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Methylheteroaromatic Carbonitriles as Building Blocks for Synthesis of Condensed Heteroaromatics: Novel Syntheses of [1]Benzo[2,3]pyrano[3,4-*c*]-pyridines, Naphtho[2′,1′:5,6]pyrano[3,4-*c*]pyridines, Pyrido[3,4-*c*]quinolines and Other New Condensed Pyridines

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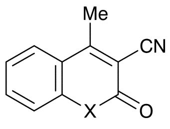
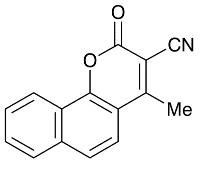
A variety of condensed pyridines were prepared via condensing alkylheteroaromatic carbonitriles with *N*,*N*-dimethylformamide dimethylacetal and subsequent cyclization of the formed products.

In conjunction with previous work we report here on the utility of the methylheteroaromatic carbonitriles **1a**, **b**, **2** and **3** as building blocks for the synthesis of condensed pyridines. Thus compounds **1a**, **b** and **2** condensed with dimethylformamide dimethylacetal (DMF DMA) to yield the (*E*)-dimethylaminoethylene derivatives **4a**, **b** and **5**. Compounds **4a**, **b** and **5** were assigned the (*E*) structure based on ^1H NMR, which revealed ethylene protons as two doublets at δ 5.7 and δ 8.5 ppm with $J = 13$ Hz.



1a X = O
b X = NH



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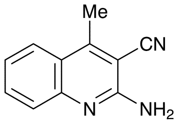

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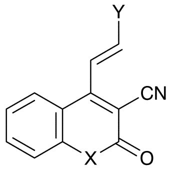
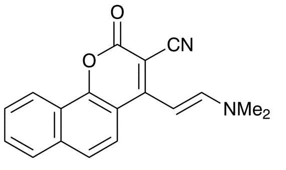


4a X = O, Y = NMe₂
b X = NH, Y = NMe₂
c X = O, Y = NHPh
d X = NH, Y = NHPh



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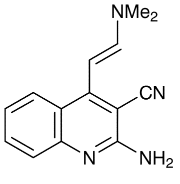
The reaction of **3** with DMF DMA in refluxing xylene afforded a xylene-insoluble product and a xylene soluble one in a 3:1 ratio. The xylene-soluble product was identified as the (*E*)-dimethylaminoethylene quinoline derivative **6** while the xylene-insoluble part proved to be the amidine derivative **7**. Structures **6** and **7** were assigned to these products based on spectral data. Thus the IR spectrum of **6** revealed the presence of an NH_2 absorption. The ^1H NMR spectrum of **6** did not exhibit a methyl group signal but showed two one-proton doublets at δ 6.51 and δ 8.11 ppm with $J = 13$ Hz, for the *trans* olefinic protons. The ^1H NMR spectrum of **7** exhibited a methyl group signal at δ 2.82 ppm and the absence of the D_2O exchangeable amino signal at δ 8.57 ppm. It showed, in addition to the $-NMe_2$ signal, an aromatic multiplet, and a singlet at δ 8.62 ppm for the iminomethylene proton.



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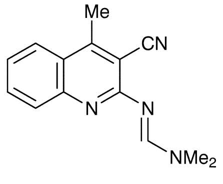

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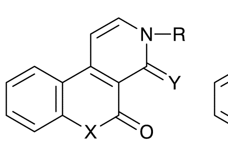
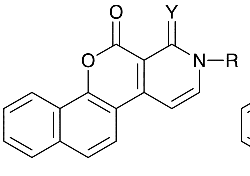
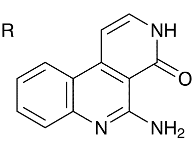
Compounds **4a**, **b**, **5** and **6** were converted into the pyridone derivatives **8a**, **b**, **9a** and **10** upon reflux in acetic acid in the presence of concentrated hydrochloric acid. We believe that under these reaction conditions the cyano function is first hydrolysed into the corresponding amide which then adds to the activated double bond, affording a tetrahydropyridine that then undergoes aromatization via loss of dimethylamine (Chart 1).



8a R = H, X = O, Y = O
b R = H, X = NH, Y = O
c R = Ph, X = O, Y = NH
d R = Ph, X = Y = NH



9a R = H, Y = O
b R = Ph, Y = NH



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Compound **4a**, **b** were converted into the (*E*)-anilinoethylene derivatives **4c**, **d** on treatment with aniline. The isomeric cyclic structures **8c**, **d** were readily ruled out on the basis of IR spectra that revealed, in each case, a cyano group signal at $\nu_{max} \approx 2180\,cm^{-1}$. Moreover the ^1H NMR spectra indicated the presence of *trans* olefinic proton doublets at δ 6.3 and δ 8.4 ppm with $J = 13$ Hz. Boiling **4c**, **d** under reflux in DMF for 5 min resulted in their cyclization into **8c**, **d**. It is believed that under such conditions the double bond is first isomerized into the (*Z*) form, which then cyclizes into **8c**, **d**. Similar treatment of **5**

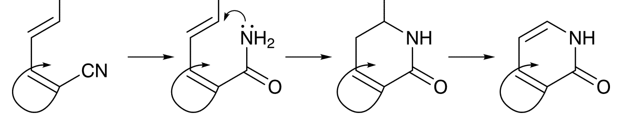

Chart 1

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*To receive any correspondence.

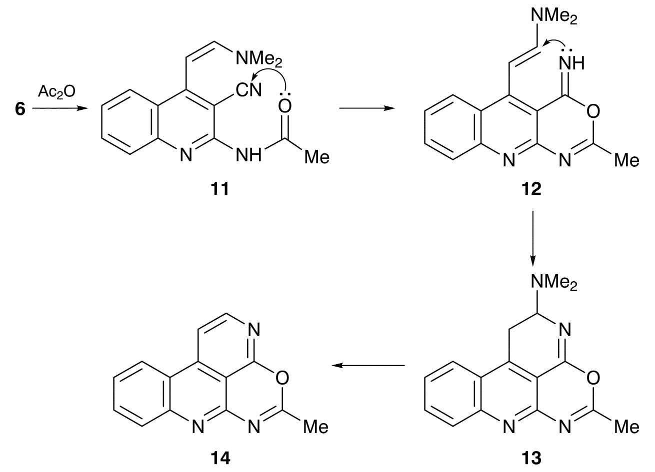
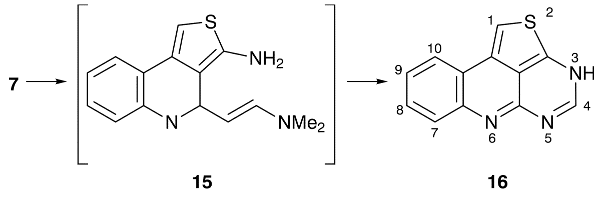


Chart 2

with aniline afforded directly the *N*-phenylnaphthopyranopyridine derivative **9b**.

Attempted acylation of **6** resulted in the formation of a product of molecular formula $C_{14}H_9N_3O$; *m/z* (%): 235 (50) [M^+]. This was thus assigned structure **14**. It is assumed that initially formed **11** cyclizes into **12** which then cyclizes further into **13** which loses dimethylamine, yielding **14** (Chart 2). This, to our knowledge, is the first reported example of this ring system. The ^{13}C NMR spectrum of this product is in complete agreement with the proposed structure.

Previously we have established that alkylazinylcarbonitriles react with sulfur in the presence of a base to yield thienoazines[7] which add to electron-poor olefins and acetylenes to yield (4 + 2) cycloadducts that either decompose into benzo fused heteroaromatics or rearrange to condensed thiepins.[4–6] It was thus thought worthwhile to investigate the behaviour of the quinolines **3** and **7** in similar reactions. Under a variety of conditions compound **3** did not react with elemental sulfur, while **7** reacted smoothly with sulfur in DMF solution in the presence of piperidine to yield a product of molecular formula $C_{12}H_7N_3S$; *m/z* (%): 225 (100) [M^+]. This was thus assigned structure **16** and is assumed to be formed via intermolecular cyclization of intermediate **15**. Attempts to isolate **15** failed. Compound **16** failed to add to both electron-poor olefins and acetylenes.



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Techniques used: IR, ^1H NMR, ^{13}C NMR, MS and elemental analysis

References: 8

Charts: 2

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