Lithium bromide as a new catalyst for carbon–carbon bond formation in the solid state

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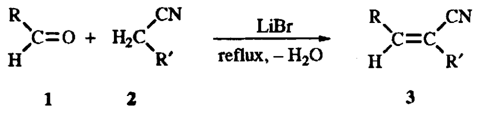
Lithium bromide catalyses the condensation of carbonyl compounds with active methylene compounds in the absence of solvent, to afford olefinic products in high yields.

Most organic reactions have been studied in solution. Not only photochemical reactions but also ground state organic reactions were found to occur efficiently in the solid state.[1] Selective carbon–carbon bond formation reactions are often induced by inorganic solids[2] and the recent use of metals in this context gives reaction under milder conditions, easier work-up procedures and higher selectivity than those conducted in solution.[3] Adsorptions on inorganic solids in the absence of solvents have been used for oxidations, reductions, alkylations, condensations and acetylations;[2a,4] until now, however, such reactions have been little used for carbon–carbon bond formation.[2a,4a] In contrast, Reformatsky and Luche reactions occurred more efficiently in the absence of solvent.[5] The Knoevenagel condensation is usually catalysed by organic bases (primary, secondary and tertiary amines, ammonia and ammonium salts), however, in recent years, new catalysts including silica gel functionalised with amine groups (Al_2O_3, $AlPO_4$–Al_2O_3, $TiCl_4$/base and doped xonontlite) have been reported.[6] Use of lithium bromide as catalyst has not hitherto, been reported.

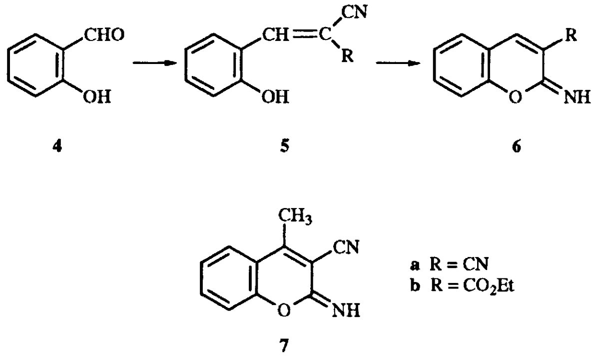
Here we wish to report the use of a new catalyst, lithium bromide, for carbon–carbon bond formation in a heterogenous reaction in the absence of solvents. It can perform the reaction to produce the olefinic products in good purity and high yields. The results obtained with different carbonyl compounds and active methylene compounds, shown in Scheme 1, are recorded in Table 1.



Scheme 1

Such reactions occur in minutes and give excellent yields of olefinic products of high purity. Aromatic α,β-unsaturated aldehydes give 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 exclusively. When the same reaction was repeated in refluxing benzene, it required a longer reaction time (approximately 15 h) and gave poor yield of **3b**.

In the reaction of *o*-hydroxybenzaldehyde with active methylene compounds (Scheme 2), the first formed Knoevenagel condensation products 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. Thus, 2-imino-2*H*-1-benzopyran-3-carbonitrile **6a** and 2-imino-2*H*-1-benzopyran-3-carboxylate **6b** were formed exclusively in 85 and 80% yields, respectively. A similar reaction has also been carried out with *o*-hydroxyacetophenone and malononitrile giving the more complex 3-cyano-4-methyliminocoumarin **7** in 82% yield, instead of the usually obtained condensed product.



Scheme 2

In conclusion, the present communication offers a convenient method for the stereospecific preparation of *E* olefins wherein the reaction is rapid, the product yields are excellent and the procedure is simple.

Experimental

Mps were taken in open capillary tubes on a Buchi apparatus and were uncorrected. IR spectra were recorded as KBr discs on a Perkin-Elmer 240C analyser. The ^1H NMR spectra were recorded with a Varian T-60 machine using tetramethylsilane (TMS) as the internal standard. The chemical shifts are recorded as δ values. Lithium bromide used was of commercial grade and obtained from Loba Chemie Indoaustranal Co., Bombay. All other chemicals were purified by distillation or crystallisation prior to use.

Knoevenagel condensations in the absence of solvent

General procedure. To a mixture of the carbonyl compound **1a** (R = Ph) (0.53 g, 5 mmol) and active methylene compound **2a** (R′ = CN) (0.34 g, 5 mmol) was added commercial grade lithium bromide (0.09 g, 1 mmol) at room temperature. After being stirred for 5 min, the resulting mixture was heated at 80 °C in a heating mantle for 10 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 (0.77 g, 90% yield). Other Knoevenagel products **3b**–**m** were similarly prepared and their characteristics are recorded in Table 2. A typical example: to a mixture of cinamaldehyde **1b** (0.66 g, 5 mmol) and malononitrile (0.34 g, 5 mmol), lithium bromide (0.09 g, 1 mmol) was added. The resulting mixture is heated at 80 °C in a heating mantle for 15 min. Then it was cooled and the solid material was treated with 1% aqueous alcohol and filtered off. The 1,1-dicyano-4-phenylbuta-1,3-dione thus obtained is recrystallised from ethanol, mp 128 °C,

Table 1 Reaction time and yield of the products **3a–m** in the Knoevenagel condensations of **1** and **2** in the absence of solvent[9]

Entry[a] 3	R	R′	Reaction time[b] (min)	Yield[c] (%)	Lit. yield (%)
a	Ph	CN	10	90	74[10]
b	(*E*)-PhCH=CH	CN	15	85	67[6a]
c	Me	CN	10	80	75[6c]
d	2-furyl	CN	8	75	56[5c]
e	4-Quinolyl	CN	12	75	98[11]
f	p-$NO_2C_6H_4$	CN	10	85	41[12]
g	Ph	CO_2Et	15	80	74[6c]
h	(*E*)-PhCH=CH	CO_2Et	10	85	79[6c]
i	p-$NO_2C_6H_4$	CO_2Et	10	81	85[6c]
j	2-Furyl	CO_2Et	10	80	89[6c]
k	4-Quinolyl	CO_2Et	12	75	90[11]
l	Ph	CO_2H	15	85	94[13]
m	(*E*)-PhCH=CH	CO_2H	12	80	25[13]

[a] The products were identified by comparison of mp/bp and spectral data with standard samples. [b] Increasing the time of reaction had no significant effect on the yield and resulted in minor decomposition. [c] Yields refers to yield of pure isolated products.

Table 2 Physical constants and microanalytical data of compounds **3a–m**

Entry 3	Mp (°C)	Lit. mp (°C)	Molecular formula	Required (%) C	H	N	Found (%) C	H	N
a	82	83[14a]	$C_{10}H_6N_2$	77.92	3.90	18.18	78.0	3.8	18.2
b	128	128[14b]	$C_{12}H_8N_2$	80.00	4.44	15.55	79.9	4.4	15.6
c	77	20[6b]	$C_5H_4N_2$	65.21	4.35	30.43	65.2	4.5	30.5
d	72	73[14c]	$C_8H_4N_2$	75.00	3.13	21.88	75.1	3.0	21.7
e	146	146–47[11]	$C_{13}H_7N_3$	76.10	3.41	20.49	76.2	3.4	20.6
f	160	159–60[12]	$C_{10}H_5N_3O_2$	60.30	2.52	21.11	60.4	2.5	21.2
g	51	50[8]	$C_{12}H_{11}NO$	74.53	6.83	8.70	74.6	7.0	8.6
h	118	116[13]	$C_{14}H_{13}NO_2$	74.01	5.73	6.17	74.1	5.8	6.1
i	168	170[14d]	$C_{12}H_{10}N_2O_2$	67.29	4.67	13.08	67.3	4.7	13.1
j	93	94[14e]	$C_{10}H_9NO_3$	62.83	4.71	7.32	62.7	4.75	7.4
k	97	98–99[11]	$C_{15}H_{12}N_2O_2$	71.43	4.76	11.11	71.5	4.7	11.2
l	179	179–80[13]	$C_{10}H_7NO_2$	69.36	4.05	8.09	69.4	4.1	8.2
m	210	212[13]	$C_{12}H_9NO_2$	72.36	4.52	7.04	72.4	4.5	7.0

lit.[14b] mp 128 °C, (0.76 g, 85% yield). Reaction of *o*-hydroxybenzaldehyde and *o*-hydroxyacetophenone with active methylene compounds were carried out in the same way, giving the corresponding imino lactones **6** and **7** in 80–85% yields. Under similar reaction conditions with a longer reaction time only polymeric material was obtained. The physical and analytical data for compounds **6** and **7** are as follows: 2-imino-2*H*-1-benzopyran-3-carbonitrile **6a** (0.72 g, 85%), mp 164 °C (decomp.) lit.,[7] mp 167 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3325, 2220 and 1645 (Found: C, 70.7; H, 3.6; N, 16.6. $C_{10}H_6N_2O$ requires C, 70.59; H, 3.53; N, 16.47%); Ethyl 2-imino-2*H*-1-benzopyran-3-carboxylate **6b** (0.86 g, 80%), mp 134 °C, lit.,[8] mp 135 °C; ν_{max}(KBr)/cm^{-1} 3330 and 1665 (Found: C, 66.4; H, 6.1; N, 6.4. $C_{12}H_{11}NO_3$ requires C, 66.36; H, 5.07; N, 6.45%). 2-Imino-3-methyl-2*H*-1-benzopyran-3-carbonitrile **7** (0.75 g, 82%), mp 150 °C, lit.,[7] 151 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3330, 2215 and 1640 (Found: C, 71.8; H, 4.4; N, 15.3. $C_{11}H_8N_2O$ requires C, 71.74; H, 4.34; N, 15.22%).

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