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Unexpected Thermal Extrusion of CO_2 from 3-Benzylthiazolidin-2-one 1,1-Dioxides to Give 2-Phenylthiazolines and Thiazoles

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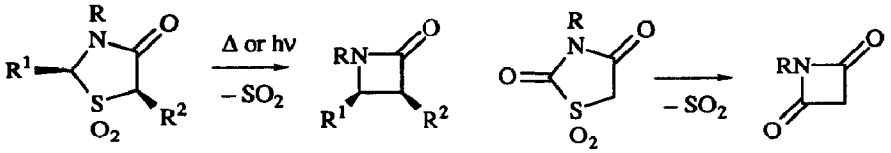
Abstract: Flash vacuum pyrolysis of a series of chiral 3-benzylthiazolidin-2-one 1,1-dioxides **5**, readily prepared from amino acids, results mainly in loss of SO_2 to give an alkene and benzyl isocyanate, but a significant minor pathway involves unexpected loss of CO_2 and water to give 2-phenylthiazolines **13** and derived thiazoles.

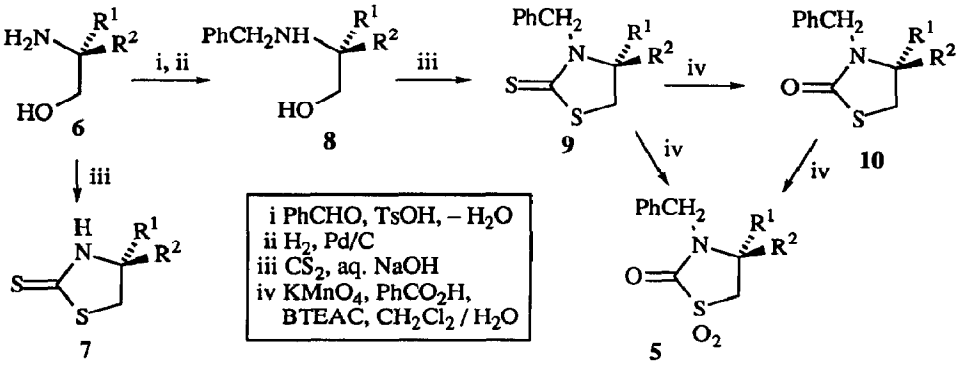
Thermal and photochemical extrusion of SO_2 from suitable ring systems has recently been used to achieve a wide variety of synthetic transformations.[1] Among the most interesting targets have been β-lactams and these have been obtained in several cases by SO_2 extrusion from appropriate thiazolidin-4-one 1,1-dioxides **1**.[2] In one case stereoselectivity was achieved with the *cis* compound **1** giving mainly the *cis* product **2** photochemically but mainly the *trans* isomer on pyrolysis.[3] The corresponding reaction of the thiazolidine-2,4-dione 1,1-dioxides **3** to give malonic acid imides **4** has also been reported.[4] We were interested to examine the isomers of **1**, the thiazolidine-2-one 1,1-dioxides **5** as possible β-lactam precursors since they have the advantage of being readily accessible in enantiomerically pure form from amino acid derived amino alcohols, and thus potentially to be suitable for asymmetric β-lactam synthesis.



1 **2** **3** **4**

We first prepared the *N*-unsubstituted thiazolidinethiones **7** which were readily obtained from *S*-valinol **6a** and *S*-phenylalaninol **6b** by treatment with CS_2 in aqueous NaOH,[5] but these were found to give problems in the subsequent oxidation step.[6] The only previous example of direct oxidation of thiazolidine-2-thiones to thiazolidin-2-one 1,1-dioxides involved the *N*-substituted compounds,[7] and so we prepared the three *N*-benzyl

examples **9a-c** in reasonable yield as shown.[8] Attempted oxidation using peracetic acid under a variety of conditions did give the desired sulfones **5** but in disappointing yield and always accompanied by some of the thiazolidinones **10**. The reagent of choice was found to be $KMnO_4$ in a mixed phase system of CH_2Cl_2 / water with both 0.1 equiv. benzyltriethylammonium chloride and 1 equiv. of benzoic acid as additives.[9] Using this system 3 equiv. of $KMnO_4$ converted **9** cleanly into **10** and either of these could be converted into **5** using 5 and 2 equiv. $KMnO_4$ respectively, the yields in all reactions exceeding 60%.[10]

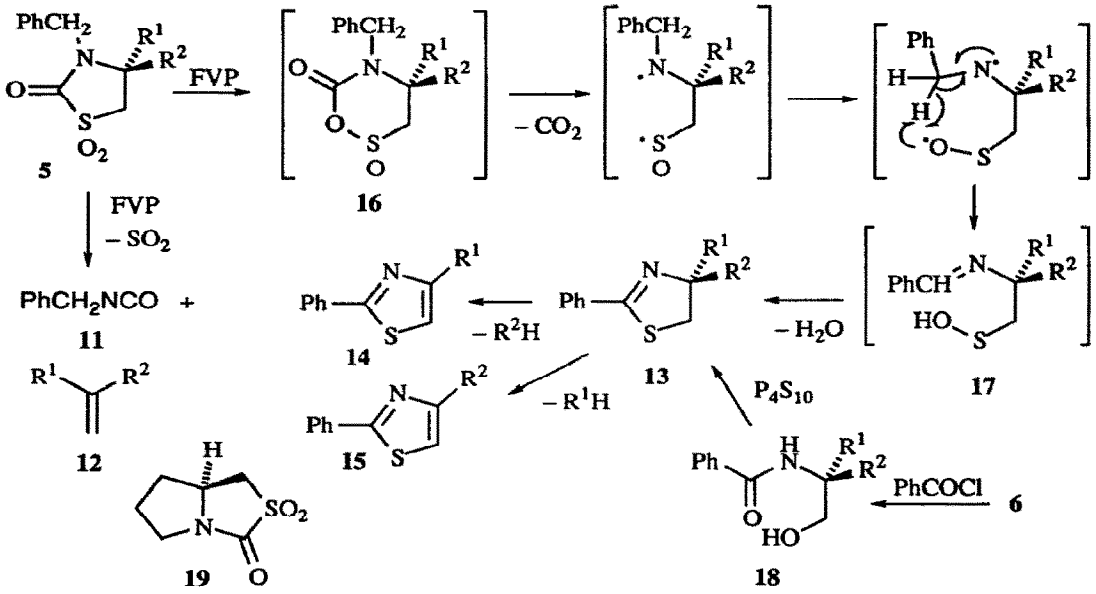


The sulfones were subjected to flash vacuum pyrolysis (FVP) using a conventional flow system with a horizontal furnace tube, operating at 10^{-2}–10^{-3} mmHg and involving contact times of ≈ 1–10 ms. Under these conditions all three examples underwent complete reaction at the relatively mild temperature of 650 °C to give rather complex mixtures of products as shown in Table 1.[11] It is disappointing to note that the desired extrusion of SO_2 does occur but is accompanied by complete fragmentation to give benzyl isocyanate **11** together with alkene **12**. It appears that the extrusion from **5** requires more forcing conditions as compared to **1** such that the β-lactam cannot survive intact. The compounds **5a-c** were also found to be photochemically inert under a variety of conditions. The formation of benzonitrile and biphenyl in all cases is probably due to fragmentation of the $PhCH_2N$ group. Most interesting however is the formation of the 2-phenyl-2-thiazolines **13** and their aromatisation products **14** and **15**. The identity of these unexpected products was demonstrated by comparison with authentic samples of **13** prepared by reaction of **6a-c** with PhCOCl to give **18** followed by cyclisation with P_4S_{10}.[12] Heating **13** with sulfur at 200–210 °C afforded samples of **14c** and **15a,b** identical with the pyrolysis products.

Table 1: Formation of thiazolidinone dioxides **5** and results of FVP

	R^1	R^2	Yield of **9** from **8**, %	Yield of **5** from **9**, %	Products of pyrolysis of **5** at 650 °C, %						
					11	**12**	**13**	**14**	**15**	PhCN	$(PhCH_2)_2$
a	H	Pr^i	36	63	10	12	4	4	4	16	6
b	H	$PhCH_2$	53	67	8	18	3	8	2	7	12
c	Et	H	72	72	24	13	5	—	3	19	10

The mechanism of this unprecedented heterocyclic transformation is believed to involve the sequence of steps shown resulting in the required net loss of CO_2 and H_2O. Ring expansion to the cyclic sulfinic/carbamic anhydride **16**, a process well known in the pyrolysis of cyclic sulfones,[1] allows ready loss of CO_2. Reorganisation of the resulting diradical and intramolecular abstraction of the benzylic CH gives the



imine/sulfenic acid **17** which can then lose water to afford **13**. Overall the process is somewhat reminiscent of the pyrolysis of benzothiophene 1,1-dioxide to give benzothiete,[13] which also involves loss of CO_2 and initial ring expansion.

In an attempt to prevent the fragmentation of **5** to alkene and isocyanate we have now prepared the bicyclic thiazolidinone dioxide **19** from *S*-proline using similar methods to those used for **5** and its FVP which seems more likely to afford a β-lactam will be reported shortly.

Acknowledgement

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8. New compounds gave satisfactory spectroscopic and microanalytical data.
9. This reagent system which is also suitable for convenient high yielding oxidation of a wide variety of other organosulfur compounds will be described in detail elsewhere: Aitken, R. A.; Mesher, S. T. E.; Ross, F. C.; Ryan, B. M. *Synlett.* submitted for publication.
10. Selected physical and spectroscopic data ($CDCl_3$, ^1H 300 MHz, ^{13}C 75 MHz):
9b; m.p. 137–139 °C; $[\alpha]_D^{25}$ –25.8 (*c* 1.60 in CH_2Cl_2); δ_H 7.5–7.2 (8 H, m), 7.1 (2 H, m), 5.85 and 4.20 (2 H, AB pattern, *J* 16, N-CH_2), 4.3–4.15 (1 H, m, 4-H), 3.20 (1 H, half AB pattern of d, *J* 12, 8), 3.15 (1 H, half AB pattern of d, *J* 14, 5), 2.88 (1 H, half AB pattern of d, *J* 12, 10) and 2.85 (1 H, half AB pattern of d, *J* 14, 10); δ_C 196.7, 135.9, 135.4, 129.1 (2 C), 129.0 (2 C), 128.9 (2 C), 128.2, 128.0 (2 C), 127.2, 67.5, 50.7, 36.3 and 32.2.
10b; m.p. 70–71 °C; $[\alpha]_D^{25}$ +11.8 (*c* 0.9 in $CHCl_3$); δ_H 7.4–7.2 (8 H, m), 7.1 (2 H, m), 5.10 and 4.00 (2 H, AB pattern, *J* 16, N-CH_2), 3.80 (1 H, m, 4-H), 3.20–3.05 (2 H, m), 2.95 (1 H, half AB pattern of d, *J* 12, 4) and 2.80 (1 H, half AB pattern of d, *J* 12, 8); δ_C 171.8, 136.4, 136.3, 129.2 (2 C), 128.7 (2 C), 128.6 (2 C), 128.0 (2 C), 127.9, 127.1, 59.5, 46.7, 37.3 and 30.4.
5b; m.p. 157–158 °C; $[\alpha]_D^{25}$ –22.6 (*c* 0.7 in $CHCl_3$); δ_H 7.5–7.3 (8 H, m), 7.1 (2 H, m), 5.15 and 4.20 (2 H, AB pattern, *J* 16, N-CH_2), 3.90 (1 H, m, 4-H), 3.30 (1 H, half AB pattern of d, *J* 16, 6), 3.20 (1 H, half AB pattern of d, *J* 12, 4), 3.05 (1 H, half AB pattern of d, *J* 12, 8) and 2.85 (1 H, half AB pattern of d, *J* 16, 10); δ_C 159.5, 134.7, 133.2, 129.4 (2 C), 129.3 (2 C), 129.2 (2 C), 129.0, 128.5 (2 C), 127.8, 51.7, 47.9, 47.4 and 38.1.
13b; b.p. 220 °C (oven temp.) / 0.1 mmHg; $[\alpha]_D^{25}$ –52.5 (*c* 1.12 in CH_2Cl_2); δ_H 7.9–7.8 (2 H, m), 7.4–7.3 (3 H, m), 7.15 (5 H, m), 5.1–4.7 (1 H, m, 4-H), 3.30 and 3.15 (2 H, AB pattern of d, *J* 10, 8), 3.30 (1 H, half AB pattern of d, *J* 12, 5) and 2.85 (1 H, half AB pattern of d, *J* 12, 9); δ_C 167.0, 138.4, 133.2, 131.0, 129.2 (2 C), 128.3 (6 C), 126.3, 78.4, 40.3 and 37.1.
15b; b.p. 250 °C (oven temp.) / 4 mmHg; δ_H 7.9 (2 H, m), 7.35 (8 H, m), 6.7 (1 H, s) and 4.2 (2 H, s); δ_C 167.5, 157.5, 139.0, 133.9, 129.8, 129.1 (2 C), 128.8 (2 C), 128.5 (2 C), 126.5 (2 C), 114.3 and 38.0.
11. Additional minor products identified included: PhMe, PhCH=NPh and PhCHO in all three cases, Pr^iCHO from **5a**, and EtCHO from **5c**.
12. Full details of the preparation and chemistry of chiral thiazolines **13** will be reported elsewhere: Aitken, R. A.; Armstrong, D. P.; Galt, R. H. B.; Mesher, S. T. E. in preparation.
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