271. Incorporation of Sulfur Dioxide into the Products of Reaction of *Schiff* Bases with Halo- or Alkylthio-ketenes in Liquid SO_2 1)

Preliminary Communication

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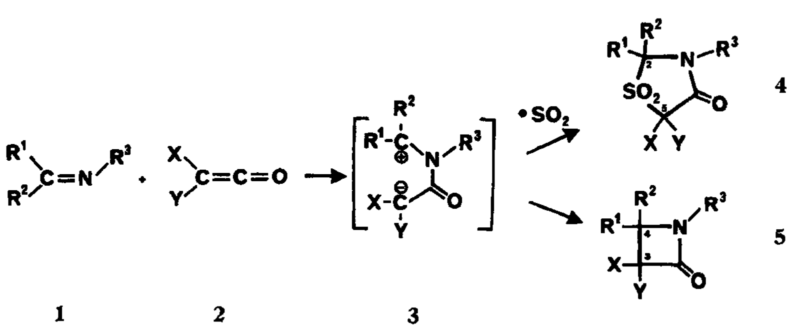
(14. X. 75)

Summary. A simple 'three-component-reaction' between halo- or alkylthio-ketenes, *Schiff* bases and sulfur dioxide, yielding 4-oxo-1,3-thiazolidine-1,1-dioxides **4** in one step, is presented.

In 1967, *Joullie & Gomez* [2] used sulfur dioxide as solvent in their study of the reactions of ketene (**2**, X = Y = H) with imines **1** to obtain azetidin-2-ones **5**. They found, however, that SO_2 participates in the reaction as an active species to give 4-oxo-1,3-thiazolidine-1,1-dioxides **4** (X = Y = H) in good yields 2). This elegant one-step synthesis of **4** suffers from one serious limitation, in that both *in substance* used dialkylketenes [4] as well as alkylketenes generated *in situ* from acid chlorides [5] failed to yield any SO_2-insertion products **4**. During our systematic search we have found so far that only the halo- and some alkylthio-ketenes can enter this reaction. As a common feature, these *in situ* generated ketenes all bear α-carbanion-stabilizing substituents [6] 3).

This communication describes the facile syntheses of **4**, where at least one of the substituents X or Y is halogen (Cl or Br) or alkylthio, and their simple and mild transformation to such derivatives of **4**, where one or both of X and Y are hydrogen atoms or alkyl groups. The latter compounds are – as was mentioned above – inaccessible by direct synthesis in liquid SO_2. For direct comparison of yields, the products of reactions with the same *Schiff* base, benzylideneaniline, are shown in the Table.

Scheme 1



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1) Synthesis and Reactivity of Compounds with Cyclobutane Ring(-s). Part VI. For Part V see [1].

2) Since that original report, various kinds of SO_2-participations in the cycloadditions of ketenes across the C=N double bonds have been reported [3].

3) However, no **4** were formed with difluorketene or with ketenes bearing α-substituents with –M effect (cyanoketene, ethoxycarbonylketene) [5].

2,3-Diphenyl-4-oxo-tetrahydro-1,3-thiazol-1,1-dioxides **4** *and 1,4-Diphenyl-azetidin-2-ones* **5** *obtained from Reaction of Haloketenes* **2a–e** *or Thioalkylketenes* **2f–i** *with Benzylideneaniline* **1** ($R^1 = R^3 = C_6H_5$, R^2 = H) *in Liquid Sulfur Dioxide*

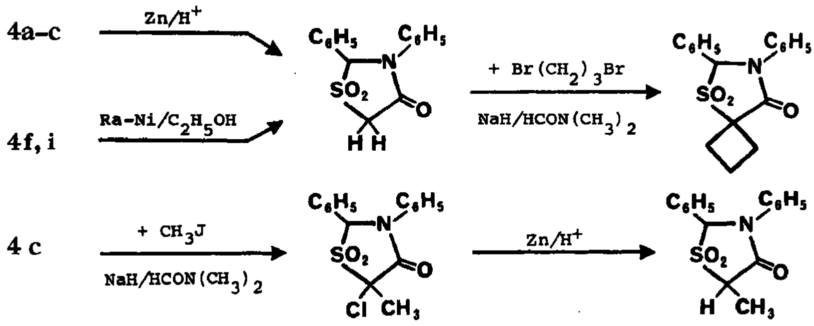
	Ketene **2**		Product yield, % [a]		M.p., °C	
	X	Y	**4**	**5**	**4**	5
a	Cl	Cl	81	–	129–130	–
b	Br	Br	67	–	137–138	–
c	Cl	H	65	–	127–129	–
d	Cl	n-C_4H_9	23	34	133–134	115–116
e	Cl	C_6H_5	14	67	184–185	118–119
f	—$S(CH_2)_2S$—		3	75	183–184	203–204
g	—$S(CH_2)_3S$—		–	69	–	175–176
h	SC_2H_5	SC_2H_5	–	73	–	108–109
i	SCH_3	H	12	37	150–153	143–144 [b]; 114 [c]

[a] Isolated products. [b] 3H,4H-*cis*-isomer; $J_{3,4\,cis}$ = 5.7 Hz. [c] 3H,4H-*trans*-isomer; $J_{3,4\,trans}$ = 2.3 Hz. For coupling constants in azetidin-2-ones, see [7].

In a typical experiment, benzylideneaniline (0.1 mol) and triethylamine (0.11 mol) were dissolved in 100 ml anhydrous SO_2 at –70°. A solution of the α-halo-[4]) or α-alkylthio-acid chloride[5]) in dry CH_2Cl_2 was then added dropwise. After 30 min at –70° and 30 min under SO_2-reflux, excess SO_2 was evaporated, the CH_2Cl_2-solution was extracted with ice-cold water, dried over $MgSO_4$ and concentrated. The residue was purified either by recrystallisation or by chromatography on silica gel.

Cycloadducts **4** and **5** were identified by spectral and chemical means. The IR. spectra of **4** exhibit strong absorption bands at 1685–1710 cm^{-1} (5-ring lactam), and at 1305–1350 and 1120–1140 cm^{-1} (sulfone). **5** show in IR. ($CHCl_3$) a typical β-lactam

Scheme 2



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[4]) Acid chlorides for generating **2a–c, e** are commercially available or described. 2-Chlorohexanoyl chloride (for **2d**) was prepared by chlorination of hexanoylchloride with SO_2Cl_2 (18 h, 70°) in the presence of iodine. Bp. 84–85°/45 Torr; 52% yield.

[5]) 2-Chloroformyl-1,3-dithiolane, b.p. 56–58°/0.015 Torr (for **2f**); 2-chloroformyl-1,3-dithiane [6], b.p. 65–69°/0.01 Torr, m.p. 46–47° (for **2g**) and di(ethylthio)acetylchloride, b.p. 81–84°/0.2 Torr (for **2h**) were prepared by treatment of the corresponding acids with oxalyl chloride. The acids were conveniently obtained by alkaline hydrolysis of their ethyl esters, which are commercialy available (*Fluka AG*). Overall yields were 67–86%. (Methylthio)acetyl chloride, b.p. 44–46°/12 Torr, was prepared by treatment of (methylthio)acetic acid [8] with oxalyl chloride.

carbonyl absorption at 1748–1780 cm^{-1}. In NMR. ($CDCl_3$), **4** and **5** are well characterized by the low-field singlets of H–C(2) in **4** ($\delta = 6.25 \pm 0.25$ ppm) and H–C(4) in **5** ($\delta = 5.1 \pm 0.3$ ppm).

4, halogenated in position 5, are quantitatively dehalogenated on brief treatment with zink in acetic acid or in an ethanol/ether/NH_4Cl system; *e.g.* **4a–c** → **6** and **8** → **9**. Similarly, the desulfurization of **4f** and **4i** by *Raney*-Nickel in ethanol affords the known [4] compound **6**.

6 is readily dialkylated in position 5, as illustrated for the formation of the spirocompound **7** (mp. 137–138°). Attempts to monoalkylate **6** led only to a mixture of mono- and di-alkylated products. However, monoalkylation of **4c** by alkyliodides, followed by reductive dehalogenation yields pure monoalkylderivatives in good yields, as shown for **4c** → **8** (two diastereoisomers with m.p. 148–149° and 138–139°, resp.) and **8** → **9** (glassy solid). We suggest that the above methods may be convenient general synthetic routes to halogen-free 4-oxo-1,3-thiazolidine-1,1-dioxides such as **6**, **7** and **9**. In the special case of **6**, its synthesis *via* **4a** allows one to avoid the handling of gaseous ketene.

Compounds **4** are thermally unstable above their m.p.-temperatures. For example **4a** loses SO_2 quantitatively in the melt at 150° in 5 min to give **5a** ($R^1 = R^3 = C_6H_5$; $R^2 = H$; $X = Y = Cl$). In solution, the rate of SO_2-extrusion from **4a** is solvent-dependent: at 95°, $t^{1/2} = 16$ min in nitromethane, whereas in toluene $t^{1/2} = 6$ h. In the presence of a large molar excess of water in CH_3NO_2, benzaldehyde and N-phenyl-dichloracetanilide were formed up to a maximum of 35% yield, thus indicating that the ring contraction **4** → **5** proceeds, at least in part, through the 1,4-dipolar intermediate **3**. In separate control experiment *no* benzaldehyde and N-phenyl-dichloracetanilide were formed from **5a** in nitromethane/water solution at 95°.

Further examples of application of the above reactions which will provide more insight into their scope will be presented in a forthcoming full paper in this journal.

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