

HETEROCYCLES FROM CHLOROSULFONYL ISOCYANATE I. REACTION WITH 2-AMINOAZINES

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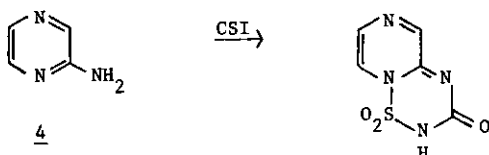
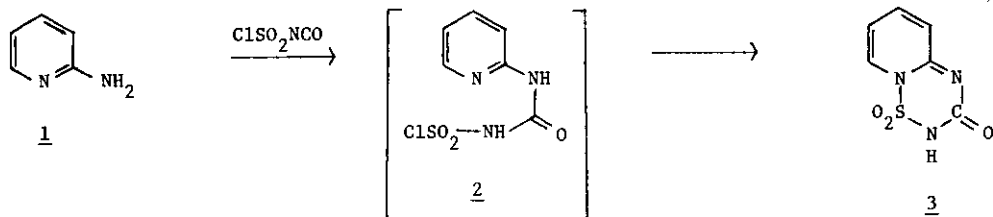
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Abstract - The reaction of chlorosulfonyl isocyanate (CSI) with 2-amino-
pyridine affords thiatriazine 3. The reaction of this heterocycle with
water, morpholine as well as alkylating agents is the subject of this
publication.

Although the chemistry of chlorosulfonyl isocyanate (CSI) has received considerable attention in recent years¹, its potential as a 1,3-dielectrophile in cyclizations has been studied only to a limited extent². A possible reason for this is the very potent electrophilic nature of CSI which makes many condensations difficult to control. In this and the following publication, we would like to demonstrate some successful cyclizations of CSI with 1,3 dinitrogen nucleophiles. The reaction of CSI with 2-aminopyridine and 2-aminopyrazine and some chemistry of the ensuing 1,2,4,6-thiatriazine-1,1-dioxide system^{2,3} are presented below⁴.

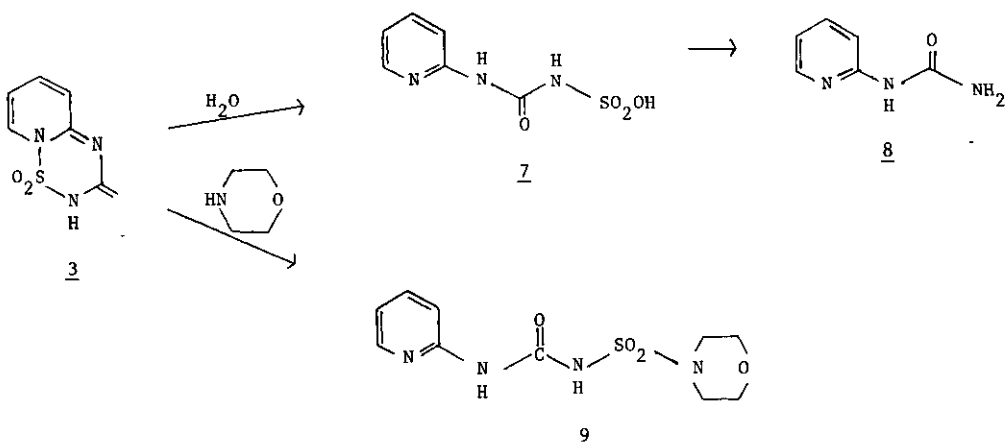
2-Aminopyridine reacts vigorously with CSI in acetonitrile at 0° producing the intermediate 2 which cyclizes on the addition of a tertiary base to afford a 50% yield of 3, mp 247°d; IR (nujol) 1680, 1620 cm⁻¹, UV (CH₃OH) λ max (ε) 302 nm (6600), 235 nm (12,000); m/e 199 (M⁺), 121 (M⁺-C₅H₄N), 107 (M⁺-C₅H₄N₂).

2-Aminopyrazine (4) reacted similarly producing a 50% yield of 5, mp 183° d; UV (MeOH) max λ (ε) 323 nm (2500), 231 nm (4000); m/e 200 (M⁺), 158 (M⁺-NCO), 121 (M⁺-SO₂NH).

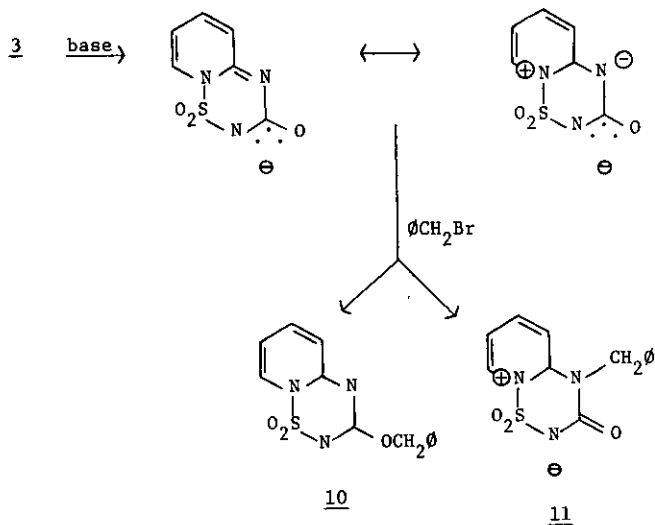


In a typical experiment one equivalent of CSI was slowly added to a solution of the 2-aminoazine in acetonitrile at 0°. After 30 minutes aging an equivalent of ethyl diisopropylamine was added, the mixture was stirred 16 hours at 20° and the product removed by filtration.

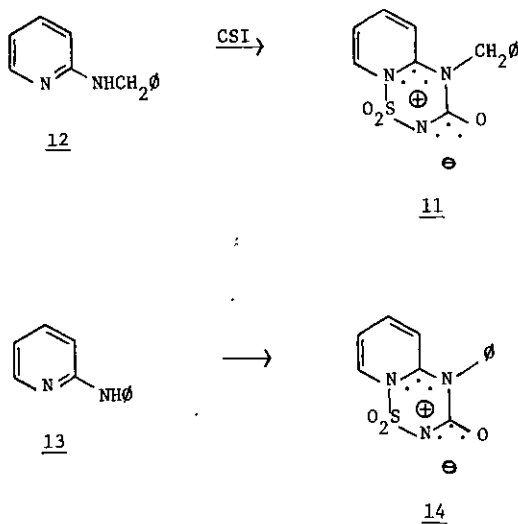
The thiatriazenes 3 and 5 are acidic and exhibit both electrophilic and nucleophilic properties. Compound 3, for example, is readily soluble in dilute aqueous sodium bicarbonate forming a sodium salt which is slowly hydrolyzed to the urea 8 via 7. The electrophilic nature of the sulfonyl group in 3 is also demonstrated in its reaction with morpholine to produce a 70% yield of 9, mp 146-148°; IR (CHCl₃) 1700 cm⁻¹; m/e 286 (M⁺), 200 (M⁺-C₄H₈NO), 137 (M⁺-C₄H₇NO₃S), 120 (C₆H₄N₂O).



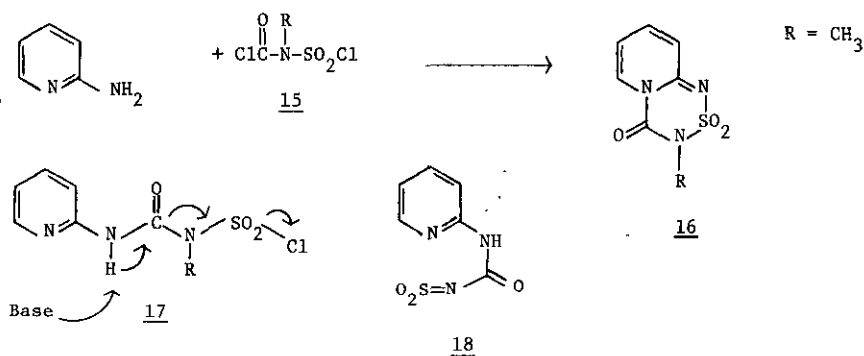
Under anhydrous conditions, the salts of 3 are stable and can be readily alkylated. Thus the reaction of 3 with benzyl bromide in acetonitrile in the presence of ethyl diisopropylamine gave equal amounts of the two alkylation products: 10, mp 124-125°, IR (CHCl₃) 1630 cm⁻¹; ¹³C NMR (CD₃CN) 71.7 ppm (δCH₂O); UV (CH₃CN) λ_{max} (ε), 332 nm (9700), 257 nm (9000); m/e 289 (M⁺), 119 (C₆H₃N₂O) and 11, mp 165-170°; IR (nujol) 1660 and 1620 cm⁻¹; ¹³C NMR (CD₃CN) 49.1 ppm (δCH₂N); UV (CH₃CN) λ_{max} (ε) 312 nm (9100); m/e 289 (M⁺), 183 (M⁺-SO₂NCO, exact mass 183.0924, calcd. for C₁₂H₁₁N₂, 183.0922).



An unequivocal structure proof for 11 was its preparation from benzylaminopyridine (12) and CSI in acetonitrile in 60% yield. Another analog of 11 was provided by the conversion of 13 into 14 in 52% yield, mp 209–212°, IR (nujol) 1690, 1620 cm^{-1} , UV (CH_3CN) λ_{max} (ϵ) 311 nm (7800), 237 nm (7800), m/e 275 (M^+), 169 ($\text{M}^+ - \text{SO}_2\text{NCO}$).



In a recent publication⁵, the reaction of 2-alkyl-2-chlorosulfonyl carbamoyl chloride (15) with 2-aminopyridine was reported to afford 16 in 20% yield. The likely reason for the opposite orientation of this reagent as compared to CSI is, the facile decomposition of the normal adduct 17 in base as shown.



The analogous product from CSI, 17 (R=H or 2) would more likely eliminate HCl to give 18, which is a possible intermediate in the cyclization process.

The conclusion of this paper is that CSI is a valuable reagent for the introduction of the C-N-S substructure into heterocycles.

†Deceased August 12, 1978.

REFERENCES

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b) R. Appel, H. Uhlenhaut and M. Montenark, Z. Naturforsch., 1974, B-29, 799.
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4. With the exception of 3 and 5 which could not be crystallized all new products gave acceptable microanalyses (C, H, N, S). Only diagnostic spectral data are given.
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