Tetrahedron Letters No. 23, pp 2037 - 2040, 1978. 0040-4039/78/0601-2037$02.00/0
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THE DESULFURIZATION OF MESOIONIC THIAZOL-4-ONES
STEREOSPECIFIC FORMATION OF β-LACTAMS

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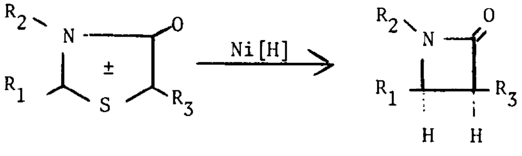
(Received in UK 31 March 1978; accepted for publication 13 April 1978)

Raney nickel desulfurizations of five-membered rings, including thiazoles, have acquired considerable importance as a synthetic and analytical tool[1]. In this communication we wish to report our preliminary results on the desulfurization of mesoionic thiazoles.

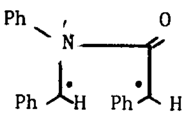
Treatment of anhydro-4-hydroxy-2,3,5-triphenyl-thiazolium hydroxide (1a) with Raney nickel in methanol, tetrahydrofuran or acetone caused disappearance of the red color of 1a within a few minutes at room temperature. Workup afforded a single product ($C_{21}H_{17}NO$, mp 182-183°, 85% yield) which was identified through its spectral properties[2] as cis-1,3,4-triphenylazetidin-2-one (2a).



1 2

a) $R_1 = R_2 = R_3 = Ph$
b) $R_1 = p\text{-}C_6H_4CH_3$, $R_2 = R_3 = Ph$
c) $R_1 = R_3 = Ph$, $R_2 = o\text{-}C_6H_4\text{-}CH_3$
d) $R_1 = R_3 = Ph$, $R_2 = p\text{-}C_6H_4Cl$
e) $R_1 = R_3 = Ph$, $R_2 = CH_2Ph$

Although ring contractions during desulfurization were observed as side reactions in a few cases[3], this smooth transformation to a four-membered ring is very unusual, and several possible mechanistic pathways have to be considered. Lactam formation via cyclization of a diradical (3) is highly unlikely, as carbon-carbon bonds are usually formed in substantial yields only on working at high temperature with degassed Raney nickel[4]. It is also to be expected that internal rotation would be faster than cyclization[5] and stereospecifity would be lost. Other possibilities are desulfurizations of either a bicyclic (4) or open (5)[6] forms of the mesoions. No spectral or chemical evidence for a contribution of these forms to the structure of 1 was found (1a did not react with phosphines or enamines). Moreover, reaction through 5 via cleavage and cycloaddition should give trans-lactams.



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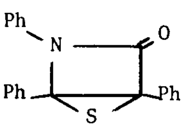

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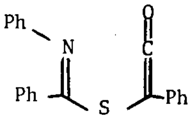

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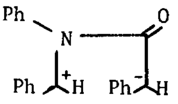

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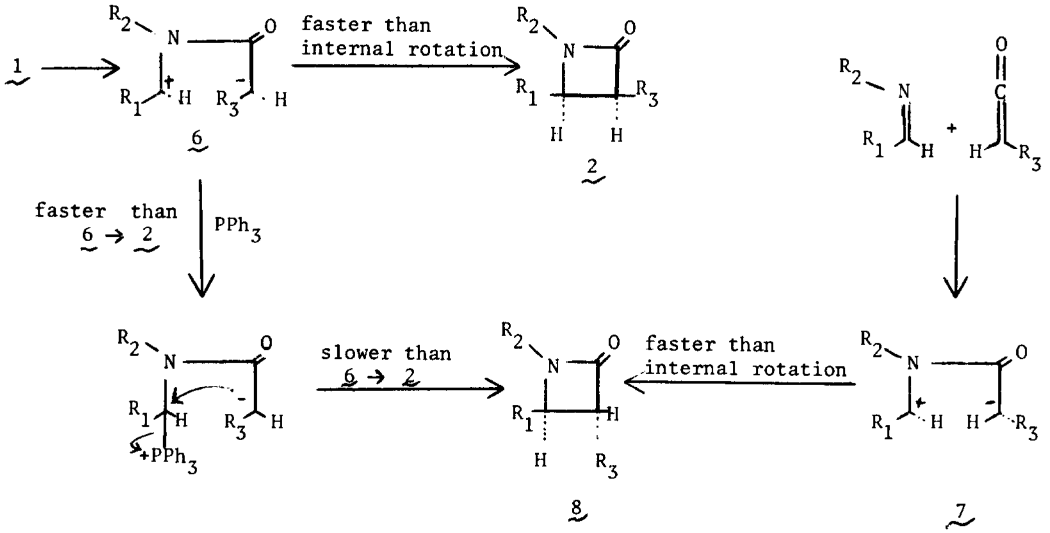
The most plausible mechanism involves conservation of the dipolar character through the desulfurization and intermediacy of the dipole 6. The same type of dipole (7) was shown to be an intermediate in the cycloaddition of ketenes to imines, which gives exclusively the *trans*-lactam 8[7]. Dipoles 6 and 7 thus differ in configuration. The cyclic precursor 1 enforces the *cis*-configuration on 6, (replacements of sulfur by hydrogen are known to proceed with retention of configuration[1])while 7 is formed from its two components in the less hindered manner (*trans*-configuration). Both 6 and 7 then collapse before internal rotation can take place[5], to give the azetidinones 2 and 8 respectively.

Although we were not able to trap 6, some indirect evidence for this mechanism has been obtained. On carrying out the desulfurization in the presence of an equimolar amount of triphenylphosphine, pure *trans*-lactam (8) was formed. With smaller amounts of phosphine, mixtures were obtained, in which the *trans*/*cis* ratios correspond to the molar amounts of the phosphine. This striking influence of the added phosphine can be ascribed to the relative rates of the reaction steps involved, as shown in Scheme I.

Scheme I



Several substituted cis-lactams were obtained by this method. The starting mesoions (1)[8] were prepared from the corresponding thioamides and α-bromophenylacetic acid according to a published procedure[9]. Properties of the lactams are summarized in Table I.

The lactam 2d is exceptional in this series by its easy thermal isomerization to the corresponding trans-lactam 8d[10]. This transformation occurs at 90-100°, and the probable mechanism is either fragmentation to ketene and imine with subsequent recombination, or dissociation to the dipole 6d, finally yielding 8d under thermodynamic control. Clarification of this point, as well as a study on the scope and applications of the desulfurization are in progress.

Table I

No.	Yield %	mp °C	$\nu C{=}O$ cm^{-1}	δH-3 ppm	δH-4 ppm	$J_{3,4}$ Hz	δ-others(a) ppm
2a	85	182-3	1745	4.96	5.44	7	
2b	80	156-7	1750	5.10	5.73	7	2.2 (3H,s)
2c	18	176-7	1755	4.98	5.75	7	2.18 (3H, s)
2d	78	80-95(b)	1740	4.95	5.40	7	
2e	80	117	1745	4.836(c)	4.843(c)	5.72	3.93 (1H,d) 5.02(1H,d)(d) J=15Hz
8a	56	127-8	1750	4.25	4.94	3	
8d	52	143	1740	4.21	4.82	3	

(a) Aromatic protons not included. (b) Transformation to 8d (see text). (c) These two doublets appear as a singlet at 60 or 100 MHz. Separation was achieved only on recording the spectrum at 270 MHz (Brucker WH-270 spectrometer, The Weizmann Institute of Science, Rehovot). (d) Such nonequivalence of benzylic protons in N-benzyllactams has been reported[11].

References and Footnotes

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