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THE KINETIC STUDY ON THE DESULFURIZATION OF 4,5-TRANS- AND 4,5-CIS-5-PHENYLTHIOOXAZOLIDIN-2-ONES VIA CYCLIC CARBAMOYLOXYRADICAL SPECIES

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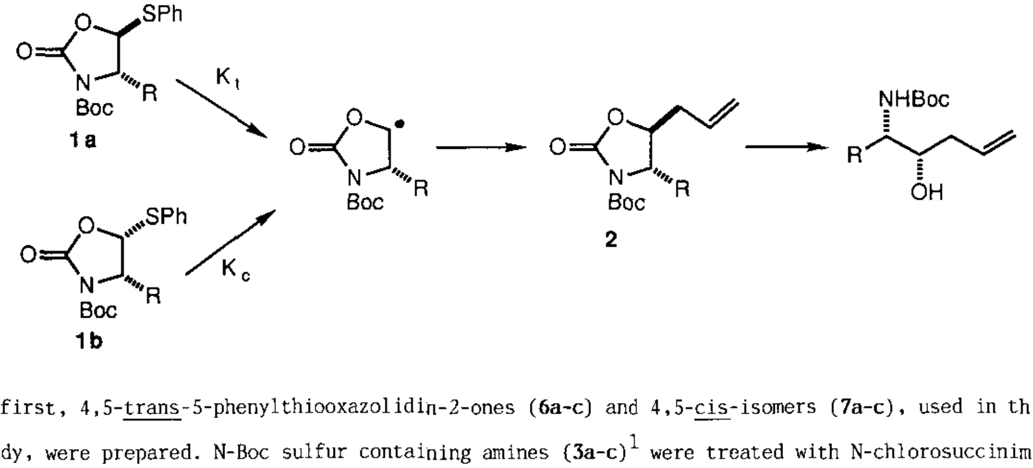
Abstract —— The relative rate for generation of cyclic carbamoyloxy radicals from 4,5-trans-5-phenylthiooxazolidin-2-ones (**6a-c**) and cis-isomers (**7a-c**) was determined and trans-isomers were found to be about six times as reactive as cis-isomers by comparison with their half life.

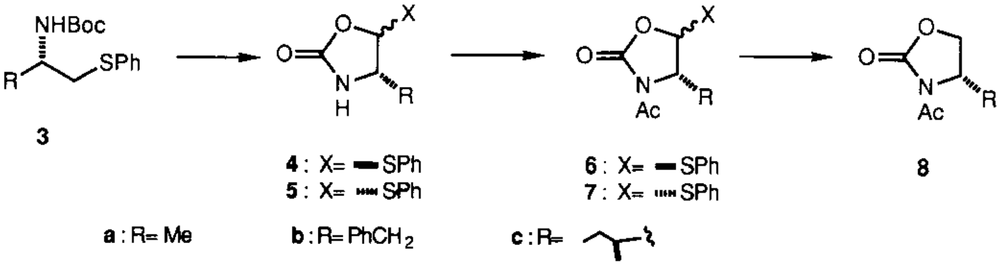
In the previous paper,[1] we reported a highly diastereoselective synthesis of 4,5-trans-5-allyloxazolidin-2-ones (**2**), protective form of threo 2-amino alcohols, by the photo-initiated radical allylation reaction[2] of 5-phenylthiooxazolidin-2-ones (**1**) (Scheme 1). The interesting observation in this reaction was that the rate for the formation of the products from cis-isomers was comparatively slower than that from the trans-isomers. We further studied this reaction to determine the relative rate for generation of radical species (K_t/K_c in Scheme 1). The results of our studies were described in this paper.

Scheme 1



At first, 4,5-trans-5-phenylthiooxazolidin-2-ones (**6a-c**) and 4,5-cis-isomers (**7a-c**), used in this study, were prepared. N-Boc sulfur containing amines (**3a-c**)[1] were treated with N-chlorosuccinimide and successively the chlorination products were cyclized with $SnCl_4$ at -78°C. When the reaction temperature was raised to room temperature (20 min), the 4,5-trans-isomers (**4a-c**) were obtained as single products.[1] The method for giving the cis-isomers was devised. Upon quenching the reaction with Et_3N at -78°C within 5 min, cis-isomers (**5a-c**) were obtained accompanied with **4a-c**. Since it was difficult to separate **5a-c** from **4a-c** as a pure state, these mixtures were subsequently subjected to N-acetylation. The mixture of **4** and **5** was treated with Ac_2O in the presence of Et_3N and catalytic amount of 4-dimethylaminopyridine in THF to give the corresponding 3-acetyl derivatives (**6a**/**7a**, **6b**/**7b**, **6c**/**7c**), respectively. Separation of **7a-c** from **6a-c** was easily achieved by column chromatography on silica gel. Each of these (0.5 M solution in C_6D_6) was subjected to photolysis (300 W Hg lamp) in the presence of Bu_3SnH (2 equiv.) at 20°C by monitoring with ^{1}H-nmr spcetra. Desulfurization of the **6a-c** was found to proceed smoothly to give **8a-c** and its half life was determined to be about 1 h. However, **7a-c** are considerably less reactive toward a generation of radical species and its half life was determined to be about 6 h. It was also found that the reaction rate was not affected by the size of the substituent at the 4-position. Thus, the trans-isomers are found to be about six times as reactive as the corresponding cis-isomers. The difference in the reactivity between each isomers could be accounted for by the rather difficulty for the approach of stanyl radical to phenylthio group in the case of cis-isomers because of steric hindrance.

Scheme 2



EXPERIMENTAL SECTION

General: Melting points are not corrected. ^{1}H-Nmr spcetra were taken with Bruker AM-400 (400 MHz) in $CDCl_3$ unless otherwise stated. For the monitoring of the reaction rate, Varian EM-390 (90 MHz) was used. Mass Spectra were taken with Hitachi RMU-7L spectrometer. The optical rotations were measured with JASCO DIP-4.

General Procedure for the Preparation of 5-Phenylthiooxazolidin-2-ones (**4** and **5**) To a stirred solution of N-Boc amines (**3a-c**)^1 (0.01 mol) in CCl_4 (35 ml) was added N-chlorosucccinimide (1.86 g, 14 mmol) in small portions at room temperature. The stirring was continued for 2 h at the same temperature, and the solvent was evaporated after removal of the precipitate by filtration. To a solution of the remaining residue in CH_2Cl_2 (35 ml) was added $SnCl_4$ (3.64 g, 14 mmol) at -78°C. After 5 min, Et_3N (5 ml) was added to the reaction mixture at the same temperature and then diluted with water. The mixture was filtered through celite pad and extracted with $CHCl_3$ and the extract was washed with water and evaporated. The resulting residue was chromatographed on silica gel (20 g). Elution with hexane-AcOEt (4:1) afforded a mixture of **4** and **5** which was used for the following reaction.

General Procedure for a Preparation of 3-Acetyl-5-phenylthiooxazolidin-2-ones (**6**,**7**) To a stirred mixture of **4** and **5** (10 mmol), Et_3N (10 mmol), 4-dimethylaminopyridine (122 mg, 1 mmol) and THF (20 ml) were added Ac_2O (2 g, 20 mmol) at room temperature. After the mixture was stirred for 1 h, the solvent was evaporated. The residue was extracted with $CHCl_3$ and extract was washed with water, dried (Na_2SO_4) and evaporated. The resulting residue was chromatographed on silica gel (35 g) by using hexan/AcOEt (7:1) to give **6** and successively **7**. Yields (based on **3**), representative physical data and microanalysis are as follows.

6a: 30 % yield, an oil, $[\alpha]_D$ -269.96° (c 1.0, chloroform), ms m/z 251 (M^+), exact ms m/z 251.0596, Calcd for $C_{12}H_{13}NO_3S$: 251.0614, ^{1}H-nmr ($CDCl_3$) δ 7.59-7.55 (2H, m), 7.39-7.34 (3H, m), 5.31 (1H, d, J=2.92 Hz), 4.42 (1H, dq, J=2.92, 6.42 Hz), 2.31 (3H, s), 1.46 (3H, d, J=6.42 Hz).

7a: 30 % yield, mp 117-119°C, $[\alpha]_D$ +256.7° (c 1.0, chloroform), ms m/z 251 (M^+), ^{1}H-nmr ($CDCl_3$) δ 7.57-7.53 (2H, m), 7.37-7.34 (3H, m), 5.80 (1H, d, J=6.12 Hz), 4.77 (1H, dq, J=6.12, 6.50 Hz), 2.51 (3H, s), 1.51 (3H, d, J=6.50 Hz). Anal. Calcd for $C_{12}H_{13}NO_3S$: C, 57.35; H, 5.21; N, 5.57. Found: C, 57.35; H, 5.25; N, 5.52).

6b: 36 % yield, mp 79-80°C, $[\alpha]_D$ -194.5° (c 1.0, chloroform), ms m/z 327 (M^+), ^{1}H-nmr ($CDCl_3$) δ 7.45-7.43 (1H, m), 7.35-7.30 (8H, m), 7.15 (1H, br d, J=6.76 Hz), 5.44 (1H, d, J=2.36 Hz), 3.28 (1H, dd, J=3.59, 13.92 Hz), 2.85 (1H, dd, J=9.00, 13.92 Hz), 2.34 (3H, s). Anal. Calcd for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.23; N, 4.28. Found: C, 66.00; H, 5.24; N, 4.21.

7b: 25 % yield, mp 84-86°C, $[\alpha]_D$ +107.35° (c 1.0, chloroform), ms m/z 327 (M^+), ^{1}H-nmr ($CDCl_3$) δ 7.53-7.50 (2H, m), 7.36-7.24 (5H, m), 5.79 (1H, d, J=6.84 Hz), 4.99 (1H, ddd, J=3.91, 6.84, 7.45 Hz), 3.24 (1H, dd, J=7.45, 14.54 Hz), 3.21 (1H, dd, J=3.91, 14.54 Hz), 2.43 (3H, s). Anal. Calcd for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.23; N, 4.28. Found: C, 65.83; H, 5.29; N, 4.22.

6c: 39 % yield, an oil, $[\alpha]_D$ -258.3° (c 0.9, chloroform), ms m/z 293 (M^+), exact ms m/z 293.1094, Calcd for $C_{15}H_{19}NO_3S$: m/z 293.1085, ^{1}H-nmr ($CDCl_3$) δ 7.59-7.57 (2H, m), 7.39-7.37 (3H, m), 5.47 (1H, d, J=2.51 Hz), 4.43 (1H, dd, J=2.51, 3.69 Hz), 2.31 (3H, s), 1.68-1.45 (2H, m), 1.25-1.12 (1H, m), 0.96-0.92 (6H, m).

7c: 26 % yield, mp 69-70°C, $[\alpha]_D$ +152.05° (c 0.5, chloroform), ms m/z 293 (M^+), ^{1}H-nmr ($CDCl_3$) 7.56-7.53 (2H, m), 7.36-7.34 (3H, m), 5.79 (1H, d, J=6.92 Hz), 4.77 (1H, dd, J=2.55, 6.92 Hz), 2.51 (3H, s), 2.14-2.02 (1H, m), 1.82-1.72 (1H, m), 1.39-1.28 (1H, m), 1.11 (3H, d, J=7.07 Hz), 0.99 (3H, t, J=7.37 Hz). Anal. Calcd for $C_{18}H_{19}NO_3S$: C, 61.41; H, 6.53; N, 4.77. Found: C, 61.39; H, 6.55; N, 4.67.

Desulfurization of 6 and 7 A mixture of 0.5 M solution of **6** (or 7) in C_6D_6, 2 equiv. of n-Bu_3SnH, Me_4Si in a sealed nmr tube was irradiated through pyrex filter with 300 W Hg lamp under standing at 20°C in a incubator. The reaction rate was monitored by the observation of the disapperance of the signals due to 5-H and $NCOCH_3$ of **6** and **7** in their ^1H-nmr (90 MHz). Thus, the half life for conversion of **6a-c** to **8a-c** was determined as about 1 h and that of **7a-c** to **8a-c** was determined as about 6 h.

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