

The Reaction of Sulfamide with Diketene.
Synthesis of an *s*-Dioxo Analog of 6-Methyluracil

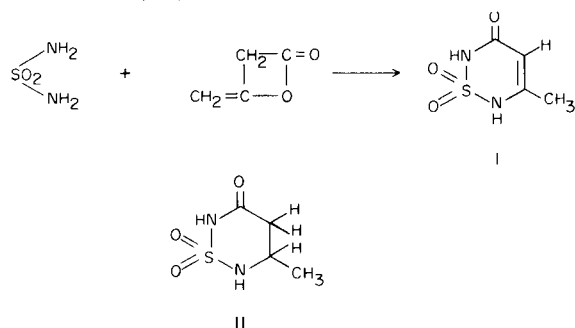
R. Die, J. Díez, G. García-Muñoz, R. Madroñero and M. Stud

Instituto de Química Orgánica General, Departamento de Química Médica,
Juan de la Cierva, 3. Madrid-6, Spain

Received May 23, 1972

Sir:

In this paper we describe the synthesis of the heterocyclic system I, an isosteric analog of 6-methyluracil in which a carbonyl group is replaced by a sulfone group.



Despite the early observation that in some cases the application of the urea reactions to sulfamide were inoperable (1), we have found that sulfamide reacts with diketene under mild conditions to give 3-methyl-5,6-dihydro-2H-1,2,6-thiadiazin-5-one 1,1-dioxide (I) in 22% yield, probably through the intermediate formation of acetoacetylsulfamide (2). In a typical experiment, to a well-stirred solution of 2 g. of sodium hydroxide and 4.8 g. of sulfamide in 45 ml. of water at 10-15° was added dropwise 5 g. of diketene. After 2 hours stirring at room temperature, 45 ml. of water was added, then the solution was carefully acidified with concentrated hydrochloric acid and the mixture was extracted repeatedly with ethyl acetate. The crude product obtained from evaporation at reduced pressure of the solvent was recrystallized from nitromethane to give 1.78 g. (22% yield based on sulfamide) of I as white needles, m.p. 173-174°.

Anal. Calcd. for C₄H₆N₂O₃S: C, 29.62; H, 3.70; N, 17.28; S, 19.75. Found: C, 29.72; H, 3.65; N, 17.27; S, 19.32.

The structure of I is apparent from its spectral characteristics: the mass spectrum shows the molecular ion peak at *m/e* 162; ir spectrum (nujol) exhibits bands at 3250 and 3105 (>NH), 1625 (>C=O), 1310 and 1180 cm⁻¹ (>SO₂); the nmr spectrum (60 MHz, DMSO-d₆) shows a three-proton singlet at 7.90 τ (-CH₃),

one-proton singlet at 4.57 τ (-CH=) and two-proton singlet at -1.97 τ (NH). This nmr spectrum is similar to that of 6-methyluracil (3).

An especially significant feature of I is the almost instantaneous hydrogen-deuterium exchange of H-4 ring proton as observed by the disappearance in the nmr spectrum (DMSO-d₆ + deuterium oxide solution) of the signal at 4.57 τ (5).

Catalytic hydrogenation of I in ethyl acetate solution with platinum oxide at room temperature and 3 atm afforded 3-methyl-3,4,5,6-tetrahydro-2H-1,2,6-thiadiazin-5-one 1,1-dioxide (6) (II), m.p. 180-181° (from ethyl acetate-cyclohexane). The nmr spectrum (60 MHz, DMSO-d₆) of the product shows a doublet at 2.49 τ (*J* = 10.5 Hz) assigned to the proton at the 2-position. The signals of the H-4 protons (multiplets centered at 7.78 and 7.50 τ) are observed as the AB portion of an ABX system, where X is H-3 (6.25 τ) (*J*_{4,4'} = 17.6 Hz, *J*_{3,4} = 12.4 Hz, *J*_{3,4'} = 3.7 Hz). Finally, the methyl group appears as a doublet at 8.8 τ.

The synthesis of *N*-substituted derivatives of I and studies on the chemical reactivity of these compounds are currently under investigation in our laboratories.

Acknowledgment.

We wish to thank Professor M. Lora-Tamayo for his encouragement and assistance.

REFERENCES

- (1) A. Lawson and R. B. Tinkler, *Chem. Rev.*, **70**, 593 (1970) and references cited therein.
- (2) S. Petersen, *Chem. Ber.*, **83**, 551 (1950).
- (3) The nmr spectrum (60 MHz, DMSO-d₆) of a sample of 6-methyluracil obtained from urea and diketene (4) shows a three-proton singlet at 7.97 τ and one-proton singlet at 4.66 τ.
- (4) S. I. Zavialov, V. I. Gunar, I. A. Mikhailopulo and L. F. Ovechkina, *Tetrahedron*, **22**, 2003 (1966).
- (5) When 6-methyluracil was treated under the same conditions no noticeable exchange of H-5 occurred.
- (6) Satisfactory analysis was obtained for this compound.