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Synthesis of Pyrido[1',2':1,2]imidazo[4,5-b]quinoxaline Derivatives from 2-Amino-3-chloroquinoxaline and Pyridines

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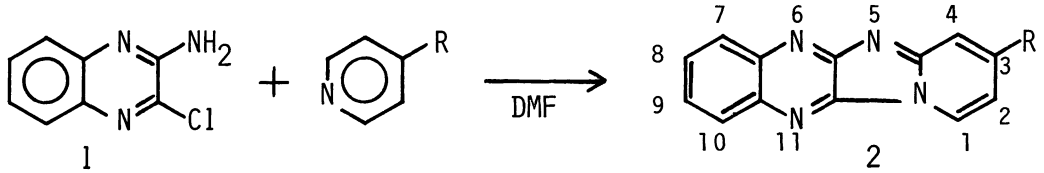
Pyrido[1',2':1,2]imidazo[4,5-b]quinoxaline was synthesized from 2-amino-3-chloroquinoxaline and pyridine. 3-Substituted pyridoimidazoquinoxalines were obtained from pyridines substituted at 4-position. These pyridoimidazoquinoxalines showed intense greenish yellow fluorescence.

Nitrogen-containing fused polycyclic compounds such as pyrido[1,2-a]benzimidazoles,[1] dipyrido[1,2-a:2',3'-d]imidazoles,[2] and pyrido[1',2':1,2]imdazo[4,5-b]pyrazine[3-5] have been attracting much attention because of not only the characteristic skeletons with bridgehead nitrogen but their use as pharmaceutical drugs and pesticides. However, there have been only a few reports[6,7] on a fused ring containing quinoxaline. We have developed the synthesis of 2-amino-3-chloroquinoxaline (1) from 2,3-dichloroquinoxaline by a rather convenient method.[8] The self-condensation of 1 in DMF gave 6,13-dihydropyrazino[2,3-b;5,6-b']diquinoxaline (fluorubin) in a low yield (30%). Thus, we attempted this reaction by using pyridine in place of DMF as a solvent with an expectation of some improvement of the yield. Pyrido[1',2':1,2]imidazo[4,5-b]quinoxaline (2), an unexpected product, was obtained by cyclization between 1 and pyridine. In this letter, we wish to report on the synthesis of the corresponding 3-substituted pyridoimidazoquinoxaline derivatives from 1 and 4-substituted pyridines.



1 2

A typical experimental procedure is as follows: A mixture of 1 (5 mmol) and a pyridine (15 mmol) in DMF (5 cm^3) was heated at 100 °C for 48 h and then allowed to cool to room temperature. The yellow precipitate was collected by filtration, washed with benzene or ethanol, and recrystallized from benzene or chloroform. The structures of the products were identified by IR, NMR and MS spectra, and by elemental analyses.

Pyridine was unreactive to 1 at room temperature, but it gave 2 in 59% at 100 °C. The reaction also took place in DMF solution, so that 4-substituted

pyridines were allowed to react with 1 in DMF. Table 1 shows the results. 4-Formylpyridine did not give the corresponding adduct, but 1 was recovered. The cyclization of isopropylpyridine with 1 was carried out at 80 °C, because the reaction at a higher temperature (100 °C) caused some contamination of 6,13-dihydropyrazino[2,3-b;5,6-b']diquinoxaline (fluorubin). The cyclizations of ethyl- and propylpyridines with 1 were carried out at 80 °C. The reactions at 100 °C gave rise to formation of uncharacterized byproducts which could not be separated from the reaction mixture.

Table 1. Yields of Pyridoimidazoquinoxalines[9]

4-R-Pyridine R	Yield /%	Mp θ_m/°C	Absorption[a] λ_{max}/nm	Fluorescence[b] Emission λ_{max}/nm
H[c]	59	293-294	355	505
H	49	(295[6];265[7])		
CH_3	26	284-285	356	507
C_2H_5[d]	38	245-247	356	506
$(CH_2)_2CH_3$[d]	40	220-223	356	505
$CH(CH_3)_2$[d]	38	202-204	356	507
$C(CH_3)_3$	66	285-286	356	507
$C(CH_3)_3$[e]	61			
$CH_2C_6H_5$	45	247-249	358	508
C_6H_5	65	321-322		
C_6H_5[e]	61			
$COCH_3$	46	314-315	363	535
COC_6H_5	25	257-258		
$COOC_2H_5$	52	268-270	364	528
$COOC_6H_5$	20	309-310		
CN	trace			
CN[f]	3.0	<350(sublime)	368	528
CHO	0			
OH	0			

a) 3×10^{-5} mol dm^{-3} (in EtOH) b) 3×10^{-6} mol dm^{-3} (in EtOH)(λ_{ex}=366 nm). c) Pyridine (10 cm^3) was used without DMF. d) Reaction temperature was 80 °C. e) Reaction period was 24 h. f) Reaction period was 96 h.

2-Methylpyridine did not react with 1 and the starting materials were recovered unchanged. The 2-substituents may sterically prevent the sufficient access of the pyridine nitrogen to 1. 3-Substituted pyridines react with 1 to give pyridoimidazoquinoxaline derivatives. But the orientation of the ringclosure is not clarified yet.

The solutions of products show intense greenish yellow fluorescence.

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9)R = H [^{1}H-NMR($CDCl_3$)δ:8.92(d,1H),8.37(d,1H),8.27(d,1H),7.86(t,1H),7.80(d,1H),7.79(t,1H),7.72(t,1H),7.02(t,1H)]. R = CH_3 [8.71(d,1H),8.32(d,1H),8.20(d,1H),7.81(t,1H),7.73(t,1H),7.50(s,1H),6.80(d,1H),2.52(s,3H)]. R = $C(CH_3)_3$ [8.69(d,1H),8.28(d,1H),8.12(d,1H),7.76(t,1H),7.67(t,1H),7.63(s,1H),7.03(d,1H),1.41(s,3H)]. R = C_6H_5 [8.95(d,1H),8.37(d,1H),8.27(d,1H),7.99(s,1H),7.86(t,1H),7.80(d,2H),7.78(t,1H),7.61-7.50(m,3H),7.32(d,1H)].

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