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Isomerization of 3-pentyl-5-methyl-γ-sultine with Iodine

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Abstract: Isomerization of 3-pentyl-5-methyl-1,2-oxathiolane-2-oxide in the presence of iodine is described. A mechanistic pathway which involves a ring-opening reaction by cleavage of the C-O bond with or without epimerization at the sulfur atom is proposed, consistent with the stereochemical investigations. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Key words: iodine, sultines, 1,2-oxathiolane-2-oxides, isomerization, epimerization.

Recently we have described a new synthesis of sultines via a disulfide intermediate with sodium metaperiodate oxidation of sulfanyl-alcohols[1]. We showed the presence of iodine coming from the reduction of $NaIO_4$. Surprisingly, we have observed that trans isomer of the 3-propyl-1,2-oxathiolane-2-oxide and 3,3,5-trimethyl-1,2-oxathiolane-2-oxide was partly converted into the cis one, when the sultines remained in the reaction medium. It is important to note that when iodine present in the reaction medium is reduced by a solution of sodium thiosulfate, the ratio of isomers is stable. These results prompted us to investigate a possible mechanism for the isomerization of γ-sultines.

For this purpose, we examined the behaviour of the 3-pentyl-5-methyl-1,2-oxathiolane-2-oxide which may exist in four racemic forms, distinguished on the basis of their NMR spectra after separation by silica-gel column chromatography. As a syn-diaxial orientation between a proton and a sulfinyl group results in significant downfield shift for the proton[2-5], the shielding of the proton H_5 in isomers A and C (4.6 and 4.8 ppm respectively) may indicate that the SO bond should lie *trans* to the proton H_5 whereas the deshielding of the proton H_5 in isomers B and D (5.1 and 5.2 ppm respectively) may indicate that the SO bond should lie *cis* to the proton H_5. From NOESY experiments, we can conclude that the ring substituents are in *cis* position in sultines A and D and in *trans* position in sultines B and C. According to Dodson et al.[2] who previously reported the isomerization of the *trans*-3,5-diphenyl-1,2-oxathiolane-2-oxide to the *cis*-3,5-diphenyl-1,2-oxathiolane-2-oxide, we suggest that racemics A and D exist in half-chair conformation with both substituents pseudoequatorial whereas racemics B and C exist in envelope conformation with pseudoequatorial pentyl group and pseudoaxial methyl group.

In order to confirm the role played by iodine, we treated the 3-pentyl-5-methyl-1,2-oxathiolane-2-oxide, synthesized with hydrogen peroxide or 3-chloroperoxybenzoic acid oxidation of 4-sulfanyl-nonan-2-ol, with I_2 in acetonitrile and in pentane solution, respectively, at room temperature. We observed the same evolution than with sodium metaperiodate but in shorter time (Table 1). In contrast, when the sultine is mixed with KI in aqueous acetonitrile, no isomerization reaction took place. These results indicate that only iodine and not iodide is directly involved in the mechanism of isomerization and that a polar medium is not necessary for the reaction.

Table 1

Time	Ratio of racemics (%)[a]			
	A	B	C	D
t_o	15	18	26	41
t_1: 1 hour	27	26	18	29
t_2: 1 day	34	25	14	27
t_3: 3 days	39	25	13	23
t_4: 6 days	41	24	13	22

a: ratio established by G.C

On the basis of these observations and configurational assigments, a detailed mechanism of isomerization can be proposed: initial nucleophilic attack by the non bonding pair of electrons on sulfur atom at iodine followed by cleavage of the cyclic C-O bond, a reaction known to proceed with some sultines in the presence of halogens[6,7], affords ring-opened intermediate X. Due to steric hindrance between iodine and the pentyl group in *cis* position, a

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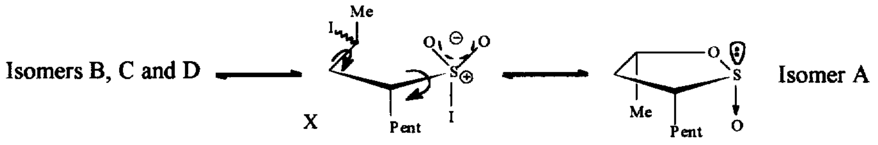
rotation around the C-S bond may occur, except the isomer B for which iodine and the pentyl substituent are in *trans* position. At the same time, a rotation around the C(4)-C(5) bond may take place leading to the inversion of the C(5) configuration. An intramolecular nucleophilic attack of the sulfinyl group causes ring closure to afford the isomer A (Scheme 1). According to this mechanism, the isomers C and D evolve towards the isomers A and B then, this latter rearranges to the A one. This is in agreement with experimental results. However, none of the ring-opened intermediates could be isolated.

Scheme 1



Conclusion

A mechanistic pathway for the unexpected isomerization of the 3-pentyl-5-methyl-1,2-oxathiolane-2-oxide in which iodine plays a key role is proposed. Study of conformational energy of the four isomers and ring-opened intermediates, performed at the B3LYP/6-31G*[8] level of calculation is in progress to explain the evolution towards the isomer A.

References and Notes:

1. Yolka, S.; Fellous, R.; Lizzani-Cuvelier, L.; Loiseau, M. *Tetrahedron Lett.* **1998**, *39*, 991-992.
2. Dodson, R. M.; Hammen, P. D.; Davis, R. A. *J. Org. Chem.* **1971**, *36*, 2693-2698.
3. Sharma, N. K.; De Reinach-Hirtzbach, F.; Durst, T. *Can. J. Chem.* **1976**, *54*, 3012-3025.
4. Haasnoot, C. A. G.; Liskamp, R. M. J.; Van Dael, P. A. W.; Noordik, J. H.; Ottenheijm, H. C. J. *J. Am. Chem. Soc.* **1983**, *105*, 5406-5414.
5. Holland, H. L.; Munoz, B. *Can. J. Chem.* **1988**, *66*, 2299-3303.
6. Liskamp, R. M. J.; Zeegers, H. J. M.; Ottenheijm, H. C. J. *J. Org. Chem.* **1981**, *46*, 5408-5413.
7. King, J. F.; Skonieczny, S.; Khemani, K. C.; Stothers, J. B. *J. Am. Chem. Soc.* **1983**, *105*, 6514-6515.
8. Becke, A. D. *J.Chem.phys.* **1993**, *98*, 5648-5652.

9 Spectroscopic data for the four isomers of the 3-pentyl-5-methyl-1,2-oxathiolane-2-oxide are given below. ^{1}H and ^{13}C{^{1}H} NMR were run on Bruker AC-200 spectrometer with CDCl$_3$ as solvent.

A isomer: (3,5)-*cis*-3-pentyl-5-methyl-1,2-oxathiolane (2,3)-*cis*-2-oxide:
^{1}H NMR: δ (ppm) 4.70-4.50 (m, 1H), 3.05-2.85 (m, 1H), 2.38-2.22 (m, 1H), 1.92 (td, 1H, ^{2}J=^{3}J=12.7Hz, ^{3}J=9.9Hz), 1.81-1.16 (m, 8H), 1.50 (d, 3H, ^{3}J=6.2Hz), 0.84 (t, 3H, ^{3}J=7.0Hz); ^{13}C{^{1}H} NMR: δ (ppm) 86.9 (CH), 69.7 (CH), 35.9 (CH$_2$), 31.8 (CH$_2$), 28.1 (CH$_2$), 26.8 (CH$_2$), 23.5 (CH$_3$), 22.5 (CH$_2$), 14.0 (CH$_3$); MS (70 eV): 190 (M$^+$, <1), 172 (4), 146 (3), 125 (9), 92 (11), 83 (49), 69 (100), 55 (60), 41 (34).

B isomer: (3,5)-*trans*-3-pentyl-5-methyl-1,2-oxathiolane (2,3)-*cis*-2-oxide:
^{1}H NMR: δ (ppm) 5.19-5.00 (m, 1H), 3.17-2.94 (m, 1H), 2.28 (td, 1H, ^{2}J=^{3}J=12.6Hz, ^{3}J=8.2Hz), 1.93 (ddd, 1H, ^{2}J=12.6Hz, ^{3}J=7.7Hz, ^{3}J=2.7Hz), 1.87-1.12 (m, 8H), 1.28 (d, 3H, ^{3}J=6.4Hz), 0.87 (t, 3H, ^{3}J=7.0Hz); ^{13}C{^{1}H} NMR: δ (ppm) 83.8 (CH), 67.4 (CH), 34.4 (CH$_2$), 31.7 (CH$_2$), 28.1 (CH$_2$), 26.9 (CH$_2$), 22.3 (CH$_2$), 21.4 (CH$_3$), 13.9 (CH$_3$); MS (70 eV): 190 (M$^+$, <1), 172 (2), 146 (2), 125 (12), 92 (17), 83 (53), 69 (100), 55 (64), 41 (36).

C isomer: (3,5)-*trans*-3-pentyl-5-methyl-1,2-oxathiolane (2,3)-*trans*-2-oxide:
^{1}H NMR: δ (ppm) 4.84-4.66 (m, 1H), 3.32-3.13 (m, 1H), 2.40 (ddd, 1H, ^{2}J=13.2Hz, ^{3}J=9.9Hz, ^{3}J=6.6Hz), 2.11 (ddd, 1H, ^{2}J=13.2Hz, ^{3}J=5.8Hz, ^{3}J=1.2Hz), 1.53 (d, 3H, ^{3}J=6.2Hz), 1.50-1.11 (m, 8H), 0.85 (t, 3H, ^{3}J=6.6Hz); ^{13}C{^{1}H} NMR: δ (ppm) 87.0 (CH), 73.1 (CH), 35.7 (CH$_2$), 31.5 (CH$_2$), 27.6 (CH$_2$), 27.1 (CH$_2$), 23.7 (CH$_3$), 22.4 (CH$_2$), 14.0 (CH$_3$); MS (70 eV): 190 (M$^+$, 2), 172 (<1), 146 (<1), 125 (13), 92 (17), 83 (54), 69 (100), 55 (72), 41 (42).

D isomer: (3,5)-*cis*-3-pentyl-5-methyl-1,2-oxathiolane (2,3)-*trans*-2-oxide:
^{1}H NMR: δ (ppm) 5.25-5.04 (m, 1H), 3.18-2.98 (m, 1H), 2.56 (ddd, 1H, ^{2}J=12.7Hz, ^{3}J=7.5Hz, ^{3}J=5.4Hz), 1.89-1.58 (m, 2H), 1.41 (d, 3H, ^{3}J=5.6Hz), 1.40-1.13 (m, 7H), 0.85 (t, 3H, ^{3}J=6.9Hz); ^{13}C{^{1}H} NMR: δ (ppm) 83.6 (CH), 76.9 (CH), 38.8 (CH$_2$), 31.4 (CH$_2$), 30.5 (CH$_2$), 27.8 (CH$_2$), 22.3 (CH$_2$), 20.0 (CH$_3$), 13.9 (CH$_3$); MS (70 eV): 190 (M$^+$, 1), 146 (<1), 125 (15), 92 (17), 83 (55), 69 (100), 55 (71), 41 (40).