A Simple Synthesis of 5-Fluorouracil by a Novel Ring Transformation Reaction (1)

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A very simple method for the preparation of 5-fluorouracil (**1**) from 1,3-dimethyl-5-azauracil (**2**) by a novel ring transformation reaction is reported.

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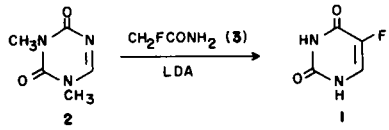
5-Fluorouracil (**1**) one of the most extensively used drugs in the treatment of advanced solid cancers (2), has been prepared either *via* cyclization of α-formyl fluoroacetate with isothiourea (3) or by fluorination of uracil with fluoroxytrifluoromethane (4). Recent development of a novel *s*-triazine to pyrimidine ring transformation reaction in our laboratories (5) prompted us to extend the reaction for preparation of **1** from 1,3-dimethyl-5-azauracil (**2**). Treatment of **1** with fluoroacetamide (**3**) in alcoholic sodium alkoxide, the conditions employed for the *s*-triazine to pyrimidine transformation, did not afford **1**. We found, however, that the transformation reaction occurred very smoothly in the presence of lithium diisopropylamide (LDA) and pure **1** was obtained in 88% yield from **2** and **3**. This procedure may have wide applicability to the synthesis of a variety of fluorine subsituted heterocyclic compounds.



2 1

EXPERIMENTAL

5-Fluorouracil (**1**).

A mixture of **2** (5,6) (1 g, 6 mmoles) and **3** (0.52 g, 6 mmoles) in 10% (w/w) LDA in ether (60 ml) was stirred at 0° for 4 hours under nitrogen. The precipitate was collected by filtration and recrystallized from methanol-ether to give 0.6 g (88%) of **1** mp 282-284° [lit (4), mp 282-283°]. The ^{1}H nmr and ir spectra of this sample were identical with those of an authentic sample.

REFERENCES AND NOTES

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