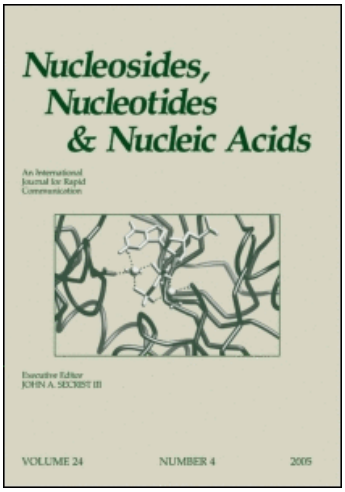

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Synthesis of 2' -Deoxypyrihidine Nucleosides Via Copper (I) Iodide Catalysis

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SYNTHESIS OF 2'-DEOXYPYRIMIDINE NUCLEOSIDES VIA COPPER (I) IODIDE CATALYSIS

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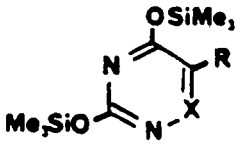
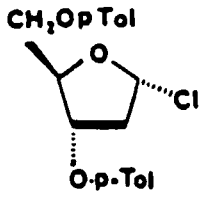
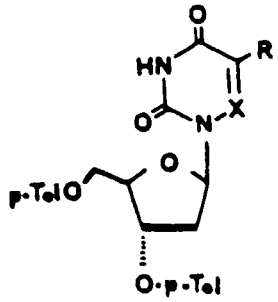
The high current interest in the use of 2'-deoxypyrimidine nucleosides as potential anti-viral agents has made a high-yield route favoring the biologically active β-anomers desirable. To this end the coupling of pyrimidine 1b with 2 in EDC or $CHCl_3$ was studied using weak Lewis Acid catalysts. Of the catalysts studied only copper (I) iodide gave β-selective reactions.







1 2 3

a R=H, X=CH
b R=CH_3, X=CH
c R=C_2H_5, X=CH
d R=I, X=CH
e R=F, X=CH
f R=NO_2, X=CH
g R=H, X=N
h R=CH_3, X=N

a R=H, X=CH
b R=CH_3, X=CH
c R=C_2H_5, X=CH
d R=I, X=CH
e R=F, X=CH
f R=NO_2, X=CH
g R=H, X=N
h R=CH_3, X=N

TABLE I. Yields and Anomeric Ratios of CuI Catalyzed Reactions of Protected Uracils with 2 in $CHCl_3$.

Base	Overall Yield	ß:α Ratio[a]
1a	93	92:8
1b	92	93:7
1c	92	93:7
1d	b	88:12
1e	90	73:27
1f	b	mainly ß
1g	92	92:8
1h	92	97:3

(a) determined by 360 MHz ^{1}H-NMR integration of anomeric protons

(b) Not determined

Thus, couplings of 2 with other silated pyrimidines were conducted using CuI in $CHCl_3$. The results are shown in Table I. Generally, nucleosides were obtained in $\geq$ 90% yields and high ß:α ratios by using freshly prepared silyl bases and distilled $CHCl_3$. When reactive bases (i.e., 1a-c,g,h) were employed, fast reactions with high ß:α selectivity were observed. However, like the uncatalyzed reaction, rate and selectivity decreases as the electronegativity of the substituent in the 5-position increases.

In summary, the use of CuI as a catalyst in the synthesis of various 2'-deoxypyrimidine nucleosides often results in improved ß:α selectivity and increased reaction rates.