REACTION OF PYRIDINE-*N*-OXIDE WITH A STRAINED SEVEN-MEMBERED CYCLOALKYNE
A CORRECTION

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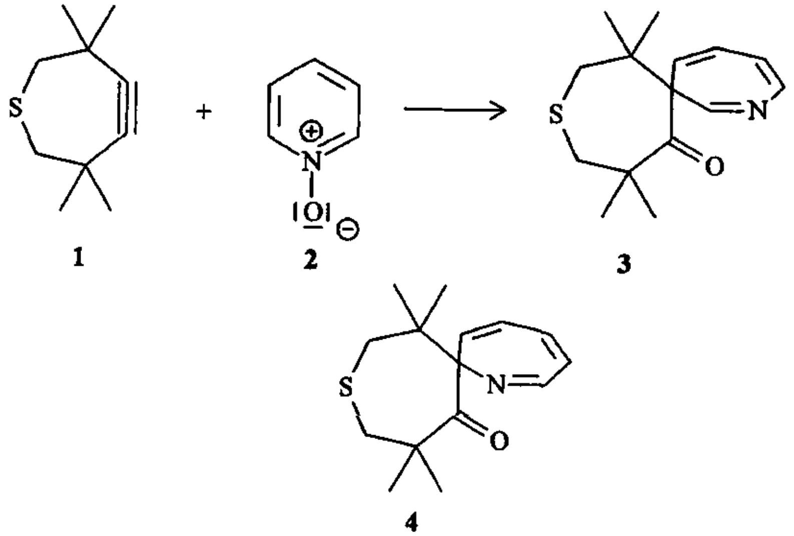
Abstract - Pyridine-*N*-oxide adds at room temperature to 3,3,6,6-tetramethyl-1-thia-cycloheptyne to give the 3*H*-azepine (**3**). A mechanism of formation for **3** is discussed. On heating **3** rearranges to yield the 3-substituted pyridine (**8**).

The strained 3,3,6,6-tetramethyl-1-thia-4-cycloheptyne (**1**) reacts at room temperature with pyridine-*N*-oxide (**2**) to give a 1:1-addition product (**3**) in 54% yield; a recent X-ray crystal structure analysis and a detailed NMR study revealed that the structure of this product was that of a 3*H*-azepine derivative (**3**) and not that of a 2*H*-azepine derivative (**4**) as previously suggested on the basis of an X-ray crystal structure analysis.[1]



Scheme 1

In connection with the synthesis of unsubstituted 2*H*-azepine[2] the reaction of **1** with **2** was reinvestigated. To our surprise the 400 MHz ^{1}H-NMR spectrum of the product showed a singlet at $\delta = 6.42$ ppm which was not significantly coupled to any of the other azepine protons. This fact and the evaluation of a ^{1}H-^{1}H-COSY spectrum suggested structure (**3**) for the isolated product; indeed, this structure was confirmed by a second X-ray analysis.

Compound (**3**) crystallized in colorless triclinic needles. The structure was determined by using direct methods (SHELXL-86[3]). The non hydrogen atoms were refined anisotropically. The hydrogen atoms were localized in a difference fourier map and refined isotropically. (SHELXL-93[4]). For details see Table 1 and ref. 5. The molecular. structure of **3** is shown in Figure 1 .[6]

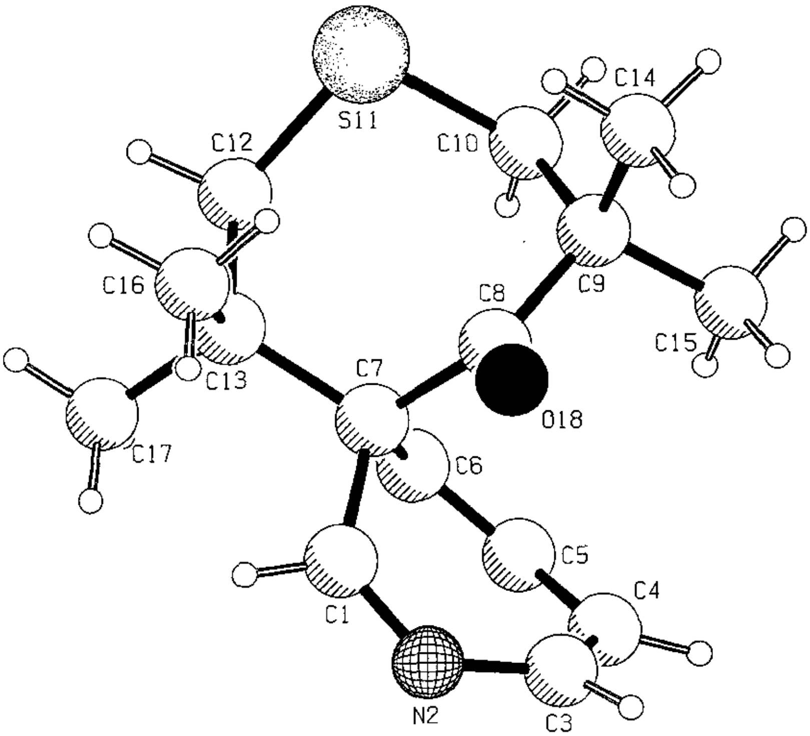
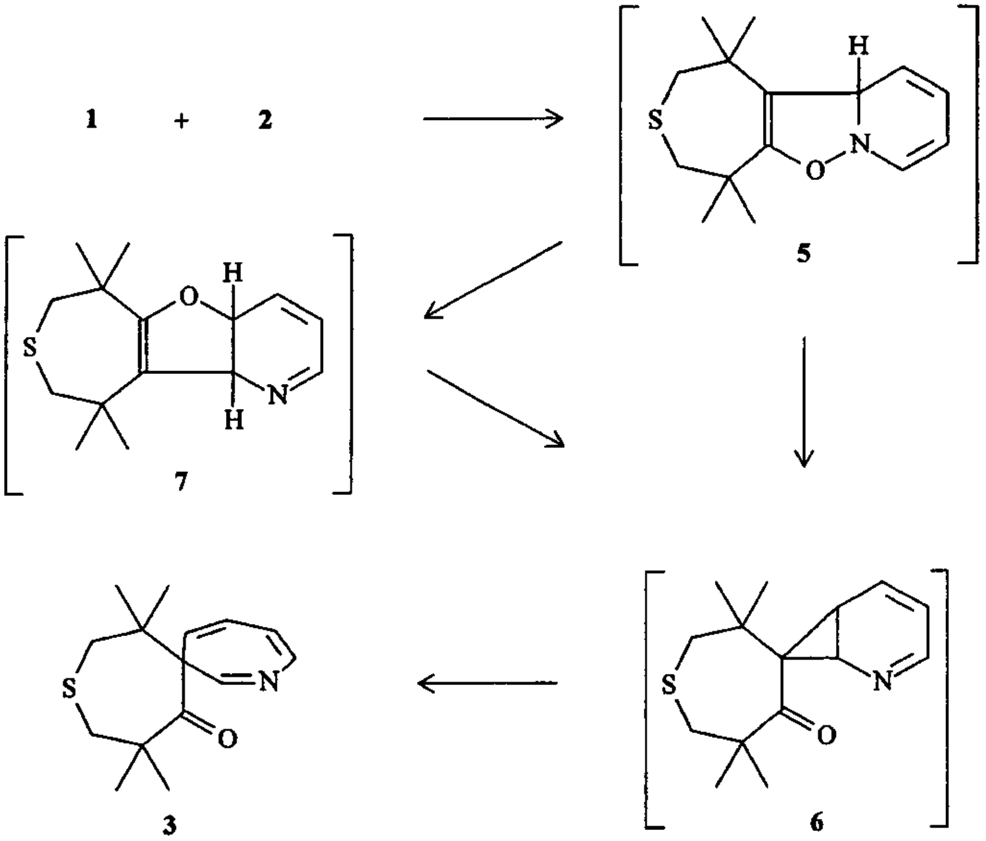


Figure 1: Molecular Structure of **3**

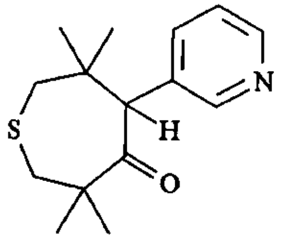
In the 400 MHz ^{1}H-NMR spectrum of **3** at room temperature in addition to signals for the main conformer a second set of signals was present for another conformer (ratio ~7:1). From the coalescence temperature of the 2-H signals (363 K) and the shift difference (0.71 ppm) at room temperature $\Delta G^{\#}_1 = 78.4$ kJmol^{-1} ($\Delta G^{\#}_2 = 71.0$ kJmol^{-1}) was calculated[7] for the inversion process of the azepine ring system. The mechanism of formation of **3** can be rationalized by the following sequence (Scheme 2):



Scheme 2

The first step is a 1,3-dipolar cycloaddition of **1** with **2** to yield the unstable intermediate (**5**) which rearranges to **3** *via* the azanorcaradiene (**6**). An alternative mechanism would be a 1,5-sigmatropic rearrangement of **5** to **7** which in turn could give **6** and subsequently **3**. There are analogies for both mechanisms in the literature[8] although in our case the direct rearrangement of **5** to **6** seems to be more likely.[9] However, in none of the previous cycloadditions of **2** formation of an azepine was observed.

The isomeric 3-substituted pyridine (**8**) can be obtained by heating **3** at 145°C for one hour in almost quantitative yield; the structure (**8**) was proved by an X-ray crystal structure analysis. This rearrangement probably proceeds *via* **6**, which opens regioselectively to afford **8**.



8

Scheme 3

The crystal structure of **8** was determined by direct methods and refined with positioned hydrogen atoms (SHELXL-86[3], SHELXS-93[4]); see Table 1 and ref. 5. The molecular structure of **8** is shown in Figure 2.

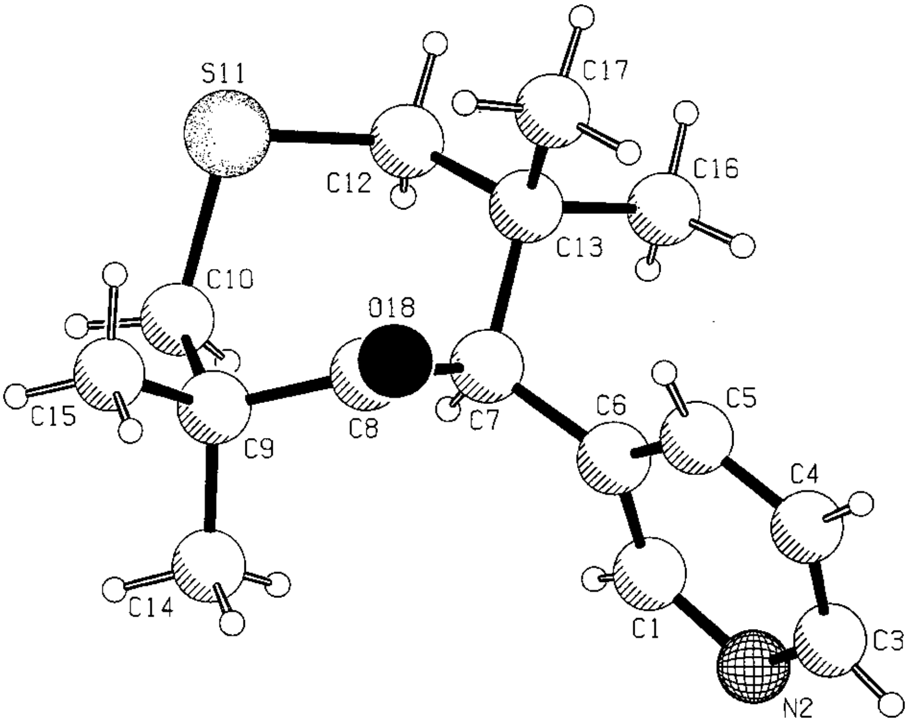


Figure 2: Molecular structure of **8**

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Table 1: Crystal data and refinement for **3** and **8**

Compound	**3**	**8**
Empirical formula	$C_{15}H_{21}NOS$	$C_{15}H_{21}NOS$
Formula weight	263.4	263.4
Temperature, K	299	299 (2)
Diffractometer	STOE IPDS	CAD 4
Wavelength, Å	0.71073	0.71069
Crystal system	Triclinic	Monoclinic
Space group	P 1	P21/c
Unit cell dimensions, Å; deg	a=6.2857 (9) alpha=85.16 (1) b=8.730 (1) beta=89.79 (1) c=13.415 (3) gamma=82.40 (1)	a = 17.839 (3) alpha = 90 b=5.9520 (1) beta = 100.97 (2) c=13.728 (4) gamma = 90
Volume, Å^3	727.0 (2)	1431.0 (5)
Z	2	4
Density (calculated) gcm^{-3}	1.203	1.223
Absorption coefficient mm^{-1}	0.212	0.212
F (000)	284	568
Crystal size, mm	0.875 x 0.075 x 0.05	0.375 x 0.25 x 0.075
Theta range for data collection, deg	2.70 to 22.50	1.16 to 19.99
Index ranges	-7<=h<=7, -11<=k<=11, -17<=l<=17	-19<=h<=19, 0<=k<=6, -15<=l<=9
Reflections collected	4568	2476
Independent reflections	1811[R(int)=0.1158]	1343[R-(int)=.0662]
Absorption correction	None	None
Refinement method	Full-matrix least-squares on F^2	Full-matrix least squares on F^2
Data/restraints/parameters	1805 / 0 / 247	1337 / 0 / 180
Goodness-of-fit on F^2	0.938	1.183
Final R indices [I>2sigma (I)]	R =0.0461, wR2=0.1000	R1=0.0686, wR2=0.1959
R indices (all data)	R1=0.0744, wR2=0.1112	R1=0.0882, wR2=0.2087
Largest diff. peak and hole, cÅ^{-3}	0.126 and -0.161	0.264 and -0.252
Extinction coefficient		0.014 (4)

REFERENCES and NOTES

1. A. Krebs, H. Colberg, U. Höpfner, H. Kimling, and J. Odenthal, *Heterocycles*, 1979, **12**, 1153.
2. D. Hamprecht, K. Polborn, and W. Steglich, *Angew. Chem.*, 1995, **107**, 1639, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1469.
3. G.M. Sheldrick: SHELXL93, a program for crystal structure determination. University of Göttingen, Germany 1993.
4. G.M. Sheldrick: SHELXS86. Program for the solution of crystal structures. University of Göttingen, Germany 1986.
5. Full details of the crystal structure analyses are available on request from the Fachinformationszentrum Karlsruhe, D-76344 Eggenstein-Leopoldshafen, on quoting the depositary numbers CSD 406066 (**3**) and CSD 406067 (**8**), the names of the authors, and the journal citation.
6. A.L. Spek: PLUTON93. Program for the display and analysis of crystal and molecular structures. University of Utrecht, the Netherlands 1993.
7. M. Oki, Application of Dynamic NMR Spectroscopy to Organic Chemistry, VCH Verlagsgesellschaft Weinheim, 1986, 6.
8. R.A. Abramovitch and I. Shinkai, *Acc. Chem. Res.*, 1976, **9**, 192 and references cited therein.
9. None of the postulated intermediates (**5**, **6** or **7**) have been observed in a ^{1}H-NMR study of the reaction at room termperature.

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