

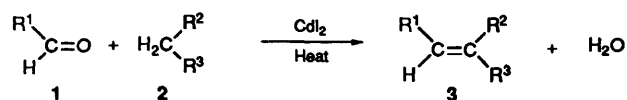
Cadmium Iodide as a New Catalyst for Knoevenagel Condensations

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Cadmium iodide catalyses the condensation of aldehydes with active methylene compounds, in the absence of solvent, to afford olefinic products in high yields.

Selective carbon-carbon bond formation is often induced by inorganic solids¹ and the recent^{2,3} use of metal or metal halides in this connection gives reactions which involve milder conditions, easier work-up procedures and higher selectivity than those conducted in solution.⁴ Adsorptions on inorganic solids in the absence of solvents (dry reactions) have been used for oxidations,⁵ reductions,⁶ alkylations,⁷ condensations,⁸ and acetylations,⁹ until now, however, such reactions have been little used for carbon-carbon bond formation.^{8a,d} The Knoevenagel condensation,^{10,11} is usually catalysed by organic

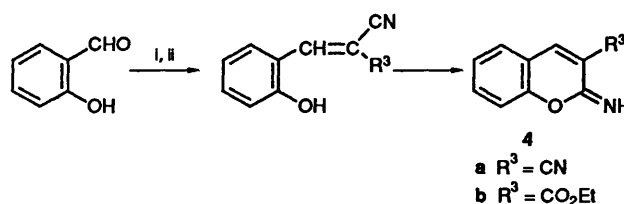


Scheme 1

bases (primary, secondary and tertiary amines, ammonia and ammonium salts),¹⁰ however, in recent years, new catalysts including silica gel functionalised with amine groups (Al₂O₃, AlPO₄-Al₂O₃, TiCl₄/base and doped xonontlite) have been reported.¹² Use of cadmium iodide as catalyst has not, hitherto, been studied.^{10,13}

Here we report its use¹³ in the heterogeneous phase and in the absence of solvents for Knoevenagel condensations. Such reactions occur in minutes and give excellent yields of olefinic products of high purity (see Scheme 1 and Table 1). Aromatic α,β -unsaturated aldehydes gave the corresponding olefinic Knoevenagel products with no evidence for the formation of Michael-type addition products. Thus, cinnamaldehyde with

malononitrile gave 1,1-dicyano-4-phenylbuta-1,3-diene (90% conversion after 10 min) (entry 3b). In the reaction of *o*-hydroxybenzaldehyde with active methylene compounds (Scheme 2) the first-formed Knoevenagel condensation pro-



Scheme 2 Reagents and conditions: i, Malononitrile; ii, Cadmium iodide, heat

ducts underwent further transformations as a result of nucleophilic attack by the phenolate ion on the cyano group, which is held in a stereochemically favourable position by the olefinic bond. The reaction, in the absence of solvent, was carried out by mixing the carbonyl compound, active methylene compound and cadmium iodide at room temperature and heating for a specified time to give, after work-up, excellent yields of the corresponding Knoevenagel products (see Table 2). Some yields (e.g. 3a, 95%) were much higher than for reactions carried out in boiling benzene (74%).¹⁰

In conclusion, the Knoevenagel condensation reported here is an attractive addition to existing methodologies¹⁰⁻¹³ since the reaction is rapid, the product yields are excellent and the procedure is simple.

Table 1 Reaction time and yield of the product 3 in the Knoevenagel condensations of 1 and 2 in the absence of solvent^{13,14}

Entry 3	R ¹	R ²	R ³	Reaction time (min)	Yield (%)	Lit. yield (%)
a	Ph	CN	CN	5	95	74 ¹⁰
b	(<i>E</i>)-PhCH=CH	CN	CN	10	90	67 ^{12a}
c	Me	CN	CN	9	80	75 ^{8b}
d	2-Furyl	CN	CN	10	85	56 ^{12c}
e	4-Quinolyl	CN	CN	6	91	98 ^a
f	<i>p</i> -NO ₂ C ₆ H ₄	CN	CN	6	92	41 ^b
g	Ph	CO ₂ Et	CN	12	90	74 ^{12c}
h	(<i>E</i>)-PhCH=CH	CO ₂ Et	CN	10	85	79 ^{12c}
i	<i>p</i> -NO ₂ C ₆ H ₄	CO ₂ Et	CN	6	91	85 ^{12c}
j	2-Furyl	CO ₂ Et	CN	15	82	89 ^{12c}
k	4-Quinolyl	CO ₂ Et	CN	8	90	90 ^a
l	Ph	CO ₂ H	CN	10	92	94 ^c
m	(<i>E</i>)-PhCH=CH	CO ₂ H	CN	8	85	25 ^c
n	Ph	CONH ₂	CN	10	90	85 ^{8b}
o	(<i>E</i>)-PhCH=CH	CONH ₂	CN	10	93	—
p	<i>p</i> -MeOC ₆ H ₄	CONH ₂	CN	12	92	75 ¹⁰
q	Ph	CO ₂ Et	CO ₂ Et	15	90	89 ^d
r	Ph	MeCO	CO ₂ Et	12	80	83 ^d

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Table 2 Physical constants and microanalytical data of compounds **3a-r**

Compound	M.p. (°C)	Lit. m.p./ (°C)	Molecular formula	Required (%)			Found (%)		
				C	H	N	C	H	N
3a	82	83 ^a	C ₁₀ H ₆ N ₂	77.92	3.90	18.18	78.0	4.0	18.1
3b	127	128 ^b	C ₁₂ H ₈ N ₂	80.00	4.44	15.55	79.9	4.4	15.6
3c	77	20 ^{bb}	C ₅ H ₄ N ₂	65.21	4.35	30.43	65.3	4.4	30.5
3d	72	73 ^c	C ₈ H ₄ N ₂	75.00	3.13	21.88	75.1	3.0	22.0
3e	146	146–147 ^d	C ₁₃ H ₇ N ₃	76.10	3.41	20.49	76.0	3.3	20.6
3f	159	159–160 ^c	C ₁₀ H ₅ N ₃ O ₂	60.30	2.52	21.11	60.4	2.6	21.2
3g	51	50 ^f	C ₁₂ H ₁₁ NO	74.53	6.83	8.70	74.6	7.0	8.55
3h	118	116 ^g	C ₁₄ H ₁₃ NO ₂	74.01	5.73	6.17	74.1	5.8	6.0
3i	168	170 ^h	C ₁₂ H ₁₀ N ₂ O ₂	67.29	4.67	13.08	67.4	4.6	13.2
3j	93	94 ⁱ	C ₁₀ H ₈ NO ₃	62.83	4.71	7.32	62.8	4.75	7.4
3k	97	98–99 ^d	C ₁₅ H ₁₂ N ₂ O ₂	71.43	4.76	11.11	71.5	4.7	11.2
3l	179	179–180 ^g	C ₁₀ H ₈ N ₂ O	69.36	4.05	8.09	69.5	4.2	8.1
3m	210	212 ^g	C ₁₂ H ₉ NO ₂	72.36	4.52	7.04	72.2	4.4	7.1
3n	121	123 ^{bb}	C ₁₀ H ₈ N ₂ O	69.77	4.65	16.28	69.8	4.8	16.2
3o	142		C ₁₂ H ₁₀ N ₂ O	72.73	5.05	14.14	72.8	5.2	14.1
3p	216	216 ¹⁰	C ₁₁ H ₁₀ N ₂ O ₂	65.35	4.95	13.86	65.5	5.0	13.9
3q	Oil	Oil	C ₁₄ H ₁₆ O ₄	67.75	6.45	—	67.6	6.5	—
3r	Oil	Oil ^h	C ₁₃ H ₁₄ O ₃	71.56	6.42	—	71.6	6.5	—

^a For a similar type of reaction see: T. Naota, H. Taki, M. Mizuno and S. Murahashi, *J. Am. Chem. Soc.*, 1989, **111**, 5954; ^b S. Dutt, *J. Ind. Chem. Soc.*, 1925, **1**, 297; J. Martelli and R. Carrie, *Bull. Soc. Chim. Fr.*, 1977, 1182; ^c B. B. Corson and R. W. Stoughton, *J. Am. Chem. Soc.*, 1928, **50**, 2825; ^d See Table 1, a; ^e See Table 1, b; ^f Ref. 15; ^g See Table 1, c; ^h J. Zabicky, *J. Chem. Soc.*, 1961, 683; ⁱ N. Singh and J. S. Sandhu, *J. Ind. Chem. Soc.*, 1956, **33**, 709.

Experimental

M.p.s were taken in open capillary tubes on a Buchi apparatus and were uncorrected. IR spectra were recorded as KBr discs on a Perkin-Elmer 237B IR spectrometer. Microanalyses were performed on a Perkin-Elmer 240C analyser. The ¹H NMR spectra were recorded at Varian T-60 machine using tetramethylsilane (TMS) as the internal standard. The chemical shifts are recorded as δ values. Cadmium iodide used was of commercial grade and procured from Loba Chemie Indoaustral Co. Bombay. All other chemicals were purified by distillation or crystallisation prior to use.

General Procedure for the Knoevenagel Condensations in the Absence of Solvent.—A mixture of the carbonyl compound **1a** (R¹ = Ph) (1.06 g, 10 mmol), the active methylene compound **2a** (R² = R³ = CN) (1.06 g, 10 mmol) and commercial grade cadmium iodide (0.37 g, 1 mmol) was thoroughly mixed at room temperature. After being stirred for 3 min, the mixture was heated in an oil-bath at 75 °C for 5 min. It was then stirred and allowed to cool to room temperature when it solidified. The solid material was treated with 1% aqueous alcohol. The product was then filtered off, dried and recrystallised from ethanol (95% yield). Other Knoevenagel products **3b-r** were similarly prepared (see Table 2). Reaction of *o*-hydroxybenzaldehyde with active methylene compounds, carried out in the same way gave the imino lactones **4** (30–35%). A similar reaction for a longer period gave only polymeric material. The physical and analytical data for compounds **4** are as follows: 2-imino-2*H*-1-benzopyran-3-carbonitrile **4a** (30%), m.p. 163 °C (decomp.) [lit.,¹⁴ m.p. 167 °C (decomp.); ν_{\max} (KBr)/cm⁻¹ 3330, 2225 and 1640 (Found: C, 70.7; H, 3.6; N, 16.5. C₁₀H₆N₂O requires C, 70.59; H, 3.53; N, 16.47%). Ethyl 2-imino-2*H*-1-benzopyran-3-carboxylate **4b** (35%), m.p. 133 °C (lit.,¹⁵ m.p. 135 °C); ν_{\max} (KBr)/cm⁻¹ 3325 and 1670 (Found: C, 66.5; H, 4.9; N, 6.4. C₁₂H₁₁NO₃ requires C, 66.36; H, 5.07; N, 6.45%).

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