Solvent-Free Condensation of Aromatic Aldehydes and 2,3-Dimethyl-1-phenyl-3-pyrazolin-5-one by *p*-Toluenesulfonic Acid

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Solvent-free condensation easily occurred by mixing aromatic aldehydes and 2,3-dimethyl-1-phenyl-3-pyrazoline-5-one (antipyrine) in the presence of *p*-toluenesulfonic acid as a solid acid catalyst at room temperature to give the corresponding disubstituted products as sole products in high yields.

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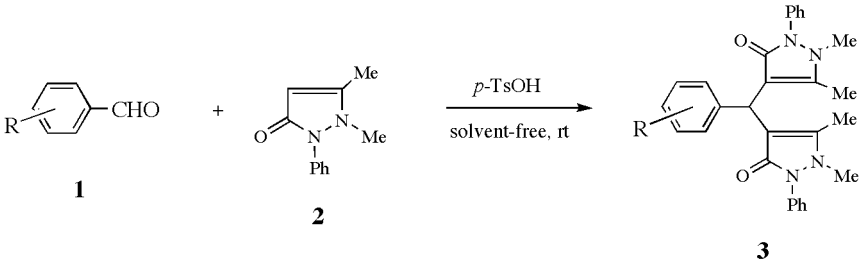
Introduction.

Organic reactions in the solid state and in the absence of solvents are of increasing interest [1-3]. Most solid state reactions occur more efficiently and with higher selectivity than solution phase reactions, providing the synthetic utility for various types of organic reactions. Further, such solvent-free organic synthesis is valuable from the environmental aspect and preservation of our earth [4]. Solid-state photochemical reaction between 4-hydroxybenzaldehyde and 2,3-dimethyl-1-phenyl-3-pyrazoline-5-one (antipyrine) in polycrystalline simple mixtures gives disubstituted product [5]. Solvent-free thermal reactions have been reported between aromatic aldehydes and 3-methyl-1-phenyl-2-pyrazolin-5-one [6]. Herein we report efficient condensations of aromatic aldehydes with antipyrine by *p*-toluenesulfonic acid as a solid acid catalyst in the absence of solvent (Scheme 1).

Scheme 1

Reaction of Aldehydes with Antipyrine



Results and Discussion.

In the context of our work on the condensation of aromatic aldehydes **1** with 1-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one **2** in the absence of solvent, we first examined the extent that *p*-toluenesulfonic acid should be used as a solid protic acid catalyst. For the reaction of 2-nitrobenzaldehyde **1b** and **2** in 1:2 molar ratio at room temperature for 1 hour, the presence of 1, 3, 5 and 10-fold excess of *p*-toluenesulfonic acid gave bis[1-(2,3-dimethyl-1-phenyl-3-pyrazolin-5-one)]-2-nitrophenylmethane **3b** as a sole product in 40%, 74%, 96% and 96% yield, respectively. Thereafter 5 molar equivalents *p*-toluenesulfonic acid was used for the reaction.

Solvent-free reactions of substituted benzaldehydes **1a**–**f** and **2** in the presence of *p*-toluenesulfonic acid were undertaken to give the corresponding bis[1-(2,3-dimethyl-1-phenyl-3-pyrazolin-5-one)]arylmethane **3a**–**f** in high yields (Table 1). Most reactions were completed within 1 hour, except 24 hours for 3- and 4-nitrobenzaldehyde **1c**, **1d**, probably due to the deactivation of the carbonyl carbon by the nitro moiety (entries 3 and 4). The products were separated by extraction into chloroform because filtration of the aqueous reaction mixture gave incomplete separation due to their high solubility in water. These reactions proved to be more highly selective than the solid state photoreaction. Because in the previous report [5], irradiation of polycrystalline mixtures of 4-hydroxybenzaldehyde **1e** and **2** for 24 hours gave **3e** in only 11% yield and 4-hydroxybenzoic acid in 37% yield.

The solvent-free condensation of aldehyde **1** with antipyrine **2** occurs by the activation of carbonyl carbon by protonation because absence of *p*-toluenesulfonic acid does not cause any reaction. Further study is necessary to elucidate the reaction mechanism.

Table 1

p-TsOH Catalyzed Reaction of Aldehydes with Antipyrine in the Absence of Solvent

Entry	Aldehyde	Reaction time (h)	Product	Yield (%)
1	**1a**	1	**3a**	80
2	**1b**	1	**3b**	99
3	**1c**	24	**3c**	93
4	**1d**	24	**3d**	79
5	**1e**	1	**3e**	87
6	**1f**	1	**3f**	77

EXPERIMENTAL

^{1}H nmr spectra were measured on a JEOL JNM-GSX270 spectrometer with tetramethylsilane as an internal standard. IR spectra were recorded on a Horiba FT-IR-210 spectrophotometer. Melting points (mp) were not corrected. Elemental analysis was carried out with a Yanaco CHN Corder MT-5. All the reagents were commercially available.

General Procedure for Solvent-free Reaction.

A mixture of aldehyde **1** (5 mmol) and antipyrine **2** (10 mmol) was ground with *p*-toluenesulfonic acid monohydrate (*p*-TsOH•H_2O, 25 mmol) in a mortar in the absence of solvent and allowed to stand for 1 hour at room temperature. After completion of the reaction (TLC), water (30 ml) was added to the reaction mixture and the slurry was extracted twice with chloroform (20 and 10 ml). The organic solution was washed with saturated $NaHCO_3$ and then water, dried over $NaSO_4$, and evaporated under reduced pressure.

Bis[1-(2,3-dimethyl-1-phenyl-3-pyrazolin-5-one)]phenylmethane (**3a**).

This compound was obtained as a white powder; mp 203-205 °C (from ethyl acetate); IR (KBr) 1664 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform) δ 7.18-7.46 (m, 15H), 5.30 (s, 1H), 3.03 (s, 6H), 2.13 (s, 6H).

Anal. Calcd. for $C_{29}H_{28}N_4O_2$: C, 74.97; H, 6.08; N, 12.06. Found: C, 75.07; H, 6.10; N, 12.05.

Bis[1-(2,3-dimethyl-1-phenyl-3-pyrazolin-5-one)]-2-nitrophenylmethane (**3b**).

This compound was obtained as a yellow powder; mp 186-187 °C (from ethyl acetate); IR (KBr) 1632 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform) δ 7.32-8.13 (m, 14H), 6.28 (s, 1H), 3.10 (s, 6H), 2.21 (s, 6H).

Anal. Calcd. for $C_{29}H_{27}N_5O_4$: C, 68.34; H, 5.34; N, 13.74. Found: C, 68.51; H, 5.39; N, 13.60.

Bis[1-(2,3-dimethyl-1-phenyl-3-pyrazolin-5-one)]-3-nitrophenylmethane (**3c**).

This compound was obtained as yellow prisms; mp 175-176 °C (from ethyl acetate); IR (KBr) 1632 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform) δ 7.19-8.23 (m, 14H), 5.37 (s, 1H), 3.08 (s, 6H), 2.18 (s, 6H).

Anal. Calcd. for $C_{29}H_{27}N_5O_4$: C, 68.34; H, 5.34; N, 13.74. Found: C, 68.35; H, 5.51; N, 13.72.

Bis[1-(2,3-dimethyl-1-phenyl-3-pyrazolin-5-one)]-4-nitrophenylmethane (**3d**).

This compound was obtained as yellow prisms; mp 238-240 °C (from ethyl acetate); IR (KBr) 1660 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform) δ 7.26-8.18 (m, 14H), 5.36 (s, 1H), 3.07 (s, 6H), 2.17 (s, 6H).

Anal. Calcd. for $C_{29}H_{27}N_5O_4$: C, 68.34; H, 5.34; N, 13.74. Found: C, 68.32; H, 5.45; N, 13.60.

Bis[1-(2,3-dimethyl-1-phenyl-3-pyrazolin-5-one)]-4-hydroxyphenylmethane (**3e**).

This compound was obtained as red prisms; mp 245-246 °C (from ethyl acetate) ; IR (KBr) 3226 (OH), 1672 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform) δ 7.21-7.46 (m, 14H), 5.21 (s, 1H), 3.02 (s, 6H), 2.12 (s, 6H).

Anal. Calcd. for $C_{29}H_{28}N_4O_3$: C, 72.48; H, 5.87; N, 11.66. Found: C, 72.50; H, 5.95; N, 11.45.

Bis[1-(2,3-dimethyl-1-phenyl-3-pyrazolin-5-one)]-4-phenylphenylmethane (**3f**).

This compound was obtained as a white powder; mp 224-226 °C; IR (KBr) 1672 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform) δ 7.06-7.73 (m, 19H), 5.20 (s, 1H), 3.49 (s, 6H), 2.67 (s, 6H).

Anal. Calcd. for $C_{35}H_{32}N_4O_2$: C, 77.75; H, 5.97; N, 10.36. Found: C, 67.70; H, 6.11; N, 10.31.

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