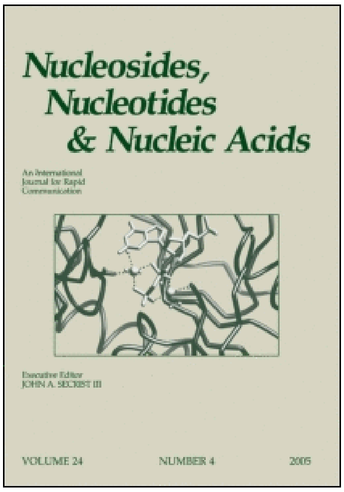

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Synthesis of the Sulfonylpyrimidine Derivatives as a New Type of Sulfonylcycloureas

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SYNTHESIS OF THE SULFONYLPYRIMIDINE DERIVATIVES AS A NEW TYPE OF SULFONYLCYCLOUREAS

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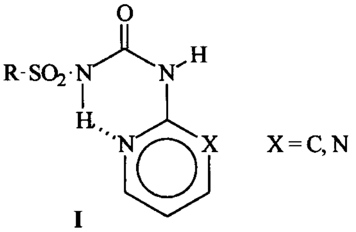
Abstract: The synthesis of several novel N-1 and N-1,NH-4-disulfonylpyrimidine derivatives are described.

As a part of our research programme directed to the syntheses of novel sulfonylurea derivatives as potential herbicides, we have performed the computer modelling studies of some sulfonylurea derivatives with potent herbicide activity based on their known X-ray structures. These results suggested that, in general, intramolecular H-bonding giving sixmembered pseudocycle stabilises a low energy conformations (I) of such derivatives.



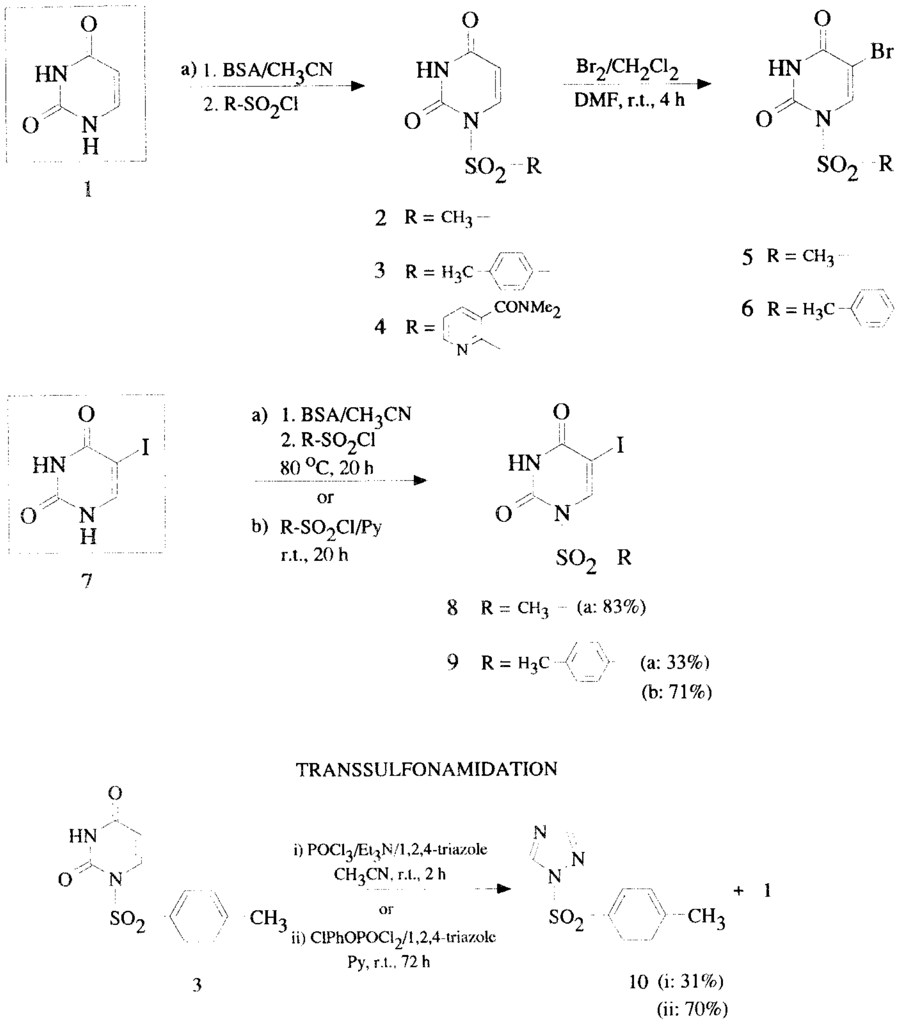
I

The possible existence of sixmembered hydrogen bonded pseudocycle (I) possessing common structural features to pyrimidine and triazine heterocycles inspired the synthesis of novel sulfonylcycloureа derivatives, as potential herbicides.

For the synthesis of sulfonylpyrimidine derivatives we used two methods: a) condensation of silylated pyrimidine bases with different sulfonyl chlorides in acetonitrile; b) reaction of pyrimidine bases with sulfonyl chlorides in pyridine.

Reaction of silylated uracil with different sulfonylchlorides gave corresponding N-1 sulfonyl products in satisfactory yields. Using method b) only a trace of product was formed.

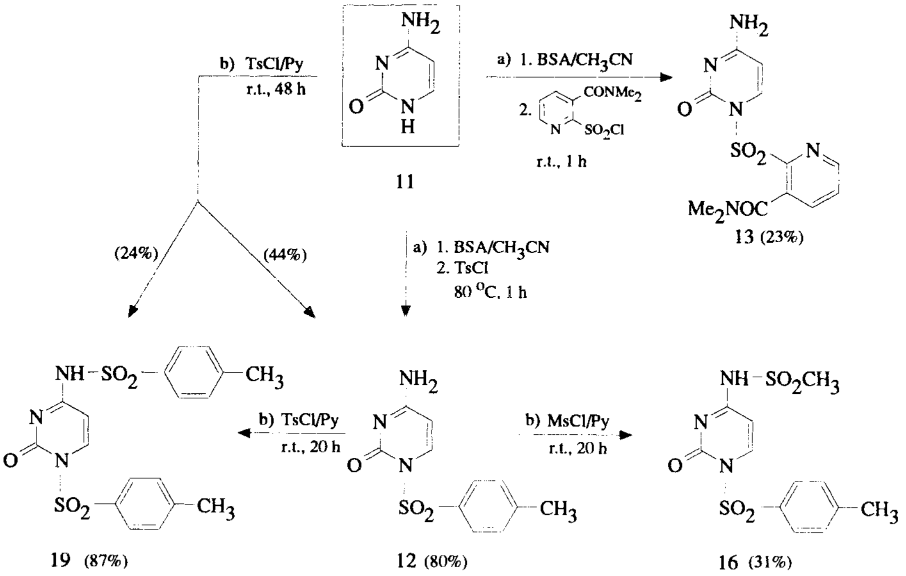
It has been reported that reaction of silylated uracil and tosyl chloride gave 1-tosyluracil in 46% yield.[1] We have found that the reaction of silylated uracil with mesyl or tosyl chlorides in acetonitrile (80 °C, 20 h) gave corresponding N-1 sulfonyl products **2** and **3** in 74% and 95% yield, respectively (Scheme 1). When the silylated



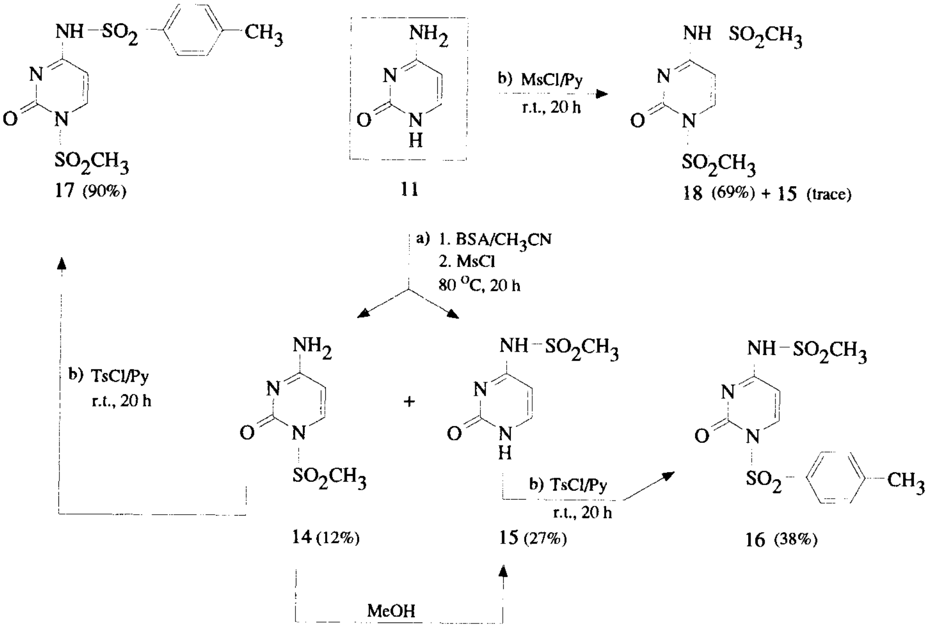
SCHEME 1

uracil reacted with 2-chlorosulfonyl-3-*N*,*N*-dimethylnicotinamide, prepared *in situ*[2] (53%), at room temperature for 1 h, product **4** was formed in 33% yield.

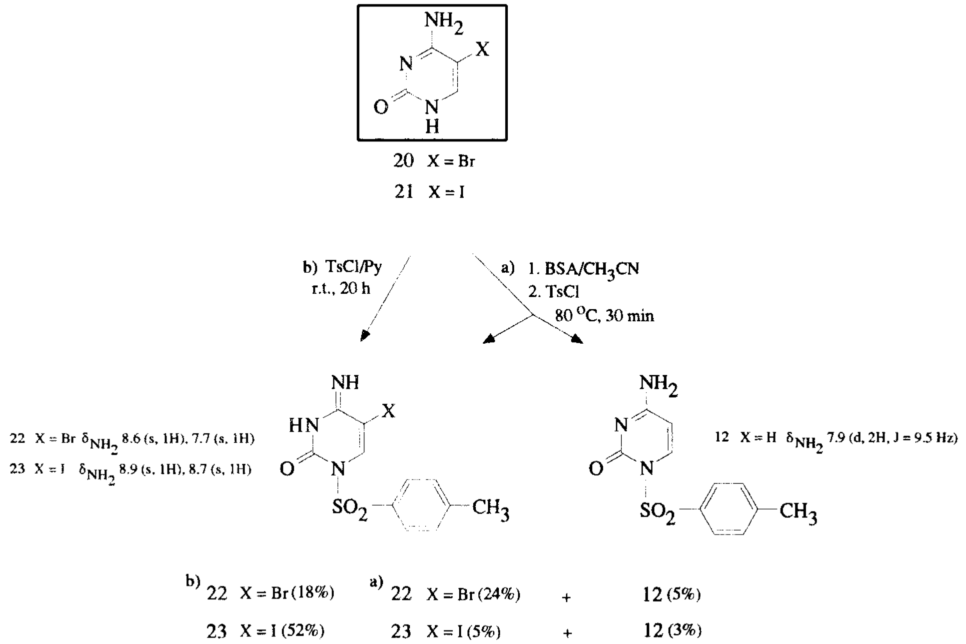
The bromination of **2** and **3** using bromine in CH_2Cl_2/DMF at 20 °C afforded the corresponding 5-bromo products **5** and **6** in 60% and 54% yields, respectively. The corresponding 5-iodo analogues **8** and **9** were synthesized (83% and 33%) using silylated 5-iodouracil and MsCl or TsCl in acetonitrile. 5-Iodo product **9** was also synthesized in 71% yield using method b).



SCHEME 2a



SCHEME 2b



SCHEME 2c

In order to prepare the corresponding cytosine analogue from **3**, we used well established procedures *via* triazolyl intermediates.[3,4] However, instead of the desired product we obtained compound **10** and uracil (**1**) by transsulfonamidation reaction.

When the silylated cytosine reacted with TsCl or 2-chlorosulfonyl-3-*N*,*N*-dimethylnicotinamide, in acetonitrile only N-1 isomers, **12** and **13** were obtained in 80% and 23% yield, respectively (Scheme 2a). On the other hand, reaction with MsCl was not selective giving N-1 (**14**) and NH-4 (**15**) mesylated products in 12% and 27% yield, respectively (Scheme 2b). Using method b), N-1,NH-4-dimesylated product **18** was isolated in 69% yield.

NH-4 Mesyl isomer **15** was transformed into N-1,NH-4-disubstituted product **16** (38%), which was also obtained in the reaction of 1-tosylcytosine (**12**) with MsCl in pyridine in 31% yield.

In order to prepare corresponding 5-halogeno-1-tosylcytosine derivatives, we used 5-bromo and 5-iodo cytosine as starting materials (Scheme 2c). Both methods, a) and b), give sulfonylated products in relatively low yields. Using method a) the dehalogenated compound **12** was also formed as by-product. ^{1}H NMR spectra of **22** and **23** revealed formation of imino-tautomer being at variance with **12**.

The prepared sulfonylcyclourea derivatives are crystalline solids. All new compounds were fully characterized by spectroscopic methods and elemental analyses. The synthesis of the corresponding triazine sulfonyl derivatives are in progress. The preliminary testing revealed herbicide activity of **6** and **13**.

REFERENCES

1. Z. A. Martirosyan, V. I. Gundar, and S. I. Zav'yalov, *Izv. Akad. Nauk SSSR, Ser. Khim.* (8), 1841 (1971).
2. M. A. Hanagan, (E. I. du Pont de Nemours and Co) *Eur. Pat. Appl.* EP 0237.292 A2. 1987.
3. D. G. Norman, C. B. Reese, and H. T. Serafinowska, *Synthesis* 751 (1985).
4. W. L. Sung, *J. Org. Chem.* **47**, 3623 (1982).