

Polycyclic Pyrazoles: Routes to New Pyrazoloazines

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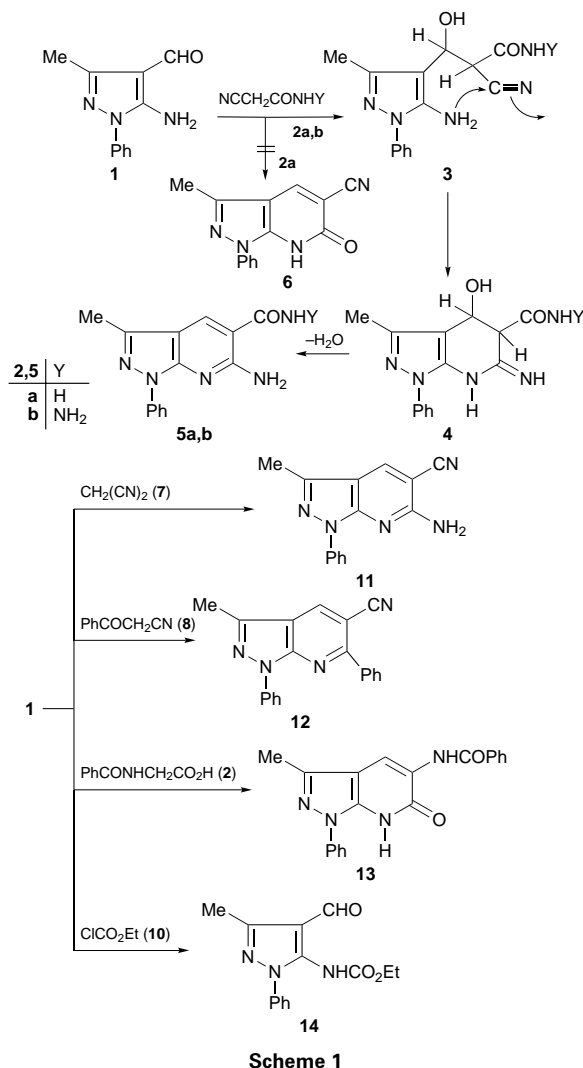
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A number of substituted pyrazolo[3,4-*b*]pyridines and pyrazolo[4',3':5,6]pyrido[2,3-*d*]-pyrimidinones and -1,2,3-triazinones have been made, starting from 5-amino-3-methyl-1-phenylpyrazole-4-carbaldehyde.

Pyrazoles have been found to be excellent precursors for the syntheses of condensed polyfunctionally substituted pyrazoles.^{10–11} We report here the facile synthesis of some new pyrazolo[3,4-*b*]pyridines from 5-amino-3-methyl-1-phenylpyrazole-4-carbaldehyde (**1**) which was first described by Häufel and Breitmaier.¹² Cyclocondensation of **1** with cyanoacetamide (**2a**) in refluxing ethanolic piperidine yielded a product which could have been either the cyano-pyridone **6** or the amino-amide **5a** (Scheme 1). Structure **5a** was considered to be the only reaction product on the basis of spectroscopic data. Compound **1** also reacted with cyanoacetamide hydrazide **2b** to yield the pyrazolo[3,4-*b*]pyridine **5b**.

Similarly **1** reacted with malononitrile (**7**) in refluxing ethanolic piperidine to yield the corresponding pyrazolopyridine **11** via addition followed by elimination of water. In analogy,



Scheme 1

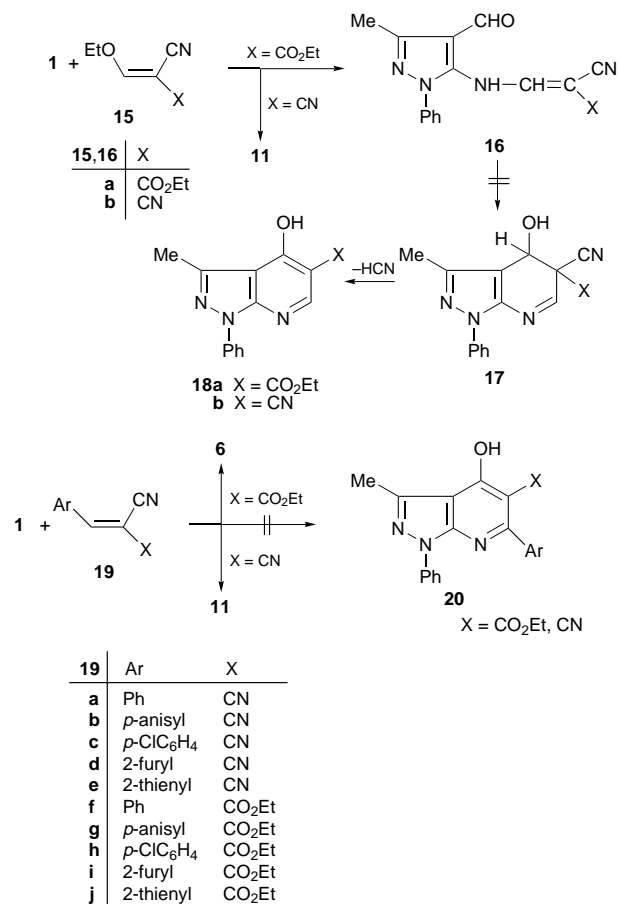
cyclocondensation of **1** with benzoylacetonitrile (**8**) afforded the pyrazolopyridine derivative **12**.

The reaction of **1** with hippuric acid was also investigated. Thus, cyclocondensation of **1** with hippuric acid (**9**) in glacial acetic acid afforded the pyrazolopyridine **13**. Also, the reaction of **1** with ethyl chloroformate **10** in ethanolic piperidine yielded the urethane **14**.

Compound **1** reacted with ethyl ethoxymethylidenecyanoacetate (**15a**) to yield the substitution product **16** (Scheme 2). Efforts to cyclize **16** under various reaction conditions failed. Also, ethoxymethylidenemalononitrile (**1b**) failed to yield **18** in reaction with **1**, compound **11** instead being formed under the reaction conditions.

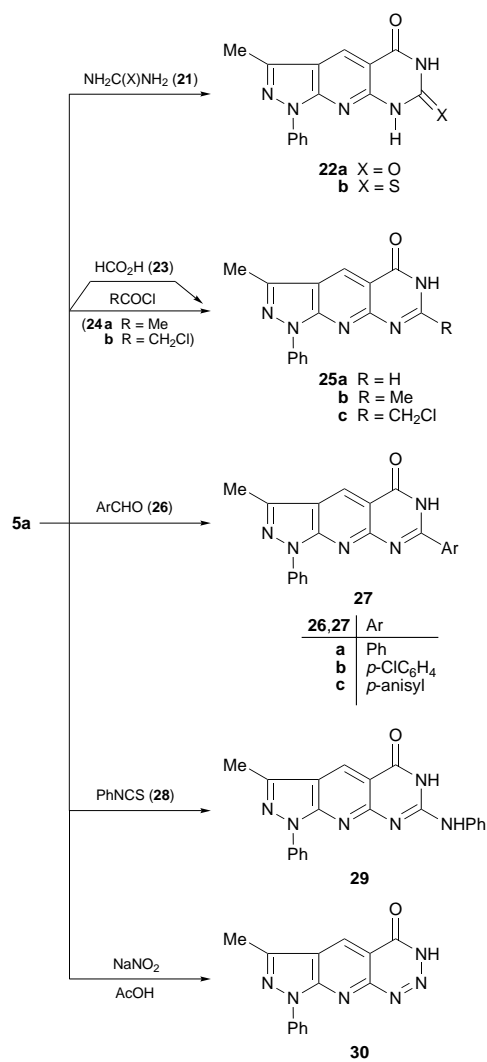
Efforts to cyclize **1** with arylmethylidenes **19a–j** to afford **20a–j** were not successful; instead, **6** and **11** were isolated.¹²

Synthetic approaches to aminocarboxamide derivatives have been extensively studied, and many syntheses using aminocarboxamides as starting materials have been reported.^{13–16} We found that the aminocarboxamide **5a** reacted with urea derivatives to yield the pyrazolopyridopyrimidine derivatives **22a,b** (Scheme 3). Similarly, formic acid, acid chlorides, aryl aldehydes and phenyl isothiocyanate reacted with **5a** to give



Scheme 2

*To receive any correspondence.



Scheme 3

the corresponding pyrazolopyridopyrimidine derivatives **25**, **27** and **29** respectively.

Treatment of the aminocarboxamide **5a** with sodium nitrite in acetic acid at room temperature afforded the 1,2,3-triazinone derivative **30**.

Techniques used: IR, NMR (^1H , ^{13}C), mass spectrometry, microanalysis

References: 16

Table 1: Mps, yields and elemental analysis of **5a-c**, **11**, **12**, **13**, **14**, **16**, **22a,b**, **25a-c**, **27a-c**, **29** and **30**

Table 2: IR and ^1H NMR of **5a,b**, **11**, **12**, **13**, **14**, **16**, **22a,b**, **25a-c**, **27a-c**, **29** and **30**

Table 3: ^{13}C NMR of **22a** and **27b**

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