Molybdenum hexacarbonyl-catalyzed condensation of malononitrile with ketones and aldehydes*

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Molybdenum hexacarbonyl activated with pyridine or morpholine catalyzes the condensation of malononitrile with ketones and aldehydes at 140 °C, which leads to alkylidenemalononitriles in 75—100% yield.

Key words: malononitrile, aldehydes, ketones, catalysis, molybdenum complexes, pyridine, morpholine.

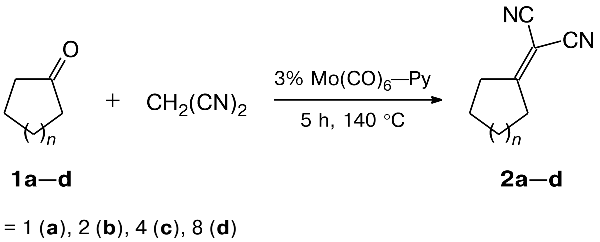
Malononitrile due to its high reactivity is widely used in the synthesis of medicinal drugs, pesticides, fungicides, dyes, *etc*. One of the most important reactions of malononitrile is the condensation with carbonyl compounds, mainly, with aromatic aldehydes. Reports on similar reactions of malononitrile with ketones are seldom encountered with, possibly, because of the low reactivity of the latter. Thus, the high conversions of ketones in their condensations with malononitrile under the classic Knoevenagel reaction conditions can be reached upon a prolonged reflux in benzene with the simultaneous removal of water.[1] The better results were obtained when ionic liquids,[2] hexamethyldisilazane,[3] and $\mathrm{TiPr^i_4}$ (see Ref. 4) were used as catalysts, as well as other organometallic[5] and heterogeneous[6] catalysts upon conventional or microwave heating. The use of bases such as morpholine, piperidine, and $\mathrm{AcONH_4}$ (see Ref. 7) as the catalysts decreased the reaction time to 1—2 h, but the yields of the target products were only 20—30% because of the polymerization of the starting compounds. The introduction of methanesulfonic acid into the composition of catalysts decreases the polymerization[7] and increases the yields of the condensation products to 80—90%.

The purpose of the present work was a development of a new catalytic method for the preparation of alkylidenemalononitriles by the reaction of ketones and aldehydes with malononitrile in the presence of homogeneous metal complex catalysts.

The examination of Mo, Fe, Mn, V, Cr, and other metal salts and complexes showed that molybdenum compounds such as $\mathrm{MoCl_5}$, $\mathrm{MoO_3}$, $\mathrm{MoO(acac)_2}$, and $\mathrm{Mo(CO)_6}$ activated with the nitrogen-containing ligands (pyridine and morpholine) can serve as efficient catalysts of the condensation of ketones with malononitrile. Molybdenum hexacarbonyl appeared to be the best out of the precatalysts studied, whose presence did not require a solvent for the reaction to proceed. At the same time, it is desirable to carry out reactions involving solid-state ketones in dichloromethane at the molar ratio of the catalyst and reactants [Mo] : [Py] : [ketone] : [malononitrile] = = 3 : 1—4 : 100 : 120.

We studied this reaction for cyclopentanone (**1a**), cyclohexanone (**1b**), cyclooctanone (**1c**), and cyclododecanone (**1d**) (Scheme 1). Cycloalkanones **1a**,**b** in the condensation with malononitrile under the optimal conditions (4—5 h, 140 °C) were completely converted to cyclopentylidene- and cyclohexylidenemalononitriles **2a**,**b**, respectively, as the only products (99% yields). As the size of the ring in the ketone molecule increased, the yield of the condensation products decreased, in particular, for cyclooctanone (**1c**) and cyclododecanone (**1d**) the yields of the corresponding cycloalkylidenemalononitriles **2c**,**d** were 75 and 30%.

Scheme 1



n = 1 (**a**), 2 (**b**), 4 (**c**), 8 (**d**)

Adamantan-2-one (**3**) reacted with malononitrile with the formation of 2-adamantylidenemalononitrile (**4**) in quantitative yield (Scheme 2).

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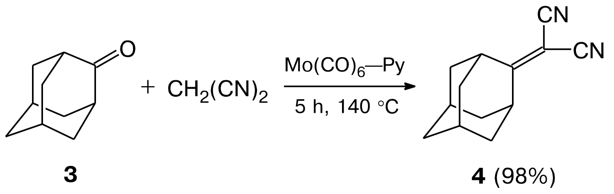
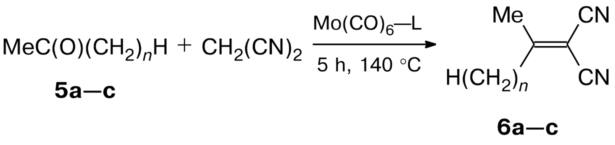
Scheme 2



The aliphatic unbranched methyl ketones **5a—c** showed fairly high activity in the reaction with malononitrile (Scheme 3). In this case, the yields of the reaction products **6a—c** did not depend on the size of the alkyl chain.

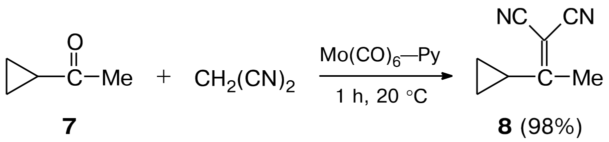
Scheme 3



n = 1 (**a**), 5 (**b**), 8 (**c**); L is the Py or morpholine

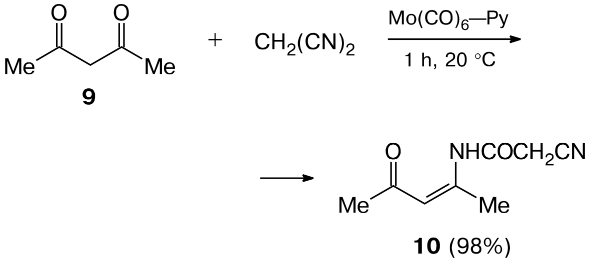
Methyl cyclopropyl ketone (**7**) reacted with malononitrile under mild conditions (1 h, 20 °C) with the formation of the condensation product **8** in high yield, with the cyclopropane ring remained intact (Scheme 4). At the same time, methyl ketones having bulky (acetyladamantane) and aromatic (acetophenone) substituents in the molecule did not react with malononitrile.

Scheme 4



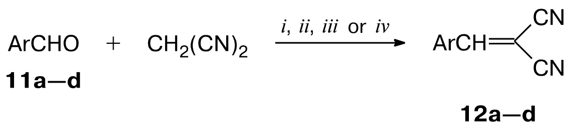
The outcome of the reaction of ketones containing two keto groups in the molecule depends on the distance between them. Thus, diacetyl virtually instantly underwent an exothermic polymerization, while acetylacetone **9** was completely converted to amide **10** at room temperature within 1 h (Scheme 5). In the latter case, acetylacetone reacted with malononitrile in the enol form at the alcohol group following the amidation scheme involving one nitrile group, whereas the second CN substituent remained intact.

Scheme 5



Aromatic aldehydes **11a—d** also exhibited high activity in the condensation reactions with malononitrile in the presence of the catalytic system $Mo(CO)_6$—pyridine (morpholine) (Scheme 6). If the reaction was carried out with a preliminary activation of the catalyst (reflux of the solution of $Mo(CO)_6$ and the ligand in dichloromethanne for 1 h at 40 °C) with subsequent addition of malononitrile and aldehyde, it took only 3—5 min for the reaction to reach completion and give quantitative yields of the products.

Scheme 6



Ar = Ph (**a**), 4-$Me_2NC_6H_4$ (**b**), 4-$MeOC_6H_4$ (**c**), 1-naphthyl (**d**)

Reagents and conditions: *i.* $Mo(CO)_6$ + Py (1 : 4), 20 °C, 5 min (for **11a**); *ii.* $Mo(CO)_6$ + morpholine (1 : 4), 20 °C, 5 min (for **11a**); *iii.* $Mo(CO)_6$ + Py (1 : 4), 40 °C, 1 h (for **11b—d**); *iv.* $Mo(CO)_6$ + morpholine (1 : 4), 40 °C, 1 h (for **11d**).

In contrast to aromatic aldehydes, in the case of alkanals $Me(CH_2)_nCHO$ (n = 2, 5, 6), a similar reaction with malononitrile gave polymers (in the absence of the catalyst, both reactants were recovered unchanged).

The optimal molar ratios of the catalyst and reactants were as follows: [Mo] : [Py] : [$R^1C(O)R^2$] : [malononitrile] = 3 : 1—4 : 100 : 120, the preferable reaction conditions in the case of ketones are 3—4 h, 140 °C, in the case of aldehydes 1 h, 20—40 °C.

In conclusion, the systems $Mo(CO)_6$—Py and $Mo(CO)_6$—morpholine were shown to be active catalysts of the condensation of ketones and aldehydes with malononitrile leading to alkylidene- or cycloalkylidenemalononitriles.

Experimental

Reaction progress and purity of compounds obtained were monitored by GC on a Chrom-5 instrument equipped with flame-ionization detectors, 1.2- and 3-m columns 3 mm in diameter; silicon SE-30 (5%) on Chromaton-N-HMDS (0.125—0.160 mm) was used as a stationary phase, temperature regime from 50 to 280 °C (8 deg min^{-1}), carrier gas helium (50 mL min^{-1}). IR spectra in the range 550—3600 cm^{-1} were recorded on a Bruker-Vertex 70V spectrometer in KBr pellets or as a suspension in Nujol. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 spectrometer (400.13 and 100.62 MHz, respectively) in $CDCl_3$, chemical shifts are given relative to Me_4Si. Mass spectra were obtained on Shimadzu GCMS-QP2010Plus spectrometer (capillary column SPB-5 30 m × 0.25 mm, carrier gas helium, temperature regime from 40 to 300 °C at the rate of 8 deg min^{-1}, injector temperature 280 °C, source of ions temperature 200 °C, ionization energy 70 eV). Elemental composition of the samples was determined on a Karlo Erba 1106 elemental analyzer.

The starting aldehydes, ketones, malononitrile, pyridine, and morpholine were commercially available from Acros, dichloromethane (reagent grade) from Component-Reactant, which were distilled or recrystallized before use.

Molybdenum hexacarbonyl (Acros) was recrystallized and dried in a vacuum desiccator before use.

Reactions were carried out in a 10-mL glass tube placed into a 17-mL stainless steel microautoclave with continuous stirring and controlled heating or in a flask equipped with a reflux condenser with stirring.

Reaction of carbonyl compounds with malononitrile catalyzed by $Mo(CO)_6$ (general procedure). The compound $Mo(CO)_6$ (0.1—0.3 mmol), the ligand (morpholine or pyridine) (0.1—0.3 mmol), ketone or aldehyde (10 mmol), malononitrile (12 mmol), and dichloromethane (2 mL) (for solid ketones or aldehydes) were placed into a stainless steel microautoclave (V = 17 mL) or into a glass tube (the results of the parallel experiments were virtually the same) under argon. The autoclave (tube) was sealed and the reaction mixture was heated at 140 °C for 5 h for ketones or at 20—40 °C for 1—2 h for aldehydes with stirring. After the reaction reached completion, the autoclave (tube) was cooled to room temperature and opened, the reaction mixture was filtered through a layer of silica gel, washing down with hexane. The solvent was evaporated, the residue was distilled *in vacuo* or recrystallized from ethanol. The yields are given in calculation based on the isolated alkylidenemalononitrile. The structure of the synthesized compounds was established by spectroscopic methods and/or by their comparison with known samples and literature data.

Cyclopentylidenemalononitrile (2a). The yield was 99%, b.p. 120—121 °C (7 Torr) (*cf.* Ref. 8: b.p. 113—114 °C (4 Torr)). IR, ν/cm^{-1}: 1610 (C=C), 2250 (CN). ^{13}C NMR ($CDCl_3$), δ: 25.42 (C(3), C(4)); 36.25 (C(2), C(5)); 81.40 (C(6)); 112.04 (C(7), C(8)); 178.15 (C(1)). Found (%): C, 72.68; H, 6.08; N, 21.24. $C_8H_8N_2$. Calculated (%): C, 72.70; H, 6.10; N, 21.20.

Cyclohexylidenemalononitrile (2b). The yield was 98%, b.p. 118—119 °C (4 Torr) (*cf.* Ref. 8: b.p. 137 °C (10 Torr)). IR, ν/cm^{-1}: 1590 (C=C), 2240 (CN). ^{13}C NMR ($CDCl_3$), δ: 24.98 (C(4)); 27.83 (C(3), C(5)); 34.61 (C(2), C(6)); 82.09 (C(7)); 111.70 (C(8), C(9)); 185.46 (C(1)). MS, m/z (I_{rel} (%)): 146 $[M]^+$ (30), 145 (32), 131 (30), 118 (20), 105 (28), 92 (18), 81 (15), 68 (15), 55 (100), 41 (30). Found (%): C, 73.91; H, 6.85; N, 19.24. $C_9H_{10}N_2$. Calculated (%): C, 73.94; H, 6.89; N, 19.16.

Cyclooctylidenemalononitrile (2c). The yield was 75%, b.p. 100—101 °C (2 Torr). IR, ν/cm^{-1}: 1595 (C=C), 2255 (CN). ^{13}C NMR ($CDCl_3$), δ: 25.08 (C5)); 25.21 (C(3), C(7)); 25.94 (C(4), C(6)); 37.75 (C(2), C(8)); 84.56 (C(9)); 112.53 (C(10), C(11)); 182.57 (C(1)). Found (%): C, 75.75; H, 8.09; N, 16.17. $C_{11}H_{14}N_2$. Calculated (%): C, 75.82; H, 8.10; N, 16.08.

Cyclododecylidenemalononitrile (2d). The yield was 30%, b.p. 215—217 °C (10 Torr). IR, ν/cm^{-1}: 1592 (C=C), 2254 (CN). ^{13}C NMR ($CDCl_3$), δ: 23.10 (C(6), C(8)); 24.56 (C(5), C(9)); 25.29 (C(3), C(11)); 26.78 (C(4), C(7), C(10)); 33.39 (C(2), C(12)); 86.17 (C(13)); 112.09 (C(14), C(15)); 186.58 (C(1)). Found (%): C, 78.17; H, 9.65; N, 12.18. $C_{15}H_{22}N_2$. Calculated (%): C, 78.21; H, 9.63; N, 12.16.

(Adamant-2-ylidene)malononitrile (4). The yield was 95%, m.p. 180—181 °C (ethanol) (*cf.* Ref. 7: m.p. 180—182 °C). IR, ν/cm^{-1}: 1595 (C=C), 2240 (CN). ^{13}C NMR ($CDCl_3$), δ: 27.02 (C(5), C(7)); 36.15 (C(6), C(10)); 38.92 (C(1), C(3)); 40.18 (C(4), C(8), C(9)); 77.80 (C(11)); 111.98 (C(12), C(13)); 193.7 (C(2)). Found (%): C, 78.75; H, 7.16; N, 14.05. $C_{13}H_{14}N_2$. Calculated (%): C, 78.75; H, 7.12; N, 14.13.

(Prop-2-ylidene)malononitrile (6a). The yield was 98%, b.p. 79—80 °C (5 Torr) (*cf.* Ref. 8: b.p. 75 °C (4 Torr)). IR, ν/cm^{-1}: 1600 (C=C), 2250 (CN). ^{13}C NMR ($CDCl_3$), δ: 24.28 (C(1), C(3)); 80.15 (C(4)); 110.33 (C(5), C(6)); 174.55 (C(3)). Found (%): C, 67.87; H, 5.69; N, 26.44. $C_6H_6N_2$. Calculated (%): C, 67.90; H, 5.70; N, 26.40.

(Hept-2-ylidene)malononitrile (6b). The yield was 95%, b.p. 125—126 °C (8 Torr) (*cf.* Ref. 8: b.p. 113—114 °C (4 Torr)). IR, ν/cm^{-1}: 1600 (C=C), 2250 (CN). ^{13}C NMR ($CDCl_3$), δ: 13.89 (C(7)); 22.44 (C(6)); 22.52 (C(1)); 26.83 (C(4)); 29.70 (C(5)); 37.75 (C(3)); 85.81 (C(8)); 111.76 (C(9)); 111.97 (C(10)); 182.80 (C(2)). Found (%): C, 73.98; H, 8.69; N, 17.33. $C_{10}H_{14}N_2$. Calculated (%): C, 74.03; H, 8.70; N, 17.27.

(Dec-2-ylidene)malononitrile (6c). The yield was 98%, b.p. 180—181 °C (4 Torr). ^{13}C NMR ($CDCl_3$), δ: 14.10 (C(10)); 22.70 (C(9)); 24.86 (C(1)); 29.08 (C(7)); 29.27 (C(5)); 29.54 (C(4)); 30.28 (C(6)); 33.08 (C(8)); 37.12 (C(3)); 84.59 (C(11)); 111.57 (C(12)); 112.37 (C(13)); 179.15 (C(2)). Found (%): C, 76.40; H, 9.86; N, 13.74. $C_{13}H_{20}N_2$. Calculated (%): C, 76.42; H, 9.87; N, 13.71.

(1-Cyclopropylethylidene)malononitrile (8). The yield was 98%, b.p. 91—92 °C (4 Torr). ^{13}C NMR ($CDCl_3$, δ: 1.01 (C(4), C(5)); 16.55 (C(1)); 27.95 (C(3)); 83.47 (C(6)); 112.43 (C(7)); 112.49 (C(8)); 182.86 (C(2)). Found (%): C, 72.68; H, 6.07; N, 21.25. $C_8H_8N_2$. Calculated (%): C, 72.70; H, 6.10; N, 21.20.

4-[*N*-(2-Cyanoacetyl)amino]pent-3-en-2-one (10). The yield was 98%, m.p. 102—103 °C. ^{13}C NMR ($CDCl_3$), δ: 21.20 (C(5)); 26.00 (C(7)); 29.35 (C(1)); 109.01 (C(3)); 110.37 (C(8)); 153.86 (C(4)); 162.68 (C(6)); 206.54 (C(2)). MS, m/z (I_{rel} (%)): 166 $[M]^+$ (100), 164 (70), 133 (35), 131 (58), 129 (65), 98 (8), 96 (20), 94 (32), 82 (10), 59 (15). Found (%): C, 57.78; H, 6.06; N, 16.91. $C_8H_{10}N_2O_2$. Calculated (%): C, 57.82; H, 6.07; N, 16.86.

Benzylidenemalononitrile (12a). The yield was 99%, m.p. 81—82 °C. ^{13}C NMR ($CDCl_3$), δ: 82.73 (C(8)); 112.67 (C(9)); 113.81 (C(10)); 129.67 (C(3), C(5)); 130.83 (C(2), C(6)); 134.70 (C(4)); 160.13 (C(7)). Found (%): C, 77.88; H, 3.91; N, 18.21. $C_{10}H_6N_2$. Calculated (%): C, 77.91; H, 3.92; N, 18.17.

[4-(*N*,*N*-Dimethylamino)benzylidene]malononitrile (12b). The yield was 98%, m.p. 163—164 °C. ^{13}C NMR ($CDCl_3$), δ: 39.90 (C(12), C(13)); 71.76 (C(9)); 111.63 (C(3), C(5)); 113.06 (C(10), C(11)); 116.05 (C(7)); 133.83 (C(2), C(6)); 154.28 (C(4)); 158.11 (C(8)). Found (%): C, 73.02; H, 5.60; N, 21.38. $C_{12}H_{11}N_3$. Calculated (%): C, 73.07; H, 5.62; N, 21.30.

(4-Methoxybenzylidene)malononitrile (12c). The yield was 99%, m.p. 108—108.5 °C. ^1H NMR, δ: 3.92 (s, 3 H, OCH_3); 7.01—7.03 (d, 2 H, H(3) arom., H(5) arom.); 7.67 (s, 1 H, CH=C); 7.90—7.92 (d, 2 H, H(2) arom., H(6) arom.). ^{13}C NMR ($CDCl_3$), δ: 55.86 (C(11), CH_3); 78.37 (C(8)); 113.44 (C(9)); 114.52 (C(10)); 115.18 (C(3), C(5)); 124.03 (C(1)); 133.50 (C(2), C(6)); 159.01 (C(7)); 164.88 (C(4)). Found (%): C, 71.68; H, 4.37; N, 15.22. $C_{11}H_8N_2O$. Calculated (%): C, 71.73; H, 4.38; N, 15.21.

(1-Naphthylmethylidene)malononitrile (12d). The yield was 98%, m.p. 162—162.5 °C. ^{13}C NMR ($CDCl_3$), δ: 85.13 (C(12)); 112.54 (C(13)); 113.75 (C(14)); 125.40 (C(3)); 127.32 (C(9)); 128.52 (C(5)); 128.59 (C(4)); 129.45 (C(8)); 131.08 (C(6)); 133.55 (C(1)); 134.95 (C(2), C(7), C(10)); 157.75 (C(11)). Found (%): C, 82.28; H, 3.94; N, 13.78. $C_{14}H_8N_2$. Calculated (%): C, 82.33; H, 3.95; N, 13.72.

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