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**PYRAZOLO[3,4-*b*]PYRIDINE NUCLEOSIDES: TOTAL SYNTHESIS OF THE
GUANOSINE, ISOGUANOSINE AND XANTHOSINE ANALOGUES***

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Summary. An expeditious and total synthesis of the guanosine (**3a**), isoguanosine (**3b**) and xanthosine (**3c**) analogues in the pyrazolo[3,4-*b*]pyridine ring system has been accomplished for the first time from the precursor 5-amino-1-(2,3-*O*-isopropylidene- β -D-ribofuranosyl)pyrazole (**8**) by various ring closure procedures.

We described the rationale behind the regio- and stereoselective synthesis of certain pyrazolo[3,4-*b*]pyridine nucleosides (**1** and **2**), which are structurally related to adenosine and inosine.¹ In this report we describe the first example of 4,6-disubstituted pyrazolo[3,4-*b*]pyridine ribonucleosides from hitherto unreported 5-amino-1-(2,3-*O*-isopropylidene- β -D-ribofuranosyl)pyrazole (**8**) by unique ring annulation procedures.

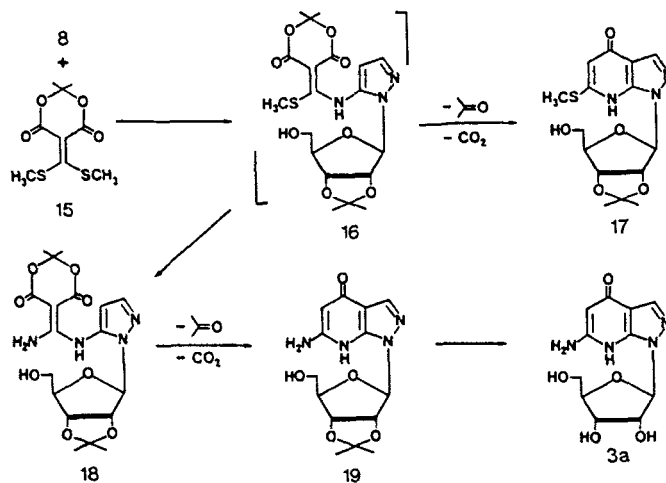
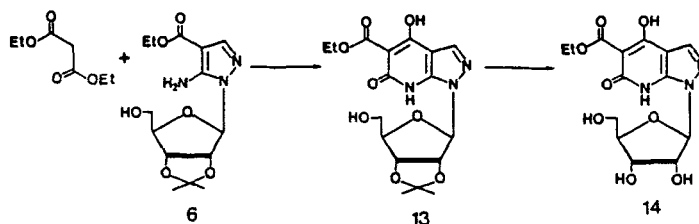
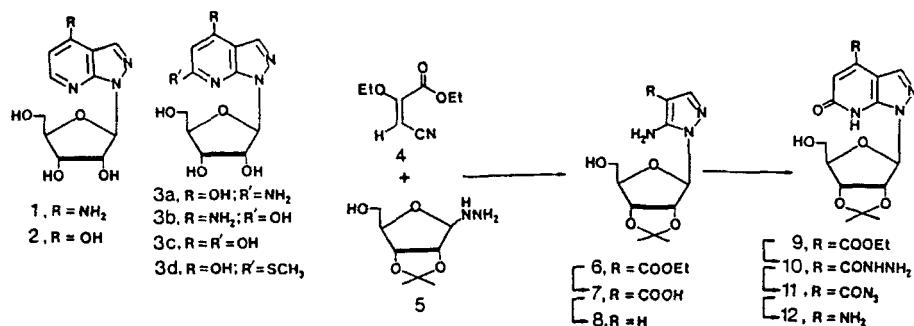
Compound **6**², was saponified to give **7** (98% yield), which on subsequent decarboxylation (in Ph₂O at 220° C) furnished the key starting material **8** as a crystalline compound (84% yield). The pyrazole **8** was converted to **12** in 4-steps as follows: When pyrazole **8** was heated with the sodium salt of diethyl oxalacetate in glacial AcOH, compound **9** was obtained, which on treatment with hydrazine furnished the hydrazide **10**. Compound **10** was allowed to react with NaNO₂/AcOH to provide the azide **11**, which on Curtius rearrangement afforded the isopropylidene blocked nucleoside **12** in 51% overall yield for 4-steps starting from **8**.

The carboxylate **6** was reacted³ with diethyl malonate in NaOEt/EtOH to provide nucleoside **13** in 62% yield. Blocking of **13** with 90% aq TFA gave compound **14**, which on saponification and decarboxylation furnished the xanthosine analogue **3c**.

Using compound **15**⁴, we have now prepared for the first time, the guanosine analogue **3a** from the nucleoside **8**. The ketene dithioacetal **15** reacted with **8** in EtOH to provide **16**, which on subsequent ammonolysis in the presence of HgCl₂ furnished crystalline **18** (mp 172° C). Thermal cyclocondensation gave the isopropylidene derivative **19**. Deblocking of **19** gave the guanosine congener **3a** in ca. 9% overall yield. A similar reaction of **15** with **8** in DMF (120° C) furnished the ring annulated product **17** in one step (via the intermediate **16**) in 86% yield.

* Dedicated to Professor C.B. Reese on the occasion of his 60th Birthday.

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REFERENCES

1. Y.S. Sanghvi, S.B. Larson, R.C. Willis, R.K. Robins, and G.R. Revankar, *J. Med. Chem.*, **32**, 945 (1989); *Nucleosides Nucleotides*, **8**, 887 (1989).
2. B.K. Bhattacharya, R.K. Robins, and G.R. Revankar, *J. Heterocycl. Chem.*, **1990**, **27**, 787 (1990).
3. S.W. Schneller and D.R. Moore, *J. Heterocycl. Chem.*, **15**, 319 (1978).
4. F.-C. Ye, B.-C. Chen, and X. Huang, *Synthesis*, 317 (1989).