Differences between the Reaction of 2-Benzylidenecyclopentanone with Malononitrile and the Reaction of Cyclopentylidenemalononitrile with Aromatic Aldehydes; Synthesis of Strong Fluorescent o-Aminonitriles

Julian Mirek* and Piotr Milart

Department of Organic Chemistry, Jagiellonian University, Karasia 3, 30060 Kraków, Poland

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It was found that instead of the Knoevenagel condensation of cyclopenylenemalononitrile with aromatic aldehydes, a complex reaction takes place leading to 5,7-dicyano-1-aryliden-4-arylindanes. The same compounds were formed in the reaction of the cyclopenylenemalononitrile dimer with aldehydes. It is suggested that the cyclopenylenemalononitrile dimers undergo an electrocyclic ring opening leading to conjugated triene systems. These species are very reactive intermediates and may react with aldehydes in the next step. Bulky substituents in 2,5-dibenzylidenecyclopentanone hindered its Knoevenagel condensation with malononitrile but did not hinder its Michael addition leading to a 4H-pyran derivative. Solutions of the obtained o-aminonitriles exhibit strong fluorescence in a variety of solvents.

The reaction course of the α,β-unsaturated ketones with malononitrile depends on the catalyst used and the structure of the ketone. A Michael adduct was formed in the reaction of benzylideneacetophenone with malononitrile catalyzed by basic aluminium oxide [1]. This adduct undergoes the Dimroth rearrangement in the presence of sodium ethoxide leading to 3-cyano-2-ethoxyopyridine [2]. Similar rearrangement can be performed without isolation of the adduct: as an example may serve the reaction of 2-benzylidene-1-tetralone with malononitrile in the presence of sodium alcoxides giving appropriate derivatives of 3-cyano-2-alkoxyopyridine [3]. When the reaction of α,β-unsaturated ketones with malononitrile is conducted in ethanol or benzene in the presence of ammonium acetate, the Michael adducts form in the beginning cyclize subsequently to 2-amino-3-cyanopyridines [4]. Similar reaction of chalcones with an excess of malononitrile in the presence of piperidine gave usually a mixture of compounds [5]. However, α,β-unsaturated ketones heated to reflux with malononitrile and ammonium acetate-acetic acid in benzene with use of a Dean-Stark trap give Knoevenagel condensation products exclusively. This method was used to obtain ylidene-malononitriles from 2-cyclohexyldienecyclohexane [6], 2-cyclopentylidenecyclopentanone [7] and mesityl oxide [8]. ApSimon et al. [9] investigating intensively the reaction of malononitrile with a variety of α,β-unsaturated ketones performed in DMF in the presence of dry potassium fluoride have found that the steric factors have a strong influence on the ratio of the Michael to Knoevenagel products. When the steric hindrance is located near the carbonyl group, the Michael addition of malononitrile prevails; in other instances, the Knoevenagel condensation is preferred.

Results and Discussion

Heating under reflux for several hours of 2-benzylidenecyclopentanone (1) [10] with malononitrile and a catalytic amount of ammonium acetate-acetic acid in benzene with use of a Dean-Stark trap gave (2-benzylidene)-cyclopentylidenemalononitrile (2) (Knoevenagel condensation product) with a moderate yield (Scheme 1).

The moderate yield of 2 prompted us to look for another procedure for its synthesis. We tried to apply the Carrie [11] method which gave good result in the condensation of benzaldehyde with 1-phenylethylidenemalononitrile in the presence of piperidine. However, the use of cyclopentylidenemalononitrile (3) [12] changed completely the reaction course. The obtained yellow product 4a possesses properties different from those of 2. Although both compounds, 2 and 4a, showed a CN band in their IR spectra, the band of 2 appeared at 2200 cm⁻¹ and that of 4a at...
Scheme 1.

Scheme 2.

2220 cm\(^{-1}\). Beside that, the IR spectrum of 4a showed additional three bands at 3280–3500 cm\(^{-1}\) which may be attributed to an amino group. The observed band system of 4a is typical for \(\alpha\)-amino-nitriles [13–16]. Similar products were obtained when other aromatic aldehydes were used: 4b from \(p\)-methylbenzaldehyde and 4c from \(p\)-chlorobenzaldehyde. Mass spectra of 4 showed that the molecules contain the moieties of two molecules of the aldehyde and possess three nitrogen atoms (nitrogen rule) what is in accord with the elementary analytical data and the proposed structure.

The given structure suggests the complexity of the reaction pathway of cyclopentylidenemalononitrile with aldehydes. More detailed discussion of the problem will be given later.

Synthesis of the “mixed dimers” of cyclohexylidenemalononitrile and benzylidenemalononitrile from the mixture of ketone, aldehyde and malononitrile carried in ethanol with the catalytical amount of piperidine is well known [13, 15]. By adoption of this procedure to the mixture containing cyclopentanone instead of cyclohexanone we obtained the unknown “mixed dimers” 5 (Scheme 2).

However, the compound 5a yielded 4a when it was heated with benzaldehyde in DMF or acetonitrile in the presence of a catalytical amount of piperidine. Similarly behaved 5b giving 4b in the reaction with \(p\)-methylbenzaldehyde. This observation suggests that 5a or other “mixed dimer” 5 should give a mixture of products 4 in the reaction with other aldehydes. Indeed, presence of four different compounds in the reaction mixture was confirmed by MS spectroscopy. Formation of the mixture of compounds 4 (I–IV) may result from the recyclization of 5 under the conditions used.

It is well known that cyclopentylidenemalononitrile (3) [12, 17] undergo dimerization in the pres-
ence of bases (Scheme 3). We have found that dimer 6 react with aldehydes to give 4, so the dimerization of cyclopentylidenemalononitrile may be considered as the first step of the investigated reaction sequence.

\[
\begin{align*}
\text{3} & \xrightarrow{\text{base}} \text{6} \\
\text{2} & \xrightarrow{\text{HCN}} \text{CN} \\
\text{CN} & \xrightarrow{\text{CN}} \text{CN} \\
\end{align*}
\]

Scheme 3.

The ability of the mentioned “dimers” to undergo the electrocyclic ring opening to the reactive conjugated triene derivatives is described in the literature \[18\]. It supports the discussed reaction mechanism (Scheme 4). Compounds 7 and 8 may be practically treated as the Knoevenagel condensation products of 1,1,3-tricyanopropene with the malononitrile dimer (2-amino-1,1,3-tricyanopropene) \[19\].

\[
\begin{align*}
\text{5a} & \xrightarrow{\text{DMF or CH3CN}} \text{11} \\
\text{CN} & \xrightarrow{\text{NC}} \text{CN} \\
\text{CN} & \xrightarrow{\text{CN}} \text{CN} \\
\end{align*}
\]

Scheme 4.

Gewald \[13\] and Sharanin \[15\] have pointed out that an exchange of the carbonyl components occurred in some instances of the Thorpe cyclization. The same is also very probable in our case. Furthermore, compounds 7 and 8 possess an active methylene group which may undergo condensation with aldehydes rather easily. The aldehyde released from 7 in the first reaction step can compete with the aldehyde added in the next step what leads to a mixture of 9. An electrocyclic reaction of 9 gave cyclic dienes 10 (Scheme 5).

Immediately after the cyclization, molecules of 10 undergo aromatization to indane derivatives (4). The reaction is catalyzed by the present base and accelerated by the high temperature used.

The “mixed dimer” 5a boiled with a few drops of piperidine in DMF or acetonitrile gave yellowish crystals of 11, 6-amino-5,7-dicyano-4-phenylindane, which is very stable and do not change when boiled with benzaldehyde under the same conditions (Scheme 6).

\[
\begin{align*}
\text{5a} & \xrightarrow{\text{HCN, CH3CN or DMF}} \text{11} \\
\text{CN} & \xrightarrow{\text{NC}} \text{CN} \\
\text{CN} & \xrightarrow{\text{CN}} \text{CN} \\
\end{align*}
\]

Scheme 6.

Unexpected results were obtained from the aromatization of 5b. Instead of the expected indane derivative of 11, compound 4b was obtained with a poor yield. Here, the elimination of HCN can proceed by an electrocyclic ring opening of the type (5 = 7) and an exchange of the benzylidene moiety at the methylene fragment of the opened molecule. In this reaction one molecule of 5b is a source of the benzyliden group for another molecule. Compound 9 formed in this reaction is transformed then to 4b according to the Scheme 5.

The attempted reaction of 1-indanone with benzaldehyde and malononitrile carried in ethanol in the presence of piperidine at room temperature was un-
successful. A complex mixture of unidentified products was obtained very quickly. However, the Thorpe cyclization of 1-indanyldenemalononitrile (12) [20] with benzylidenemalononitrile (13) [21] gave an yellowish crystalline product having the high melting point. Its spectroscopical data and elemental analysis correspond very well with 3-amino-2,4-dicyano-1-phenylfluorene (14) (Scheme 7).

The reaction course is changed here a bit. The present aromatic ring increased the tendency of the molecule to adopt a planar structure and facilitated its aromatization at room temperature.

It appeared that compound 11 can be obtained very easily from 2-benzylidenecyclopentanone (1) and malononitrile when the reaction is carried in ethanol in the presence of piperidine at room temperature. In this case, the reaction course must be different from that of 2-benzylidene-1-tetralone [3] which gave a heterocyclic compound. The less hindered molecule of 2-benzylidenecyclopentanone may react with two molecules of malononitrile (Knoevenagel condensation and Michael addition) as was illustrated in Scheme 8.

In order to check this suggestion, a reaction of the much more hindered molecule, 2,5-dibenzylidene-cyclopentanone (15) [22], with malononitrile was carried under the same reaction conditions. 4H-Pyrrane derivative (16) was obtained in good yield (Scheme 9), although compound 4a might be expected as the product in analogy to 11. Here, the Knoevenagel condensation was retarded and the Michael addition was facilitated.

A similar compound was obtained by H.-H. Otto [23] from 2,6-dibenzylidenecyclohexanone.

For comparison, we have checked if the “mixed dimer” derived from cyclohexanone, benzaldehyde and malononitrile [13, 15] can react with benzadehyde. Despite of a variety of solvents and basic catalysts tried, only one well known product, 2-amino-1,3-dicyano-5,6,7,8-tetrahydro-1,3-naphthalenetetrahydronaphthalene [14, 15], was always separated. However, a MS spectrum of the crude product showed its contamination (less than 5.0%) by a derivative formed in the condensation with benzaldehyde but this was not separated in a pure form. It seems to be interesting that such a small difference in the structure of the starting materials (five- or six-membered ring) can cause such dramatic differences in their reactivities.

Solutions of compounds 4 in a variety of organic solvents showed a very strong luminescence evoked by daylight. The yellow solutions emitted blue-green light. The absorption and emission spectra [24] of 4a...
were obtained and are shown in Fig. 1, to give more precise picture of that phenomenon.

According to the molecular spectroscopy theory, the absorption spectrum is, in the first approximation, a mirror reflection of the emission one and this can be seen in Fig. 1. Compound 11 has strong blue fluorescence evoked by the 365 nm wave length.

Experimental

Melting points were determined in open capillary tubes and are uncorrected. Elemental analyses were performed by the Regional Laboratory of Physico-Chemical Analyses, Kraków. The IR spectra were obtained on a IR-75 (Carl Zeiss Jena) spectrometer in nujol. The $^1$H NMR spectra were recorded on Tesla BS-487 (80 MHz) and Tesla BS-567 A (100 MHz) spectrometers using CDCl$_3$ as solvent and TMS as internal standard. The MS spectra were taken on LKB-9000 s and LKB-2091 instruments at 70 eV.

The absorption electronic spectra were recorded on a UV/VIS (Carl Zeiss Jena) spectrophotometer in 0.1 cm silica transmission cells using spectrally pure ethanol (c = 5 x $10^{-4}$ mol/l). The emission spectra were taken on a spectrometer constructed in the Department of Physical Chemistry and Electrochemistry, Jagiellonian University (c = 10$^{-2}$ mol/l, ethanol, room temperature). The used known ylidene-cyclopentanones, ylidene-malononitriles and ylidene-malononitrile dimers were synthesized according to the cited literature.

(2-Benzylidene)-cyclopentylidenemalononitrile (2)

2-Benzylidenecyclopentanone (1) (3.4 g, 0.02 mol), malononitrile (1.3 g, 0.02 mol), ammonium acetate (0.3 g) and acetic acid (1.2 g) were refluxed for 5 h in benzene (20 ml) under a Dean-Stark water separator. Then, benzene was removed under reduced pressure and the oily residue was diluted with ethanol (10 ml) and left for the next day in
a refrigerator. The separated product was recrystallized from ethanol.
Yield 1.0 g (23%); m.p. 119–120 °C.

\[
\text{C}_{15}\text{H}_{12}\text{N}_2 \quad (220.29)
\]
- Calcd C 81.78 H 5.50 N 12.72.
- Found C 81.63 H 5.46 N 12.59.
- IR [cm\(^{-1}\)]: 2205 (C=N), 1605, 1520 (C=C).
- \(\text{H} \text{NMR (3 ppm)}: 8.07 \text{ (t, 1H, J = 4 Hz, benzylidene proton)}, 7.45 \text{ (m, 5H, aromatic protons)}, 2.95 \text{ (m, 4H, } 2\times \text{ CH}_2 \text{), 1.92 \text{ (quintette, 2H, } J = 12 \text{ Hz, CH}_3 \text{).}
- MS [m/z]: M\(^+\) = 220 (100%), 192 (64%), 155 (25%), 117 (23%), 91 (25%).

3-Amino-2,4,4-tricyano-5-arylbicyclo[4.3.0]nona-2,9-dienes (5) (for the mixture of tautomers); general procedure

To a stirred mixture of cyclopentanone (8.4 g, 0.1 mol), malononitrile (13.2 g, 0.2 mol) and the appropriate aldehyde (0.1 mol) in ethanol (400 ml) was added piperidine (1.0 ml) at room temperature. After 1–2 h, the white precipitate began to separate. The precipitate was recrystallized from ethanol.

\[
\text{C}_{18}\text{H}_{14}\text{N}_4 \quad (300.39)
\]
- Calcd C 75.96 H 5.38 N 18.66.
- Found C 75.72 H 5.27 N 18.79.
- IR [cm\(^{-1}\)]: 3400, 3390, 3280 (NH\(_2\)), 2220 (C=N), 1650 (NH\(_2\)), 1570 (C=C). - \(\text{H} \text{NMR (3 ppm)}: 7.80 \text{ (t, 1H, J = 2 Hz, benzylidene proton)}, 7.25 \text{ (m, 8H, aromatic protons), 5.22 \text{ (s, 2H, NH\(_2\)), 3.05 \text{ (m, 2H, CH\(_2\)), 2.80 \text{ (m, 2H, CH\(_2\)), 2.43 (s, 3H, CH\(_3\), 2.38 \text{ (s, 3H, CH\(_3\).}
- MS [m/z]: M\(^+\) = 375 (100%), 256 (26%), 105 (89%). - UV/VIS \(\lambda\text{max} \text{ [nm] absorption spectrum: 411 (} \varepsilon = 18600\text{), emission spectrum: 480.}"

6-Amino-5,7-dicyano-1-arylidene-4-arylidanes (4)

Method A; general procedure

To a solution of cyclopentylidenemalononitrile (3) (2.6 g, 0.02 mol) or its dimer (2.6 g, 0.01 mol) and the appropriate benzaldehyde (0.04 mol in DMF (10 ml) was added piperidine (0.5 ml) and the obtained mixture was refluxed for 1 h. Dilution of the slightly cooled mixture with ethanol (10 ml) caused a precipitation. The obtained precipitate was recrystallized from nitromethane.
6-Amino-5,7-dicyano-1-(4'-chloro)benzylidene-4-(4'-chlorophenyl)indane (4)

Yield 2.5 g (62%) from cyclopentylidenemalononitrile or 2.7 g (67%) from its dimer; m.p. 252–253 °C.

C$_{24}$H$_{15}$N$_5$Cl$_2$ (416.32)
Calcd C 69.23 H 3.64 N 10.09,
Found C 69.11 H 3.56 N 9.90.

IR [cm$^{-1}$]: 3500, 3390, 3280 (NH$_2$), 2220 (C=N), 1650 (NH$_2$), 1600, 1580, 1560, 1500 (C=C). –
$^1$H NMR δ [ppm]: 7.85 (t, 1H, $J$ = 4 Hz, benzylidene proton), 7.40 (m, 8H, aromatic protons), 5.30 (s, 2H, NH$_2$), 3.05 (m, 2H, CH$_2$), 2.80 (m, 2H, CH$_2$). – MS [m/z]: M$^+$ = 417 (68%), 416 (32%), 415 (100%), 290 (22%), 127 (28%), 125 (83%). –

UV/VIS $\lambda_{max}$ [nm] absorption spectrum: 408 ($\varepsilon$ = 15100), emission spectrum: 467.

Method B; general procedure

To a solution of the “mixed dimer” 5 (0.01 mol) in DMF (10 ml) was added the appropriate aldehyde (0.01 mol) and piperidine (0.5 ml). Further work up as in the Method A.

Compound 4a, yield 2.3 g (66%), compound 4b, yield 2.6 g (70%).

6-Amino-5,7-dicyano-4-phenylindane (11)

Method A

To a solution of the compound 5a (2.7 g, 0.01 mol) in DMF or acetonitrile (10 ml) was added piperidine (0.5 ml) and the obtained mixture was refluxed for 1 h. Ethanol (10 ml) was added and the mixture was left aside for crystallization. Recrystallization of the crude product from nitromethane gave yellowish crystals.

Yield 1.8 g (74%); m.p. 226–228 °C.

C$_{17}$H$_{13}$N$_3$ (259.33)
Calcd C 78.33 H 5.06 N 16.21,
Found C 78.33 H 5.12 N 16.09.

IR [cm$^{-1}$]: 3380, 3330, 3240 (NH$_2$), 2205 (C=N), 1640 (NH$_2$), 1570 (C=C). –
$^1$H NMR δ [ppm]: 7.52 (m, 8H, aromatic protons), 7.27 (s, 1H, aromatic proton), 5.30 (s, 2H, NH$_2$), 3.72 (s, 2H, CH$_2$). – MS [m/z]: M$^+$ = 259 (100%), 258 (59%), 182 (19%). –

UV/VIS $\lambda_{max}$ [nm] absorption spectrum: 363 ($\varepsilon$ = 7700), emission spectrum: 417.

Method B

To a solution of 2-benzylidenecyclopentanone (1) (3.4 g, 0.02 mol) in ethanol (30 ml) was added a solution of malononitrile (2.6 g, 0.04 mol) in ethanol (20 ml) and piperidine (1.0 ml). The mixture was stirred for 24 h. The obtained precipitate was separated and recrystallized from nitromethane. All physical properties of the obtained compound were identical with that obtained from Method A.

Yield 1.5 g (29%).

3-Amino-2,4-dicyano-1-phenylfluorene (14)

A solution of 1-indanyldimalononitrile (12) (3.6 g, 0.02 mol), benzylidenedimalononitrile (13) (3.1 g, 0.02 mol) and piperidine (2.0 ml) in ethanol (400 ml) was stirred for 48 h at room temperature. During this time, evolution of hydrogen cyanide was observed and the solution turned blue-green. Then, half of the ethanol volume was removed by distillation and the obtained yellow precipitate was recrystallized twice from nitromethane.

Yield 1.3 g (21%); m.p. 303–305 °C.

C$_{22}$H$_{18}$N$_3$O (326.42)
Calcd C 80.94 H 5.57 N 8.58,
Found C 80.88 H 5.50 N 8.44.

IR [cm$^{-1}$]: 3490, 3370, 3240 (C=N), 2205 (C=C), 1690 (C=C), 1650 (NH$_2$), 1590 (C=C). –
$^1$H NMR δ [ppm]: 7.42 (m, 8H, aromatic protons), 7.27 (s, 1H, aromatic proton), 5.30 (s, 2H, NH$_2$), 3.72 (s, 2H, CH$_2$). – MS [m/z]: M$^+$ = 326 (79%), 325 (21%), 219 (44%), 218 (23%).

2-Amino-3-cyano-7-benzylidene-4-phenyl-4,5,6,7-tetrahydro-4H-cyclopenta[b]pyrane (16)

A suspension of 2,5-dibenzylidenecyclopentanone (15) (2.6 g, 0.01 mol) in ethanol was stirred with malononitrile (1.0 g, 0.015 mol) and piperidine (1.0 ml), and refluxed for 3 h. During this time, the colour and structure of the suspension was changed. The obtained precipitate was recrystallized twice from nitromethane.

Yield 2.8 g (86%); m.p. 227–228 °C.

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