HETEROCYCLES, Vol. 24, No. 5, 1986

# 1,3-ANIONIC CYCLOADDITION OF 1,3-DIPHENYL-2-AZAALLYL LITHIUM TO THIOKETENES AND THIOKETENE S-OXIDES

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Abstract - Cycloaddition of 1,3-diphenyl-2-azaallyl lithium (4) to the thioketenes 5a,b leads to thiazolidines 7a,b. Evidence for an open-chain anionic intermediate 8 is obtained by trapping with methyl iodide and through the stereochemistry of 7a as revealed in an X-ray crystallographic study. With thioketene S-oxides 10a,b, 4 yields thiazoles 15 via a 'second-generation' Pummerer reaction.

The work of Kauffmann has established 1,3-anionic cycloaddition as an important method for synthesis of five-membered heterocyclic rings[1]. Among the possible reagents, 2-azaallyl anions, e. g. 4, have proven to be particularly reactive toward electrophilic $\pi$-electron systems. The generation of 4 via ring-opening of the aziridine anion 2 and isomerization of the short-lived intermediate 3[2] in the absence of an additional base allows cycloadditions with substrates which would react with amines or amides. Thus, 4 can be added to heterocumulenes such as phenyl iso(thio)cyanate or carbon disulfide to give heterocycles[3]. As part of our investigation of thioketene chemistry, we now report on 1,3-anionic cycloaddition of 4 to thioketenes 5 and their S-oxides 10.

Electrocyclic ring-opening of 2 was achieved in THF as previously described[2] and the reaction mixture refluxed for 2 h to achieve complete conversion into the trans, trans anion 4. Then thioketene 5a[4] was added at - 60°C and the mixture allowed to warm to room temperature. Workup by hydrolysis and chromatography (silica gel; eluent petroleum ether) to remove some unreacted 5a and benzyl(benzylidene)amine afforded a 1:1 adduct[5] in 83% yield [mp 154°C; IR(KBr): 1545, 1595,

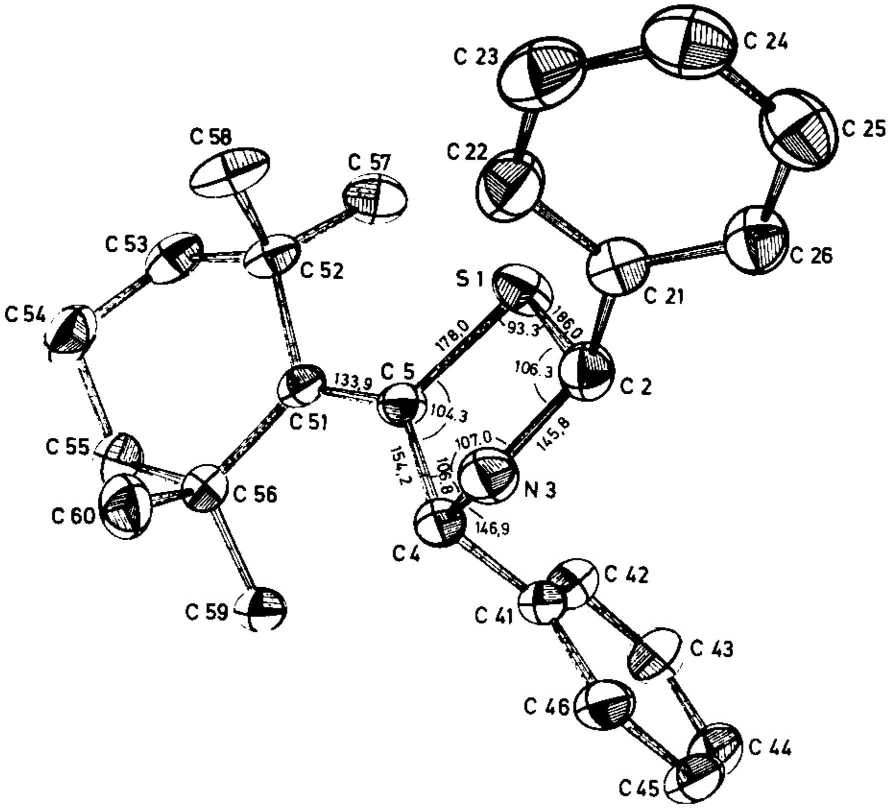
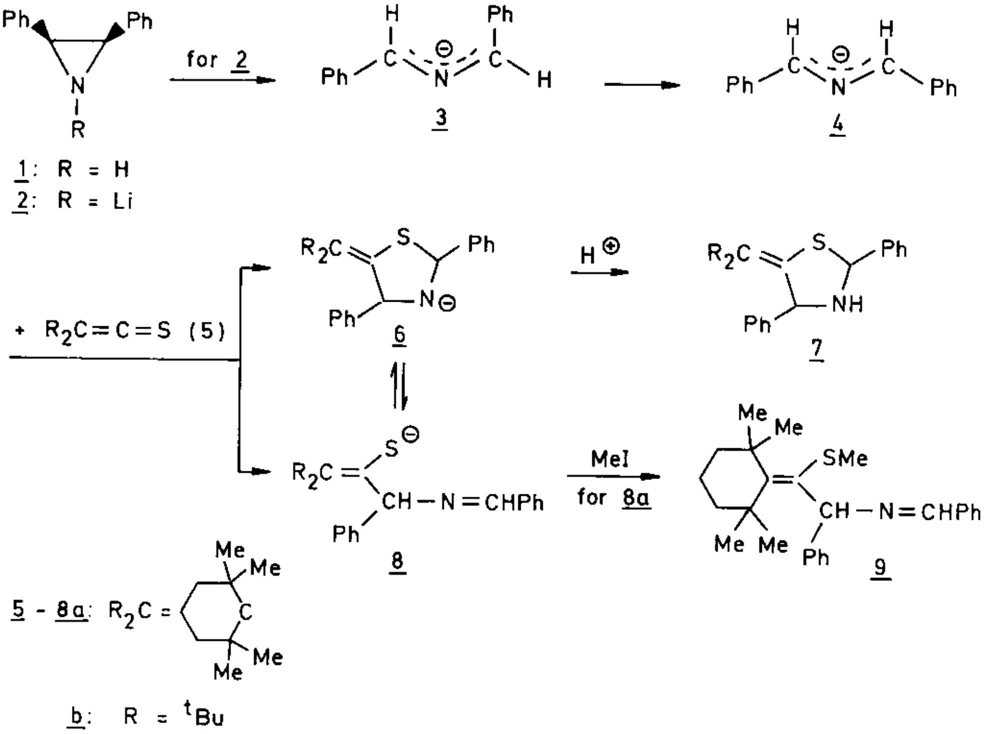


Figure 1. Computer-generated ORTEP drawing of 7a with important bond lengths [pm] and angles [°].

1640 cm$^{-1}$; $^{1}$H NMR (CDCl$_3$): δ 0.98, 1.28, 1.42, 1.55 (each s, 3H), 1.53 (m, 6H), 2.02 (broad, 1H, exchanges with D$_2$O), 5.02, 5.91 (each broad s, 1H), 7.15-7.77 ppm (m, 10H)] as a single diastereomer. The $^{13}$C NMR spectrum of the product lacks a signal at low field which might be due to a thiocarbonyl carbon. On the other hand, peaks at δ 142.2, 140.5, 139.1, 139.0, 128.5, 128.3, 127.7, 127.3, 127.0 can be assigned to the carbons of the phenyl rings and of the exocyclic C=C moiety in 7a, which results from cycloaddition of 4 across the C=S bond of 5a apparently via 6. However, these data provide no evidence for the stereochemistry of the product and even some doubt as to the constitution 7a is raised by the magnetic equivalence of C2 and C4 ( δ 69.6 ppm) and by the lack of an unambiguous NH absorption in the IR spectrum (KBr or 0.0017 M in CCl$_4$). Therefore, the structure 7a was finally confirmed by an X-ray structure analysis (Figure 1)[6].



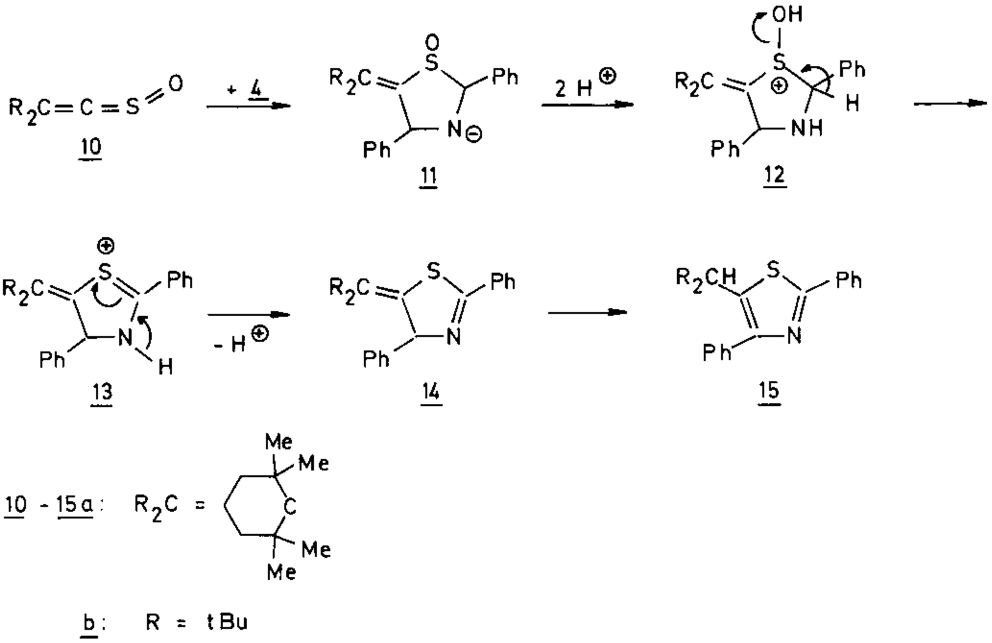
The X-ray investigation of 7a reveals a half-chair conformation of the heterocyclic ring with C4 being tilted out of the approximate plane formed by C5, S1, C2, N3 (dihedral angle 9.6°). The phenyl residues on C2, C4 are *trans*-oriented. The bond lengths are in the expected range based on van-der-Waals radii and, for the heterocyclic ring, roughly match those reported for the thiazolidine unit in a 2-alkylidene penam derivative[7] .

Not unexpectedly, starting from the sterically more hindered thioketene 5b[4] and following the same procedure, cycloadduct 7b[5] (oil, IR: 3200, 1675 cm$^{-1}$) is formed in only 18% yield.

In a modification of the workup procedure, instead of water methyl iodide was added to the reaction mixture from 4 and 5a. Interestingly, no indication for N-methylation of 6a was found, but S-methyl derivative 9[5] (19%, mp 74°C) was isolated. The structure assignment is based on the spectroscopic evidence IR (KBr): 1610 (C=C), 1540 cm$^{-1}$ (C=N); $^1$H NMR (CDCl$_3$): $\delta$ = 1.28, 1.46, 1.53, 1.58 (each s, 3H; CCH$_3$), 1.0-1.95 (m, 6H; CH$_2$), 2.12 (s, 3H; SCH$_3$), 6.16 (s, 1H, CHN), 7.25-7.95 (m, 10H; aryl H), 8.45 ppm (s, 1H, CH=N)] . In an independent experiment, thiazolidine 7a was deprotonated by the action of sodium hydride or butyl lithium in THF and then methyl iodide added. Again, the $^1$H NMR spectrum of the resulting product mixture showed no N-methyl signal, but the presence of 9, which was isolated in 9% yield.

Previous evidence on 1,3-anionic cycloadditions of 4 to C=C systems had corroborated a concerted pathway[8] . However, formation of 9 on methylation of the reaction mixture from 4 and 5a proves the presence of anion 8, which would be the expected intermediate in a two-step 1,3-anionic cycloaddition. Moreover, the trans arrangement of the phenyl residues in 7a (Figure 1) can only be understood in terms of an acyclic intermediate 8 of the cycloaddition between the trans, trans anion 4 and 5. However, this evidence does not necessarily exclude a mechanism in which anion 6 with cis oriented phenyl rings is formed in a concerted fashion and then isomerizes via an equilibrium with the acylic anion 8. In a third, though less likely reaction pathway, only 8 would be formed, and 7 would result from 5-endo-trig[9] cyclization of protonated 8.

Following the same procedure as with 5a, b, addition of 4 to thioketene S-oxides 10a, b[10] yields complex reaction mixtures from which a defined product could be isolated in low yield only after chromatography (silica gel; eluent ethyl acetate/petroleum ether 1:50). According to the elemental analyses, no 1:1 adduct such as the S-oxide of 7 is formed, but a product resulting from the loss of water. Based on the spectroscopic evidence, the thiazole structures 15a [yield 18%, mp 117°C, IR (KBr): 1595 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 0.75, 1.17, (s, 6H each; $CCH_3$), 1.45 (mc, 6H; $CH_2$), 2.98 (s, 1H; CH), 7.36-8.18 ppm (m, 10H; aryl H)] and 15b [yield 11%, m. p. 139°C; IR (KBr): 1600, 1575 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 1.10 (s, 18H, tBu), 3.43 (s, 1H, CH), 7.33-8.17 ppm (m, 10H; aryl H)] are suggested for the product from 10a and b, respectively. Particularly informative is the $^{13}$C NMR spectrum of 15a in which signals at $\delta$ 164.0 (C2), 155.8 (C4), 137.0, 133.9, 132.8, 129.9, 129.5, 128.8, 128.1, 127.6, 126.4 (C5, aryl C) can be assigned to the (het)arene carbons in 15[11] . Furthermore, C1 of the cyclohexane ring gives rise to a peak at $\delta$= 54.5 excluding structures like 14 in which this carbon is sp$^2$ hybridized; in the off-resonance spectrum, this peak is split into a doublet as expected based on structure 15.



A plausible mechanism for the formation of 15 assumes an initial one- or two-step 1,3-anionic cycloaddition of 4 to 10 to give anion 11. Protonation on nitrogen and oxygen provides intermediate 12 which triggers a 'second-generation' Pummerer reaction[12]. The resulting thiazolidine 14 should aromatize to yield thiazole 15.

In conclusion, the reactions of thioketenes 5 and their S-oxides 10 with anion 4 yield quite different products. However, branching occurs after the addition step and the difference is not due to a change in site selectivity of the cycloaddition as is the case in the reaction of 5[13] and 10[14] with diazo compounds.

ACKNOWLEDGEMENT

We thank the 'Fonds der Chemischen Industrie', Frankfurt, for financial support of this work and Mr. Torsten Marr for experimental assistance.

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Received, 27th January, 1986