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SHORT COMMUNICATIONS

On the Reaction of Malononitrile with Acetylacetone

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Abstract—The reaction of malononitrile with acetylacetone in alkaline medium afforded a mixture of 2-amino-4,6-dimethylbenzene-1,3-dicarbonitrile and 4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile, whereas only the latter was formed in alcoholic medium in the absence of a catalyst. The alkylation of 4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile with allyl bromide gave a mixture of *N*- and *O*-allyl derivatives.

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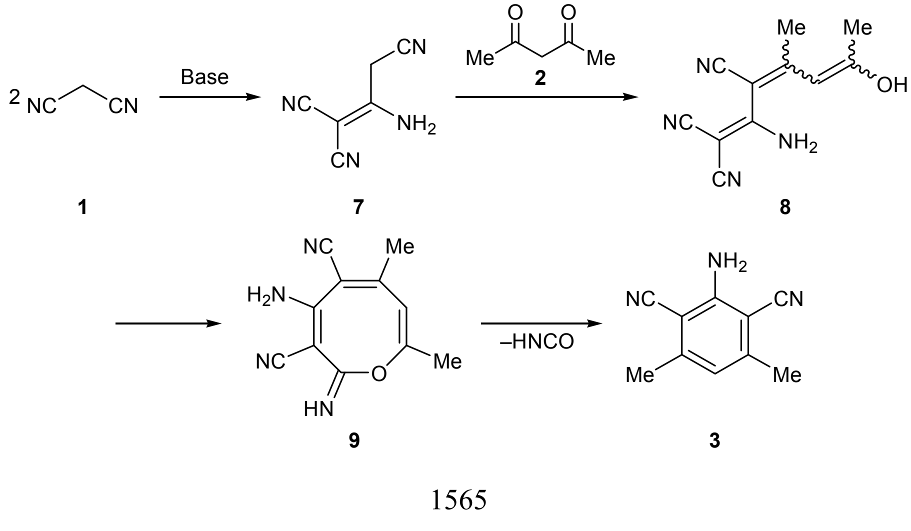
The reaction of malononitrile (**1**) with acetylacetone (**2**) in water in the presence of sodium hydroxide was reported for the first time in [1] to produce a mixture of 2-amino-4,6-dimethylbenzene-1,3-dicarbonitrile (**3**) and 2-(4-hydroxypent-3-en-2-ylidene)malononitrile (**4**). Later it was shown [2] that compound **3** is also formed in 33–55% yield in the reaction of nitrile **1** with diketone **2** in alcohols or dioxane in the presence of KOH at room temperature, but nothing was said about formation of a second product.

We have found that malonotnitrile (**1**) reacts with acetylacetone (**2**) in water or ethanol in the presence of $NaHCO_3$ or NaOH to give a mixture of substituted aniline **3** and pyridinone **5**, the latter being isomeric to **4**. The structure of **3** and **5** was proved by GC/MS with the use of NIST.08 library [3]. The melting point of **5** coincided with the melting point reported for compound **4** and that of a sample of **5** obtained by the reaction of acetylacetone with cyanoacetamide (**6**) [4].

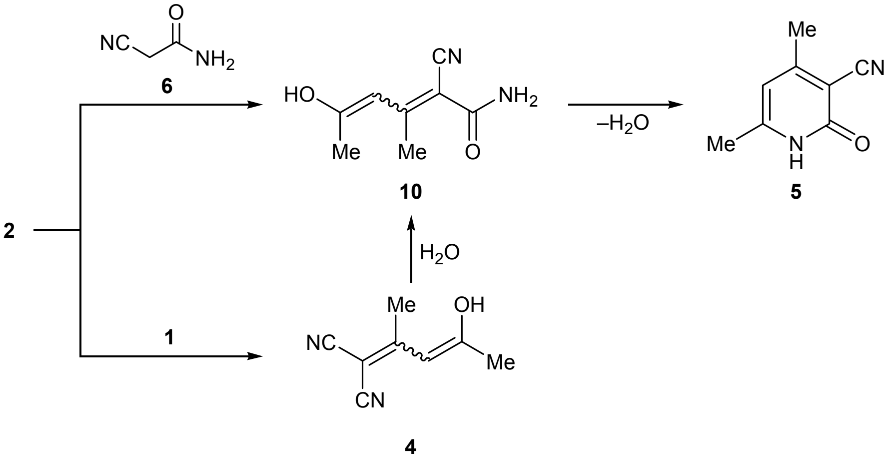
Presumably, compound **3** is formed according to the following scheme. Base-catalyzed dimerization of malononitrile gives 2-aminoprop-1-ene-1,1,3-tricarbonitrile (**7**) which reacts with acetylacetone to produce 2-amino-6-hydroxy-4-methylhepta-1,3,5-triene-1,1,3-tricarbonitrile (**8**); compound **8** undergoes intramolecular cyclization to eight-membered 4-amino-2-imino-6,8-dimethyl-2*H*-oxocine-3,5-dicarbonitrile (**9**), and elimination of isocyanic acid from the latter yields final product **3** (Scheme 1).

The reaction of malononitrile with acetylacetone in methanol or ethanol in the absence of a base afforded pyridinone **5** as the only product. Compound **5** is likely

Scheme 1.



Scheme 2.



to be formed by reaction of diketone **2** with cyanoacetamide **6** which appears in the reaction mixture as a result of hydrolysis of malononitrile with traces of water present in the solvent. The yield of **5** increased (to 56%) if the initial dinitrile already contained traces of amide **6** which is formed on prolonged storage of malononitrile (**1**). Theoretically, pyridinone **5** can also be formed from dienol **4** which is the condensation product of dinitrile **1** with diketone **2**. Hydrolysis of **4** gives 1-amino-5-hydroxy-3-methyl-1-oxohexa-2,4-diene-2-carbonitrile (**10**), and cyclodehydration of the latter leads to compound **5** (Scheme 2).

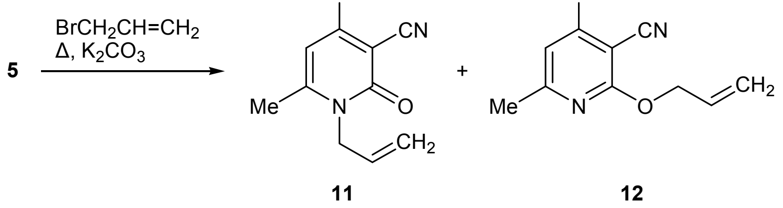
The question arises why a mixture of **3** and **5** is formed in the presence of alkali whereas pyridinone **5** is formed as the only product in the absence of a base? We believe that alkali catalyzes dimerization of malononitrile (**1**) to aminopropene **7** which is then converted to aniline **3** while no dimerization occurs in the absence of a base.

The structure of **5** was also confirmed by its alkylation with allyl bromide in acetone or DMF in the presence of potassium carbonate, which led to the formation of a mixture of 1-allyl-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (**11**) and 2-allyloxy-4,6-dimethylpyridine-3-carbonitrile (**12**) (Scheme 3). *N*-Allyl derivative **11** was isolated from the reaction mixture by treatment with hexane, and its structure was confirmed by ^{1}H NMR, IR, and mass spectra. Compound **11** was synthesized for the first time by condensation of allylamine with acetylacetone and ethyl cyanoacetate [5].

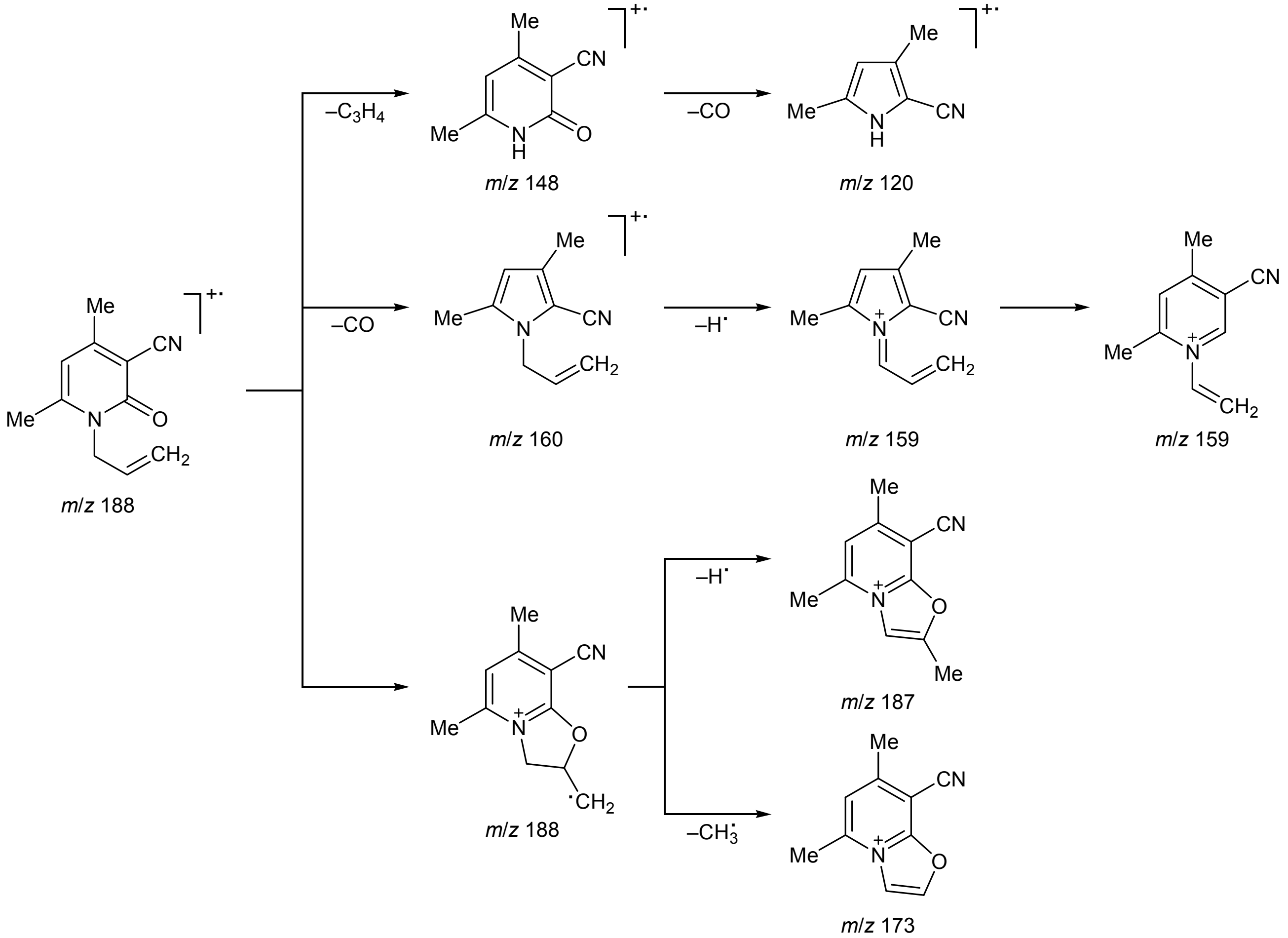
The ^{1}H NMR spectrum of **11** contained signals of protons of the allyl group and proton on C^5 of the pyridine ring (δ 6.34 ppm). The 5-H signal of isomer **12** was located in a weaker field (δ 6.98 ppm). Isomers **11** and **12** were characterized by fairly similar mass spectra, indicating similarity of the fragmentation patterns of their molecular ions. Analogous similarity of the fragmentation patterns was reported previously for *N*- and *O*-allyl derivatives of pyridin-2(1*H*)-one [6] and 5-nitropyridin-2(1*H*)-one [7]. The molecular ion peak of **11** was less intense (39%) than that of ether **12** (56%). The base peak in the spectra of both compounds **11** and **12** was that of the $[M - \mathrm{CH_3}]^+$ ion (*m*/*z* 173) resulting from elimination of methyl radical from the molecular ion and having aromatic 5,7-dimethyl-8-cyanooxazolo[3,2-*a*]pyridinium structure (Scheme 4). The IR spectrum of **11** showed a strong carbonyl stretching vibration band at 1643 cm^{-1} and C≡N stretching band at 2220 cm^{-1}.

4,6-Dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (5). A solution of 0.66 mL (10 mmol) of

Scheme 3.



Scheme 4.



malononitrile (**1**) in 3 mL of methanol or ethanol was refluxed for 2.5 h with stirring, and 1 mL (10 mmol) of acetylacetone (**2**) was added with vigorous stirring to the boiling solution. After 7 h, light brown solid precipitated. The mixture was left to stand for 24 h in the cold, and the precipitate was filtered off and dried. Yield 0.55 g (56%), colorless crystals, mp 286–287°C; published data [8, 9]: mp 290°C. IR spectrum, ν, cm^{-1}: 3100 (C^5–H, CH$_2$), 3001, 2962, 2918 (CH$_3$, CH), 2218 (CN), 1660 s (C=O). Mass spectrum, m/z (I_{rel}, %): 149 (10) $[M + 1]^+$, 148 (100) $[M]^{+\cdot}$, 121 (4), 120 (46), 119 (82), 105 (18), 93 (5), 92 (6), 80 (3), 79 (3), 78 (14), 77 (5), 76 (5), 67 (4), 66 (7), 65 (8), 64 (5), 63 (4), 53 (3), 52 (8), 51 (11), 50 (3), 42 (16), 41 (6), 40 (3), 39 (12), 38 (4).

2-Amino-4,6-dimethylbenzene-1,3-dicarbonitrile (3, in a mixture with 5). A solution of 0.66 mL (10 mmol) of malononitrile and 1.68 g (20 mmol) of NaHCO$_3$ in 7 mL of water was stirred for 2.5 h at 50–60°C, and 1 mL (10 mmol) of acetylacetone was added with vigorous stirring. After 12 h, the precipitate was filtered off, washed with cold water (3×5 mL), and dried. Yield 1.3 g. Mass spectrum, m/z (I_{rel}, %): 172 (11) $[M + 1]^+$, 171 (100) $[M]^{+\cdot}$, 170 (40) $[M - \text{H}]^+$, 157 (4), 156 (40) $[M - \text{CH}_3]^+$, 144 (5), 143 (10), 142 (3), 129 (7), 117 (5), 116 (10), 115 (3).

1-Allyl-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (11). A mixture of 2.07 g (15 mmol) of potassium carbonate, 8 mL of acetone, and 1.48 g (10 mmol) of compound **5** was refluxed for 15 min. A solution of 1.3 mL (15 mmol) of allyl bromide in 3 mL of acetone was added, and the mixture was refluxed for 10 h. The mixture was cooled and filtered, the filtrate was evaporated, and the residue was washed with hexane (3×3 mL). Yield 0.96 g (51%), colorless crystals, mp 112°C; published data [5]: mp 114°C. IR spectrum, ν, cm^{-1}: 3085 (C^5–H, CH$_2$), 2954, 2875 (CH$_3$, CH), 2220 (CN), 1643 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, Me), 2.40 s (3H, Me), 4.65 t.d (2H, NCH$_2$, J = 4.74, 1.75 Hz), 4.92 t.d (1H, =CH$_2$, J = 4.90, 1.64 Hz), 5.18–5.15 m (1H, =CH$_2$), 5.95–5.86 m (1H, CH=), 6.34 s (1H, 5-H).

Mass spectrum, *m*/*z* (I_{rel}, %): 189 (5) $[M + 1]^+$, 188 (39) $[M]^{+\cdot}$, 187 (34) $[M - \mathrm{H}]^+$, 174 (11), 173 (100) $[M - \mathrm{CH_3}]^+$, 172 (7), 171 (15), 161 (6), 160 (3) $[M - \mathrm{CO}]^+$, 159 (9) $[M - \mathrm{CO} - \mathrm{H}]^+$, 158 (3), 156 (4), 149 (3), 148 (10) $[M - \mathrm{C_3H_4}]^+$, 146 (4), 145 (4), 133 (4), 132 (11) $[M - \mathrm{CO} - \mathrm{C_2H_4}]^+$, 131 (9), 130 (3), 120 (5) $[M - \mathrm{C_3H_4} - \mathrm{CO}]^+$, 119 (9) $[M - \mathrm{CO} - \mathrm{H} - \mathrm{C_3H_4}]^+$, 118 (5), 105 (4), 104 (5), 92 (3), 78 (5), 77 (6), 66 (3), 65 (5), 52 (3), 51 (5), 42 (4), 41 (21), 39 (13).

2-Allyloxy-4,6-dimethylpyridine-3-carbonitrile (12) was isolated in a mixture with **11**. Oily liquid. ^{1}H NMR spectrum, δ, ppm: 2.41 s (3H, Me), 2.42 s (3H, Me), 4.90 t (1H, $\mathrm{OCH_2}$, *J* = 1.51 Hz), 4.96 d.d (1H, $\mathrm{OCH_2}$, *J* = 2.97, 1.78 Hz), 5.27 q.d (1H, $=\mathrm{CH_2}$, *J* = 10.51, 1.39 Hz), 5.41 q.d (1H, $=\mathrm{CH_2}$, *J* = 17.23, 1.70 Hz), 6.07 t.d.d (1H, CH=, *J* = 17.21, 10.55, 5.30 Hz), 6.98 s (1H, 5-H). Mass spectrum, *m*/*z* (I_{rel}, %): 189 (7) $[M + 1]^+$, 188 (56) $[M]^{+\cdot}$, 187 (40) $[M - \mathrm{H}]^+$, 174 (11), 173 (100) $[M - \mathrm{CH_3}]^+$, 172 (6), 171 (16), 162 (3), 161 (11), 160 (10) $[M - \mathrm{CO}]^+$, 159 (48) $[M - \mathrm{CO} - \mathrm{H}]^+$, 156 (3), 149 (4), 148 (13) $[M - \mathrm{C_3H_4}]^+$, 146 (5), 145 (5), 133 (12), 132 (44) $[M - \mathrm{CO} - \mathrm{C_2H_4}]^+$, 131 (24), 130 (2), 120 (9) $[M - \mathrm{C_3H_4} - \mathrm{CO}]^+$, 119 (16) $[M - \mathrm{CO} - \mathrm{H} - \mathrm{C_3H_4}]^+$, 118 (5), 117 (3), 106 (3), 105 (8), 104 (11), 92 (4), 91 (3), 79 (3), 78 (10), 77 (12), 76 (3), 66 (4), 65 (6), 64 (3), 63 (3), 52 (5), 51 (8), 42 (6), 41 (39), 39 (19).

The mass spectra (electron impact, 70 eV) were recorded on a Shimadzu GCMS-QP2010 instrument. The ^{1}H NMR spectra were measured on a Bruker DRX-400 spectrometer at 400 MHz using DMSO-d_6 as solvent and tetramethylsilane as internal standard. The IR spectra were recorded in KBr on a Shimadzu IR Affinity-1S spectrometer with Fourier transform. The melting points were measured with a PTP (M) melting point apparatus.

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