sub>CF</sub> = 245.9 Hz), 152.8, 149.2, 140.5, 131.9 (d, <sup>3</sup>*J*<sub>CF</sub> = 8.1 Hz), 129.1, 127.5, 127.0, 125.9, 116.1, 115.9 (d, <sup>2</sup>*J*<sub>CF</sub> = 21.6 Hz), 12.4, 8.9. IR (neat):  $\nu$  1602, 1506 cm<sup>-1</sup> (C=C, C=N), 1095 cm<sup>-1</sup> (C=F). Anal. Calcd. for C<sub>17</sub>H<sub>15</sub>FN<sub>2</sub>: C, 76.71; H, 5.63; N, 10.52. Found: C, 76.52; H, 5.51; N, 10.31.

**2b**: Orange oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.06 (s, 3H), 2.35 (s, 3H), 2.36 (s, 3H), 7.01 (m, 4H), 7.13 (d, 2H), 7.44 (d, 2H). IR (neat):  $\nu$  1606, 1515 cm<sup>-1</sup> (C=C, C=N), 1161 cm<sup>-1</sup> (C=F). Anal. Calcd. for C<sub>18</sub>H<sub>17</sub>FN<sub>2</sub>: C, 77.12; H, 6.11; N, 9.99. Found: C, 77.20; H, 6.16; N, 9.89.

**2c**: Orange oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.12 (s, 3H), 2.33 (s, 3H), 7.43 (m, 5H), 7.64 (m, 4H). IR (neat):  $\nu$  1590, 1500 cm<sup>-1</sup> (C=C, C=N), 1070 cm<sup>-1</sup> (C–Br). Anal. Calcd. for C<sub>17</sub>H<sub>15</sub>BrN<sub>2</sub>: C, 62.40; H, 4.62; N, 8.56. Found: C, 62.49; H, 4.57; N, 8.63.

**2d**: Orange oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.0 (s, 3H), 2.34 (s, 3H), 7.0 (d, 2H), 7.15 (m, 3H), 7.28 (d, 2H), 7.47 (d, 2H). IR (neat):  $\nu$  1600, 1500 cm<sup>-1</sup> (C=C, C=N), 1060 cm<sup>-1</sup> (C–Br). Anal. Calcd. for C<sub>17</sub>H<sub>15</sub>BrN<sub>2</sub>: C, 62.40; H, 4.62; N, 8.56. Found: C, 62.45; H, 4.54; N, 8.59.

**2e**: Orange oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.12 (s, 3H), 2.39 (s, 3H), 7.14 (d, 1H), 7.30 (m, 5H), 7.44 (m, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  146.5, 138.7, 134.5, 132.7, 130.0, 129.8, 129.6, 129.4, 128.7, 128.0, 127.8, 119.3, 113.6, 12.6, 9.3. IR (neat):  $\nu$  1595, 1500 cm<sup>-1</sup>(C=C, C=N), 1028 cm<sup>-1</sup> (C–Cl). Anal. Calcd. for C<sub>17</sub>H<sub>14</sub>Cl<sub>2</sub>N<sub>2</sub>: C, 64.37; H, 4.45; N, 8.83. Found: C, 64.43; H, 4.52; N, 8.74.

**2f**: Purple oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.17 (s, 3H), 2.35 (s, 3H), 6.22 (broad, 1H), 6.45 (broad, 1H), 7.24–7.40 (m, 5H), 7.45 (broad, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  151.3, 144.8, 143.4, 140.3, 129.8, 128.2, 126.6, 120.6, 115.9, 109.5, 107.8, 12.3, 9.4. IR (neat):  $\nu$  1595, 1500 cm<sup>-1</sup> (C=C, C=N), 1142 cm<sup>-1</sup> (C=O). Anal. Calcd. for C<sub>15</sub>H<sub>14</sub>N<sub>2</sub>O: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.55; H, 5.84; N, 11.83.

**2g**: Orange oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.31 (s, 3H), 2.40 (s, 3H), 7.28 (m, 6H), 7.40 (broad, 1H). IR (neat):  $\nu$  1600, 1500 cm<sup>-1</sup> (C=C, C=N), 1535 cm<sup>-1</sup> (NO<sub>2</sub>), 1355 cm<sup>-1</sup> (NO<sub>2</sub>), 1070 cm<sup>-1</sup> (C=O). Anal. Calcd. for C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>: C, 63.60; H, 4.63; N, 14.83. Found: C, 63.72; H, 4.58; N, 14.77.

**2h**: Orange oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.25 (s, 3H), 2.62 (s, 3H), 7.26 (m, 2H), 7.43 (m, 6H). IR (neat):  $\nu$  1595, 1500 cm<sup>-1</sup> (C=C, C=N). Anal. Calcd. for C<sub>15</sub>H<sub>14</sub>N<sub>2</sub>S: C, 70.83; H, 5.55; N, 11.01. Found: C, 70.77; H, 5.60; N, 10.92.

**2i**: Orange oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.08 (s, 3H), 2.38 (s, 3H), 7.04 (d, 1H), 7.22 (m, 6H), 7.44 (m, 1H), 7.62 (m, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  149.3, 140.1, 139.3, 134.6, 133.2, 130.2, 130.1, 128.5, 128.4, 128.3, 127.2, 125.1, 115.5, 12.5, 9.0. IR (neat):  $\nu$  1600, 1500 cm<sup>-1</sup> (C=C, C=N), 1050 cm<sup>-1</sup> (C–Cl). Anal. Calcd. for C<sub>17</sub>H<sub>15</sub>ClN<sub>2</sub>: C, 72.21; H, 5.35; N, 9.91. Found: C, 72.30; H, 5.42; N, 9.80.

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