Sodium carbonate: A versatile catalyst for Knoevenagel condensation

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Received 17 November 2009; accepted (revised) 17 August 2010

Catalytic amounts of sodium carbonate (Na$_2$CO$_3$) catalyze the condensation of aromatic aldehydes with active methylene compounds to afford arylmethylidene products under the grindstone method. The reactions go to completion within 1-5 min at 26ºC and give products in excellent yield.

Keywords: Grindstone method, aromatic aldehydes, active methylene compounds, sodium carbonate, solvent-free reaction

Toda introduced a method called the grindstone method$^1$. In this method, solids are ground together using a pestle and mortar to get the products. The method is advantageous over the existing methods as the yields of the products are high and one can avoid the use of solvents, and the method matches the green chemistry protocols.

The Knoevenagel condensation of araldehydes with active methylene compounds is an important and widely employed method for carbon-carbon bond formation in organic synthesis$^2$. Usually gaseous ammonia, amines and their salts are used as catalysts in this condensation$^3$. Recently TEBA$^4$, diammonium hydrogen phosphate$^5$, [bmim]OH (Ref. 6), lithium bromide$^7$, hydrotalcite$^8$, nanocrystalline magnesium oxide$^9$, hexadecyltrimethyl ammonium bromide$^{10}$, MgO/ZrO$_2$ (ref. 11), CeCl$_3$-7H$_2$O-NaI (ref. 11), imidazoles$^{13}$, gem-diamines$^{14}$, methylammonium FAU zeolite$^{15}$, and poly(vinylchloride) supported tetraethylenepentamine$^{16}$ has been reported to bring about this reaction. Although some of these methods represent convenient procedures with good to high product yields, representation of a new, efficient and facile procedure for synthesis of these compounds can be very significant.

On one hand, studies on use of readily available and an inexpensive environmentally benign sodium carbonate has greatly expanded all around the world; and search for application of sodium carbonate has pulled up numerous records$^{17}$. On the other hand, Aramendia has reported the Knoevenagel condensation of malononitrile with benzaldehyde using potassium carbonate, rubidium carbonate and cesium carbonate to get benzylidenemalononitrile, but the reactions proceed further to give benzylmalononitrile (also, the Michael addition of malononitrile to certain double bonds occurred in the presence of K$_2$CO$_3$) (ref. 18a). Siebenhaar et al in 2001 used a 1:4 mixture of sodium carbonate-4 Å molecular sieves at 50°C and at 90°C for Knoevenagel condensation$^{18b}$. Esteb et al have performed the Knoevenagel condensation of aldehydes and malononitrile at RT for 30 min in water using sodium bicarbonate, sodium acetate, and potassium carbonate$^{18c}$.

Results and Discussion

An earlier report from our laboratory described the synthesis of bis(indolyl) methanes under the grindstone method$^{19}$. The same methodology has now been extended to synthesize arylmethylidene compounds from aromatic aldehydes with active methylene compounds. The reaction requires catalytic amounts of sodium carbonate, and is possible in the absence of a solvent under the grindstone method at 26°C. The products are obtained in good purity with excellent yields within 1-5 min (Scheme I).

The reaction of benzaldehyde with ethyl cyanoacetate using catalytic amount of Na$_2$CO$_3$ at 26°C was initially carried out in different solvents (Table I). It is clear from this table that, when non polar solvent is used, after stirring for 20 min the yield of the product is less than 35%, with polar solvent, after stirring for 10 min the yield of the product is 85% (polar solvents assist the reaction), whereas in the absence of a solvent under the grindstone method yield is 96% (Entry 8).

In order to find a suitable catalyst for the

\[
\text{ArCHO} + \begin{array}{c}
\text{CN} \\
\text{X}
\end{array} \xrightarrow{\text{Grindstone method}} \text{Ar}^+\text{CN} \\
\xrightarrow{\text{Solvent-free}} \text{Ar}^+\text{CN} \\
\text{X} = \text{COOEt, CN} \\
\text{Na}_2\text{CO}_3 , 1-5 \text{ min.}
\]

Scheme I

Note
Knoevenagel condensation under grindstone method, we worked with different bases which were available in our laboratory we found that, sodium carbonate gives best yield of the product (in the absence of a solvent under the grindstone method) in our experiment. Use of just 0.1 mmole sodium carbonate in the solvent-free grindstone method is sufficient to push the reaction forward. Therefore 0.1 mmole of sodium carbonate was chosen for further work.

By using 0.1 mmole sodium carbonate in the solvent-free grindstone method, a systematic study was undertaken to investigate the Knoevenagel condensation reaction of aromatic aldehydes bearing electron-withdrawing and electron-donating groups with active methylene compounds. The results are summarized in Table III which shows that in all the cases respective products are obtained in excellent yield within 1-5 min.

### Experimental Section

Araldehydes, methylene compounds and sodium carbonate are purchased from S D fine-chem limited and are of LR grade and used without further purification. Solvents were distilled before use. Reactions were monitored on TLC by comparison with the authentic samples. Melting points were determined on a Buchi melting point apparatus. IR, ¹H NMR and LC-MS were recorded on a Nicolet 400D FT-IR, 400 MHz Brucker spectrophotometers and an Agilent Technologies 1200 series instrument respectively.

### General procedure for Knoevenagel condensation

A mixture of an aldehyde (1 mmole), active methylene compound (1 mmole) and sodium carbonate (0.1 mmole) were ground together in a mortar at 26°C. The reaction mixture was solidified within 1-5 min After completion of the reaction (TLC), water was added, stirred for a min, filtered and dried. Recrystallization was not necessary. The melting point, IR, ¹H NMR and LC-mass spectral data of novel arylmethylidene compounds prepared by this procedure is presented below.

### Spectroscopic and analytical data of the novel products

**Ethyl-(E)-2-cyano-3-(4-fluorophenyl)-2-propenoate 9.** m.p: 98-100°C; IR: 2990, 2226, 1725, 1616, 1517 cm⁻¹; ¹H NMR (CDCl₃): δ 8.22 (s, 1H, H-C=C), 8.02-8.06 (m, 2H, ArH), 7.18-7.23 (t, 2H, J = 8Hz, ArH), 4.37-4.42 (q, 2H, J = 8Hz, -OCH₂CH₃), 1.39-1.43 (t, 3H, J = 8Hz, -OCH₂CH₃); MS: (m/z) 219.8 (M⁺).

**Ethyl-(E)-2-cyano-3-(4-cyanophenyl)-2-propenoate 10.** m.p: 169-171°C; IR: 2997, 2221, 1724, 1616, 1553 cm⁻¹; ¹H NMR (CDCl₃): δ 8.26 (s, 1H, H-C=C),
8.06-8.08 (d, 2H, J = 8Hz, ArH), 7.79-7.82 (d, 2H, J = 12Hz, ArH), 4.39-4.45 (q, 2H, J = 8Hz, OCH3). The reaction works at RT;
 excellent product yields are obtained in a short reaction time with elimination of solvents.

References