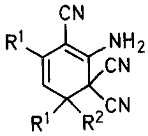
Syntheses with Unsaturated Nitriles; I.
Selective Hydrolysis of 1-Amino-2,6,6-tricyano-1,3-cyclohexadienes to 2,6,6-Tricyano-2-cyclohexenones

Julian Mirek, Maciej Adamczyk, Maria Mokrosz

Department of Organic Chemistry, Jagiellonian University,
Pl-30-060 Kraków, Poland

The condensation of ketones with malononitrile leading to alkylidenemalononitriles is well known[1,2]. Under the usual reaction conditions, cyclodimerization products may be formed. These products were first described as alkylidenemalononitriles and later as linear dimers[3]. Based on spectral data, a cyclic structure was finally formulated[4,5].



We have examined the dimerization reaction of some alkylidenemalononitriles. We found that of the various

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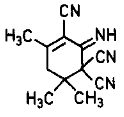
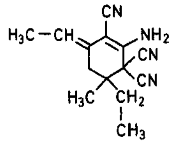
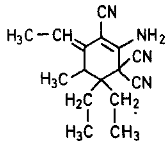
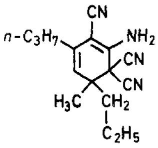
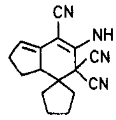
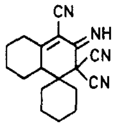
Table 1. Dimers **2** prepared from Alkylidenemalononitriles **1**

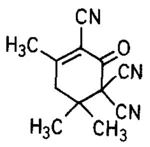
2	Yield[a] [%]	m.p.[°C] (Lit.m.p.[°C])	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]	References
a 	77	171.0 (168–170)[4]	1.32 [d, 6H, $(CH_3)_2$]; 1.92 (s, 3H, CH_3); 5.12 (m, 1H, =NH); 5.45 (m, 1H, =CH–)	4, 5, 11
b 	71	158–160 (167–169)[8]	1.0–2.0 (m, 11H); 2.4 (s, 2H, $-CH_2-$); 5.0 (s, 2H, $-NH_2$); 5.81 (q, 1H, =CH–)	5, 8, 11
c 	69	160.0 (165–167)[8]	1.0–2.0 (m, 16H); 2.8 (q, 1H, $C\underline{H}-CH_3$); 5.08 (s, 2H, $-NH_2$); 5.72 (q, 1H, =CH–)	5, 8
d 	79	175–176[b]	1.0–2.5 (m, 17H); 5.1 (s, 1H, =CH–); 5.68 (s, 2H, $-NH_2$)	
e 	81	181–182 (178–182)[11]	1.0–3.25 (m, 13H); 5.12 (s, 2H, $-NH_2$); 5.74 (m, 1H, =CH–)	11
f 	79	181–183 (172–173)[8]	1.0–3.4 (m, 19H); 9.25 (s, 1H, =NH)	5, 8, 11

[a] Yield of isolated product.

[b] $C_{16}H_{20}N_4$ calc. C 71.60 H 7.15 N 20.87
(268.3) found 71.52 7.59 20.80

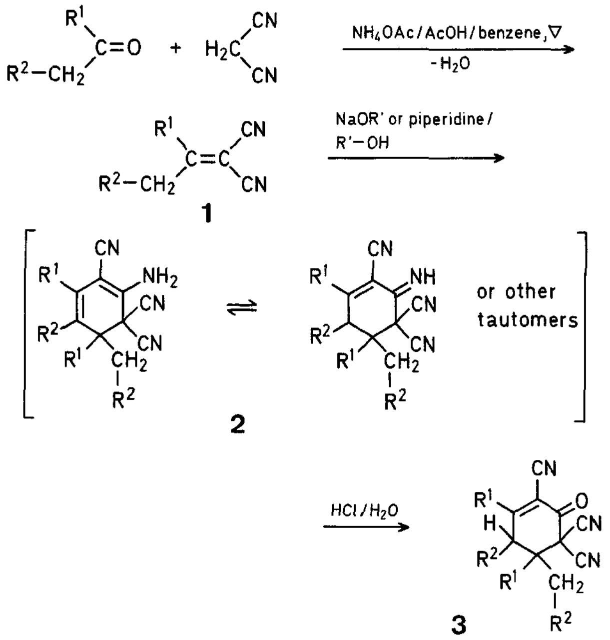
methods[3,5–9] for condensing ketones with malononitrile, the use of ammonium acetate/acetic acid/benzene with heating under a Dean-Stark trap was the most efficient one. Coenen[3] and others[5,8,10,11] using piperidine without solvent for the dimerization of alkylidenemalononitriles obtained a crude glassy product which was difficult to purify. We carried out the dimerization in alcoholic solution in the presence of only catalytic amounts of sodium alkoxides or piperidine and obtained the dimers in ~80% yield and in high purity.

Based on the structural assignment by Williams[4] of the hydrolysis product **3a** obtained from isopropylidenemalononitrile dimer,

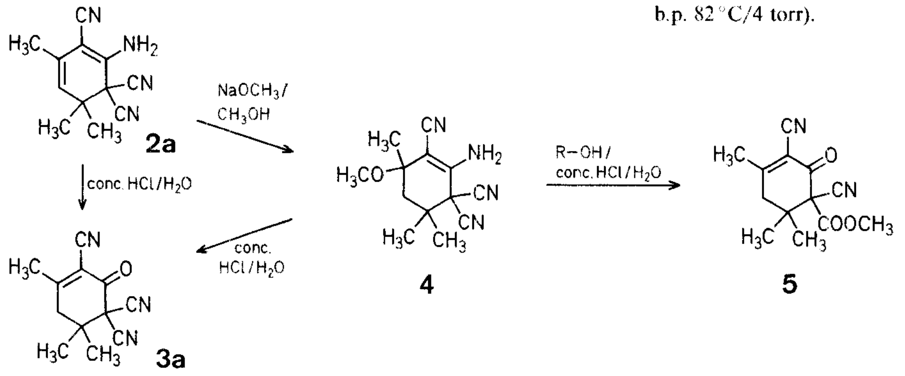


3a

we developed a convenient synthesis of 2,6,6-tricyano-2-cyclohexenones (3-oxocyclohexene-2-carbonitriles, **3**) starting from alkylidenemalononitriles **1**.



In this reaction sequence, hydrolysis of the dimer **2** with concentrated hydrochloric acid leads directly to the cyclohexenone **3**. When the dimerization of the alkylidenemalononitriles (e.g. isopropylidenemalononitrile) is carried out in the presence of more than a catalytic amount of alkoxide ion (e.g., sodium methoxide) the formation of alkoxylation products of **2** (e.g. **4**) is observed. Hydrolysis of compound **4** with concentrated hydrochloric acid affords the tricyanocyclohexenone **3a** whereas the reaction of **4** with aqueous-ethanolic hydrochloric acid leads to the formation of the dicyanooxocyclohexenecarboxylic ester **5**[4].



Alkylidenemalononitriles (1); General Procedure:
A ketone (0.2 mol), malononitrile (0.2 mol), ammonium acetate (3 g), acetic acid (9.6 g), and benzene (60 ml) are refluxed under a Dean-Stark trap until water ceases to separate (~6 h). The mixture is then washed with water (3 × 50 ml) and half saturated aqueous sodium chloride (1 × 50 ml), and is dried with magnesium sulfate. Benzene is removed and the remaining liquid is distilled under reduced pressure.

Isopropylidenemalononitrile (**1a**); yield: 58%; b.p. 108 °C/23 torr (Ref.[6], b.p. 107–108 °C/23 torr).

2-Butylidenemalononitrile (**1b**); yield: 69%; b.p. 82 °C/4 torr (Ref.[7], b.p. 82 °C/4 torr).

3-Pentylidenemalononitrile (**1c**): yield: 68%; b.p. 92 °C/5 torr (Ref.[6], b.p. 125 °C/23 torr).

2-Pentylidenemalononitrile (**1d**); yield: 69%; b.p. 96 °C/5 torr (Ref.[3], b.p. 113 °C/12 torr).

Cyclopentylidenemalononitrile (**1e**); yield: 72%; b.p. 115 °C/5 torr (Ref.[3], b.p. 113 °C/4 torr).

Cyclohexylidenemalononitrile (**1f**); yield: 67%; b.p. 125 °C/5 torr (Ref.[6], b.p. 137 °C/10 torr).

Cyclodimerization of Alkylidenemalononitriles (1) to 1-Amino-2,6,6-tricyano-1,3-cyclohexadienes (2) or Their Tautomers; General Procedure:
The alkylidenemalononitrile (**1**; 0.02 mol) is dissolved in absolute ethanol (40 ml), and a few drops of a 15% solution of sodium ethoxide in ethanol or a few drops of piperidine are added. After 1 h, the precipitated crystalline product **2** is isolated by filtration and washed with cold methanol.

3-Oxo-2,6,6-tricyanocyclohexenes (3); General Procedure:
The 1-amino-2,6,6-tricyano-1,3-cyclohexadiene (**2**; 5 g) is suspended in concentrated hydrochloric acid (50 ml), the mixture stirred for 2 h at 80 °C, and then allowed to cool. The crystalline product is isolated by filtration, washed with water, and dried. The product thus obtained is of satisfactory purity. For further purification it may be recrystallized from methanol.

1-Amino-3-methoxy-2,6,6-tricyano-3,5,5-trimethylcyclohexene (4):
To a solution of isopropylidenemalononitrile (**1a**; 4.24 g, 0.02 mol) in methanol (40 ml), a solution of sodium methoxide (0.02 mol) in methanol (~10 ml) is added with stirring. After 24 h, the crystalline product is isolated by filtration and washed with methanol; yield: 2.94 g (60%); plates from methanol or ethanol, m.p. 210–212 °C (Ref.[4], m.p. 210–212 °C).

Methyl 1,3-Dicyano-2-oxo-4,6,6-trimethyl-3-cyclohexene-1-carboxylate (5):
Compound **4** (4.9 g, 0.02 mol) is dissolved in conc. hydrochloric acid (35 ml) + ethanol (35 ml). After 15 min, the crystalline product is isolated by filtration and washed with ethanol; yield: 4.4 g (90%); m.p. 142–143 °C (Ref.[4], m.p. 142.8–143.4 °C). [The use of different alcohols in this reaction gives the same product].

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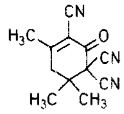
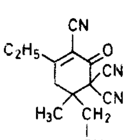
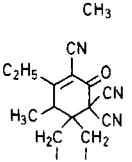
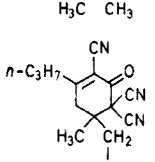
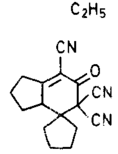
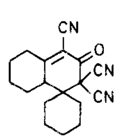
Table 2. 3-Oxo-2, 6, 6-tricyanocyclohexenes **3**

3	Yield[a] [%]	m.p. [°C]	Molecular formula or Lit. m.p. [°C]	M.S. m/e (M$^+$)	I.R. (KBr) ν[cm^{-1}]
a 	98	129–131	126–127[4]	213	2260(C≡N); 1720(C=O); 1620(C=C)
b 	96	94.0	$C_{14}H_{15}N_3O$ (241.3)	241	2245(C≡N); 1720(C=O); 1620(C=C)
c 	97	101–103	$C_{16}H_{19}N_3O$ (269.4)	269	2240(C≡N); 1705(C=O); 1615(C=C)
d 	97	101–102	$C_{16}H_{19}N_3O$ (269.4)	269	2240(C≡N); 1725(C=O); 1610(C=C)
e 	98	153.0	$C_{16}H_{15}N_3O$ (265.3)	265	2240(C≡N); 1720(C=O); 1640(C=C)
f 	98	148–150	$C_{18}H_{19}N_3O$ (293.4)	293	2240(C≡N); 1720(C=O); 1615(C=C)

[a] Yield of isolated product.
[b] The microanalyses were in good agreement with the calculated values: C, ± 0.24; H, ± 0.17; N, ± 0.19.

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