

Studies with 3-oxoalkanenitriles: novel rearrangements observed while exploring the utility of 2-cyanoacetyl-1-methylpyrrole as a precursor to pyrrole substituted heterocyclic compounds

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Abstract

2-Cyanoacetyl-1-methylpyrrole **1** reacts with acetylacetone in glacial acetic acid in presence of ammonium acetate to yield a polysubstituted pyridine derivative **5**. In contrast, ethyl acetoacetate reacts with **1** to yield a pyranone derivative **8**, formed via a rearrangement process. Enaminonitrile **3**, generated by reaction of 2-cyanoacetyl-1-methylpyrrole **1** with the dimethylformamide dimethylacetal (DMFDMA), undergoes condensation with malononitrile to yield a 2-dialkyl-aminopyridine again via a rearrangement pathway. Structural assignments to 2-cyanoacetyl-1-methylpyrrole **1**, enaminonitrile **3**, pyrrole-substituted pyran **8**, and pyridine **14** were made using X-ray crystallographic analysis. Finally, 2-cyanoacetyl-1-methylpyrrole **1** undergoes coupling with benzenediazonium chloride to yield the arylhydrazone **2** that reacts with hydroxylamine hydrochloride to yield an amidoxime **19** that participates in ready cyclization to form the pyrrole-substituted 1,2,3-triazole **20** whose structure could be also established by X-ray crystallography.

Keywords: 3-Oxoalkanenitrile, cyanoacetylation, cyanoacetic acetic anhydride, *NOE* difference experiments, X-ray

Introduction

Over more than a thirty year period, our studies have focused on the utility of 3-oxoalkanenitriles as starting materials for the synthesis of functionally substituted heterocyclic and aromatic compounds.¹⁻³ These efforts have led to the development of methods based on 3-oxoalkanenitrile precursors to prepare pyrazoles,⁴ isoxazoles,⁵ pyridazines,⁶ pyrans,¹ thiazoles,^{7,8} as well as poly functional aromatic compounds.⁹ One limitation encountered in these investigations concerned difficulties associated with the preparation of substituted 3-oxoalkanenitriles by using simple eco-friendly procedures. For example, 3-oxoalkanenitriles were synthesized either by reactions

of haloketones with cyanide ion,¹⁰ a completely eco-unfriendly approach, or by dehydration of non-readily available aldehyde oximes.^{9,11} In 2004, a new route for the synthesis of 3-oxoalkanenitriles was reported by Slätt *et al.*¹² that involves reactions of electron rich aromatic compounds with cyanoacetic acid anhydride. Since that time, several publications have appeared describing explorations of the potential of this methodology along with the chemistry of the resulting 3-oxoalkanenitriles.¹¹⁻¹⁴ In continuing studies in this area described below, we have devised a high yielding synthesis of 3-oxoalkanenitriles and have probed the potential utility of these substances as precursors in routes for the preparation of pyrrole-substituted heterocyclic compounds. In this effort, we have also observed the operation of several unprecedented rearrangement reactions.

Results and Discussion

2-Cyanoacetyl-1-methylpyrrole **1** was prepared using a modification of a published procedure¹⁵ where only 1-methylpyrrole, cyanoacetic acid, and acetic anhydride were heated together. We could obtain X-ray crystal structure for this product (Figure 1).

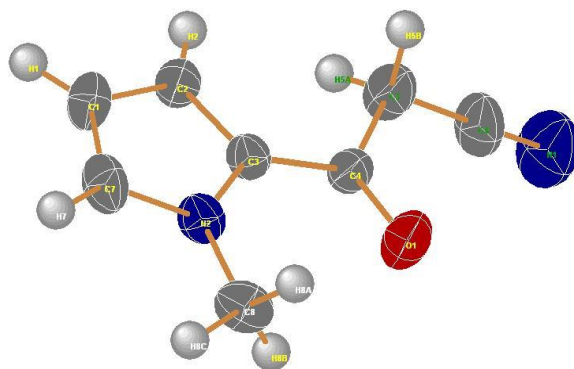
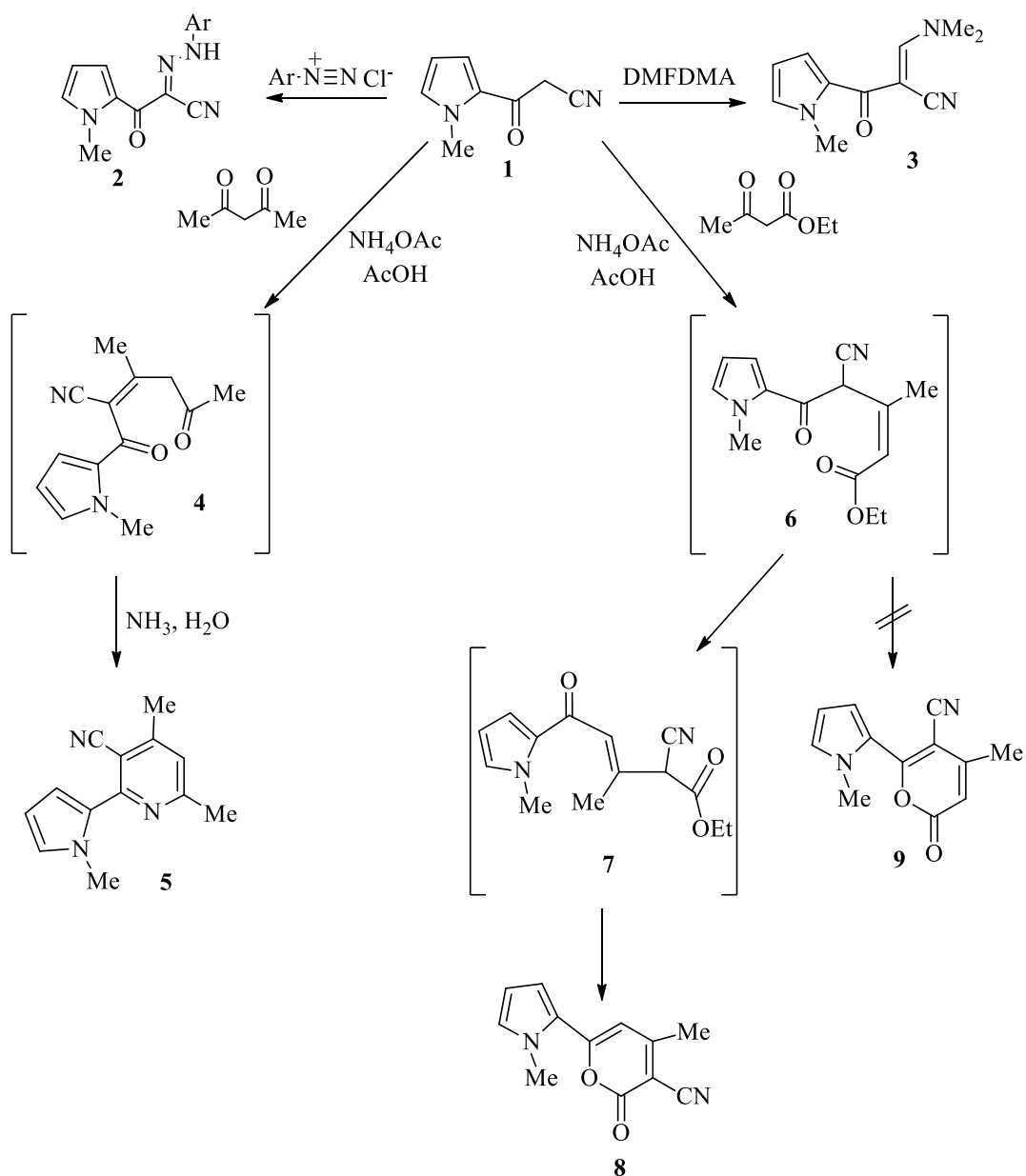


Figure 1. X-ray crystal structure of 2-cyanoacetyl-1-methylpyrrole **1**.

In the expected manner, 2-cyanoacetyl-1-methylpyrrole **1** participates in a coupling reaction with benzenediazonium chloride to yield the *p*-chlorophenylhydrazine **2** (Scheme 1), which was assigned to be the anti-isomer based on analogy to established structures of 2-arylhydrazono-3-oxoalkanenitriles.¹⁶ 2-Cyanoacetyl-1-methylpyrrole **1**, as anticipated, also condenses with the dimethylformamide dimethylacetal (DMFDMA) to yield enaminonitrile **3**, reported earlier in the patent literature.¹⁷ The structure of assignment of **3** was confirmed by using X-ray crystallographic analysis (Figure 2). In addition, reaction of **1** with acetylacetone in refluxing acetic acid containing ammonium acetate affords the pyrrole-substituted pyridine **5**. It is believed

that in this process, diketone **4** is produced initially and it then condenses with ammonia to generate **5**.



Scheme 1

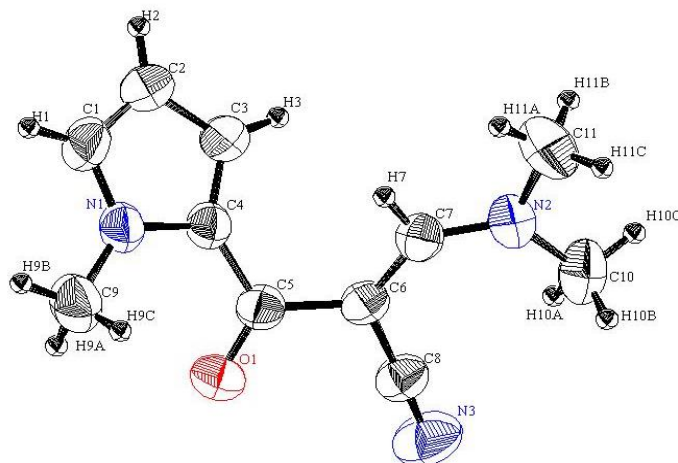


Figure 2. X-ray crystal structure of enaminonitrile **3**.

A study of the reaction of **1** with ethyl acetoacetate led to an interesting observation. This condensation process, which takes place in the presence of ammonium acetate, occurs via ethanol and water elimination to afford a pyranone. Based on analogy to the reaction of **1** with acetylacetone, we assumed that the ketoester **6** was produced initially and that it then cyclized to form **9** rather than condensing with ammonia, however, surprisingly X-ray crystallographic analysis of the product revealed that it was pyranone **8** rather than **9** (Figures 3 and Table 1). It is believed that the reaction initially afforded intermediate **6** that underwent a formal 1,3-cyano group shift to give **7** that then cyclized into **8**. Similar 1,3-cyano group migrations have been previously noted.¹⁸⁻²⁰ At the moment we are exploring the potential of this migration.²¹

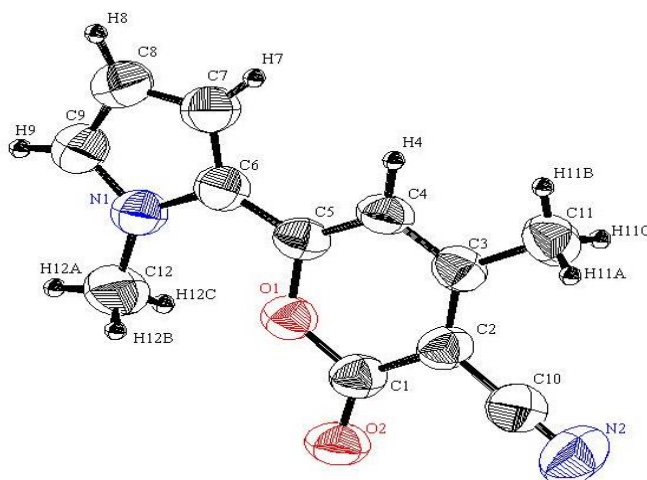


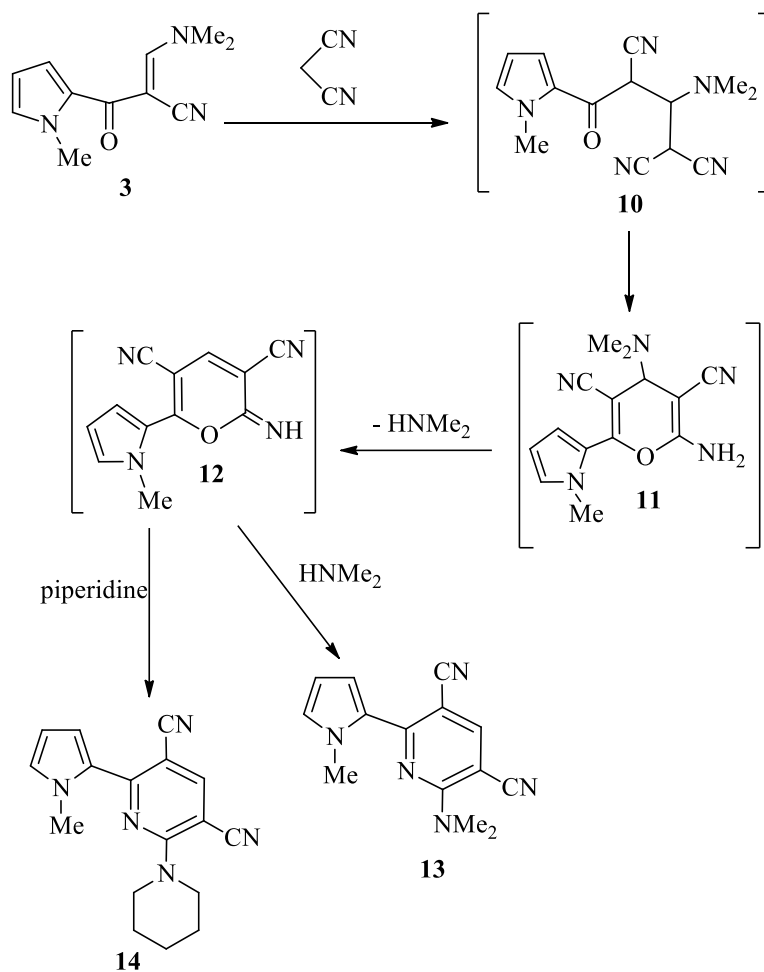
Figure 3. X-ray crystal structure of pyranilpyrrole **8**.

Table 1. Selected bond lengths and bonds angles of the pyranylpyrrole **8**

| (a) Bond lengths (Å) | | | |
|----------------------|----|--|----------|
| C1 | C2 | | 1.438(5) |
| C2 | C3 | | 1.374(6) |
| C3 | C4 | | 1.404(5) |
| C4 | C5 | | 1.358(5) |
| O1 | C5 | | 1.363(5) |
| O1 | C1 | | 1.389(4) |
| O2 | C1 | | 1.207(5) |

| (b) Bond angles (°) | | | |
|---------------------|----|----|----------|
| C1 | O1 | C5 | 123.8(3) |
| C1 | C2 | C3 | 122.5(3) |
| C2 | C3 | C4 | 118.2(4) |
| C3 | C4 | C5 | 120.9(4) |
| O1 | C5 | C4 | 119.8(3) |
| O1 | C1 | C2 | 114.7(3) |

Our attention then shifted to an exploration of the chemistry of enaminonitrile **3**. Reaction of **3** with malononitrile in the presence of piperidine was observed to afford a mixture of pyridines **13** and **14** (Scheme 2). The structure of **14** was established by employing X-ray crystallography (Figure 4 and Table 2). The products of this process are assumed to form via initial addition of malononitrile to **3** to afford trinitrile **10** that cyclizes to generate intermediate pyran **11** which gives **12** *via* dimethylamine elimination. Reactions of **12** with dimethylamine and piperidine would generate the respective pyridine derivatives **13** and **14** (Scheme 2). Although to the best of our knowledge the rearrangement involved in the conversion of enaminone **3** and malononitrile to the amino pyridines **13** and **14** has not been observed previously, a similar process was recently reported to participate in the formation of enedieneamides through reactions of enaminones with malononitrile.^{14,22,23}



Scheme 2

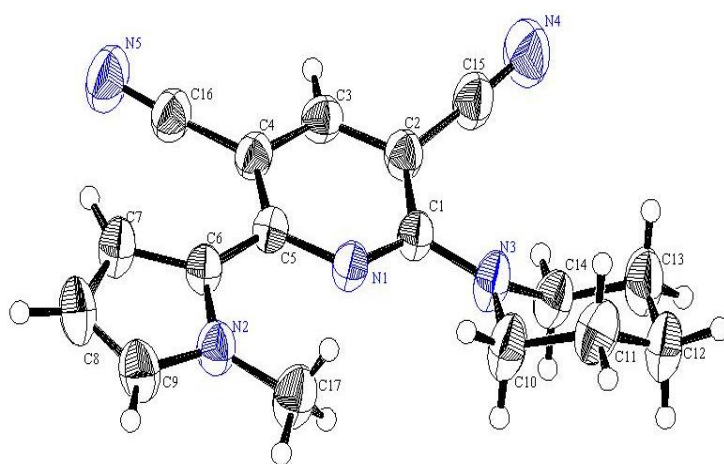
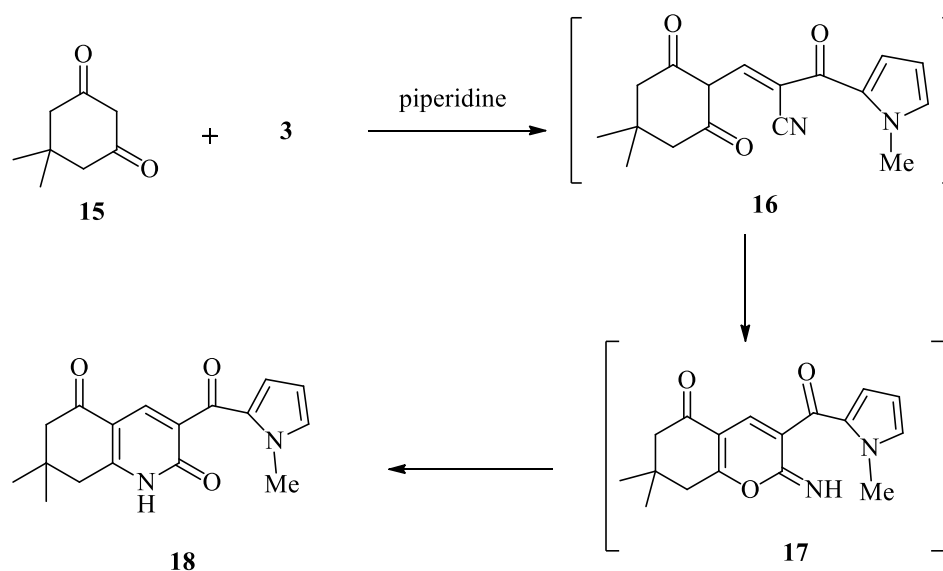
Figure 4. X-ray crystal structure of pyrrrole-substituted pyridine **14**.

Table 2. Selected bond lengths and bond angles of the pyrrole-substituted pyridine **14**

| (a) Bond lengths (Å) | | | |
|----------------------|----|----|------------|
| C1 | C2 | | 1.428(3) |
| C2 | C3 | | 1.373(3) |
| C3 | C4 | | 1.387(3) |
| C4 | C5 | | 1.428(3) |
| N1 | C5 | | 1.3423(18) |
| N1 | C1 | | 1.344(3) |
| (b) Bond angles (°) | | | |
| C1 | N1 | C5 | 122.02(17) |
| N1 | C1 | C2 | 119.97(13) |
| C1 | C2 | C3 | 118.23(16) |
| C2 | C3 | C4 | 121.11(19) |
| C3 | C4 | C5 | 118.29(14) |
| N1 | C5 | C4 | 119.84(15) |

The reaction of enaminonitrile **3** with dimedone **15** was also explored. This process carried out in the presence of piperidine produces the fused 2-pyridone **18**, *via* a pathway that likely involves addition of the enolate of dimedone to the activated double bond in **3** to yield an adduct (Scheme 3) that eliminates dimethylamine to form intermediate **16**. Cyclization of **16** then generates the iminopyran **17**. As we have noted earlier,¹³ heterocyclic imines like **17** are highly unstable substances that often undergo hydrolysis to form corresponding 2-pyranones. However, in the process described above it appears that **17** follows a Dimroth-type rearrangement route to form the 2-pyridone ring in the polyhydroquinoline product **18**.²² Support for the assignment of the structure of **18** comes from the results of a *NOE* difference experiment that shows enhancements of resonances for methylene protons at δ 2.38 and 2.76 upon irradiation of the NH resonance at δ 12.29 and vice versa.



Scheme 3

Finally, we have also observed that the *p*-chlorophenylhydrazone **2** reacts with hydroxylamine hydrochloride *via* the amidoxime intermediate **19** to form the 1,2,3-triazole **20** (Scheme 4) as established by single crystal X-ray crystallography (Figure 5 and Table 3). It worth mentioning that formation of 1,2,3-triazole in this reaction finds parallel to repeatedly reported cyclization of derivatives of **19** under similar conditions.^{16,24,25} Although cyclization into isoxazoles in acid medium has since long been reported²⁶ also cyclization into 1,2,4-triazole *via* a Tiemann like rearrangement has been noted by us in one case.²⁷

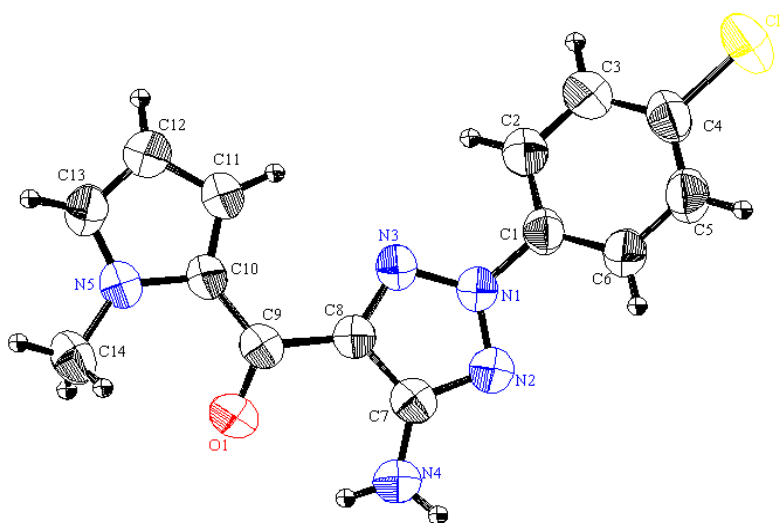
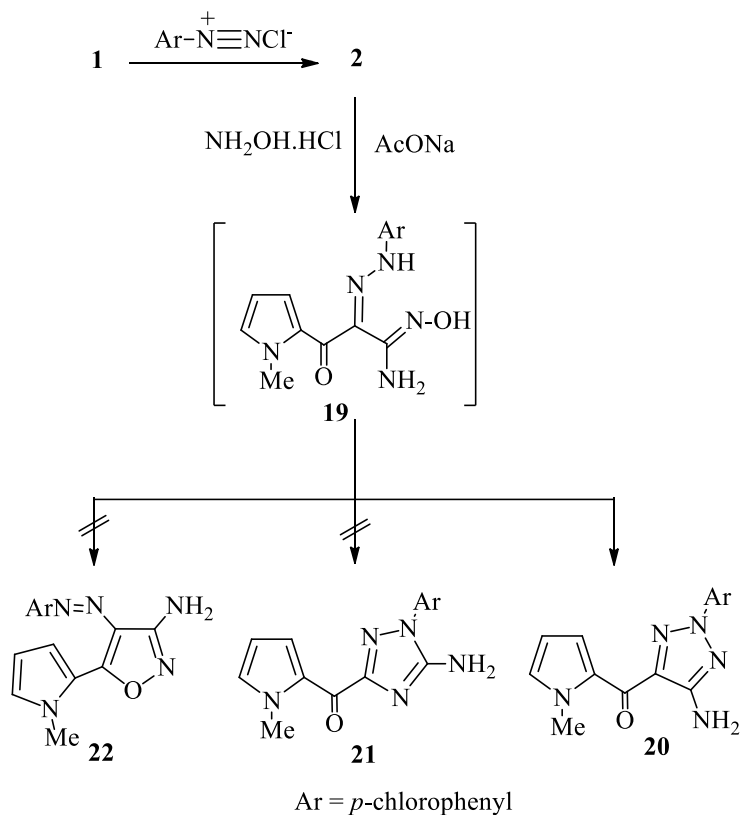


Figure 5. X-ray crystal structure of 1,2,3-triazole **20**.

Table 3. Selected bond lengths and bond angles of the 1,2,3-triazole **20**

| (a) Bond lengths (Å) | | | |
|----------------------|----|--|----------|
| N1 | N2 | | 1.358(3) |
| N1 | C1 | | 1.420(3) |
| N3 | C8 | | 1.331(3) |
| N1 | N3 | | 1.325(3) |
| N2 | C7 | | 1.331(3) |
| C1 | C2 | | 1.386(3) |
| C2 | C3 | | 1.371(4) |
| C4 | C5 | | 1.379(4) |
| C7 | C8 | | 1.414(3) |
| C3 | C4 | | 1.377(4) |
| C5 | C6 | | 1.374(4) |
| C1 | C6 | | 1.375(3) |

| (b) Bond angles (o) | | | |
|---------------------|----|----|------------|
| N2 | N1 | N3 | 115.49(17) |
| N1 | N3 | C8 | 104.24(17) |
| C2 | C1 | C6 | 120.1(2) |
| C2 | C3 | C4 | 119.7(3) |
| C4 | C5 | C6 | 120.2(3) |
| N1 | N2 | C7 | 102.78(17) |
| C1 | C2 | C3 | 120.1(3) |
| C3 | C4 | C5 | 120.3(3) |
| C1 | C6 | C5 | 119.7(3) |
| N2 | C7 | C8 | 109.16(19) |
| N3 | C8 | C7 | 108.33(19) |



Scheme 4

Conclusions

In the effort described above, several novel rearrangement reactions have been observed and plausible mechanisms for these processes have been presented. The work clearly indicates that cyano shift during condensing aroyl acetonitrile with β -ketoesters should be always considered as a possibility and the spectra of end product in such reaction should be carefully inspected, otherwise wrong conclusion might be drawn. This applies also to reactions of enaminonitrile moiety in aroyl diethylaminoacrylate and active methylene reagents. Investigations are currently underway exploring the scope and limitations of these rearrangement processes.

Experimental Section

General. Melting points were recorded on a Gallenkamp apparatus and are uncorrected. Infrared spectra (KBr) were determined on a Perkin-Elmer 2000 FT-IR system. NMR measurements were determined on a Bruker DPX spectrometer, at 600 MHz for ^1H -NMR and 100 MHz for ^{13}C -NMR, in DMSO-d_6 as solvent using TMS as internal standard. NMR coupling constants (J) are

given in Hz. Mass spectra were measured on MS 30 and MS 9 (AEI) spectrometers, with EI 70 eV. Elemental analyses were measured by means of LECO CHNS-932 Elemental Analyzer. Copies of original data can be provided upon request.

2-Cyanoacetyl-1-methylpyrrole (1). A mixture of cyanoacetic acid (0.85 g, 10 mmol) and acetic anhydride (1.02 g, 10 mmol) was refluxed for 20 min and then the resulting mixture was mixed with *N*-methylpyrrole (0.81 g, 10 mmol) and the reaction mixture was heated at reflux again for 1 h. On cooling to *ca.* 20 °C the reaction mixture was poured over water and crude solid product was collected by filtration and recrystallized (EtOH) to give the *title compound 1* as pale yellow crystals (mp 106 °C, lit.,¹⁵ 109-110 °C), (3.2 g, 90%). IR (KBr): $\nu = 2258$ (C≡N), 1640 (C=O) cm^{-1} . ¹H-NMR: $\delta = 3.86$ (s, 3H, CH₃), 4.44 (s, 2H, CH₂), 6.17-6.19 (m, 1H, C-4 pyrrole), 7.13 (d, 1H, *J* = 2.5 Hz, C-5 pyrrole), 7.26 (d, 1H, *J* = 2.5 Hz, C-3 pyrrole). ¹³C-NMR: $\delta = 29.7$ (q, CH₃), 37.4 (t, CH₂), 109.0 (d, CH, C-4 pyrrole), 116.6 (C≡N), 121.7 (d, CH, C-3 pyrrole), 128.4 (s, C, C-2 pyrrole), 133.7 (d, CH, C-5 pyrrole), 178.7 (C=O). MS, *m/z* (%), 148 (M⁺, 76), 108.0 (100). Calcd. Accurate mass for (C₈H₈N₂O): 148.0637. Found: 148.0637 (M⁺). CCDC 842880 contains the supplementary crystallographic data for compound **1**, which can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk

4,6-Dimethyl-2-(1-methyl-1*H*-pyrrol-2-yl)nicotinonitrile (5). A mixture of 2-cyanoacetyl-1-methylpyrrole (1.48 g, 10 mmol), ammonium acetate (1.54 g, 20 mmol) and acetylacetone (1.00 g, 10 mmol) was dissolved in glacial acetic acid (20 mL). The mixture was then heated at reflux for 24 h. On cooling to *ca.* 20 °C the reaction mixture was poured over cold water and the precipitate that formed was collected by filtration and recrystallized (EtOH) to give the title compound **5** as a bright orange powder (mp 98-100 °C), (1.22 g, 85%). IR (KBr): $\nu = 2217$ (C≡N) cm^{-1} . ¹H-NMR: $\delta = 2.48$ (s, 3H, CH₃), 2.52 (s, 3H, CH₃), 3.82 (s, 3H, CH₃), 6.14-6.16 (m, 1H, C-4 pyrrole), 6.78 (d, 1H, *J* = 2.5 Hz, C-5 pyrrole), 7.01 (d, 1H, *J* = 2.5 Hz, C-3 pyrrole), 7.23 (s, 1H, C-5 pyridine). ¹³C-NMR: $\delta = 20.3$ (q, CH₃), 24.5 (q, CH₃), 36.1 (q, CH₃), 103.8 (s, C, C-3 pyridine), 107.5 (d, CH, C-4 pyrrole), 113.8 (d, CH, C-3 pyrrole), 117.5 (C≡N), 121.4 (s, C, C-2 pyrrole), 127.7 (d, CH, C-5 pyridine), 128.5 (d, CH, C-5 pyrrole), 152.7 (s, C, C-4 pyridine), 153.0 (s, C, C-2 pyridine), 160.9 (s, C, C-6 pyridine). MS, *m/z* (%), 210.1 [(M⁺-1), 100]. Calcd. Accurate mass for (C₁₃H₁₃N₃): 211.1109. Found: 211.1101 (M⁺).

4-Methyl-6-(1-methyl-1*H*-pyrrol-2-yl)-2-oxo-2*H*-pyran-3-carbonitrile (8). A mixture of 2-cyanoacetyl-1-methylpyrrole (1.48 g, 10 mmol), ammonium acetate (1.54 g, 20 mmol) and ethyl acetoacetate (1.30 g, 10 mmol) was dissolved in glacial acetic acid (20 mL). The reaction mixture was then heated at reflux for 24 h. On cooling to *ca.* 20 °C the reaction mixture was poured over water and crude solid product was collected by filtration and recrystallized (EtOH) to give the *title compound 8* as green crystals (mp 199 °C), (1.3 g, 90%); IR (KBr): $\nu = 2215$ (C≡N), 1711 (C=O) cm^{-1} . ¹H-NMR: $\delta = 2.40$ (s, 3H, CH₃), 3.90 (s, 3H, CH₃), 6.25-6.27 (m, 1H, C-4 pyrrole), 7.07 (d, 1H, *J* = 2.5 Hz, C-5 pyrrole), 7.25 (d, 1H, *J* = 2.5 Hz, C-3 pyrrole), 6.94 (s, 1H, C-5 pyran). ¹³C-NMR: $\delta = 21.2$ (q, CH₃), 37.4 (q, CH₃), 91.4 (d, CH, C-5 pyran), 102.6 (d,

CH, C-4 pyrrole), 109.9 (d, CH, C-3 pyrrole), 115.1 (s, C, C-3 pyran), 117.6 (C≡N), 121.3 (d, CH, C-5 pyrrole), 132.8 (s, C, C-2 pyrrole), 157.8 (s, C, C-6 pyran), 158.4 (C-2, C=O pyran), 166.3 (s, C, C-4 pyran). MS, m/z (%), 214.1 (M^+ , 100); Calcd. Accurate mass for ($C_{12}H_{10}N_2O_2$): 214.0742. Found: 214.0736 (M^+). CCDC 845130 contains the supplementary crystallographic data for compound **8**, which can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk

3-(Dimethylamino)-2-(1-methyl-1H-pyrrole-5-carbonyl)acrylonitrile (3). A mixture of 2-cyanoacetyl-1-methylpyrrole (1.48 g, 10 mmol), with dimethylformamide dimethylacetal (2.38 g, 20 mmol) was dissolved in PhMe (20 mL). The mixture was then heated at reflux for 24 h. The reaction mixture was then cooled in fridge at 0 °C and the precipitate that formed was collected by filtration and recrystallized (EtOH) to give the *title compound 3* as pale yellow crystals (mp 101-102 °C), (2 g, 98.5%). IR (KBr): $\nu = 2198$ (C≡N), 1636 (C=O) cm^{-1} . 1H -NMR: $\delta = 3.25$ (s, 3H, CH₃), 3.34 (s, 3H, CH₃), 3.77 (s, 3H, CH₃), 6.07 (m, 1H, C-4 pyrrole), 6.95 (d, 1H, $J = 2.5$ Hz, C-5 pyrrole), 7.03 (d, 1H, $J = 2.5$ Hz, C-3 pyrrole), 7.90 (s, 1H, enamine H). ^{13}C -NMR: $\delta = 36.4$ (q, CH₃), 38.5 (q, CH₃), 47.5 (q, CH₃), 78.0 (s, C, C-CN), 107.0 (d, CH, C-4 pyrrole), 117.2 (C≡N), 120.7 (d, CH, C-3 pyrrole), 129.3 (d, CH, C-5 pyrrole), 129.7 (s, C, C-2 pyrrole), 158.9 (d, CH enamine), 178.7 (C=O). MS, m/z (%), 203.1 (M^+ , 70), 108.0 (100); Calcd. Accurate mass for ($C_{11}H_{13}N_3O$): 203.1059. Found: 202.0974 (M^+-1). CCDC 845129 contains the supplementary crystallographic data for compound **3**, which can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk

Synthesis of 2-(dimethylamino)-6-(1-methyl-1H-pyrrol-2-yl)pyridine-3,5-dicarbonitrile (13) and 2-(1-methyl-1H-pyrrol-2-yl)-6-(piperidin-1-yl)pyridine-3,5-dicarbonitrile (14)

To a stirred solution of enamionitrile **3** (2.03 g, 10 mmol) and malononitrile (0.66 g, 10 mmol) in EtOH (20 mL) was added piperidine (5 drops, 0.5 mL). The mixture was then heated at reflux for 24 h. On cooling to *ca.* 20 °C a precipitate was collected by filtration and the crude solid product, so formed, was separated by column chromatography (EtOAc/n-hexane, 1:3) to give the title products **13** and **14**

2-(Dimethylamino)-6-(1-methyl-1H-pyrrol-2-yl)pyridine-3,5-dicarbonitrile (13). Pale yellow powder (mp 109-110 °C) (EtOH), (1.2 g, 48%). IR (KBr): $\nu = 2209$ (2 x C≡N) cm^{-1} . 1H -NMR: $\delta = 3.34$ (s, 6H, two CH₃), 3.91 (s, 3H, CH₃), 6.19-6.21 (m, 1H, C-4 pyrrole), 7.04 (d, 1H, $J = 2.5$ Hz, C-3 pyrrole), 7.12 (d, 1H, $J = 2.5$ Hz, C-5 pyrrole), 8.50 (s, 1H, C-4 pyridine); ^{13}C -NMR: $\delta = 37.3$ (q, three CH₃), 86.0 (s, C, C-3 pyridine), 91.8 (s, C, C-5 pyridine), 108.1 (d, CH, C-4 pyrrole), 116.2 (d, CH, C-3 pyrrole), 117.9 (C≡N), 118.4 (C≡N), 127.5 (s, C, C-2 pyrrole), 130.0 (d, CH, C-5 pyrrole), 150.9 (d, CH, C-4 pyridine), 153.6 (s, C, C-2 pyridine), 157.1 (s, C, C-6 pyridine). MS, m/z (%), 251.1 (M^+ , 100); Calcd. Accurate mass for ($C_{14}H_{13}N_5$): 251.1171. Found: 251.1165 (M^+).

2-(1-Methyl-1H-pyrrol-2-yl)-6-(piperidin-1-yl)pyridine-3,5-dicarbonitrile (14). Pale yellow crystals (mp 102 °C) (EtOH), (0.8 g, 30%). IR (KBr): $\nu = 2210$ (2 x C≡N) cm^{-1} . 1H -NMR: $\delta = 1.66$ (s, 6H, piperidine), 3.83-3.85 (m, 4H, piperidine), 3.89 (s, 3H, CH₃), 6.20-6.21 (m, 1H, C-4

pyrrole), 7.03 (d, 1H, $J = 2.5$ Hz, C-3 pyrrole), 7.13 (d, 1H, $J = 2.5$ Hz, C-5 pyrrole), 8.53 (s, 1H, C-4 pyridine); $^{13}\text{C-NMR}$: $\delta = 23.8$ (t, 2CH_2 , C-3, C-5 piperidine), 25.6 (t, CH_2 , C-4 piperidine), 37.1 (q, CH_3), 48.3 (t, 2CH_2 , C-2, C-6 piperidine), 87.4 (s, C, C-3 pyridine), 92.5 (s, C, C-5 pyridine), 108.1 (d, CH, C-4 pyrrole), 116.2 (d, CH, C-3 pyrrole), 117.3 ($\text{C}\equiv\text{N}$), 118.2 ($\text{C}\equiv\text{N}$), 127.6 (s, C, C-2 pyrrole), 130.0 (d, CH, C-5 pyrrole), 150.8 (d, CH, C-4 pyridine), 153.8 (s, C, C-2 pyridine), 157.5 (s, C, C-6 pyridine). MS, m/z (%), 291.1 (M^+ , 100); Calcd. Accurate mass for ($\text{C}_{17}\text{H}_{17}\text{N}_5$): 291.1484. Found: 291.1478 (M^+). CCDC 845131 contains the supplementary crystallographic data for compound **14**, which can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk

7,7-Dimethyl-3-(1-methyl-1H-pyrrole-2-carbonyl)-7,8-dihydroquinoline-2,5(1H,6H)-dione (18). To a stirred mixture of enamionitrile **3** (2.03 g, 10 mmol) and dimedone (1.40 g, 10 mmol) in EtOH (20 mL) was added 5 drops of piperidine (0.5 mL). The mixture was then heated at reflux for 24 h. On cooling to *ca.* 20 °C a precipitate formed which was collected by filtration and then recrystallized (EtOH) to give the title compound **18** as pale yellow crystals (mp 272 °C), (1.2 g, 89%). IR (KBr): $\nu = 1674$ (C=O), 1644 (C=O), 1627 (C=O) cm^{-1} . $^1\text{H-NMR}$: $\delta = 1.05$ (s, 6H, two CH_3), 2.38 (s, 2H, C-8 quinoline), 2.76 (s, 2H, C-6 quinoline), 3.92 (s, 3H, CH_3), 6.11-6.12 (m, 1H, C-4 pyrrole), 6.64 (d, 1H, $J = 2.5$ Hz, C-5 pyrrole), 7.23 (d, 1H, $J = 2.5$ Hz, C-3 pyrrole), 7.81 (s, 1H, C-4 quinoline), 12.43 (s, 1H, NH). $^{13}\text{C-NMR}$: $\delta = 27.7$ (q, two CH_3), 32.7 (s, C, C-7 quinoline), 36.9 (q, CH_3), 50.1 (t, 2CH_2 , C-6, C-8 quinoline), 108.3 (d, CH, C-4 pyrrole), 110.8 (s, C, C-4a quinoline), 122.5 (d, CH, C-3 pyrrole), 128.9 (d, CH, C-5 pyrrole), 130.2 (s, C, C-3 quinoline), 132.8 (s, C, C-2 pyrrole), 135.5 (s, C, C-8a quinoline), 157.4 (d, CH, C-4 quinoline), 160.8 (C=O, C-2 quinoline), 181.8 (C=O), 193.2 (C=O, C-5 quinoline). MS, m/z (%), 298.2 (M^+ , 100); Calcd. Accurate mass for ($\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_3$): 298.1317. Found: 298.1311 (M^+).

2-[2-(4-Chlorophenyl)hydrazono]-3-(1-methyl-1H-pyrrol-2-yl)-3-oxopropanenitrile (2)

2-Cyanoacetyl-1-methylpyrrole (1.48 g, 10 mmol) was dissolved in 20 mL ethanol in presence of (1.36 g, 10 mmol) sodium acetate then cooled to *ca.* 0 °C using an ice-bath for 5 min. The above solution was added dropwisely into a solution of 4-chlorobenzenediazonium chloride (prepared from *p*-chloroaniline (1.27 g, 10 mmol) with the 6 mL concentrated hydrochloric acid and (2.1 g, 20 mmol) sodium nitrite). The resulting solution was left in a fridge at 0 °C for 24 h and the precipitate, so formed, was collected by filtration and was recrystallized from ethanol to give the title compound **2** as a yellow powder (mp 169 °C), (2.28 g, 80%). IR (KBr): $\nu = 3231$ (NH), 2213 ($\text{C}\equiv\text{N}$), 1613 (C=O) cm^{-1} . $^1\text{H-NMR}$: $\delta = 3.89$ (s, 3H, CH_3), 6.22-6.23 (m, 1H, C-4 pyrrole), 7.20 (d, 1H, $J = 2.5$ Hz, C-3 pyrrole), 7.27 (d, 1H, $J = 2.5$ Hz, C-5 pyrrole), 7.43-7.49 (m, 4H, *p*-chlorophenyl), 12.08 (s, 1H, NH). $^{13}\text{C-NMR}$: $\delta = 37.1$ (q, CH_3), 108.5 (d, CH, C-4 pyrrole), 111.5 (d, CH, C-3 pyrrole), 114.5 (d, 2CH, C-2, C-6 *p*-chlorophenyl), 117.6 ($\text{C}\equiv\text{N}$), 121.9 (s, C, C-4 *p*-chlorophenyl), 127.4 (d, CH, C-5 pyrrole), 128.2 (s, C, C-2 pyrrole), 129.4 (d, 2CH, C-3, C-5 *p*-chlorophenyl), 132.4 (s, C, C-1 *p*-chlorophenyl), 141.3 (s, C, C-CN), 175.2 (C=O); MS, m/z (%), 286.0 (M^+ , 100); Calcd. Accurate mass for ($\text{C}_{14}\text{H}_{11}^{35}\text{ClN}_4\text{O}$): 286.0621. Found: 286.0615 (M^+).

[5-Amino-2-(4-chlorophenyl)-2H-1,2,3-triazol-4-yl]-(1-methyl-1H-pyrrol-2-yl)methanone (20). A mixture of the *p*-chlorophenylhydrazone **2** (2.86 g, 10 mmol), hydroxylamine hydrochloride (1.38 g, 20 mmol) and sodium acetate (1.36 g, 10 mmol) was dissolved in EtOH (20 mL) and then heated at reflux for 24 h. On cooling to *ca.* 20 °C a precipitate formed that was collected by filtration and recrystallized (EtOH) to give the *title compound 20* as yellow crystals (mp 150 °C), (2.57 g, 85%). IR (KBr): $\nu = 3310$ (NH₂), 1614 (C=O) cm⁻¹. ¹H-NMR: $\delta = 3.97$ (s, 3H, CH₃), 6.23-6.25 (m, 1H, C-4 pyrrole), 7.28 (d, 1H, *J* = 2.5 Hz, C-5 pyrrole), 7.76 (d, 1H, *J* = 2.5 Hz, C-3 pyrrole), 6.41 (s, 2H, NH₂), 7.62 (d, 2H, *J* = 8.0 Hz, *p*-chlorophenyl), 7.98 (d, 2H, *J* = 8.0 Hz, *p*-chlorophenyl). ¹³C-NMR: $\delta = 37.5$ (q, CH₃), 108.6 (d, CH, C-4 pyrrole), 119.8 (d, 2CH, C-2, C-6 *p*-chlorophenyl), 122.1 (d, CH, C-3 pyrrole), 128.8 (d, CH, C-5 pyrrole), 129.7 (d, 2CH, C-3, C-5 *p*-chlorophenyl), 131.4 (s, C, C-2 pyrrole), 131.7 (s, C, C-1 *p*-chlorophenyl), 132.6 (s, C, C-4 *p*-chlorophenyl), 137.7 (s, C, C-4 triazole), 156.2 (s, C, C-5 triazole), 175.8 (C=O). MS, *m/z* (%), 301.1 (M⁺, 100), 108 (100). Anal. Calcd. For (C₁₄H₁₂³⁵ClN₅O): C, 55.73. H, 4.01; N, 23.21. Found: C, 55.73; H, 3.99; N, 23.18. CCDC 845132 contains the supplementary crystallographic data for compound **20**, which can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk

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