Acta Chemica Scandinavica, 1997: 51: 1104–1111
Printed in UK – all rights reserved

Copyright © Acta Chemica Scandinavica 1997

ACTA
CHEMICA SCANDINAVICA
ISSN 0904–213X

Dimerization of Cyclopropanecarbonitrile Mediated by Grignard Reagents. Formation of Highly Substituted Pyridines

Per Kolsaker,* Pål Songe and Christian Rømming

Department of Chemistry, University of Oslo, PO Box 1033 Blindern, 0315 Oslo, Norway

Kolsaker, P., Songe, P. and Rømming, C., 1997. Dimerization of Cyclopropanecarbonitrile Mediated by Grignard Reagents. Formation of Highly Substituted Pyridines. – Acta Chem. Scand. 51: 1104–1111. © Acta Chemica Scandinavica 1997.

The reaction of cyclopropanecarbonitrile with ethylmagnesium bromide in diethyl ether followed by quenching with malononitrile gave the expected 2-cyano-3-cyclopropylpent-2-enonitrile (**1a**) in high yields. When the solvent was changed to tetrahydrofuran (THF) using ethylmagnesium chloride, low yields of **1a** (12%) were obtained; the main products were two pentasubstituted pyridines, 2-amino-5-(2-chloroethyl)-3-cyano-6-cyclopropyl-4-ethylpyridine (**2a**, 70%) and 2-amino-3-cyano-5-(3,3-dicyanopropyl)-6-cyclopropyl-4-ethylpyridine (**2c**, 10%). In addition, their isomers, 2-amino-5-(2-chloroethyl)-3-cyano-4-cyclopropyl-6-ethylpyridine (**3a**, 7%) and 2-amino-3-cyano-5-(3,3-dicyanopropyl)-4-cyclopropyl-6-ethylpyridine (**3c**, 1%), were observed and identified by combined gas chromatography–mass spectrometry (GC–MS). When methylmagnesium chloride was used (solvent THF), in addition to **1b** and the isomers **2d**, **2e**, **3d** and **3e**, a tetrasubstituted pyridine, 2-amino-3-cyano-4,6-dicyclopropylpyridine (**11**), was formed. Similar reaction between cyclopropylmagnesium bromide and cyclopropanecarbonitrile gave after hydrolysis about equal yields of dicyclopropyl ketone and a diketone, 1,1-di(cyclopropanecarbonyl)cyclopropane (**8b**). The structures of **2c** and **2d** were established by X-ray crystallography.

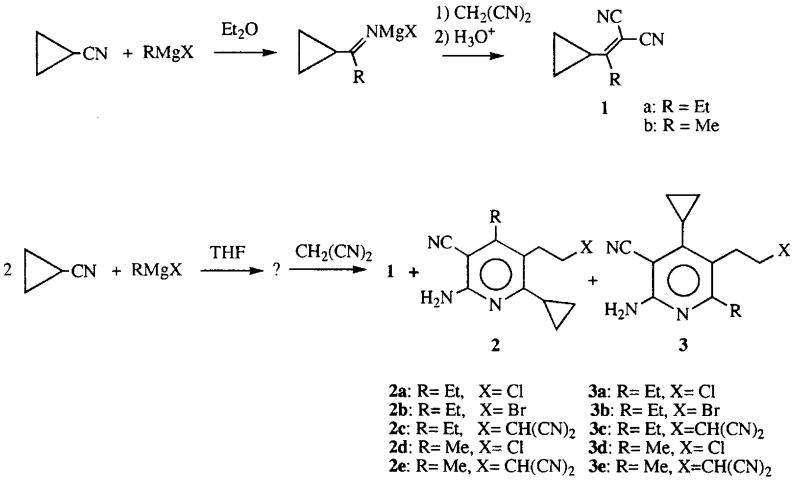
During continued studies of the chemistry of nucleophilic reactions involving substituted 1,1-dicyanoallyl anions,[1] it was of interest to synthesize 2-cyano-3-cyclopropylpent-2-enonitrile (**1a**). A one-pot procedure[2] has earlier been applied with success[3] in which an alkane nitrile is reacted with a Grignard reagent and, instead of the usual hydrolysis step, the reaction solution was 'quenched' with malononitrile. Indeed, when the proper reagents (ethylmagnesium bromide and cyclopropanecarbonitrile, followed by malononitrile) were mixed in the usual way using diethyl ether as solvent, **1a** was obtained in very good yields. However, when commercial ethylmagnesium chloride [FLUKA, solvent tetrahydrofuran (THF)] was used, **1a** was produced in only low yields (12%) and instead the pentasubstituted pyridines **2a** (70%) and **2c** (10%) were isolated. In addition, their isomers [**3a** (7%) and **3c** (1%)] were identified by combined gas chromatography–mass spectrometry (GC–MS) (Scheme 1). Similar results were obtained (apart from a change of the halogen atom to give **2b**) using ethylmagnesium bromide.

The formation of the pyridines deserves some comment. Stoichiometrically, with regard to the number of carbon atoms, two moles of cyclopropanecarbonitrile and one mole each of ethylmagnesium chloride and malononitrile must be involved. As shown below, compound **4** is a real intermediate and its formation, shown in Scheme 2, could be explained by two alternative routes, **A** or **B**. The former route could be a result of a Thorpe-like dimerization to form an imine which most likely would react with a second mole of alkylmagnesium halide with expulsion of the corresponding alkane to give intermediate **4**.

A serious objection to such a proposal is that the acidity of the cyclopropyl proton probably is not high enough to take part in a Thorpe reaction. A better explanation might be that the acidity is high enough to protonate the Grignard reagent (Route **B**).

To distinguish between these two possibilities cyclopropanecarbonitrile was allowed to react completely with equimolar amounts of ethereal ethylmagnesium bromide, as no dimerization took place in this solvent. Then, equimolar amounts of ethylmagnesium bromide in THF were added and the evolution of ethane was followed volumetrically and within 24 h one mole equivalent was

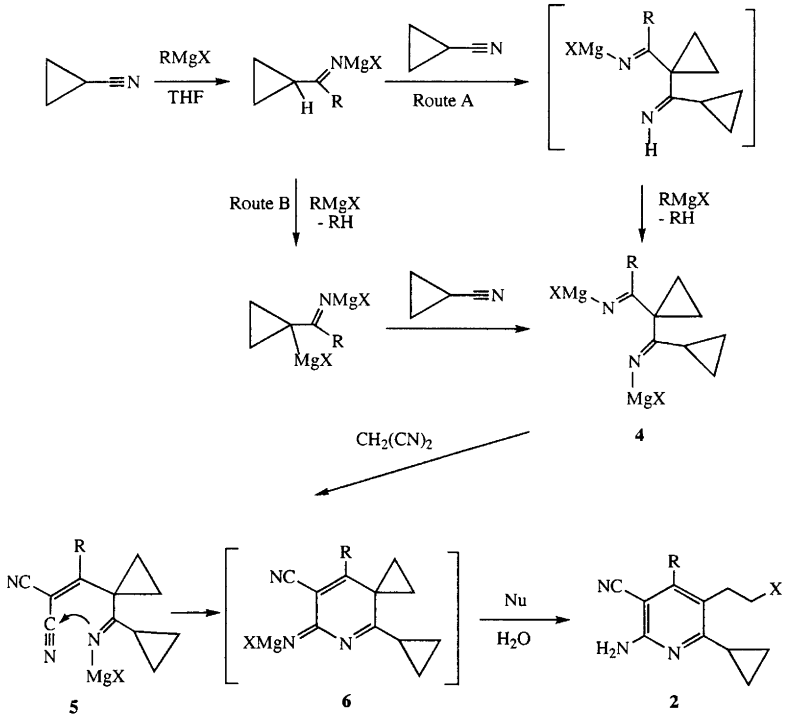
* To whom correspondence should be addressed.



1 a: R = Et
b: R = Me

2 3

Scheme 1.



5 6 2

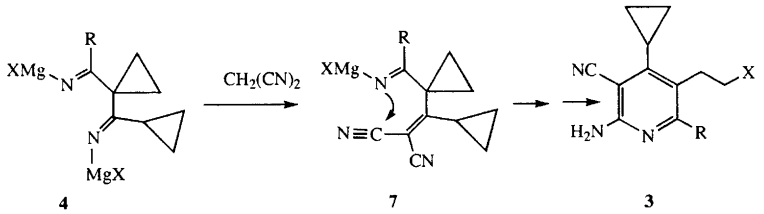
Scheme 2.

collected. Its identity was established using gas chromatography and HRMS. This reaction clearly indicates that the alkane is evolved before an extra mole equivalent of cyclopropanecarbonitrile is added, according to Route **B**.

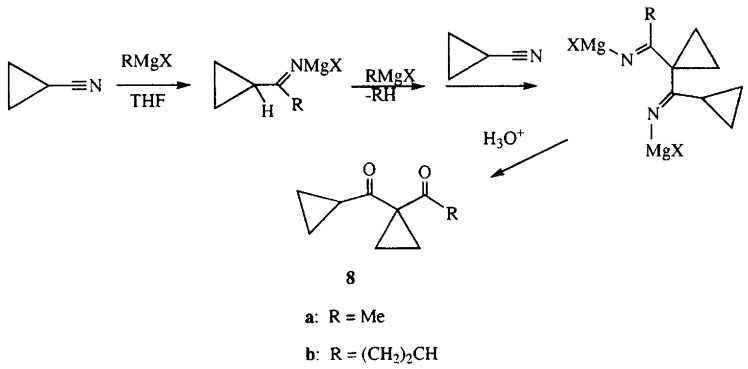
When malononitrile is added, **5** is formed as a possible intermediate, which is probably cyclized to the quinonoid structure **6**. Whether **6** is an actual intermediate or it is immediately cleaved by ethylmagnesium halide or malononitrile to form **2** is not quite clear. As shown below, a similar fragment is quite abundant in MS. An indication of **6** being an intermediate was also obtained when the Grignard reagent was ethylmagnesium bromide. The reaction solution was hydrolyzed using aqueous HCl to give tiny amounts of **2a** in addition to **1a** and **2b**. The possibility of a nucleophilic displacement of bromide in **2b** by chloride ion to give **2a** was excluded in a separate experiment.

Similar nucleophilic ring openings of cyclopropanes with geminal electron-withdrawing substituents are quite common.[4] In the present case the driving force is the formation of an aromatic system, acting as the electron-withdrawing component in the process.

The route to the isomers **3** is parallel to Scheme 2 (Scheme 3). The difference in yields of the isomers reflects different free activation energies for their formation. Thus the lower yields of **3** indicate that, in the nucleo-



Scheme 3.



Scheme 4.

philic attack of malononitrile (or its anion) on one of the imino carbons in **4**, the cyclopropyl group imposes greater steric hindrance compared with the alkyl group.

The key process in the pyridine formation must be the formation of the intermediate **4**. Its existence was confirmed by hydrolysis instead of reaction with malononitrile to give the diketone **8** using methyl- or cyclopropylmagnesium halide as the Grignard component in THF solvent (Scheme 4). It must be added that when using diethyl ether as the solvent the expected monoketones (methyl cyclopropyl or dicyclopropyl ketone) were the only products. Of the diketones only **8a** has been described in the literature.[5] Further developments in the study of this interesting synthetic chemistry will be reported separately.

When the Grignard reagent was methylmagnesium chloride (in THF) a tetrasubstituted pyridine (**11**) was observed in low yields. This could be explained by competetive proton abstraction from the primary adduct in Route **B** (Scheme 2) as depicted in Scheme 5.

The observed large solvent effect in the present study is most likely due to the position of the Schlenk equilibria. [eqn. (1)].[6] In contrast with the reaction in diethyl ether, these equilibria are displaced towards the monomeric side in THF over a wide concentration range (0.1–3.5 M) for the Grignard reactants applied in this work. Furthermore, it was also observed that the left-hand side of the Schlenk equilibrium in THF is displaced more to the dialkylmagnesium side by a factor of two powers of ten, compared with the equilibrium in diethyl ether,[7] and it is also reported that dialkylmagnesium is somewhat more basic than the corresponding alkylmagnesium halide.[8]

$$2\ RMgX \rightleftharpoons R_2Mg + MgX_2 \rightleftharpoons R_2MgMgX_2 \qquad (1)$$

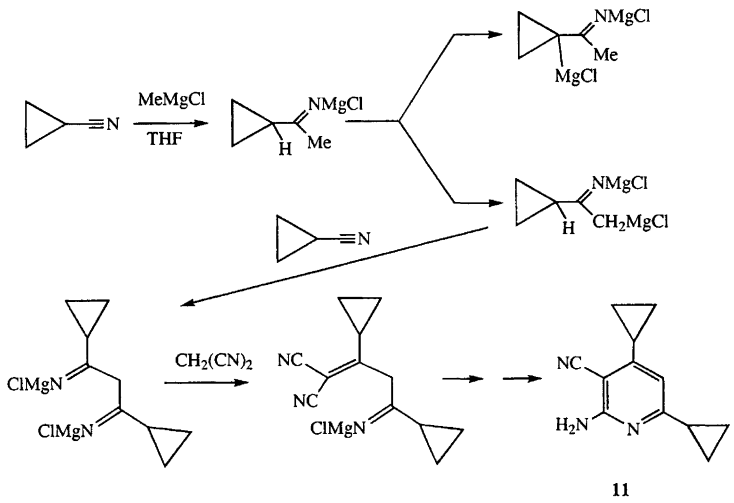
Mass spectrometry. The identity of the positional isomers **3** (**a** and **c**) was established using mass spectrometry. HRMS was used to verify the elemental composition. Comparison of the fragmentation patterns down to *m/z* 200 of **2** with those of **3** revealed close similarities, Table 1.

From *m/z* 200 and downwards the spectra are almost identical.

Complete absence of the $[M-H]^+$ peaks in **3** is somewhat puzzling as the corresponding peak in the spectrum of 2-ethylpyridine is much more abundant than in 4-ethylpyridine.[9] On the other hand, the $[M-H]^+$ peak from 2-cyclopropylpyridine (**9**) is, in relative terms (% total ion current), more than twice as abundant as the corresponding peak from 4-cyclopropylpyridine (**10**) (Table 1).* The almost identical appearance in this high mass region in the spectrum of **2c** compared with **2a** itself is also a good indication of this process.

The high abundance of $[M-X]^+$ is somewhat surprising since simple elimination of the X·-radical should result in a primary carbocation. However, the structure of this ion is most likely similar to the intermediate **6** as shown in Scheme 6, stabilized by the ring amino substituent. A similar stabilizing effect may also explain the abundance of the $[M-CH_2X]^+$ peak, it being the base peak in **2** (**a** and **c**) and **3a**.

*The cyclopropylpyridines was synthesized according to a literature procedure.[10]



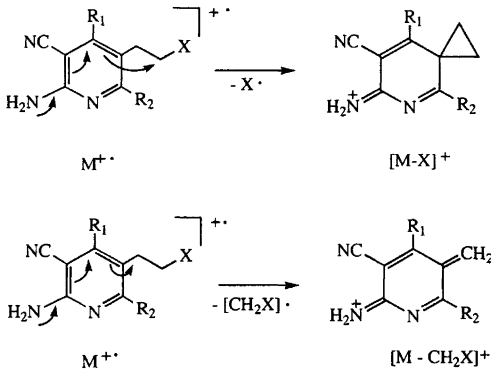
Scheme 5.

Table 1. Percentage ion current of the high mass fragments (*m/z*) of the substituted pyridines **2**, **3**, **11** and the cyclopropylpyridines **9** and **10**.[a]

Compound	$M^{+\cdot}$	$[M-H]^+$	$[M-X]^+$	$[M-CH_2X]^+$	Σ TIC[b]
2a	4.2 (249) 1.3 (251)	1.7 (248) 0.6 (250)	10.6 (214)	14.3 (200)	32.7
3a	3.9 (249) 1.3 (251)	0 0	2.6 (214)	20.4 (200)	28.2
2c	4.3 (279)	1.6 (278)	4.1 (214)	8.3 (200)	18.3
2d	3.5 (235) 1.2 (237)	1.7 (234) 0.5 (236)	6.9 (200)	13.7 (186)	27.5
3d	1.1 (235) 0.4 (237)	0 0	0.2 (200)	5.3 (186)	6.3
9	10.0 (119)	28.0 (118)			38.0
10	15.6 (119)	19.3 (118)			34.9
11	21.7 (199)	14.6 (198)			36.3

[a]Relative intensities of the fragments are given in Experimental. [b]Total ion current of the high mass fragments (above *m/z* 185 for **2**, **3**, **11** and *m/z* 117 for the cyclopropylpyridines **9** and **10**).

The spectrum of the tetrasubstituted pyridine **11** is distinctly different from the other pyridine products since it lacks the 5-substituent which is involved in the formation of the fragments discussed in Scheme 6, thereby furnishing a further indication of the proposed process. In contrast with the pentasubstituted pyridines where the fragments $[M-X]^+$ and $[M-CH_2X]^+$ constitute a major part of the total ion current of the high mass fragments (Table 1), the ions $M^{+\cdot}$ and $[M-H]^+$ carry all the high mass ionic current in **11**.



Scheme 6.

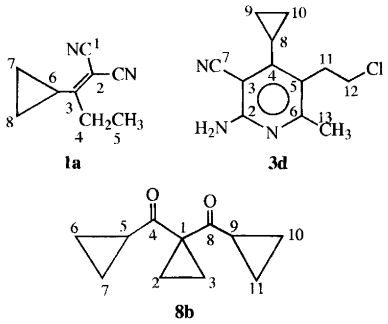
Experimental

General. Melting points are uncorrected. Boiling points (uncorrected) were determined using a Mettler FP1 apparatus. Infrared spectra were recorded on a Nicolet Magna 550 FTIR spectrometer, using an attenuated total reflectance (ATR) ZnSe plate for solid samples, ultraviolet spectra on a Shimadzu UV-260 spectrophotometer, mass spectra on a Fison Instrument VG ProSpec Q, and high-resolution NMR spectra (^1H and ^{13}C) on a Bruker Spectrospin Avance DPX 300 spectrometer.

All solvents used were dried according to literature recommendations.[11]

^{13}C NMR peak assignments were made using the Bruker pulse programs XHcorr (HETCOR) and Coloc (Long-range HETCOR). The numbering of the carbon atoms for compounds **2b**, **2c** and **2d** is given in the crystal structure in Figs. 1 and 2, respectively, and for **2a** it

follows the numbering in Fig. 1, except that the dicyanocarbon element is exchanged with Cl. For compounds **1a**, **3d** and **8b** the numbering is given in the formulae below.



1a **3d**

8b

2-Cyano-3-cyclopropylpent-2-enonitrile (**1a**).[2] To a solution of ethylmagnesium bromide made from magnesium (0.65 g, 26 mmol) and bromoethane (2.83 g, 26 mmol) in diethyl ether (15 ml) was added dropwise cyclopropanecarbonitrile (1.5 g, 22 mmol) in diethyl ether (15 ml). The reaction was refluxed for 5 h after which malononitrile (1.5 g, 22 mmol) in diethyl ether (25 ml) was added dropwise. After continued reflux for 1 h, HCl (1 M, 25 ml) was added. The organic phase was washed twice with HCl (1 M, 25 ml), dried ($MgSO_4$) and evaporated. The oily residue was dissolved in dichloromethane and precipitated with pentane to give 2.5 g (74%) white crystals. M.p. 36–38 °C. Anal. Found C 74.35, H 7.18, N 18.55. Calc. for $C_9H_{10}N_2$: C 73.94, H 6.89, N 19.16. FTIR: ν_{max} 3019 (w), 2984 (m), 2227 (s), 1564 (s) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.2–2.3 (1 H, m), 2.06 (2 H, q, *J* 7.6 Hz), 1.2–1.3 (2 H, m), 1.15 (3 H, t, *J* 7.6 Hz), 1.0–1.1 (2 H, m). ^{13}C NMR ($CDCl_3$): δ 188.6 (C3), 112.6 and 112.2 (2 × CN), 83.0 (C2), 23.3 (C4), 18.2 (C5), 13.6 (C6), 10.7 (C7 and C8). MS [EI, 70 eV: *m/z* (% rel. int.)]: 146 (22, $[M]^{+\cdot}$), 145 (24, $[M-H]^+$, 91 (70), 41 (100, $C_3H_5^+$). UV [MeOH, (log ε)]: λ 269.9 (4.21).

Reaction of cyclopropanecarbonitrile with ethylmagnesium chloride and malononitrile in tetrahydrofuran (THF). Cyclopropanecarbonitrile (1.5 g, 22 mmol, Fluka) dissolved in dry THF (15 ml) was added dropwise to 2.8 M ethylmagnesium chloride (9.6 ml, 26.9 mmol, Fluka) in THF. The reaction was refluxed for 5 h after which malononitrile (1.6 g, 24 mmol) dissolved in THF (25 ml) was added dropwise with vigorous stirring and the mixture was refluxed for 1 h. HCl (1 M, 25 ml) and diethylether (25 ml) were added. The organic phase was washed with aqueous sodium chloride, dried ($MgSO_4$) and evaporated. The resulting brown oil (2.3 g) was flash-chromatographed on silica gel using dichloromethane as the eluent. The following compounds were isolated in order of elution.

1a, 0.4 g [(12% in crude product (GC)].

2-Amino-5-chloroethyl-3-cyano-6-cyclopropyl-4-ethylpyridine (**2a**), 1.5 g [70% in crude product (GC)]. M.p. 107–109 °C. Anal. (HRMS): Found 249.1043/251.1027. Calc. for $C_{13}H_{16}ClN_3$: 249.1033/251.1027. FTIR: ν_{max} 3490 (w), 3342 (s), 3014 (w), 2977 (w), 2217 (s), [1625 (s) and 1560 (s) (pyridine quadrant stretch)].[12] ^1H NMR ($CDCl_3$): δ 4.95 (2 H, br s), 3.6–3.5 (2 H, m), 3.2–3.1 (2 H, m), 2.73 (2 H, q, *J* 7.9 Hz), 2.0–1.9 (1 H, m), 1.19 (3 H, *J* 7.9 Hz), 1.1–1.0 (2 H, m), 1.0–0.9 (2 H, m). ^{13}C NMR ($CDCl_3$): δ 165.1 (C6), 158.2 (C3), 156.0 (C4), 118.9 (C5), 116.7 (C7), 88.2 (C2), 42.9 (C11), 30.7 (C10), 25.3 (C8), 14.6 (C9), 13.8 (C12), 10.6 (C13 and C14). MS [EI, 70 eV: *m/z* (% rel. int.)]: 249/251 (30/9, $[M]^{+\cdot}$), 248/250 (12/9, $[M-H]^+$), 214 (74, $[M-Cl]^+$), 200 (100, $[M-CH_2Cl]^+$). UV [MeOH, (log ε)]: λ 330.6 (3.96), 252.8 (4.11), 225.7 (4.35), 204.7 (4.17) nm.

2-Amino-3-cyano-5-(3,3-dicyanopropyl)-6-cyclopropyl-4-ethylpyridine (**2c**), 0.3 g [10% in crude product (GC)]. M.p. 155–157 °C. X-Ray crystallography, see below. FTIR: ν_{max} 3486 (m), 3378 (s), 2975 (m), 2256 (w), 2208 (s), [1612 (s) and 1569 (s) (pyridine quadrant stretch)].[12] ^1H NMR ($CDCl_3$): δ 4.93 (2 H, br s), 3.86 (1 H, t, *J* 6.2 Hz), 3.0–2.9 (2 H, m), 2.72 (2 H, q, *J* 7.6 Hz), 2.3–2.2 (2 H, m), 2.0–1.9 (1 H, m), 1.23 (3 H, t, *J* 7.6 Hz), 1.1–1.0 (2 H, m), 1.0–0.9 (2 H, m). ^{13}C NMR ($CDCl_3$): δ 164.8 (C6), 158.3 (C3), 155.6 (C4), 119.0 (C5), 116.6 (C7), 112.2 (C16, C17), 88.3 (C2), 31.1 (C15), 25.2 (C8), 24.0 (C11), 22.5 (C10), 14.7 (C9), 13.8 (C12), 10.8 (C13, C14). MS [EI, 70 eV: *m/z* (% rel. int.)]: 279 (52, $[M]^{+\cdot}$), 278 (19, $[M-H]^+$), 214 (49, $[M-C_3HN_2]^+$), 200 (100, $[M-C_4H_3N_2]^+$). UV [MeOH, (log ε)]: λ 331.6 (3.96), 252.3 (4.10), 225.5 (4.35), 203.8 (4.16) nm.

Gas chromatography on the crude product showed a peak (7%) very close to that of **2a** which by GC–MS gave a spectrum very similar to **2a** and most likely is an isomer, *viz. 2-amino-5-chloroethyl-3-cyano-4-cyclopropyl-6-ethylpyridine* (**3a**), Cf. mass spectra discussion above. MS [EI, 70 eV: *m/z* (% rel. int.)]: 249/251 (19/7, $[M]^+$), 214 (12, $[M-Cl]^+$), 200 (100, $[M-CH_2Cl]^+$). Likewise GC indicated the presence of an isomer of **2c** in about 1% yield, *viz. 2-amino-3-cyano-5-(3,3-dicyanopropyl)-4-cyclopropyl-6-ethylpyridine* (**3c**). MS [EI: 70 eV, *m/z* (% rel. int.)]: 279 (57, $[M]^{+\cdot}$), 214 (100, $[M-C_3HN_2]^+$), 200 (72, $[M-C_4H_3N_2]^+$).

Reaction of cyclopropanecarbonitrile with ethylmagnesium bromide and malononitrile in THF. Following the same procedure as above (using the same molar ratio of reagents) the brown oil obtained (3.0 g) was flash-chromatographed (SiO_2–dichloromethane) to give these compounds in order of elution.

1a, 0.8 g [27% in crude product (GC)].

2-Amino-5-bromoethyl-3-cyano-6-cyclopropyl-4-ethylpyridine (**2b**), 1.2 g [45% in crude product (GC)]. M.p. 124–126 °C. Anal. (HRMS): Found 295.0516/293.0519.

Calc. for $C_{13}H_{16}BrN_3$: 295.0507/293.0528. FTIR: ν_{max} 3458 (m), 3341 (m), 2970 (m), 2214 (s), [1619 (s), 1556 (s) (pyridine quadrant stretch)].[12] ^{1}H NMR ($CDCl_3$): δ 4.94 (2 H, br s), 3.4–3.3 (2 H, m), 3.3–3.2 (2 H, m), 2.73 (2 H, q, *J* 7.6 Hz), 2.0–1.9 (1 H, m), 1.20 (3 H, t, *J* 7.6 Hz), 1.1–1.0 (2 H, m), 1.0–0.9 (2 H, m). ^{13}C NMR ($CDCl_3$): δ 165.0 (C6), 158.2 (C3), 155.8 (C4), 120.0 (C5), 116.6 (C7), 88.2 (C2), 31.0 (C11), 30.3 (C10), 25.3 (C8), 14.6 (C9), 13.8 (C12),10.6 (C13, C14). MS [EI, 70 eV: *m/z* (% rel. int.)]: 293/295 (25/25, $[M]^{+\cdot}$), 292/294 (12/12, $[M-H]^+$), 214 (100, $[M-Br]^+$), 200 (89, $[M-CH_2Br]^+$). UV [MeOH, (log ε)]: λ 331.3 (4.00), 255.0 (4.18), 226.8 (4.41) nm.

2-Amino-3-cyano-5-(3,3-dicyanopropyl)-6-cyclopropyl-4-ethylpyridine (**2c**), 0.1 g [6% in crude product (GC)].

Identified using GC–MS: *2-amino-5-bromoethyl-3-cyano-4-cyclopropyl-6-ethylpyridine* (**3b**) [8% in crude product (GC)]. MS [EI, 70 eV: *m/z* (% rel. int.)]: 293/295 (18/18, $[M]^{+\cdot}$), 214 (23, $[M-Br]^+$), 200 (100, $[M-CH_2Br]^+$, (**2a**) [2% in crude product (GC)], (**3a**) [0.3% in crude product (GC)], (**3c**) [1.0% in crude product (GC)].

Reaction of cyclopropanecarbonitrile with methylmagnesium chloride and malononitrile in THF. Following the same procedure as above (using the same molar ratio of reagents) the brown oil obtained (2.7 g) was flash-chromatographed (SiO_2–dichloromethane) to give the following compounds in order of elution.

2-cyano-3-cyclopropylbut-2-enonitrile (**1b**), 0.6 g [36% in crude product (GC)].

2-Amino-3-cyano-4,6-dicyclopropylpyridine (**11**), 98 mg [5% in crude product (GC)]. M.p. 187–189 °C. Anal. (HRMS): Found 199.1104. Calc. for $C_{12}H_{13}N_3$: 199.1103. FTIR: ν_{max} 3395 (s), 3332 (m), 2921 (w), 2209 (m), 1658 (s), [1581 (s), 1555 (s) (pyridine quadrant stretch)].[12] ^{1}H NMR (DMSO-d_6): δ 6.47 (2 H, s), 6.10 (1 H, s), 1.9–1.8 (2 H, m), 1.1–1.0 (2 H, m). 0.9–0.8 (6 H, m). ^{13}C NMR (DMSO-d_6): δ 167.1, 161.0, 159.0, 117.9, 113.0, 105.5, 87.6, 18.1, 14.5, 11.0, 10.7, 9.3. MS [EI, 70 eV: *m/z* (% rel. int.)]: 199 (67, $[M]^{+\cdot}$), 198 (100, $[M-H]^+$). UV [MeOH, (log ε)]: λ 324 (4.09), 229.3 (4.51), 211.5 (4.48) nm.

2-Amino-5-(2-chloroethyl)-3-cyano-6-cyclopropyl-4-methylpyridine (**2d**), 0.5 g [32% in crude product (GC)]. M.p. 82–83 °C. X-ray crystallography, see below. FTIR: ν_{max} 3451 (w), 3339 (s), 3224 (w), 2216 (m), 1630 (m), 1570 (m). ^{1}H NMR ($CDCl_3$): δ 4.89 (2 H, br s), 3.6–3.5 (2 H, m), 3.2–3.1 (2 H, m), 2.41 (3 H, s), 2.0–1.9 (1 H, m), 1.1–1.0 (2 H, m), 1.0–0.9 (2 H, m). ^{13}C NMR ($CDCl_3$): δ 164.6 (C6), 158.0 (C3), 150.2 (C4), 120.0 (C5), 116.9 (C7), 89.4 (C2), 42.6 (C10), 31.1 (C9), 18.3 (C8), 13.8 (C11), 10.5 (C12 and C13). MS [EI, 70 eV: *m/z* (% rel. int.)]: 235/237 (24/8, $[M]^{+\cdot}$), 234/236 (13/8, $[M-H]^+$), 200 (48, $[M-Cl]^+$), 186 (100 $[M-CH_2Cl]^+$), 171 (37). UV [MeOH, (log ε)]: λ 329.0 (3.29), 252.9 (4.14), 224.7 (4.37) nm.

2-Amino-3-cyano-5-(3,3-dicyanopropyl)-6-cyclopropyl-4-methylpyridine (**2e**), 0.2 g [12% in crude product (GC)]. M.p. 182–184 °C ($CHCl_3$–pentane). Anal. (HRMS): Found 265.132566. Calc. for $C_{15}H_{15}N_5$: 265.132 746. FTIR: ν_{max} 3474 (m), 3373 (m), 3214 (m), 2913 (m), 2251 (m), 2209 (s), [1614 (s) and 1573 (s) (pyridine quadrant stretch)],[12] 1458 (s).^{1}H NMR ($CDCl_3$): δ 4.94 (2 H, br s), 3.81 (1 H, t, *J* 6.2 Hz), 3.1–3.0 (2 H, m), 2.42 (3 H, s), 2.2–2.1 (2 H, m), 2.0–1.9 (1 H, m), 1.1–0.9 (4 H, m). ^{13}C NMR (DMSO-d_6): δ 163.1, 158.4, 150.3, 119.6, 116.9, 114..3, 87.9, 29.1, 24.2, 22.2, 17.6, 13.4, 9.9. MS [EI, 70 eV: *m/z* (% rel. int.)]: 265 (0.5 $[M]^{+\cdot}$), 250 (15), 235 (9), 220 (31), 219 (10), 205 (100). UV [MeOH, (log ε)]: λ 330.0 (3.73), 252.4 (4.07), 224.7 (4.32)] nm.

2-Amino-3-cyano-5-(2-chloroethyl)-4-cyclopropyl-6-methylpyridine (**3d**), 0.1 g [9% in crude product (GC)]. M.p. 103–104 °C ($CHCl_3$–pentane). Anal. (HRMS): Found 237.083 957/235.086 783. Calc. for $C_{12}H_{14}N_3Cl$: 237.084 675/235.087 625. FTIR: ν_{max} 3418 (m), 3375 (s), 3330 (m), 2216 (s), 1649 (m), 1556 (s). ^{1}H NMR ($CDCl_3$): δ 5.05 (2 H, br s), 3.6–3.5 (2 H, m), 3.3–3.2 (2 H, m), 2.43 (3 H, s), 1.9–1.8 (1 H, m), 1.2–1.1 (2 H, m), 0.9–0.8 (2 H, m). ^{13}C NMR ($CDCl_3$): δ 160.6 (C6), 158.2 (C3), 154.8 (C4), 122.9 (C5), 116.5 (C7), 90.7 (C2), 42.6

Table 2. Crystal and experimental data.

	2c	**2d**
Compound	$C_{16}H_{17}N_5$	$C_{12}H_{14}ClN_3$
Crystal system	Triclinic	Triclinic
a/Å	8.118(1)	7.8618(3)
b/Å	9.890(2)	8.8618(3)
c/Å	10.266(2)	9.8959(3)
α/°	98.31(1)	108.284(2)
β/°	99.77(1)	95.969(2)
γ/°	109.24(2)	104.129(1)
V/Å^3	748.9(2)	589.55(2)
Space group	$P\bar{1}$	$P\bar{1}$
Formula weight	279.34	235.71
Z	2	2
F(000)	296	248
λ/Å	0.71073	0.71073
μ/cm^{-1}	0.73	3.00
D_x/g cm^{-3}	1.239	1.328
Crystal size/mm	0.3 × 0.3 × 0.4	0.2 × 0.4 × 0.4
T/°C	−135	−123
Scan mode	ω/2θ	ω
Scan range/°	1.3	0.3
Max 2θ/°	60	80
No. indep. meas.	4388	6217
No. with $F > 4\sigma(F)$	3603	4251
No. of parameters	258	202
Δρ max./e Å^{-3}	0.29	0.45
Δρ min./e Å^{-3}	0.21	−0.33
R_1 indices [$F > 4\sigma(F)$]	0.047	0.052
wR_2 (all data)	0.135	0.130
Goodness-of-fit on F^2	1.054	1.038

Table 3. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\times 10^3$) for **2c** and **2d**. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Atom	x	y	z	U_{eq}
2c				
N(1)	1281(1)	6675(1)	7252(1)	23(1)
N(2)	3781(1)	6705(1)	6488(1)	34(1)
N(3)	3498(1)	3179(1)	5367(1)	35(1)
N(4)	−4751(2)	−118(1)	8234(1)	42(1)
N(5)	−6767(1)	3342(1)	9185(1)	40(1)
C(2)	2168(1)	5918(1)	6688(1)	22(1)
C(3)	1499(1)	4369(1)	6397(1)	22(1)
C(4)	−83(1)	3599(1)	6749(1)	22(1)
C(5)	−1028(1)	4405(1)	7303(1)	21(1)
C(6)	−281(1)	5942(1)	7533(1)	21(1)
C(7)	2564(1)	3656(1)	5824(1)	26(1)
C(8)	−667(1)	1952(1)	6579(1)	27(1)
C(9)	−2069(2)	1079(1)	5273(1)	37(1)
C(10)	−2736(1)	3638(1)	7719(1)	23(1)
C(11)	−2367(1)	3584(1)	9221(1)	22(1)
C(12)	−1152(1)	6882(1)	8167(1)	26(1)
C(13)	−6(2)	8372(1)	9062(1)	31(1)
C(14)	−1106(2)	8278(1)	7712(1)	31(1)
C(15)	−3998(1)	2531(1)	9611(1)	24(1)
C(16)	−4470(1)	1027(1)	8842(1)	29(1)
C(17)	−5569(1)	2972(1)	9368(1)	28(1)
2d				
Cl(1)	4384(1)	2659(1)	332(1)	31(1)
N(1)	201(1)	7536(1)	3412(1)	20(1)
N(2	−1928(1)	7774(1)	4840(1)	27(1)
N(3)	−4158(1)	3448(1)	4687(1)	27(1)
C(2	−1144(1)	6735(1)	3918(1)	19(1)
C(3)	−1680(1)	4889(1)	3547(1)	19(1)
C(4)	−862(1)	3851(1)	2575(1)	18(1)
C(5)	474(1)	4693(1)	1989(1)	18(1)
C(6)	975(1)	6542(1)	2471(1)	18(1)
C(7)	−3048(1)	4084(1)	4178(1)	21(1)
C(8)	−1460(2)	1890(2)	2217(2)	26(1)
C(9)	1408(1)	3675(1)	908(1)	21(1)
C(10)	3226(2)	3723(2)	1650(1)	23(1)
C(11)	2447(2)	7523(1)	1953(1)	23(1)
C(12)	3853(2)	9091(2)	3068(2)	31(1)
C(13)	2571(2)	9370(2)	2019(1)	29(1)

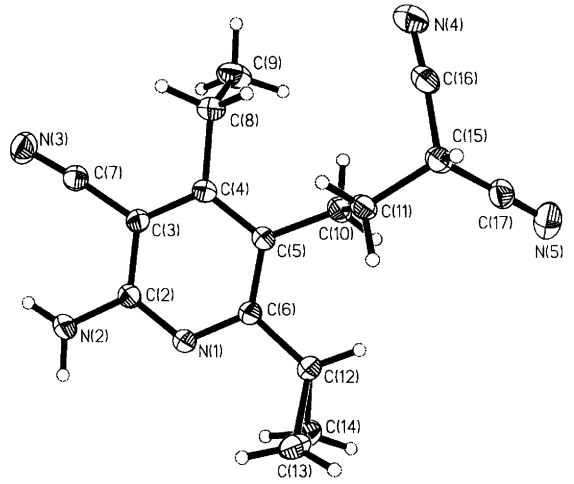


Fig. 1. ORTEP plot of **2c**.

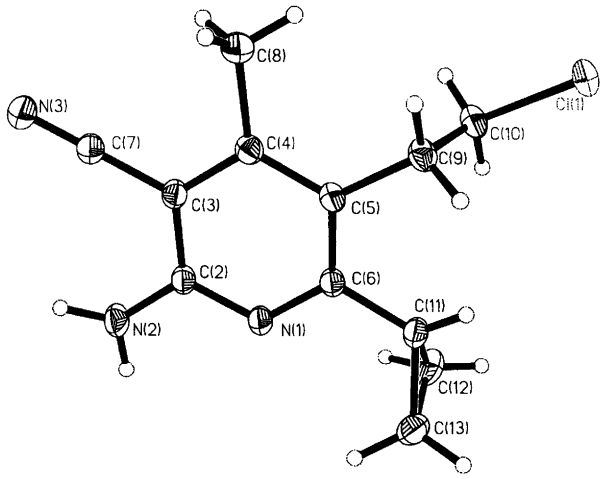


Fig. 2. ORTEP plot of **2d**.

(C12), 31.3 (C11), 22.9 (C13), 13.6 (C8), 8.0 (C9 and C10). MS [EI, 70 eV: *m/z* (% rel. int.)]: 235/237 (21/7, $[M]^{+\cdot}$), 186 (100, $[M-CH_2Cl]^+$), 171 (41). UV [MeOH, (log ε)]: λ 329.0 (3.73), 251.4 (3.99), 224.8 (4.20), 204.9 (4.12) nm.

Reaction between cyclopropanecarbonitrile and cyclopropylmagnesium bromide. To a solution of cyclopropylmagnesium bromide made from magnesium (0.65 g, 27 mmol) and bromocyclopropane (3.25 g, 27 mmol) in THF (15 ml), cyclopropanecarbonitrile (1.5 g, 22.4 mmol) in THF was added dropwise. The reaction was refluxed for 5 h, after which diethyl ether (25 ml) was added and the organic solution was washed with H_2O saturated with NH_4Cl. After drying ($MgSO_4$), the organic phase was evaporated and the crude product was filtered through a short silica column. Distillation at low pressure gave 0.82 g of a compound identified as *dicyclopropyl ketone* by comparison with commercial material (Fluka). The distillation residue (0.73 g) was quite pure, b.p. 258 °C (decomp), and identified as *1,1-di(cyclopropanecarbonyl)cyclopropane* (**8b**). Anal. (HRMS): Found 178.099 73. Calc. for $C_{11}H_{14}O_2$: 178.099 38. FTIR: ν_{max} 3351 (w), 3010 (m), 1672 (s), 1386 (s) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.1–2.0 (m, 2 H), 1.30 (4 H, s), 1.0–0.9 (4 H, m), 0.8–0.9 (4 H, m). ^{13}C NMR ($CDCl_3$): δ 206.4 (C=O), 43.9 (C1), 20.2 (C2, C3), 17.2 (C5, C9), 12.2 (C6, C7, C10, C11). MS [EI, 70 eV: *m/z* (% rel. int.)]: 178 (1.6, $M^{+\cdot}$), 150 (100, $[M-CO]^+$), 121 (23), 69 (93), 41 (71, $C_3H_5^+$). UV [MeOH, (log ε)]: λ 208 (4.21), 272 (2.73) nm.

Reaction of cyclopropanecarbonitrile with ethylmagnesium bromide and estimation of ethane. To a solution of ethylmagnesium bromide made from magnesium (0.29 g, 12 mmol) and bromoethane (1.20 g, 11 mmol) in diethylether (7 ml) was added cyclopropanecarbonitrile (0.67 g,

10 mmol) in diethyl ether (4 ml). The reaction was refluxed for 5 h (to ensure complete reaction of cyclopropanecarbonitrile), after which THF (10 ml) was added. Ethylmagnesium bromide (5 ml, 2 M THF solution) was added dropwise. The gas that evolved was collected in a gas burette. After 20 h the volume of gas collected, identified as ethane by GC–MS, was 220 ml (ca. 10 mmol). The reaction solution was hydrolyzed using ammonium chloride solution (25 ml, 1 M). Standard work-up gave 1.17 g (88%) cyclopropyl ethyl ketone.

X-Ray crystal structure determination. Crystal data and the conditions for the data collection are given in Table 2. The experiments with **2c** were carried out using a Nicolet P3/F four-circle diffractometer. Unit cell parameters were determined from the settings of 25 carefully centered general reflections. The intensity data were corrected for Lorentz and polarization effects but not for absorption and extinction. Standard deviations for the intensities were based on counting statistics with an addition of 2% of the net intensity. The data for **2d** were collected on a Siemens SMART CCD diffractometer; the data reduction and cell parameter determination were carried out by use of the SAINT program.[13] Absorption corrections were made using the program SADABS.[14] Both structures were determined and refined using the SHELXTL program package.[15] The non-hydrogen atoms were refined anisotropically; hydrogen atomic positions were calculated from geometrical criteria and refined with isotropic thermal parameters. Positional and equivalent isotropic thermal parameters for non-hydrogen atoms are listed in Table 3. ORTEP drawings of **2c** and **2d** are given in Figs. 1 and 2, respectively. Lists of structure factors, anisotropic thermal parameters, hydrogen parameters, and a complete list of bond lengths and angles may be obtained from C.R. upon request.

Acknowledgements. C.R. is grateful to the Norwegian Research Council for financial support.

References

1. Kolsaker, P., Karlsen, H., Songe, P. and Vik, I. B. Abstract, *Vth European Symposium on Organic Reactivity (ESOR V)*, Santiago de Compostela, Spain, July 16–21, 1995.
2. Campaigne, E., Mais, D. and Yokley, E. M. *Synth. Commun. 4* (1974) 379.
3. Kolsaker, P. and Hellebostad, K. *Acta Chem. Scand., Ser. B 34* (1980) 721.
4. Zefirov, N. S.. Kozhushkov, S.I. and Kuznetsova, T. S. *Tetrahedron 38* (1982) 1693; cf. Danishefsky, S. *Acc. Chem. Res. 12* (1979) 66.
5. Zefirov, N. S.. Kozhushkov, S. I. and Kuznetsova, T. S. *Khim. Geterotsikl. Soedin. 6* (1983) 801; *Chem. Abstr. 99* (1983) 139839t.
6. Cannon, K. C. and Krow, G. R. In: Silverman, G. and Rakita, P. E., Eds., *Handbook of Grignard Reagents*, Marcel Dekker, New York 1996, Chap. 13.
7. Smith, M. B. and Becker, W. E. *Tetrahedron 22* (1966) 3027; *23* (1967) 4215.
8. Chevrot, C., Folest, J., Troupel, M and Perichon, J. *Electroanal. Chem. Interfac. Electrochem. 54* (1974) 135.
9. Biemann. K. *Mass Spectrometry: Organic Chemical Application.* McGraw-Hill, New York 1962, pp. 134–135.
10. Al-Khaffaf, S. I. and Shanshal, M. *J. Prakt. Chem. 325* (1983) 517.
11. Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd edn., VCH, Weinheim 1988, pp. 414–416 and Refs. therein.
12. Lin-Vien, D., Colthup, N. B., Fateley, W. G. and Grasseli, J. G. *Hand-book of Infrared and Raman Frequencies of Organic Molecules*, Academic Press, London 1991, pp. 296–297.
13. SMART and SAINT Area-detector Control and Integration Software. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
14. Sheldrick, G. M. *Personal communication* (1996).
15. Sheldrick, G. M. SHELXTL, Version 5. Siemens Analytical Instruments Inc., Madison, Wisconsin, USA.

Received January 7, 1997.