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Product Diversion by Magnesium Chelation in the Chemistry of Cyanoesters.

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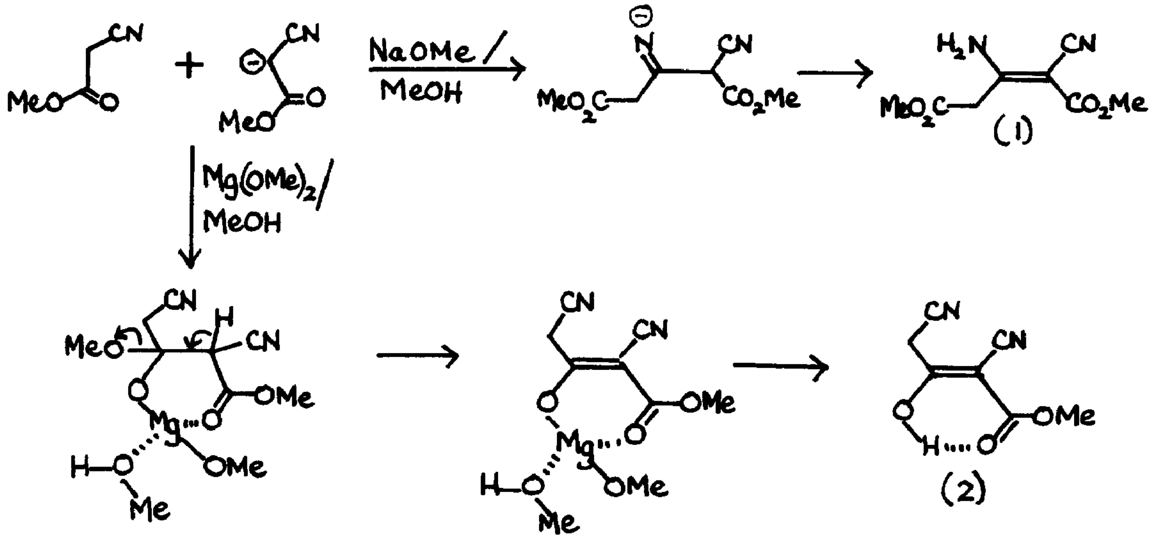
Summary: Whilst treatment of methyl cyanoacetate with sodium methoxide in methanol gives the dimer **1**, formed through 1,2-nitrile addition, the employment of magnesium methoxide in methanol as a chelating base, intercepts the Claisen product giving only **2** in excellent yield: a 'crossed example has also been found.

The ability of the chelating base magnesium methoxide in methanol to drastically alter reaction courses relative to those brought about by sodium methoxide in methanol has been demonstrated in our earlier work which involves simple and highly complex carbonyl-ester systems.[1] A new type of case involving this simple reagent with a simple reactant, under simple conditions, yet giving an excellent yield of a novel simple product is now reported.

Refluxing methyl cyanoacetate with sodium methoxide in methanol is known[2] to form the crystalline dimer dimethyl 2-amino-1-cyanoglutaconate **1**, a useful intermediate in heterocyclic synthesis. This is the product

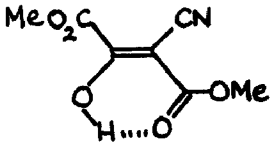


from 1,2-addition of the carbanion to the nitrile of a second molecule of cyanoacetate as shown. When the reaction is carried out using magnesium methoxide in methanol at 20°C however, a white precipitate forms and on work up of this magnesium chelate with 4M-HCl 3-hydroxy-2-methoxycarbonyl-glutaconic dinitrile **2**, needles m. p. 92 - 93°C is obtained in 78% yield. It analysed for $C_7H_6O_3N_2$, giving a deep red ferric chloride reaction.[3] The simple, yet novel, compound appears to exist entirely in the enolic form.

Dinitrile **2** is clearly intercepted and captured by magnesium chelation as the kinetic product in the 1,2-addition / Claisen competition set up by methanolic methoxide ion which normally leads to the thermodynamic product **1**. The magnesium chelate can be mono-, then di-, methylated at C-4, but released from its chelate compound **2** becomes labile towards methoxide ion. Thus, refluxing with sodium methoxide in methanol gives **1**: on the other hand, refluxing **1** with magnesium methoxide leaves it structurally unchanged.

This type of reaction is not confined to self condensation. Addition of methyl cyanoacetate to diethyl oxalate in refluxing magnesium methoxide gives no precipitate, but on acid work-up dimethyl 2-cyano-3-hydroxyfumarate **3**, m. p, 108 - 109°C, is obtained in 85% yield.

Attempted crossed condensations with methyl acetate, formate or benzoate were not successful however as self condensation of cyanoacetate to give **2** supervened.



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3. The dinitrile **2** had λ_{max} (EtOH) 262 (ε16,050) nm; ν_{max} (KBr) 2920 (chelated OH), 2260 (CN), 1660 (chelated ester) and 1595 (olefin) cm^{-1}; δ_H ($CDCl_3$) 3.97 (3H, s, ester Me), 3.81 (2H, s, 4-CH_2), 13.0 (1H, br s, chelated OH); δ_C ($CDCl_3$) 23.9 (t, C-4), 53.9 (q, ester Me), 83.3 (s, C-2), 177.8 (s, C-3), 112.7 and 111.8 (both s, CN groups); M^+ 166.0378.

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