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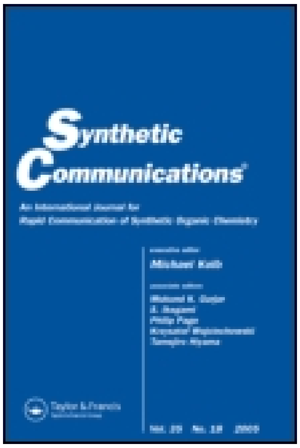

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Magnesium Ethoxide as an Effective Catalyst in the Synthesis of Dicayanomethylendihydrofurans

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Magnesium Ethoxide as an Effective Catalyst in the Synthesis of Dicayanomethylendihydrofurans

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Abstract: Magnesium ethoxide was used for the first time in the synthesis of the titled compounds. In these preparations, product yields were significantly improved compared with similar synthesis catalyzed by other metal ethoxides. The effectiveness of magnesium ethoxide as catalyst was tentatively rationalized.

Keywords: Dicayanomethylendihydrofurans, electron acceptors, magnesium ethoxide

Chromophores with push–pull π-electron-conjugated systems constitute the basic class of organic nonlinear optical materials (NLO), and electron acceptors are the key chemical structural units. 3-Cyano-2-dicayanomethylen-dihydrofuran and its derivatives are recognized as one of the best sorts of electron acceptors and have attracted extensive attention since their discovery,[1–3] particularly after the first successful use of this class of compound as an electron acceptor in an NLO chromophore in 1998.[4] In addition, these dihydrofurans may be also be used to synthesize compounds for labeling and visualizing biomolecules and biological structures.[5] Unfortunately, the yields of these acceptors are not ideal, especially for steric hindrance substituted derivatives; however, it is important to introduce hindered substituents at the 5-position of the dihydrofuran ring to inhibit

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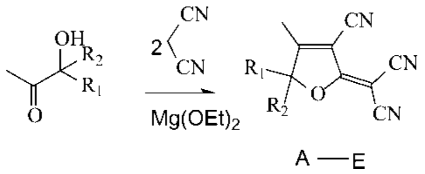
some unwanted dipole–dipole interactions between the NLO chromophore themselves. In this article, we report that magnesium ethoxide, as an effective catalyst, could improve product yields of titled compounds significantly and therefore make the synthesis of the steric hindrance substituted derivatives possible.

The synthesis of compound A to E catalyzed by lithum ethoxide[6] and sodium ethoxide[7] as well as by magnesium ethoxide were conducted in our laboratory. The results are shown in Table 1 and Table 2. There is no product yield data available for the compounds in Table 1 in literature except that product A has a reported yield of 75%[7] or 36%[8] and 88% under microwave-assisted conditions[9] when catalyzed by sodium ethoxide. As shown in Table 2, magnesium ethoxide is the base or catalyst that offers the highest product yield. The tentative explanation is given later. Steric hindrance obviously plays an important role in determining product yields. The order of steric hindrance of the substituents at 5-position basically corresponds to the order of the product yields. Compound A has highest yield of 91%, whereas a yield of only 33% is achieved for the most hindered compound E.

The mechanism of the condensation of α-hydroxy ketone with malononitrile is suggested in Scheme 1. α-Hydroxy ketone reacts with malononitrile through a Knoevenagel condensation (1), followed by intramolecular attack of the OH group on the nitrile group in **1** to form iminolactone **2**. Then, **2** reacts through an another type of Knoevenagel condensation (2) with a second malononitrile molecule to form product A to E while releasing NH_3. He and his coworkers[6] believe the Pinner reaction indicated in Scheme 1 is the crucial step in forming the desired product. They found that when the

Table 1. Synthesis of the dicayanomethylendihydrofurans catalyzed by the magnesium ethoxide



Product	R1	R2	Reaction time (h)	Isolated yield (%)
A	Methyl	Methyl	8	91
B	Methyl	Butyl	24	70
C	Methyl	Cyclohexyl	24	65
D	Methyl	2-Ethylhexyl	24	60
E	Butyl	Butyl	72	33

Table 2. Comparasion of the catalyst effect of magnesium ethoxide with commonly used compounds

	Isolated product yield (%)		
Product	Magnisium ethoxide	Lithium ethoxide[a]	Sodium ethoxide[b]
A	91	80	30 (75[6] or 36 [7])
B	70	—	—
C	65	—	—
D	60	Poor	Poor
E	33	Poor	Poor

[a] The procedure was performed according to Ref. 6.

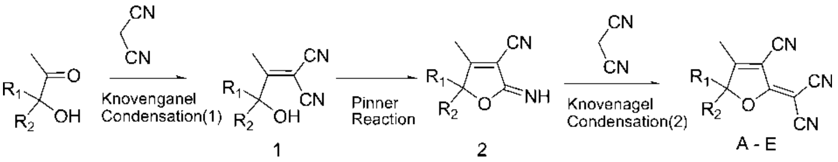
[b] The procedure was performed according to Ref. 7.

base is changed to $LiOC_2H_5$, the ring-closure reaction is more successful compared to the case of $NaOC_2H_5$ because of a tentatively presumed stronger Li-N intermediate complex between the nitrile nitrogen and the base. Our result is in agreement with this mechanism. It is reasonable to believe that an even stronger interaction between the bivalent ion Mg^{2+} and the nitrogen atom of the nitrile group in 1, as in our case, facilitates the ring-closure reaction, and a higher product yield is expected.

In conclusion, magnesium ethoxide was used for the first time as a catalyst in the synthesis of dicayanomethylendihydrofurans, and five derivatives have been prepared in clearly higher yields compared with the cases catalyzed by ethoxides of monovalent metal ion. It may be worthwhile to note that in this preparation, highly steric hindered derivatives such as compound E could also be obtained in an acceptable product yield.

EXPERIMENTAL

Reagents were purchased and used as received unless otherwise stated. Malononitrile was freshly distilled prior to use. Magnesium ethoxide was prepared according to this procedure: activated magnesium turning (4.8 g, 0.2 mol) was added to absolute ethanol (50 mL), and ethanol was kept refluxing until magnesium turning disappeared. Ethanol was evaporated, and magnesium



Scheme 1. Steps involved in the TCF ring synthesis.

ethoxde was collected as white powder. Alternatively, magnesium ethoxide could be prepared and used as catalyst without isolation for the synthesis of dicayanomethyldihydrofurans. The α-hydroxy ketones used in this work were obtained as follows: 3-hydroxy-3-methyl-2-butanone was purchased from Aldrich and used as received; 3-butyl-3-hydroxy-2-heptanone was synthesized according to a known procedure.[10] The other three α-hydroxy ketones were synthesized in this laboratory; the detailed procedures together with other work will be published later. FR-IR spectrum was determined on a BIO-RAD FTS-165 spectrometer; MS spectrum was determined on a TRIO-2000 spectrometer. ^{1}H NMR spectrum was determined on a Varian Gemini 300 (300 MHz) ^{1}H NMR spectrometer (with $CDCl_3$ as solvent and tetramethylsilane as internal reference). All melting points are uncorrected.

The general procedure: 1 molar part of α-hydroxy ketones, 2 to 3 molar parts of malononitrile, 1 to 1.5 molar parts of magnesium ethoxide, and 20 to 30 molar parts of absolute of ethanol were mixed. The reactant solution was kept at 60°C for 8–72 h and then concentrated by rotary evaporation. The residue was dissolved with methylene chloride, and the solution was filtrated. The solvent was evaporated, and the residue was collected and washed with 20–30 mL of deionized water. Then, the residue was recrystallized from ethanol to give products A–E.

2-(3-Cyano-4,5,5-trimethyl-5*H*-furan-2-ylidene)malononitrile (A): According to the general procedure, a mixture of malononitrile (3 g, 45 mmol), 3-hydroxy-3-methyl-2-butonone (1.53 g, 15 mmol), magnesium ethoxide (1.94 g, 17 mmol), and absolute ethanol (15 mL) was stirred effectively at 60°C for 8 h. Product A (3.17 g, 15.9 mmol) was obtained as light yellow crystal, yield 91%, mp 197–198°C, lit.[7] 199°C, IR (KBr): $\nu_{max}(cm^{-1})$: 2995, 2235, 2222, 1619, 1591.

2-(3-Cyano-4,5-dimethyl-5-butyl-5*H*-furan-2-ylidene)malononitrile (B): A mixture of malonontrile (3 g, 45 mmol), 3-butyl-3-hydroxy-2-butaone (2.16 g, 15 mmol), magnesium ethoxide (1.94 g, 17 mmol), and absolute ethanol (15 mL) was stirred effectively at 60°C for 24 h. Compound B (2.53 g, 10.5 mmol) was obtained as a colorless crystal, yield 70%, mp: 104°C, IR (KBr): $\nu_{max}(cm^{-1})$: 2958, 2933, 2228.5, 1620, 1596.7; MS, m/s (%): 241 (M+, 100), 184 (52), 57 (50); ^{1}H NMR (δ, ppm, $J_{H\text{-}H}$, Hz), 2.3303 (s, 3H, C_4-CH_3), 2.0384 (m, 2H), 1.7958 (m, 2H), 1.5998 (s, 3H, C_5-CH_3), 1.3271 (m, 2H, $J_{H\text{-}H} = 7$), 0.9232 (t, 3H, $J_{H\text{-}H} = 7.2$).

2-(3-Cyano-4,5,-dimethyl-5-cyclohexyl-5*H*-furan-2-ylidene)malononitrile (C): A mixture of malonontrile (3 g, 45 mmol), 3-cyclohexyl-3-hydroxy-2-butaone (2.55 g, 15 mmol), magnesium ethoxide (1.94 g, 17 mmol), and absolute ethanol (15 mL) was stirred effectively at 60°C for 24 h. Product C (2.6 g, 9.75 mmol) was obtained as a colorless crystal, yield 65%, mp: 210°C, IR (KBr): $\nu_{max}(cm^{-1})$: 2931, 2857, 2228.5, 1616.25, 1592.21, MS, m/z (%): 267 (M+, 30), 185 (42), 83 (100); ^{1}H NMR (δ, ppm): 2.3350 (s, 3H, C_4-CH_3), 1.8270 (m, 5H), 1.5743 (s, 3H, C_5-CH_3), 1.2482 (m, 6H).

2-[3-Cyano-4,5-dimethyl-5-(2-ethylhexyl)-5*H*-furan-2-ylidene]malononitrile (D): A mixture of malonontrile (3 g, 45 mmol), 5-ethyl-3-hydroxy-3-methyl-2-nonanone (3 g, 15 mmol), magnesium ethoxide (1.94 g, 17 mmol), and absolute ethanol (15 mL) was stirred effectively at 60°C for 24 h. Product D (2.68 g, 9 mmol) was obtained as a colorless crystal, yield 60%, mp: 118°C; IR (KBr): ν_{max}(cm^{-1}): 2963, 2931, 2862, 2227, 1617, 1587, MS, m/z (%): 298 (M+, 100), 184 (15), 71 (15.70), 57 (16.74); ^{1}H NMR (δ ppm): 2.3447 (s, 3H, C_4-CH_3), 1.9549 (m, 1H), 1.8251 (m, 2H), 1.5968 (s, 3H, C_5-CH_3), 1.3002–1.200 (m, 8H), 0.9056 (t, 3H, CH_3), 0.8928 (t, 3H, CH_3).

2-(3-Cyano-4-methyl-5,5-dibutyl-5*H*-furan-2-ylidene)malononitrile (E): A mixture of malononitrile (3 g, 45 mmol), 3-butyl-3-hydroxy-2-heptanone (2.8 g, 15 mmol), magnesium ethoxide (1.94 g, 17 mmol), and absolute ethanol (15 mL) was stirred effectively at 60°C for 72 h. Product E (1.49 g, 5.2 mmol) was obtained as a colorless crystal, yield 33%, mp: 92°C, IR (KBr): ν_{max}(cm^{-1}): 2926, 2970, 2221, 1619, 1595, 1465, MS: m/z (%): 284 (M+, 21), 227 (49), 184 (62), 57 (100), 41 (79); ^{1}H NMR (δ, ppm, $J_{H\text{-}H}$, Hz): 2.2962 (s, 3H, C_4-CH_3), 2.0558 (m, 2H), 1.8057 (m, 2H), 1.3326 (t, $J_{H\text{-}H} = 7.4$ H), 1.1871 (m, 4H), 0.9141 (t, $J_{H\text{-}H} = 7.44$, 6H, $2 \times CH_3$).

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