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Synthesis of 4,5-Dicyanoimidazoles

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The effective procedure of preparation of 2-trifluoromethyl-4,5-dicyanoimidazole (**3a**) from diaminomaleonitrile (**1**) and trifluoroacetic anhydride has been elaborated. The syntheses of five other 2-substituted imidazoles from appropriate acyl derivatives of **1** have been attempted. Out of them only 4,5-dicyanoimidazole (**3b**) could be obtained in good yield.

Key words: imidazoles, cyclization, diaminomaleonitrile

Recently, we were involved in syntheses of 2-substituted 4,5-dicyanoimidazoles **3**, of which trifluoromethyl derivative, **3a**, (as well as its lithium salt) was of our particular interest. For the syntheses of these compounds, several methods starting from diaminomaleonitrile (**1**) and aldehydes [1–3], ketoesters [4], orthoesters [5–8], imidates [9] or cyanogen chloride [10] have been reported. Compound **3a** was previously obtained by cyclization of appropriate Schiff base [1]. To avoid an inconvenience of using gaseous trifluoroacetic aldehyde or its acetal, we decided to check the possibility of synthesis of **3a** in reaction between diaminomaleonitril and trifluoroacetic acid or its anhydride. We were also interested, if this route could be applied to prepare other imidazole derivatives.

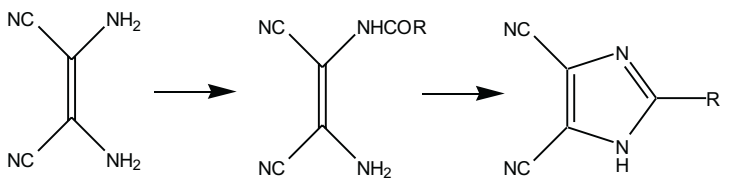
RESULTS AND DISCUSSION

The only information on synthesis of 4,5-dicyanoimidazole ring with the use of acid and **1** as starting reagents is, that concerning compound unsubstituted in position 2 (**3b**) [11]. It was obtained in two steps. In the first step, formyl derivative **2b** was obtained in the reaction between **1** and anhydrous formic acid in benzene and then was cyclized by refluxing in diglyme. Though possibility of analogous synthesis of 2-methyl derivative **3c** was also mentioned in [1], neither the procedure details nor compound data have been reported. Taking into account above information, we tried to obtain **3a** starting form **1** and trifluoroacetic acid. At first an attempt has been made to realize that in one-pot reaction. Following Ohtsuka's procedure [11] for preparation of **3b**, the mixture of **1** and TFA in ethanol, acetonitrile or diglyme was refluxed for 12–24 h. However, it resulted in formation of complex mixture of products, originating probably from the degradation of desired imidazole. Careful monitoring of this reaction by TLC has revealed, that the formation of **3a** as well as its decomposition proceeded repidly and a maximum yield of **3a** (*ca.* 30%; see Experimental) was

obtained after refluxing for 30 min. The experiments have revealed also, that ether solvents like diglyme or dioxane give better results than alcohols or acetonitrile, but still the reaction yield is far from satisfying and a large amount of by-products formed makes the purification procedure difficult. Alternative, known method of preparation of **3b** is based on the cyclization of obtained formyl derivative **2b** [11]. Analogous, trifluoroacetyl substituted compound **2a** was obtained in reaction between **1** and trifluoroacetic anhydride. On the basis of performed experiments, the optimal conditions of cyclization of **2a** have been found, which allow to obtain **3a** in *ca.* 70–80% yield. Also an alternative, effective procedure has been elaborated, in which trifluoroacetyl derivative **2a** is prepared from **1** and *in situ* generated trifluoroacetic anhydride and then cyclized without its prior separation (see Experimental). It was observed, that compound **3a** easily forms hydrate (*e.g.* when exposed to the moisture), incorporating two molecules of water. Lithium salt of **3a** was prepared in reaction with lithium carbonate. To check the generality of the above cyclization procedure, several other acyl derivatives **2** have been prepared. Compound **2b** was obtained from **1** and formic acid [9]. TLC indicated that the crude product was composed of two compounds, which were separated and proved to be *N*-(*Z*)- (main product, *ca*. 95%) and *N*-(*E*)-2-amino-1,2-dicyanoethenylformamide. Additionally, NMR spectra of both stereoisomers showed restricted rotation about amide bond. In both cases proton and carbon spectra contained two sets of signals, corresponding to the presence of two rotamers in the approximate ratio of 13:87. Observed values of NH-C(O)H coupling constants were *ca*. 11 and 1 Hz, respectively. Comparing these values with those found for formamide [12], the substituent configurations at C–N bond could be established. Isomer *Z* was found to be more abundant. High temperature proton spectra evidenced, that the amide rotation became fast in the NMR time scale at temperatures above 70°C. Other compounds **2** were prepared under mild conditions, using appropriate acid anhydrides (**c–e**) or acid chloride (**f**). The NMR spectra indicated, that in each of those cases products constituted of single *Z*-stereoisomers. Cyclization of **2** has been found to give the best result, when performed in dioxane and catalyzed by trifluoroacetic acid. However, besides mentioned above **3a**, only **3b** could be prepared in this way in good yield (73%). The highest yields reached for **3c** and **3d** were 29 and 27%, respectively. Cyclization of **2f** did not give product **3f** at all; starting amid has been recovered unchanged. In the case of **2e** the completion of reaction measured by starting amide disappearance has been reached after 2 h the only product, which could be separated from tarry reaction mixture with *ca*. 35% yield, was surprisingly **3b**. Its identity was unequivocally proved by melting point, spectra (^{1}H, ^{13}C NMR and IR) and elemental analysis. The explanation of this fact is unknown to the authors at present stage of investigation. An attempt has been undertaken to obtain compounds **3c** and **3d** by heating appropriate amides in diglyme, following the method described for preparation of **3b**. In both cases only unchanged, partially isomerized starting reagent was overed.

EXPERIMENTAL

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded using a Varian Gemini 2000 spectrometer operating at 4.7 T. Residue solvent signals were used as chemical shift references for proton (δ_{DMSO} = 2.50 ppm, δ_{CD_3CN} = 1.96 ppm, $\delta_{CD_3COCD_3}$ = 2.05 ppm) and carbon spectra (δ_{DMSO} = 39.52 ppm, δ_{CD_3CN} = 1.79 ppm, $\delta_{CD_3COCD_3}$ = 29.84 ppm). Trichlorofluoromethane was used for fluorine spectra calibration (δ_{CCl_3F} = 0 ppm). IR spectra (in KBr) were recorded using Specord M-80 spectrophotometer. Compound **1** (from Aldrich) was purified by dissolving in ethyl acetate, separating of insoluble material and evaporating of solvent to dryness. High resolution mass spectra (ESI or LSIMS) were recorded using AMD 604 instrument.



	R
a	CF_3
b	H
c	CH_3
d	n-C_3H_7
e	CCl_3
f	p-C_6H_4F

N-((Z)-2-Amino-1,2-dicyanoethenyl)trifluoroacetamide **(2a)**. A mixture of **1** (1.24 g, 11.5 mmol), trifluoroacetic anhydride (2.65 g, 12.6 mmol) and dioxane (10 mL) was stirred under argon atmosphere for 2 h at room temperature. After removal of the solvent in vacuum a crude product was dissolved in benzene and some insoluble dark solid was filtered off. The product (2.06 g, m.p. 193–195°C, yield 88%) obtained after removing the benzene in vacuum was used in cyclization reaction without further purification. Sublimation of this product in vacuum gave an analytical sample of the amide; m.p. 196–197°C ; HMRS: *m/z* calcd. for $C_6H_3F_3N_4O_3$ $[M\text{-}H]^-$ 203.0186, found 203.0187, IR (KBr, cm^{-1}): 3440, 3328, 3236, 2220, 1714, 1632, 1534, 1388, 1276, 1196, 1164, and 1152; ^{1}H NMR (acetone-d_6) 9.8 (bs,1H, NHCO), 7.19 (bs, 2H, NH_2); ^{19}F NMR (acetone-d_6) –74.6 (CF_3); ^{13}C NMR (acetone-d_6) 156.5 (q, **C**OCF_3, J = 38.3 Hz), 116.4 (q, CF_3, J = 287.5 Hz), 130.3 and 87.8 (C=C), 115.8 and 113.4 (CN).

N-((Z)-2-Amino-1,2-dicyanoethenyl)formamide (**2b**). The amide was obtained following the literature method [9]. TLC showed that a crude product (1.18 g) prepared from **1** (1.63 g, 15 mmol) and formic acid consisted of a main product (R_f = 0.6, Kieselgel 60, benzene-acetonitrile-methanol 10:5:2) and a minor one (R_f = 0.69). Crystallization of this product from methanol or acetonitrile gave a crystalline substance of m.p. 186°C (lit. [9] 182°C, 0.93 g, yield 46%) which was proved to consist exclusively of *N*-((*Z*)-2-amino-1,2-dicyanoethenyl)formamide, **2b**. IR (KBr, cm^{-1}): 3408, 3316, 3212 (NH, NH_2), 2252 w, 2212s (CN), 1664, 1636,1612, 1516, 1400, 1380, 1288, 496. The NMR spectra are composed of two sets of signals according to the presence of two stereoisomers resulting from the hindered rotation about the OC–N bond.

(Z)-N-((Z)-2-Amino-1,2-dicyanoethenyl)formamide (***Z,Z*-2b**). ^{1}H NMR (DMSO-d_6) 9.40 (bs, 1H, NHCO), 8.07 (d, 1H, CHO, J = 1.2 Hz), 7.26 (bs, 2H, NH_2); ^{13}C NMR (DMSO-d_6) 160.1 (CO), 126.8 and 87.7 (C=C), 116.7 and 113.8 (CN).

(E)-N-((Z)-2-Amino-1,2-dicyanoethenyl)formamide (***E,Z*-2b**). ^{1}H NMR (DMSO-d_6) 9.22 (bd, 1H, NHCO, J = 10.7 Hz), 8.15 (d, 1H, CHO), 7.41 (bs, 2H, NH_2); ^{13}C NMR (DMSO-d_6), 163.8 (CO), 125.8 and 89.0 (C=C), 116.7 and 113.8 (CN).

The filtrate from crystallization of crude product was evaporated to dryness and the solid residue (0.19 g) was chromatographed on silica gel with acetonitrile-benzene (2:1) as eluent to give, in addition to the *Z*-isomer (86 mg), *N*-((*E*)-2-amino-1,2-dicyanoethenyl)formamide (48 mg). M.p. 163°C (from benzene-acetonitrile 1:2); IR (KBr, cm^{-1}): 3392, 3300, 3188, 2212, 1660, 1608, 1516, 1376, 1284.

(Z)-N-((E)-2-Amino-1,2-dicyanoethenyl)formamide (***Z,E*-2b**). ^{1}H NMR (DMSO-d_6) 9.57 (bs, 1H, NHCO), 8.16 (d, 1H, CHO, J = 1.0 Hz), 7.51 (bs, 2H, NH_2); ^{13}C NMR (DMSO-d_6) 161.8 (CO), 131.6 and 84.7 (C=C), 115.3 and 112.7 (CN).

(E)-N-((E)-2-Amino-1,2-dicyanoethenyl)formamide (***E,E*-2b**). ^{1}H NMR (DMSO-d_6) 9.26 (bd, 1H, NHCO, J = 10.8 Hz), 8.09 (d, 1H, CHO), 7.72 (bs, 2H, NH_2); ^{13}C NMR (DMSO-d_6) 165.8 (CO), 132.9 and 85.3 (C=C), 116.2 and 112.7 (CN).

N-((Z)-2-Amino-1,2-dicyanoethenyl)acetamide **(2c)**. The amide was obtained following the literature procedure [9]. TLC showed that a crude product (1.0 g) prepared from **1** (1.0 g, 9.8 mmol) and acetic anhydride (4 mL) consisted exclusively of the title product (m.p. 161°C, lit. [9] 161°C, yield 68%). IR (KBr): cm^{-1}, 3432, 3336, 3236, 2244, 2208s, 1676, 1628, 1508, 1372, 1300, 456. ^{1}H NMR (CD_3CN) 7.63 (bs, 1H, NHCO), 5.65 (bs, 2H, NH_2), 2.03 (s, 3H, CH_3); ^{13}C NMR (CD_3CN) 170.7 (CO), 127.9 and 93.1 (C=C), 117.3 and 114.6 (CN), 23.5 (CH_3).

N-((Z)-2-Amino-1,2-dicyanoethenyl)butyramide **(2d)**. A mixture of **1** (0.89 g, 7.8 mmol) and butyric anhydride (3.87 g, 24.4 mmol) was heated at 65°C for 35 min. After removal of an excess of anhydride and the acid formed in vacuum a solid product was crystallized from the mixture: benzene-ethyl acetate (1:2) to yield colourless crystals (0.91 g, yield 69%); m.p. 177–178°C; HRMS ESI: calcd. for $C_8H_{10}N_4O$ $[M+Na]^+$ 201.0747, found 201.0748; IR (KBr, cm^{-1}): 3412, 3328, 3220, 2252, 2212, 1668, 1640, 1612, 1524, 1384; ^{1}H NMR (DMSO-d_6) 9.06 (s, 1H, NHCO), 7.10 (s, 2H, NH_2), 2.19 (t, 2H, CH_2CO, J = 7.4 Hz), 1.54 (tq, 2H, C**H**$_2$CH$_3$), 0.87 (t, 3H, CH_3, J = 7.4 Hz); ^{13}C NMR (DMSO-d_6) 171.3 (CO), 126.0 and 89.8(C=C), 116.8 and 113.9 (CN), 36.9 (**C**H_2CO), 18.1 (**C**H_2CH_3), 13.6 (CH_3).

N-((Z)-2-Amino-1,2-dicyanoethenyl)trichloroacetamide **(2e)**. A solution of trichloroacetic anhydride (3.58 g, 11.0 mmol) in acetonitrile (10 mL) was added dropwise with stirring and cooling (ice and water) to a solution of **1** (1.25 g, 11.5 mmol) in acetonitrile (20 mL). A mixture was stirred for 15 min at room temperature. After removal of the solvent in vacuum, the solid residue was triturated with ether to remove trichloroacetic acid. The residual solid was crystallized from acetonitrile-benzene 1:3 to give the amide (2.42 g, yield 83%). M.p. 184°C (dec), HRMS ESI: calcd. for $C_6H_3Cl_3N_4O$ $[M+Na]^+$ 274.9265, found 274.9281; IR (KBr, cm^{-1}): 3440, 3328, 3252 (NH, NH_2), 2260w, 2212s (CN), 1700, 1628, 1508, 1384, 844, 816; ^{1}H NMR (acetone-d_6) 9.76 (bs, 1H, NHCO), 7.16 (bs, 2H, NH_2); ^{13}C NMR (acetone-d_6) 161.4 (CO), 130.1 and 92.3 (C=C), 116.0 and 113.6 (CN).

N-((Z)-2-Amino-1,2-dicyanoethenyl)-p-fluorobenzamide **(2f)**. A solution of *p*-fluorobenzoyl chloride (2.3 g, 14.5 mmol) in dioxane (7 mL) was added dropwise to a stirring solution of **1** (1.56 g, 14.5 mmol) and pyridine (1.14 g) in dioxane (22 mL). The reaction mixture was stirred overnight. The solid was filtered off, washed with dioxane and water and dried in vacuum. A crude product was crystallized from methanol to give yellowish crystals (0.73 g, yield 22%); m.p. 273°C (dec); HRMS: calcd. for $C_{11}H_4FN_4O$ $[M+Na]^+$ 253.0496, found 253.0488; IR (KBr, cm^{-1}): 3412, 3328, 3220 (NH, NH_2), 2252, 2212s (CN), 1648, 1608, 1524, 1496, 1384, 1316, 1236, 852, 760; ^{1}H NMR (DMSO-d_6) 9.55 (s, 1H, NHCO), 8.08 (m, 2H, H3, H5), 7.25 (m, 2H, H2, H6), 7.25 (s, 2H, NH_2); ^{13}C NMR (DMSO-d_6) 164.4 (d, C4, ^{1}J(C,F)= 250.2 Hz), 164.2 (CO), 130.8 (d, C2, C6, ^{3}J(C,F) = 9.2 Hz), 129.4 (d, C-1, ^{4}(C,F) = 2.7 Hz), 127.5 and 89.2 (C=C), 117.0 and 113.9 (CN), 115.4 (d, C3, C5, ^{2}J(C,F) = 21.7 Hz).

2-Trifluoromethyl-4,5-dicyanoimidazole **(3a)**. Method 1. A solution of **1** (3.0 g, 0.027 mol) and trifluoroacetic acid (3.4 mL, 0.055 mol) in diglyme (32 mL) was stirred and refluxed under argon until complete disappearance of the starting material (TLC, 35 min). After removal of the solvent in vacuum, the resulting dark residue was subjected to silica gel column chromatography (eluent – benzene:ethyl acetate – 5:1) to give semisolid substance (1.5 g, 30% yield) consisted exclusively of **3a** as evidenced by TLC (R_f = 0.6, acetonitrile:benzene = 1:1) and NMR spectra. Crystallization of crude product from benzene-pentane (2:3) gave colourless crystals. M.p. 101–102°C. IR (nujol, cm^{-1}): 3564, 3532, 2252, 1524, 1462, 1318, 1176, 1002; ^{1}H NMR (acetone-d_6): 13.6 (bs, 1H, NH); ^{19}F NMR (acetone-d_6): –64.1; ^{13}C NMR (acetone-d_6): 140.7 (q, **C-**CF_3, ^{2}J(C,F) = 44.6 Hz), 118.2 (q, CF_3, ^{1}J(C,F) = 270.4 Hz), 118.2 (C=C), 110.3 (CN).

On exposure of an anhydrous sample of **3a** to moisture, successive increase in weight was observed, until two moles of water per one mole of **3a** were absorbed to yield the dihydrate of **3a**. M.p. 70–71°C (lit. [1] 86–88°C); IR (nujol, cm^{-1}): 3564, 3476, 2268, 1524, 1456, 1184, 1156, 964; ^{1}H NMR (acetone-d_6) 6.6 (s, NH+H_2O); ^{19}F and ^{13}C NMR spectra were identical as for anhydrous compound.

Method 2. A solution of **2a** (0.520 g, 2.55 mmol) in diglyme (7.3 mL) was refluxed under argon atmosphere until the substrate disappeared (TLC, 3 h). After removal of the solvent in vacuum, the dark solid residue was subjected to a silica-gel chromatography with benzene-ethyl acetate (5:1) to give the product **3a** (0.385 g, yield 69%). Crystallization from benzene-pentane (2:3) yielded an analytical sample of **3a** as colourless crystals. M.p. 101–102°C.

2-Trifluoromethyl-4,5-dicyanoimidazole lithium salt. Trifluoroacetic anhydride (2.42 g, 11.5 mmol), generated form trifluoroacetic acid and phosphorus pentoxide, was distilled directly into reactor containing a solution of **1** (1.14 g, 10.5 mmol) in dioxane (11 mL). The mixture was refluxed under argon atmosphere until the substrate disappeared (TLC, *ca*. 1 h). After removal of the solvent and trifluoroacetic acid in vacuum the solid residue was dissolved in ether (50 mL). The ether solution was extracted four times with the slurry of lithium carbonate (1 g) in water (90 mL). The aqueous solution of the lithium salt of **3a** was washed with ether. After removal of the water on a rotary evaporator, the dark residue was dried at 100°C in vacuum. The dark solid was extracted with acetonitrile (4×10 mL) and the resulting solution was filtered. The solvent was then removed and the crude salt was purified by basic alumina column chromatography using acetonitrile-benzene (2:1) as eluent. The colourless crystalline product was dried in vacuum at 120°C for two hours to give lithium salt of **3a** (1.45 g, 71% yield). An analytical sample was obtained by crystallization from acetonitrile-benzene (1:1). IR (KBr, cm^{-1}): 2248, 1650, 1500, 1464, 1428, 1182, 1136, 1000; ^{13}C NMR (CD_3CN) 148.7 (q, **C**-CF_3, $^2J(C,F) = 36.6$ Hz), 121.2 (q, CF_3, $^1J(C,F) = 268.5$ Hz), 120.4 (C=C), 115.7 (CN). ^{19}F NMR (CD_3CN) –63.0; HRMS LSIMS: m/z 291 for [M + glycerol + Li]$^+$; Calcd. for $C_6F_3LiN_4$; M = 192.

4,5-Dicyanoimidazole (**3b**). A slurry of **2b** (2.04 g, 15 mmol), trifluoacetic acid (15 mmol) and dioxane (15 mL) was stirred and refluxed in argon atmosphere. After 20 min it turned into a homogeneous dark solution. The reflux was continued, until the amide disappeared (TLC, 1.5–2 h). After removal of the solvent and acid, the dark solid residue was extracted with ether and the brownish ethereal solution was filtered through a short silica gel layer. The yellow solid (1.3 g, 73%; m.p. 168–170°C) was obtained after evaporation of ether. Further purification of this product either by silica gel chromatography with acetonitrile-benzene (2:1) or by crystallization from methanol yielded an analytical sample of **3b** as colourless needles. M.p. 178°C (lit. [11] 176°C); IR (KBr, cm^{-1}): 3264, 2248, 1400, 1340, 1120, 800; ^1H NMR (acetone-d_6) 11.6 (bs,1H, NH), 8.20 (s, H, CH); ^{13}C NMR (acetone-d_6) 141.8 (C2), 116.7 (CN), 111.3 (C=C).

2-Methyl-4,5-dicyanoimidazole **(3c)**. Method 1. A solution of the amide **2c** (0.345 g, 2.3 mmol) in diglyme (16 mL) was refluxed under argon atmosphere for 8 h. After removal of the solvent, the residue (0.300 g) was subjected to TLC, ^1H- and ^{13}C-NMR analyses which revealed that the product consisted mainly of the unchanged substrate accompanied by *ca*. 21% of its *E*-stereoisomer. The latter was isolated by silica-gel chromatography with acetonitrile-benzene (2:1) as eluent to give an analytical sample of **2c** *E*-isomer (43 mg, yield 17%); m.p. 162°C; IR (KBr, cm^{-1}): 3416, 3332, 3236, 2248, 2216, 1672, 1644, 1512, 1372, 1280; ^1H NMR (CD_3CN) 7.65 (s, 1H, NHCO), 5.61 (s, 2H, NH_2), 1.98 (s, 3H, CH_3); ^{13}C NMR (CD_3CN) 171.3 (CO), 131.8 and 90.8 (C=C), 115.3 and 112.9 (CN), 23.1 (CH_3).

Method 2. A solution of **2c** (0.400 g, 2.7 mmol) was stirred and refluxed with trifluoacetic acid (2.7 mmol) and dioxane (10 mL) under argon atmosphere for 8 h. After removal of the solvent and acid in vacuum, the dark solid residue was extracted with ether. After removal of the ether the orange solid residue (0.243 g) was found to consist mainly of **2c** and **3c** in an approximate molar ratio 1:1 (^1H NMR). The crude product was chromatographed on a silica gel with benzene-ethyl acetate (1:1) to yield **3c** (0.117 g) as yellow solid which after being treated with two small portions of ether gave colourless crystals (0.103 g, 29% yield). M.p. 230–231°C (lit. [9] 230–231°C); IR (KBr, cm^{-1}): 3432, 3160–2544, 2240, 1580, 1520, 1396, 1304, 1044, 924; ^1H NMR (CD_3CN) 11.2 (vbs,1H, NH), 2.40 (s, H, CH_3); ^{13}C NMR (CD_3CN) 151.9 (C2), 116.2 (CN), 111.6 (C=C), 14.3 (CH_3).

2-Propyl-4,5-dicyanoimidazole **(3d)**. Method 1. A solution of the amide **2d** (0.125 g, 0.7 mmol) in diglyme (5 mL) was refluxed under argon atmosphere for 8 h. After removal of the solvent, the residue (0.121 g) was subjected to TLC, ^1H and ^{13}C NMR analyses which revealed the product consisted mainly of the unchanged substrate accompanied by *ca*. 15% of the *E*-stereoisomer. The latter was isolated by silica gel chromatography with ethyl acetate-benzene (1:1) as eluent to give the *E*-isomer of **2d** (17 mg). M.p. 139°C; IR (KBr, cm^{-1}): 3412, 3332, 3256, 2248, 2216, 1664, 1644, 1616, 1516, 1272; ^1H NMR (DMSO-d_6) 9.32 (s, 1H, NHCO), 7.39 (s, 2H, NH_2), 2.16 (t, 2H, CH_2CO, J = 7.2 Hz), 1.54 (tq, 2H, C**H**$_2$CH$_3$), 0.87 (t, 3H, CH_3, J = 7.3 Hz); ^{13}C NMR (DMSO-d_6) 173.1 (CO), 131.7 and 86.5 (C=C), 115.7 and 112.8 (CN), 36.8 (**C**H$_2$CO), 18.5 (C**C**H$_2$C), 13.4 (CH_3).

Method 2. A solution of **2d** (0.528 g. 3 mmol) was stirred and refluxed with trifluoroacetic acid (1.5 mmol) and dioxane (12 mL) under argon atmosphere for 8 h. After removal of the solvent and acid in vacuum, the dark solid residue was extracted with ether. After removal of the ether the dark solid residue (0.451 g) was found to consist mainly of **2d** and **3d** in an approximate molar ratio 1.1:1 (^1H NMR). The

product was chromatographed on a silica gel with benzene-ethyl acetate (1:1) to yield **2d** (0.207 g) and **3d** (0.130 g, yield 27%). M.p. 148°C (lit. [1] 142–3°C); IR (KBr, cm^{-1}): 3428, 3148–2652, 1572, 1520, 1416, 1388, 1300, 1024, 892; ^{1}H NMR (CD_3Cl_3) 11.6 (vbs, 1H, NH) 2.81 (t, 2H, CH_2, J = 7.6 Hz), 1.79 (tq, 2H, CH_2), 0.98 (t, 3H, CH_3, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) 155.1 (C2), 116.0 (CN), 110.4 (C=C), 30.4, 21.2, 13.6 ($CH_2CH_2CH_3$).

REFERENCES

1. Begland R.W., Hartter D.R., Jones F.N., Sam D.J., Sheppard W.A., Webster O.W. and Weigert W.A., *J. Org. Chem*., **39**, 2341 (1974).
2. Booth B.L., Pritchard R. and Proenca M.F., *Synthesis-Stuttgart*, (9) 1269 (2000).
3. Johnson D.M. and Rasmussen P.G., *Macromolecules*, **33**(23), 8597 (2000).
4. Ohtsuka Y., *J. Org. Chem*., **41**, 629 (1976).
5. Woodward D.W., U.S. Patent 2534331 (1950); *C.A*. **45**, 5191 (1951).
6. O'Connell J.F., Parquette J., Yelle W.E., Wang W. and Rapoport H., *Synthesis*, 767 (1988).
7. Johnson S.J., *Synthesis*, 75 (1991).
8. Al-Azmi A., Elassar A.Z.A. and Booth B.L., *Tetrahedron*, **59**(16), 2749 (2003).
9. Bredereck H. and Schmötzer G., *Liebigs Ann. Chem.*, **600**, 95 (1956).
10. Sheppard W.A. and Webster O.W., *J. Am. Chem. Soc*., **95**, 2695 (1973).
11. Ohtsuka Y., *J. Org. Chem*., **41**, 713 (1976).
12. Drakenberg T. and Forsen S., *J. Phys. Chem*., **74**, 1 (1970).