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

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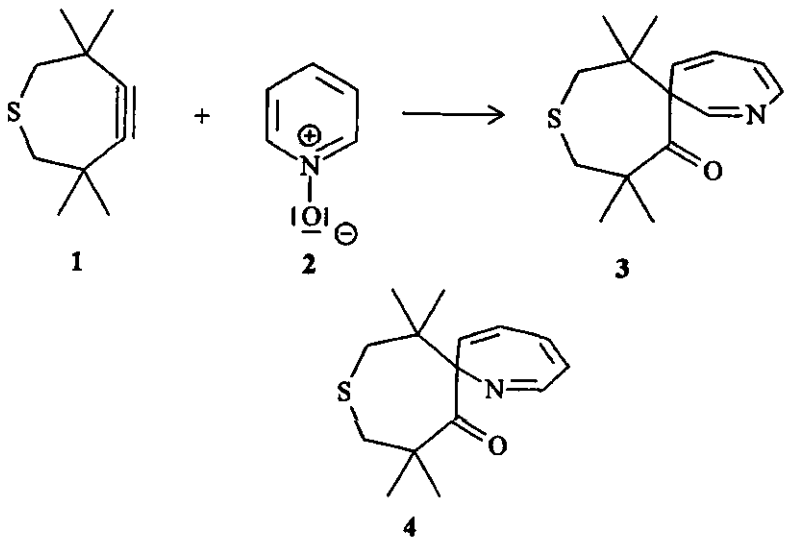
Abstract - Pyridine-*N*-oxide adds at room temperature to 3,3,6,6-tetramethyl-1-thia-cycloheptyne to give the 3*H*-azepine (**3**). A mechanism of formation for **3** is discussed. On heating **3** rearranges to yield the 3-substituted pyridine (**8**).

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]



1 **2** **3**

4

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 δ = 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]

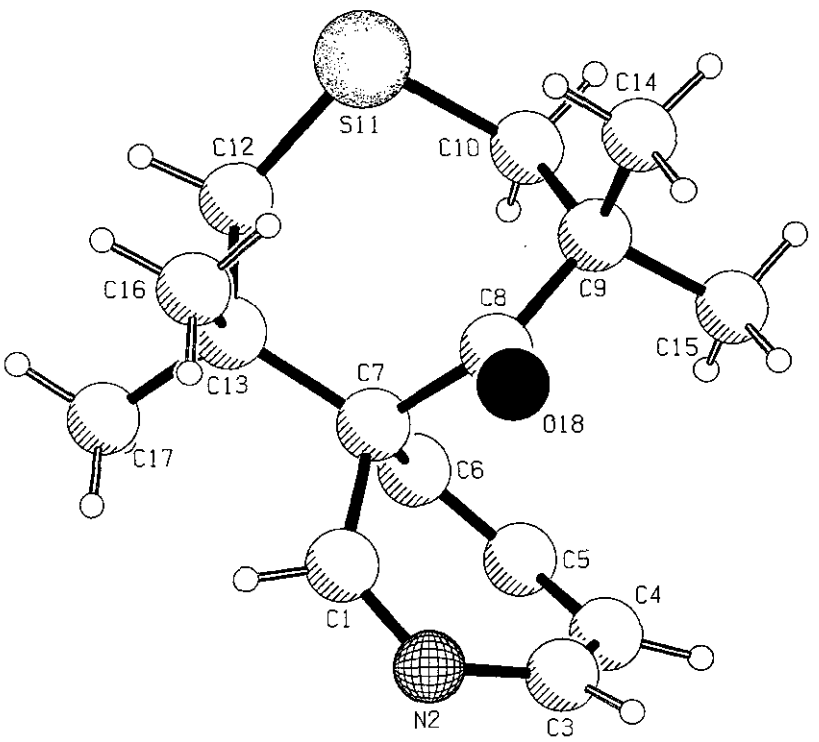
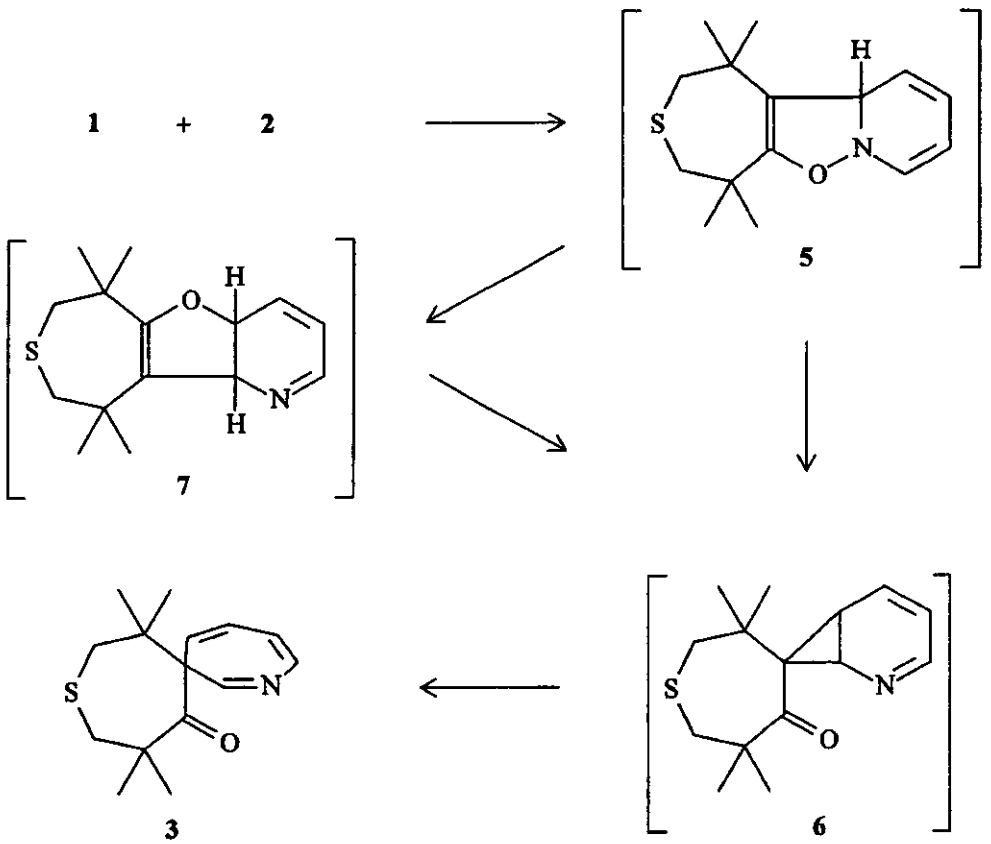


Figure 1: Molecular Structure of **3**

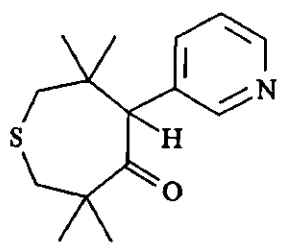
In the 400 MHz ^{1}H-NMR spectrum of **3** at room temperature in addition to signals for the main conformer a second set of signals was present for another conformer (ratio ~7:1). From the coalescence temperature of the 2-H signals (363 K) and the shift difference (0.71 ppm) at room temperature $\Delta G^{\#}_1$ = 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.

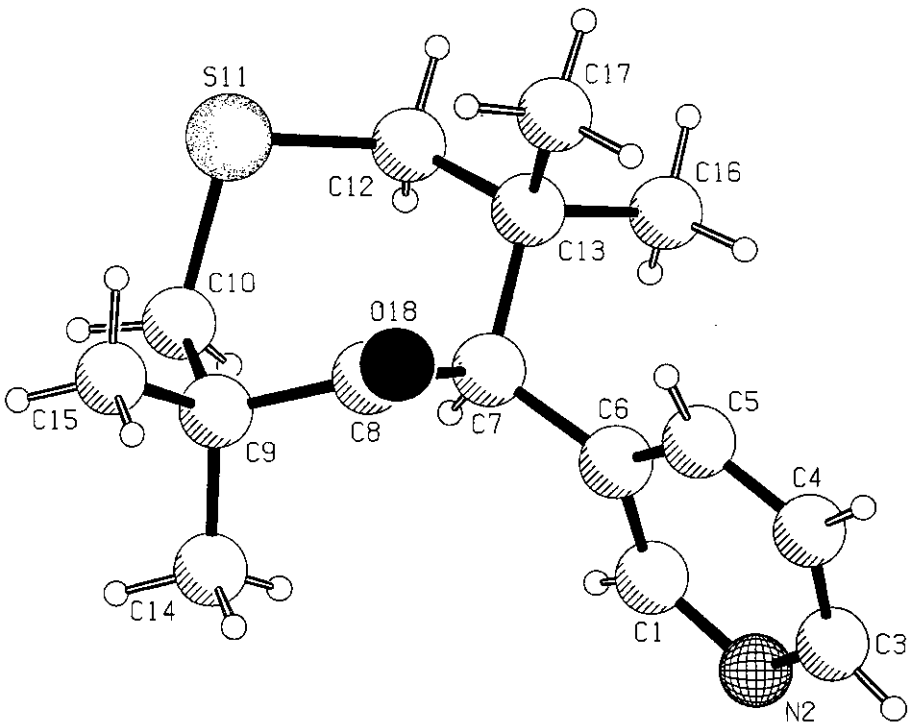


Figure 2: Molecular structure of **8**

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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)	a = 17.839 (3) alpha = 90
	b=8.730 (1) beta=89.79 (1)	b=5.9520 (1) beta = 100.97 (2)
	c=13.415 (3) gamma=82.40 (1)	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,	-19<=h<=19, 0<=k<=6,
	-17<=1<=17	-15<=1<=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

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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.
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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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