Tetrahedron Letters,Vol.26,No.18,pp 2195-2198,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

BENZYNE-INDUCED FRAGMENTATION OF 1,3-OXATHIOLANES. A NOVEL METHOD FOR DEPROTECTION OF CARBONYL GROUPS, PREPARATION OF PHENYL VINYL SULFIDES, AND 1,2-CARBONYL TRANSPOSITION

Juzo Nakayama,* Hidetoshi Sugiura, Atsuko Shiotsuki, and Masamatsu Hoshino
Department of Chemistry, Faculty of Science, Saitama University
Urawa, Saitama 338, Japan

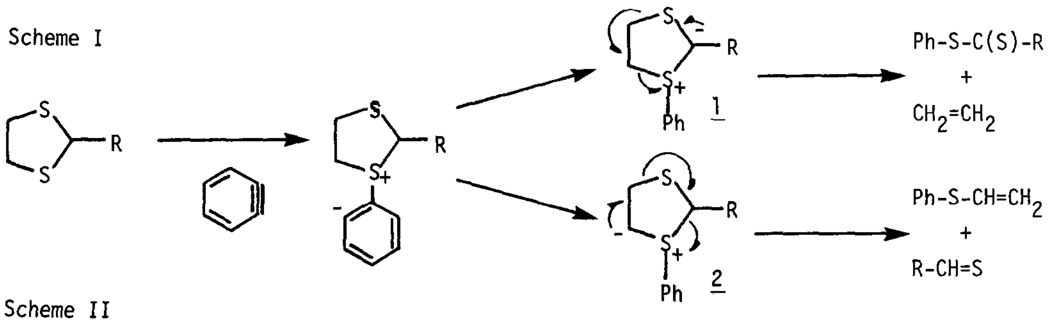
Abstract: A variety of 1,3-oxathiolanes undergo a benzyne-induced fragmentation leading to phenyl vinyl sulfides and carbonyl compounds. The reaction developed here provides a novel method for deprotection of carbonyl compounds from 1,3-oxathiolanes, preparation of phenyl vinyl sulfides, and 1,2-carbonyl transposition.

The base-induced fragmentation of 1,3-dithiolanes[1] and 1,3-oxathiolanes[2] is well documented. Especially the base-induced fragmentation of the former heterocycle has been extensively studied both from synthetic and mechanistic points of view. We have recently reported that 2-monosubstituted 1,3-dithiolanes competitively undergo two types of benzyne-induced fragmentations, one of which leads to phenyl vinyl sulfide and thioaldehydes (corresponding aldehydes as the final product) and the other provides phenyl dithiocarboxylates and ethylene (Scheme I).[3] The cyclic sulfur ylides **1** and **2** are probable intermediates. Herein we report the benzyne-induced fragmentation of 1,3-oxathiolanes. All of 1,3-oxathiolanes were prepared by acid-catalyzed condensation of 2-mercaptoethanols with carbonyl compounds.[4]

The reaction of benzyne with 2-monosubstituted and 2,2-disubstituted 1,3-oxathiolanes was first examined. Benzyne was generated by decomposing 2-carboxybenzenediazonium chloride in the presence of propylene oxide (HCl scavenger).[5] Thus, a mixture of an oxathiolane and 2-carboxybenzenediazonium chloride (1.1 equiv. unless otherwise stated) was heated in the presence of propylene oxide in refluxing 1,2-dichloroethane for ca. 45 min. Results are summarized in Table 1. The sole fragmentation leading to phenyl vinyl sulfides and carbonyl compounds occurs in the present case in a marked contrast to the results with 1,3-dithiolanes. A tentative mechanism is shown in Scheme II.[6] The use of 2-carboxybenzenediazonium chloride in excess (1.5 equiv.) gives carbonyl compounds in excellent yields (entries 2 and 6). The reaction therefore provides a novel method for deprotection of carbonyl compounds from 1,3-oxathiolanes under mild conditions.[4] The reaction is also useful for preparation of phenyl vinyl sulfide. Particularly in entry 7 phenyl vinyl sulfide is easily isolated by a single distillation of the crude mixture since the produced carbonyl compound is volatile acetone.[7]

To know more about the synthetic utility and mechanism of this reaction, a variety of 2,2-pentamethylene-1,3-oxathiolanes were prepared and allowed to react with benzyne. Results summarized in Table 2 show that the reaction provides a convenient synthesis of various phenyl vinyl sulfides which are otherwise difficult to obtain. Phenyl vinyl sulfides are useful intermediates in organic synthesis, not only as a carbonyl protecting group but

Scheme I



Scheme II

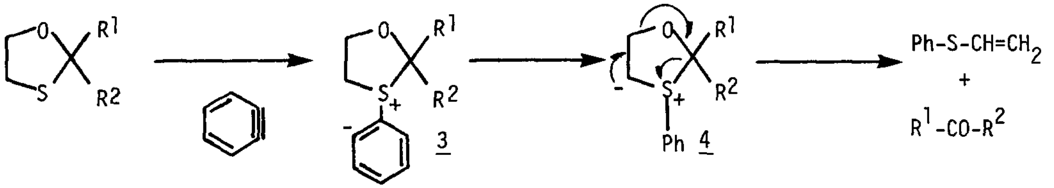


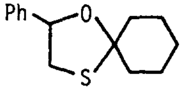
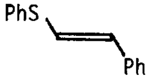
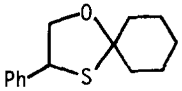
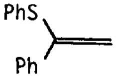
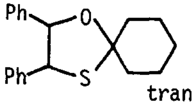
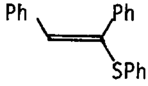
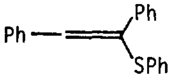
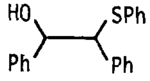
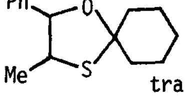
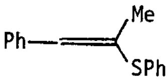
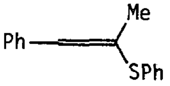
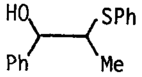
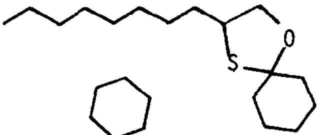
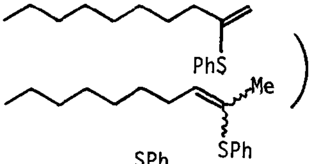
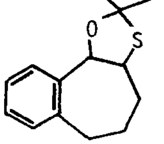
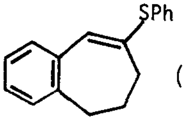
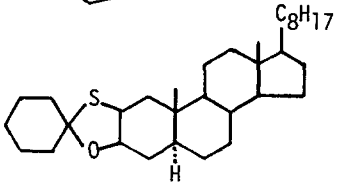
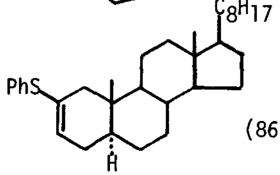
Table 1 Reaction of Benzyne with 2-Monosubstituted and 2,2-Disubstituted 1,3-Oxathiolanes[a]

entry	R^1	R^2	yield of phenyl vinyl sulfide (%)	yield of carbonyl compound (%)
1	C_6H_5	H	57	71
2	C_6H_5	H	(+)[b]	83[c]
3	4-MeOC_6H_4	H	50	76
4	4-ClC_6H_4	H	49	49
5	C_6H_5	C_6H_5	67	82
6	C_6H_5	C_6H_5	(+)[b]	100[c]
7	CH_3	CH_3	71	(+)[b]

a) Unless otherwise stated 1.1 equiv. of 2-carboxybenzenediazonium chloride was used.
b) Yield was not determined. c) 1.5 Equiv. of 2-carboxybenzenediazonium chloride was used.

in a variety of other synthetic transformations as well. As to stereochemistry, in entries 3 and 5 the reactions afford phenyl vinyl sulfides in a virtually stereospecific manner with retention of the original stereochemistry, whereas in entries 4 and 6 stereospecificity is lost. In certain cases 2-(phenylthio)ethanol derivatives are formed as a diastereoisomeric mixture (entries 4 and 6). These observations can best be explained by the mechanism that proceeds via the sulfur ylide intermediate 4 (Scheme II). In case of the fragmentation step of the ylide being slow, the inversion of the carbanionic center of the ylide may occur, thus resulting in the loss of stereospecificity in the phenyl vinyl sulfide formation. At the same time the ylide must be trapped by hydrogen chloride produced from 2-carboxybenzenediazonium chloride. Hydrolytic decomposition of the resulting sulfonium chloride yields the 2-(phenylthio)ethanol derivative and cyclohexanone.[8] Note that 2-(phenylthio)ethanols are formed as a diastereoisomeric mixture and that their formation is accompanied by the loss of stereospecificity in the phenyl vinyl sulfide formation. The initial ylides derived from the cis isomers are unstable due to steric repulsion and thus immediately undergo fragmentation to phenyl vinyl sulfides in a stereospecific manner (entries 3 and 5), while the less sterically hindered ylides derived from the trans isomers are stable enough to allow

Table 2 Reaction of 2,2-Pentamethylene-1,3-oxathiolanes with Benzyne

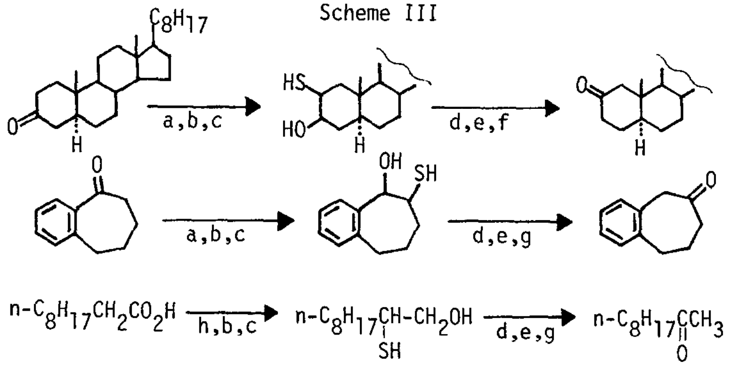
entry	oxathiolane	product (yield; %)[a]
1		 (85)[b]
2		 (70)
3	cis isomer 	 (83)[c]
4	trans isomer	 (7)[d] +  (88)[e]
5	cis isomer 	 (86.5, E:Z = 98:2)
6	trans isomer	 (50) +  (30)[e] (E:Z = 14:86)
7		 (86)[f]
8		 (78)
9		 (86)[g]

a) Cyclohexanone was formed in every case and easily removed by column chromatography on silica gel or Florisil. b) No cis isomer was formed. c) The Z-isomer was found in a trace amount. d) A mixture of E- and Z-isomers. The isomer ratio was not determined. e) A mixture of diastereomers. f) The initial product isomerized during workup. g) Yield based on the consumed oxathiolane (66% yield based on the oxathiolane used).

the inversion at the carbanionic center and its trapping with hydrogen chloride, and affords phenyl vinyl sulfides and 2-(phenylthio)ethanols in a nonstereospecific manner (entries 4 and 6).

Finally we stress the point that the reaction provides a novel method for 1,2-carbonyl transposition.[9] For example, 2β-mercaptocholestan-3β-ol, the precursor of the starting oxathiolane in entry 9, is prepared from cholestan-3-one in three steps.[10] The oxathiolane in entry 8 is also prepared from 1-benzosuberone. Hydrolysis of the phenyl vinyl

Scheme III



a: Br_2. b: $EtOC(S)S^-K^+$.
c: $LiAlH_4$.
d: cyclohexanone-$ZnCl_2$ (Na_2SO_4).
e: benzyne.
f: (i) HBr, (ii) $HgCl_2$ (THF-H_2O).
g: $HgCl_2$ (CH_3CN-H_2O).
h: (i) $SOCl_2$, (ii) NBS-HBr, (iii) aq. $NaHCO_3$.

sulfides resulting from the present reaction affords cholestan-2-one and 2-benzosuberone (25 and 33% overall yields), respectively. 2-Mercaptodecan-1-ol prepared from decanoic acid is condensed with cyclohexanone to afford the oxathiolane in entry 7. Hydrolysis of a mixture of phenyl vinyl sulfides resulting from the reaction with benzyne provides 2-decanone in 84% yield (Scheme III).

References and Notes

1. (a) Schönberg, A.; Cernik, D.; Urban, W. Ber. 1931, 64, 2577. (b) Wilson, S. R.; Georgiadis, G. M.; Khatri, H. N.; Bartmess, J. E. J. Am. Chem. Soc. 1980, 102, 3577. (c) Wilson, S. R.; Caldela, P.; Jester, M. A. J. Org. Chem. 1982, 47, 3319. (d) Tanimoto, S.; Oida, T.; Hatanaka, K.; Sugimoto, T. Tetrahedron Lett. 1981, 22, 655. (e) Hatanaka, K.; Tanimoto, S.; Oida, T.; Okano, M. Tetrahedron Lett. 1981, 22, 5195. (f) Hatanaka, K.; Tanimoto, S. Tetrahedron Lett. 1982, 23, 425. (g) Tanimoto, S.; Oida, T.; Kokubo, T.; Okano, M. Bull. Chem. Soc. Jpn. 1982, 55, 339. (h) Ikehara, H.; Tanimoto, S.; Oida, T. Bull. Chem. Soc. Jpn. 1983, 56, 2537. (i) Ikehara, H.; Tanimoto, S.; Oida, T.; Okano, M. J. Org. Chem. 1983, 48, 1120.
2. Jones, M.; Temple, P.; Thomas, E. J.; Whitham, G. H. J. Chem. Soc. Perkin Trans. 1 1974, 433.
3. Nakayama, J.; Ozasa, H.; Hoshino, M. Heterocycles 1984, 22, 1053.
4. (a) Loewnthal, H. J. E. "Protective Groups in Organic Chemistry"; McOmie, J. F. W. Ed.; Plenum Press: New York, 1973, p. 332. (b) Greene, T. W. "Protective Groups in Organic Synthesis"; John Wiley: New York, 1981, p. 139.
5. Klanderman, B. H.; Criswell, T. R. J. Org. Chem. 1969, 34, 3426.
6. The formation of the sulfur ylides via the betaine intermediates is a typical reaction of benzyne with sulfides: Hoffmann, R. W. "Dehydrobenzene and Cycloalkynes", Academic Press: New York, 1967, p. 164. The observation of the sole fragmentation indicates that the ylide 4 is exclusively formed, and hence in the betaine 3 the proton transfer occurs from the C-4 but not from the C-2, probably because the C-4 proton is more acidic than the C-2 proton. Interestingly, however, treatment of 2-phenyl-1,3-oxathiolane with a lithium dialkylamide leads to the sole fragmentation to give lithium thiobenzoate and ethylene probably as a result of the lithiation at the C-2 (ref. 2).
7. Phenyl vinyl sulfide is prepared by dehydrobromination of 1-bromo-2-(phenylthio)ethane obtainable from thiophenol and 1,2-dibromoethane. The one-pot procedure avoids the handling of 1-bromo-2-(phenylthio)ethane which can cause severe skin blistering: Carr, R. V. C.; Williams, R. V.; Paquette, L. A. J. Org. Chem. 1983, 48, 4976. The present method can avoid the route through 1-bromo-2-(phenylthio)ethane. The starting 2,2-dimethyl-1,3-oxathiolane is easily prepared from 2-mercaptoethanol and acetone.
8. An analogy is found in the reaction of benzyne (produced from 2-carboxybenzenediazonium chloride) with tetramethylene sulfide which affords 1-chloro-4-(phenylthio)butane in a good yield: Nakayama, J.; Shiotsuki, A.; Hoshino, M. unpublished results. Trapping of the ylide by hydrogen chloride followed by the thermal ring-opening reaction of the resulting sulfonium chloride gives rise to the observed product.
9. (a) Morris, D. G. Chem. Soc. Rev. 1983, 11, 397. (b) Kane, V. V.; Singh, V.; Martin, A.; Doyle, D. L. Tetrahedron 1983, 39, 345.
10. Djerassi, C.; Gorman, M.; Markley, F. X.; Oldenburg, E. B. J. Am. Chem. Soc. 1955, 77, 568.

(Received in Japan 10 January 1985)