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Can α-sultone exist as a chemical species? First experimental implication for intermediacy of α-sultone

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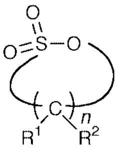
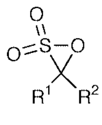
The treatment of 2,4,6-trimethylpyridine *N*-oxide 8 with $BnSO_2Cl$ and Et_3N in the presence of various olefins afforded unexpected γ-sultones 10 along with 2,4,6-trimethylpyridine 9, *via* the possible generation and/or intermediacy of an α-sultone 2 as a new reactive intermediate.

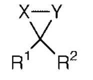
Sultones **1** are the internal esters of hydroxy sulfonic acids and are the sulfur analogs of lactones. Since the term 'sultone' was first introduced into the literature by Erdmann in 1888,[1] there have been many new developments in sultone chemistry,[2] including industrial applications, biological properties and the current mechanistic research into the role of β-sultones in olefin sulfonation.[3,4] However, most of the sultones mentioned above have been restricted to four- to seven-membered rings. Can the α-sultone **2** exist as a chemical species? To the best of our knowledge, the description of an α-sultone has never been reported in the literature. On the other hand, S- and/or O-containing three-membered ring compounds such as **3–5** have attracted recent interest as labile reactive intermediates in organic chemistry.[5] From the viewpoints of labile reactive intermediates, the chemistry of small rings containing two heteroatoms and organosulfur chemistry as well as sultone chemistry, the question of whether α-sultone **2** can exist as a chemical species or not is a very stimulating and interesting subject in organic chemistry. Here we suggest the possibility of the generation and/or intermediacy of α-sultones as new reactive intermediates for the first time.



1 $n = 2–5$

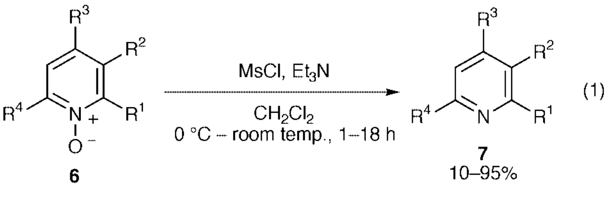


2 α-sultone



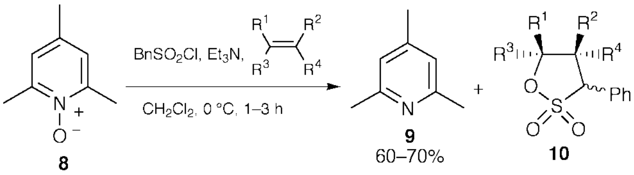
3 X = S, Y = O
4 X = Y = O
5 X = Y = S

The reason why we suspected that the α-sultone might be generated as a reactive intermediate originated from an unexpected phenomenon. In the course of our recent synthetic studies on macrocyclic marine alkaloids, halicalmines A and B,[6] it was determined that an excess of MsCl resulted in the deoxygenation of pyridine *N*-oxides **6** under standard mesylation conditions (MsCl, Et_3N, CH_2Cl_2) without chlorination of the pyridine nucleus [eqn. (1)].[7] The problem is the reaction mechanism of these unusual deoxygenations. After many unsuccessful experiments, products, which are very significant for deducing the reaction mechanism, have been trapped. The treatment of 2,4,6-trimethylpyridine *N*-oxide **8** with 7 equiv. of $BnSO_2Cl$ and 9 equiv. of Et_3N in the presence of 30 equiv. of 2,3-dimethylbut-2-ene afforded γ-sultone **10** ($R^1 = R^2 = R^3 = R^4 = Me$) in 21% yield as an isolable and identifiable product along with deoxygenated 2,4,6-trimethylpyridine **9** (entry 1 in Table 1).† How can the production of γ-sultone **10** be explained?



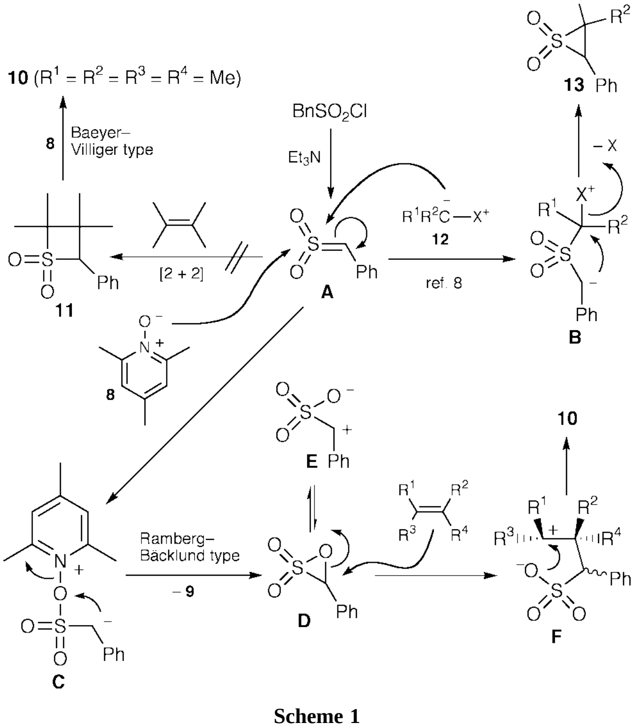
Possible reaction pathways leading to the γ-sultone **10** are depicted in Scheme 1. The generation of sulfenes by treating

Table 1 Production of γ-sultones **10** in the presence of several olefins



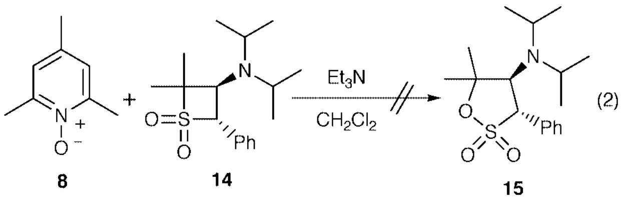
Entry	Olefin	Yield of $\mathbf{10}^a$ (%)	α-Ph:β-Ph
1	$R^1 = R^2 = R^3 = R^4 = Me$	21	—
2	$R^1 = R^2 = R^3 = Me, R^4 = H$	26	60:40^b
3	$R^1 = R^2 = Me, R^3 = R^4 = H$	36	35:65^b
4	$R^1 = R^2 = (CH_2)_6, R^3 = R^4 = H$	40	45:55^c

^{a} Isolated yield. ^{b} Ratios were determined by ^1H NMR integration of the mixture. ^{c} Ratio was based on the isolated yields.



Scheme 1

alkanesulfonyl chloride derivatives possessing an α-hydrogen with triethylamine is a well-established process in sulfene chemistry.[8] The formation of thietane 1,1-dioxide **11**[9] by [2 + 2] cycloaddition between the sulfene intermediate **A** and 2,3-dimethylbut-2-ene and the subsequent Baeyer–Villiger type oxidation of **11** with *N*-oxide **8** may be considered as one possibility. This reaction pathway, however, appears to be ruled out, because the thietane 1,1-dioxide **11** could not be produced in the reaction of $BnSO_2Cl$ and Et_3N with 2,3-dimethylbut-2-ene in the absence of the *N*-oxide **8**. Furthermore, treatment of thietane 1,1-dioxide **14**‡ with *N*-oxide **8** in the presence of Et_3N in CH_2Cl_2 did not give γ-sultone **15**, but resulted in quantitative recoveries of **8** and **14** [eqn. (2)].



On the other hand, it is also well known that the reaction of sulfenes with diazoalkanes (X = N_2) and phosphonium (X = PPh_3), sulfonium (X = SR^3R^4) and sulfoxonium (X = SOR^3R^4) ylides **12** provides episulfones **13** *via* elimination of the neutral leaving group X from the intermediary adduct **B**.[8] Therefore, another possible reaction pathway closely related to this episulfone route may be more plausible to explain the production of γ-sultone **10**. The similar attack of the *N*-oxide **8** on the sulfur atom in the sulfene intermediate **A** may generate α-sultone **D** through the ring-closing reaction[10] such as the Ramberg–Bäcklund type[11] in the adduct **C** together with liberation of 2,4,6-trimethylpyridine **9**. The α-sultone **D** is postulated to be highly labile for the following reasons: (i) an intrinsic ring strain in the three-membered rings; (ii) a large polarization of the C–O bond which is characteristic of sulfonates and makes them good leaving groups; and (iii) the presence of carbon geminally disubstituted by two kinds of heteroatoms (oxygen and sulfur). Therefore, the alternative zwitterionic structure **E**, which is produced by spontaneous cleavage of the highly strained and polarized C–O bond, may then predominate over the α-sultone structure **D**. Finally, the interaction of α-sultone **D** or zwitterion **E** with 2,3-dimethylbut-2-ene could lead to the γ-sultone **10** ($R^1 = R^2 = R^3 = R^4 =$ Me) by way of the cationic intermediate **F**.

The γ-sultones **10** were also obtained as stereoisomeric mixtures§ in the presence of olefins other than 2,3-dimethylbut-2-ene (entries 2–4). In the case of 2-methylbut-2-ene, the observation of only one regioisomeric γ-sultone **10** ($R^1 = R^2 = R^3 =$ Me, $R^4 =$ H) supports the intervention of the cationic intermediate **F** (tertiary *vs.* secondary). In entry 3, the fact that the stereochemistry of *cis*-but-2-ene was retained in the γ-sultone **10** ($R^1 = R^2 =$ Me, $R^3 = R^4 =$ H) may imply that in the carbocation **F** the ring-closure is much faster than the C–C single bond rotation. It is also of interest to note that yields of γ-sultones **10** reflect the reactivities (strain and steric hindrance) of the olefins examined.

In conclusion, we have proposed the possible generation and/or intermediacy of α-sultone **2** as a new chemical species for the first time in organic chemistry. Clarification of the detailed reaction mechanism for the production of γ-sultones **10** and determination of direct evidence for the α-sultone are in progress.

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Notes and references

† All new compounds were satisfactorily characterized using ^1H and ^{13}C NMR, IR, MS and HRMS spectra and also by elemental analyses whenever possible. *Selected data* for **10** ($R^1 = R^2 = R^3 = R^4 =$ Me): mp 190.5–191.5 °C; δ_H (400 MHz, $CDCl_3$) 7.56–7.48 (2H, m), 7.46–7.36 (3H, m), 4.52 (1H, s), 1.68 (3H, s), 1.49 (3H, s), 1.17 (3H, s), 0.97 (3H, s); δ_C (100 MHz, $CDCl_3$) 131.3, 129.2, 128.4, 127.9, 92.9, 70.6, 48.3, 24.2, 23.4, 22.1, 19.1; $\nu_{max}(CHCl_3)/cm^{-1}$ 2995, 1450, 1338, 1172, 1152, 1130, 1109, 940, 894, 835; *m/z* (EI-MS) 254 (M^+, 10%), 132 (100), 117 (67), 91 (41), 84 (54) (EI-HRMS: calc. for $C_{13}H_{18}O_3S$ (M^+), 254.0976; found, 254.0973) (Calc. for $C_{13}H_{18}O_3S$: C, 61.39; H, 7.13. Found: C, 61.46; H, 7.07%).

‡ Thietane 1,1-dioxide **14**, prepared according to the procedure of ref. 9(*b*), was subjected to the control experiment instead of the inaccessible **11**.

§ The relative stereochemistries in γ-sultones **10** were unambiguously assigned by the diagnostic coupling constants and NOE experiments in their ^1H NMR spectra.

1 H. Erdmann, *Liebigs Ann. Chem.*, 1888, **247**, 306.
2 For reviews, see: A. Mustafa, *Chem. Rev.*, 1954, **55**, 195; D. W. Roberts and D. L. Williams, *Tetrahedron*, 1987, **43**, 1027.
3 J. L. Boyer, B. Gilot and J.-P. Canselier, *Phosphorus Sulfur*, 1984, **20**, 259; W. A. Thaler and C. duBreuil, *J. Polym. Sci.*, 1984, **22**, 3905; H. Cerfontain, J. B. Kramer, R. M. Schonk and B. H. Bakker, *Recl. Trav. Chim. Pays-Bas*, 1995, **114**, 410 and references cited therein.
4 D. W. Roberts, D. L. Williams and D. Bethell, *J. Chem. Soc., Perkin Trans. 2*, 1985, 389; D. W. Roberts, P. S. Jackson, C. D. Saul and C. J. Clemett, *Tetrahedron Lett.*, 1987, **28**, 3383; J. Haller, B. R. Beno and K. N. Houk, *J. Am. Chem. Soc.*, 1998, **120**, 6468; J. O. Morley, D. W. Roberts and S. P. Watson, *J. Chem. Soc., Perkin Trans. 2*, 1999, 1819.
5 R. W. Murray and M. Singh, in *Comprehensive Heterocyclic Chemistry II*, ed. A. R. Katritzky, C. W. Rees and E. F. V. Scriven, Pergamon, Oxford, 1996, vol. 1A, p. 429; W. Adam and S. Weinkötz, *Chem. Commun.*, 1996, 177; R. Huisgen, G. Mloston, K. Polborn and F. Palacios-Gambra, *Liebigs Ann./Rec.*, 1997, 187; A. Kirschfeld, S. Muthusamy and W. Sander, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2212; A. Ishii, T. Akazawa, T. Maruta, J. Nakayama, M. Hoshino and M. Shiro, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 777.
6 Y. Morimoto and C. Yokoe, *Tetrahedron Lett.*, 1997, **38**, 8981; Y. Morimoto, C. Yokoe, H. Kurihara and T. Kinoshita, *Tetrahedron*, 1998, **54**, 12 197.
7 Y. Morimoto, H. Kurihara, C. Yokoe and T. Kinoshita, *Chem. Lett.*, 1998, 829.
8 For reviews, see: G. Opitz, *Angew. Chem., Int. Ed. Engl.*, 1967, **6**, 107; N. H. Fischer, *Synthesis*, 1970, 393; J. F. King, *Acc. Chem. Res.*, 1975, **8**, 10.
9 For the formation of the thietane 1,1-dioxides from sulfenes and nucleophilic olefins such as enamines and enol ethers, see: (*a*) W. E. Truce and J. R. Norell, *J. Am. Chem. Soc.*, 1963, **85**, 3231; (*b*) W. E. Truce and J. F. Rach, *J. Org. Chem.*, 1974, **39**, 1109.
10 The readiness for intramolecular cyclization of carbanions to three-membered rings has been theoretically suggested as a proximity effect. See: S. Gronert, K. Azizian and M. A. Friedman, *J. Am. Chem. Soc.*, 1998, **120**, 3220. During the deoxygenations of tertiary amine oxides with carbon disulfide, the formation of three-membered ring intermediates from the analogous adduct such as **C** has been invoked. See: T. Yoshimura, K. Asada and S. Oae, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 3000.
11 L. A. Paquette, in *Mechanism of Molecular Migrations*, ed. B. S. Thyagarajan, Interscience, New York, 1968, vol. I, p. 121; L. A. Paquette, *Acc. Chem. Res.*, 1968, **1**, 209.

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