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Environmentally benign synthesis of 3-methyl-4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylene]-1-phenylpyrazolin-5-(4*H*)-ones in an ionic liquid

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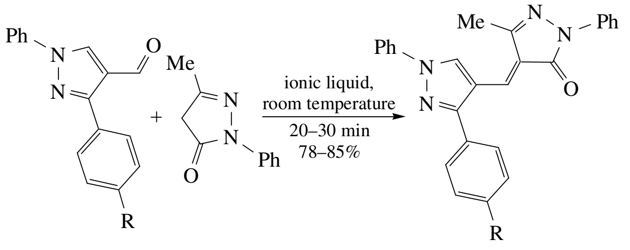
The condensation of 1,3-diphenyl-1*H*-pyrazole-3-carbaldehydes with 3-methyl-1-phenylpyrazolin-5-(4*H*)-one in an ionic liquid (ethylammonium nitrate) afforded 3-methyl-4-[(1,3-diphenyl-1*H*-pyrazolo-4-yl)methylene]-1-phenylpyrazolin-5-(4*H*)-ones in an excellent yield at room temperature.

The Knoevenagel condensation is a basic reaction for carbon–carbon bond formation, which is of paramount importance for organic synthesis. The Knoevenagel condensation reactions are classically catalysed by bases in liquid-phase systems; various catalysts are known to effect the reaction with different aldehydes.

An ideal synthesis should produce the expected products in high yields with high selectivity in safe and environmentally acceptable process. In the last decade, ionic liquids[1–4] have often been discussed as promising solvents for clean processes and green chemistry.

Here, we report the Knoevenagel condensation of 1,3-diphenyl-1*H*-pyrazole-3-carbaldehyde[5,6] with 3-methyl-1-phenylpyrazolin-5-(4*H*)-one[7–10] in an ionic liquid[9] (ethylammonium nitrate) to afford 3-methyl-4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylene]-1-phenylpyrazolin-5-(4*H*)-ones in an excellent yield for 20–30 min at room temperature (Table 1).[†] In this methodology, the reactions are completed in shorter time and with higher yields as compared with the reported methods.[6] In addition, the reaction conditions are very mild. The condensed products were isolated (*a*) by pouring the reaction mixture into ice-cold water, filtering off the obtained solid product and recrystallising it from dioxane or acetic acid or (*b*) by extraction with ethyl acetate. The ethyl acetate layer was concentrated on a rotary evaporator to afford the product.



1a–e **2** **3a–e**

The condensation reaction has been successfully carried out in the ionic liquid ethylammonium nitrate. The reaction does not require any additional catalyst because the ionic liquid acts as a solvent as well as a catalyst.[9] Therefore, this is a good methodology for the synthesis of 3-methyl-4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylene]-1-phenylpyrazolin-5-(4*H*)-ones.

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Table 1 Reaction conditions and characterization of 3-methyl-4-[(1,3-diphenyl-1*H*-pyrazol-4-yl)methylene]-1-phenylpyrazolin-5-(4*H*)-ones.

Entry	R	Reaction time/min	Yield (%)		mp/°C	Solvent for crystallization
			Method (*a*)	Method (*b*)		
3a	Br	30	80	82	228	Dioxane
3b	Cl	30	85	85	238	Dioxane
3c	NO_2	28	78	79	242	Acetic acid
3d	Me	25	81	80	235	Acetic acid
3e	H	30	84	84	212	Dioxane

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[†] *Typical experimental procedure.* A mixture of 1,3-diphenyl-1*H*-pyrazole-3-carbaldehyde **1** (10 mmol) and active methylene compound 3-methyl-1-phenylpyrazolin-5-(4*H*)-one **2** (10 mmol) in the ionic liquid ethylammonium nitrate (20 mmol) was stirred at room temperature for 20–30 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the following two methods were used for isolating the product. (*a*) The reaction mixture was poured into ice-cold water, which solidified the product; the solid product was filtered off and recrystallised from a proper solvent. (*b*) Extraction with ethyl acetate was performed; the ethyl acetate layer was concentrated on a rotary evaporator to afford the product. The other layer consisted of the ionic liquid, which can be reused for further reactions.

For **3a**: ^{1}H NMR, δ: 2.23 (s, 3H, Me), 7.85 (d, 2H, bromophenyl, J 7.2 Hz), 7.69 (d, 2H, bromophenyl, J 7.2 Hz), 7.19–7.61 (m, 11H), 10.2 (s, 1H). ^{13}C NMR, δ: 162.5, 155.2, 150.2, 139.1, 138.7, 136.1, 135.2, 134, 131.1, 129.9, 129.6, 129.2, 128.7, 128.0, 124.6, 124.1, 119.1, 115.9, 95.2, 77.8, 76.9, 76.3, 48.0, 23.7, 13.1. IR (ν/cm^{-1}): 3024, 1670, 1610, 1592, 1565, 1510, 1500, 1440, 756. MS, *m*/*z*: 482, 349, 312, 284, 271, 243, 202, 167, 140, 115, 91, 77 (base peak).

For **3b**: ^{1}H NMR, δ: 2.25 (s, 3H, Me), 7.82 (d, 2H, chlorophenyl, J 7.2 Hz), 7.66 (d, 2H, chlorophenyl, J 7.2 Hz), 7.19–7.61 (m, 11H), 10.2 (s, 1H). ^{13}C NMR, δ: 162.5, 155.8, 150.1, 138.9, 138.41, 135.47, 134.5, 134.1, 130.5, 129.8, 129.5, 129.1, 128.7, 127.8, 124.8, 124.0, 119.2, 115.8, 95.3, 77.6, 77.0, 76.3, 48.0, 23.7, 13.0.