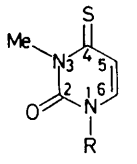
Thio-Claisen Rearrangement in the Pyrimidine Series. Access to 5-Allyl-4-thiouracil Derivatives

By JEAN-LOUIS FOURREY,* EDITH ESTRABAUD, and PATRICK JOUIN
(*Institut de Chimie des Substances Naturelles, C.N.R.S.*, 91190 *Gif sur Yvette, France*)

Summary Functionalization at C-5 of the pyrimidine system can be achieved by thio-Claisen rearrangement of 3-substituted 4-allylthiopyrimidin-2-ones.

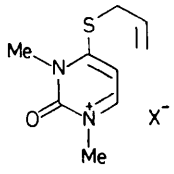
IN pyrimidine chemistry only a few examples of oxo- and amino-Claisen rearrangements are known.[1,2] The reaction of some 4-allyloxy-pyrimidine derivatives has been used to prepare, in low yield, 5-allyl-uracil.[2b]

We now report that 3-methyl-4-allylthiopyrimidin-2-ones rearrange readily to yield the corresponding 5-allyl-4-thiouracil isomers. This thio-Claisen rearrangement, the first example in pyrimidine chemistry, is of value for the synthesis, under mild conditions, of 5-alkyl substituted uracils, compounds of current interest.[3]



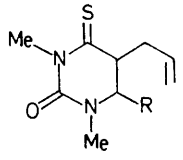
(1)

a; R = Me
b; R = H



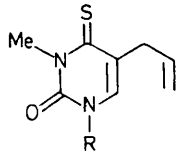
(2)

X = Br or I



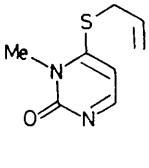
(3)

a; R = OMe
b; R = H

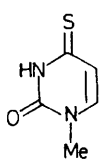


(4)

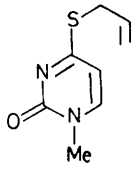
a; R = Me
b; R = H



(5)



(6)



(7)

The new 4-allylthiopyrimidin-2-ones were prepared by methods previously used for the synthesis of the 4-alkylthiopyrimidin-2-one derivatives.[4] Thus, treatment of the dimethyl thiouracil (**1a**) with allyl bromide yields the crystalline salt (**2**), from which compound (**1a**) may be regenerated on heating in the absence of solvent. However, addition, at room temperature with stirring, of acetone–methanol (6:2) to the salt (**2**) in the presence of Na_2CO_3 induces rearrangement to the 5,6-dihydropyrimidin-2-one (**3a**) as an oil,† which, when heated in refluxing $CHCl_3$, loses MeOH to give the 5-allyldimethylthiouracil (**4a**) as an oil [75% overall yield from (**1a**)]. In contrast to the dihydropyrimidinone (**3a**), compound (**4a**) has the characteristic 6-H n.m.r. signal (δ 6·90) of a 4-thiouracil, and a u.v. absorption maximum at λ 334 nm, demonstrating the presence of a conjugated thiocarbonyl.

The 5,6-dihydro-derivative (**3b**) (oil) was prepared by treatment of a methanolic solution of compound (**2**) with $NaBH_4$ [80% from (**1**)].

We have also investigated the reactivity of the mono-*N*-substituted 4-allylthiopyrimidin-2-one derivatives. Compound (**5**), m.p. 88—89 °C, can be prepared by the reaction of (**1b**) with allyl bromide in acetonitrile followed by treatment with carbonate. In the presence of MeI the sulphide (**5**) gives compound (**2**), whilst it is quantitatively converted into (**4b**), m.p. 155—157 °C, δ (6-H) 7·07, when heated in refluxing benzene. The reaction of allyl bromide with the 1-methylthiouracil (**6**) produces the sulphide (**7**), m.p. 121—123 °C.

So far, we have not been able to induce isomerization of compound (**7**). It is noteworthy that Minnemeyer and his co-workers[2a] have reported that 2-substituted 4-allylthiopyrimidines do not undergo the Claisen rearrangement. Accordingly, substitution at N-3 could be a prerequisite for observing allyl group migration in this class of molecule.

We thank Dr. J. Polonsky for encouragement.

(*Received*, 15*th October* 1975; *Com.* 1170.)

† New compounds were characterized by elemental analysis, and u.v., i.r., n.m.r., and mass spectrometry.

[1] S. J. Rhoads and N. R. Raulins, *Org. Reactions*, 1975, **22**, 1.

[2] (a) H. J. Minnemeyer, P. B. Clarke, and H. Tieckelmann, *J. Org. Chem.*, 1966, **31**, 406; (b) H. J. Minnemeyer, J. A. Egger, J. F. Holland, and H. Tieckelmann, *ibid.*, 1961, **26**, 4425; (c) J. K. Elwood and J. W. Gates, *ibid.*, 1967, **32**, 2956; (d) B. A. Otter, A. Taube, and J. J. Fox, *ibid.*, 1971, **36**, 1251.

[3] A. Wexler, R. J. Bachunis, and J. A. Swenton, *J.C.S. Chem. Comm.*, 1975, 601, and references cited therein.

[4] D. J. Brown and B. T. England, *J. Chem. Soc.* (*C*), 1971, 2507; H. Maehr, M. Leach, and V. Toome, *J. Heterocyclic Chem.*, 1972, **9**, 1389.