

EXOCYCLIZATION OF NOVEL β,β -DIFLUORO- α -PHENYLVINYL
SULFIDE WITH BIDENDATE HETEROATOM(N, O, S)
NUCLEOPHILES

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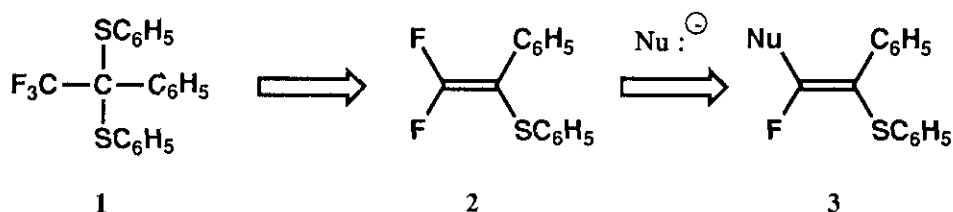
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Abstract-The exocyclization of novel β,β -difluoro- α -phenylvinyl sulfide with bidentate heteroatom (N, O, S) nucleophiles afforded various types of heterocyclic ketene acetals (O,O-, O,S-, S,S-, N,N-, N,O-, N,S-). The ease of exocyclization depended on the ring size of heterocyclic ketene acetals.

Recently, considerable effort has been paid to the synthesis of various types of heterocyclic N,N-¹, S,S-² and N,S-acetals,³ because these compounds are useful synthetic intermediates for the preparation of a wide variety of fused heterocycles. The general approach to synthesize those heterocyclic acetals was established by the reactions of α -oxoketene dithioacetals⁴ or electro-negatively substituted olefins such as 1,1-diiododinitroethylene⁵ with bidentate heteroatom (N, O, S) nucleophiles. Although a reaction of symmetrical *gem*-dichlorinated and *gem*-difluorinated ketene dithioacetals with only a bidentate sulfur nucleophile has been reported in recent years,² a reactivity study on the reaction of unsymmetrical *gem*-difluorinated vinyl sulfides with various types of bidentate heteroatom nucleophiles has not been initiated. The paucity of studies related to unsymmetrical *gem*-difluorinated vinyl sulfides ascribes to the lack of suitable methods for the preparation of unsymmetrical *gem*-difluorinated vinyl sulfides. Of particular interests in this unsymmetrical *gem*-difluorinated vinyl sulfides is β,β -difluoro- α -phenylvinyl sulfide (**2**), because this sulfide (**2**) may have a unique reactivity toward ionic species to yield substitution product (**3**) *via* loss of fluoride and utilize to synthesis of a variety of heterocyclic acetals *via* exocyclization with bidentate heteroatom nucleophiles. Recently, we found that β,β -difluoro- α -

phenylvinyl sulfide (**2**) can be easily prepared from the reaction of 2,2,2-trifluoro-1,1-bis(phenylthio)ethylbenzene (**1**) with a mixture of 2 equiv. TiCl_4 and 4 equiv. LiAlH_4 .⁶ In this communication, we wish to describe a reactivity on the exocyclization of **2** with various types of bidentate heteroatom (N,O,S) nucleophiles.



Treatment of **2** with dianionic sodium salts of 1,2-ethanediol, 2-mercaptoethanol, 1,2-ethanedithiol, and 2-aminoethanethiol resulted in the formation of only heterocyclic ketene acetals (**4a**, **4b**, **4c**, and **4f**) in good yields. Although two methylene protons of **4b** and **4f** were shown as one set of peaks in ^1H -nmr spectrum, it seems likely that **4b** and **4f** exist as a (*E*) and (*Z*) isomeric mixture, since it is very difficult to distinguish two methylene protons in (*E*) and (*Z*) isomers of **4b** and **4f**. In contrast, the similar reactions of **2** with dianionic sodium salts of ethylenediamine and 2-aminoethanol afforded only tautomers of heterocyclic ketene acetals (**5d**) and (**5e**) in good yields. In these cases, no corresponding heterocyclic ketene acetals was observed. The products (**5d**) and (**5e**) were confirmed by ^1H -nmr and ir spectra. The methine proton signals of **5d** and **5e** in ^1H -nmr spectrum were shown as a singlet peak at 5.20 and 5.05 ppm, respectively and an NH absorption peak was not detected in the ir spectrum. To support this spectroscopic analysis, the reaction of **4f** and **5e** with acetyl chloride in the presence of pyridine were performed. N-Acetylated product formed only from the reaction of **4f** with acetyl chloride was obtained in quantitative yield. This result indicates that only **4f** contains NH functionality in the structure. Tautomerization of **4f**, **5d**, and **5e** under basic condition was examined. When **4f**, **5d**, and **5e** were reacted with sodium ethoxide in ethanol, however, tautomers of **4f**, **5d**, and **5e** were not detected and only starting materials were recovered. This result implies that **4f**, **5d**, and **5e** are very stable compounds even under basic condition. The use of longer chained alkanediols in the reaction of **2** with bidentate heteroatom nucleophiles caused to diminish the formation of heterocyclic ketene acetals (**4**), while monosubstituted vinyl sulfides (**6**) were obtained as major products. Therefore, the reaction of **2** with dianionic sodium salt of 1,4-butanediol afforded monosubstituted vinyl sulfide (**6h**) in 68% yield, while heterocyclic ketene acetals (**4h**) was obtained in only 5% yield.⁷ An attempt to cyclize the compound (**6h**) in the presence of 1 equiv. of NaH was performed. However, only trace amount of **4h** was obtained, which indicates that it is

very difficult to prepare heterocyclic ketene acetals with more than six-membered ring *via* exocyclization of **2**. The reactions of **2** with bidentate heteroatom nucleophiles are summarized in Table I.

Table I. The Reaction of **2** with Dianionic Sodium Salts of Heteroatom 1,*n*-Disubstituted Alkane

X	Y	n	Products(Yield, %) ^a		
			4	5	6
O	O	2	4a (82)	-	-
O	S	2	4b (88) ^b	-	-
S	S	2	4c (89)	-	-
N	NH	2	-	5d (87)	-
N	O	2	-	5e (85)	-
N	S	2	4f (86) ^b	-	-
O	O	3	4g (77)	-	6g (12) ^b
O	O	4	4h (5)	-	6h (68) ^b
O	O	5	4i (3)	-	6i (72) ^b
O	O	6	4j (2)	-	6j (77) ^b
O	O	7	4k (trace)	-	6k (78) ^b

^a All products were isolated by silica gel column chromatography.

^b All products are (*E*) and (*Z*) isomeric mixtures.

The reactions of **2** with dianionic sodium salts of catechol and 1,2-benzenedithiol yielded only the corresponding heterocyclic ketene acetals (**7a**) and (**7b**) in 82% and 80% yields, respectively. In contrast, when the compound (**2**) was treated with dianionic sodium salts of 2-aminophenol and 1,2-phenylenediamine, only tautomers of heterocyclic ketene acetals (**8c**) and (**8d**) were obtained in 68% and 72% yields, respectively.³

However, the treatment of **2** with dianionic sodium salt of 2-aminothiophenol resulted in the formation of a mixture of corresponding benzothiazoline (**7e**) and benzothiazole (**8e**) in 35% and 38% yields, respectively.⁹ This result is sharply contrast to that obtained from the reaction of **2** with dianionic sodium salt of 2-aminoethanethiol, in which only heterocyclic ketene acetal (**4f**) was obtained in 86% yield. The results are summarized in Table II. The partial formation of **8e** can be rationalized by a better stability due to the conjugation effect than **7e**.

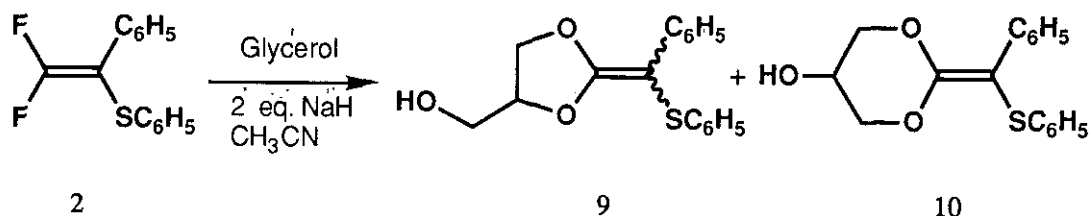
Table II. The Reaction of **2** with Dianionic Sodium Salts of Heteroatom 1,2-Disubstituted Benzene

	X	Y	Products (Yield, %) ^a	
			7	8
	O	O	7a (82)	-
	S	S	7b (80)	-
	N	NH	-	8c (68)
	N	O	-	8d (72)
	N	S	7e (35) ^b	8e (38)

^a All products were isolated by silica gel column chromatography.

^b Products is (*E*) and (*Z*) isomeric mixture.

Exocyclization reaction of **2** with triol, such as glycerol, provided a mixture of 5-membered and 6-membered heterocyclic ketene acetals (**9**) and (**10**) (ratio = 1:1).¹⁰ No selectivity was found.



In a typical experiment, sodium hydride (2.2 mmol) and 2-aminoethanethiol (1.1 mmol) in dry CH_3CN (10 ml) were stirred at room temperature for 1 h under nitrogen atmosphere. β,β -Difluoro- α -phenylvinyl sulfide (**2**) (1.0 mmol) was added dropwise at room temperature and then stirred for further 2 h. The reaction mixture was poured into water (10 ml) and extracted with ethyl acetate (10 ml x 2). The ethyl acetate solution was dried and chromatographed on a SiO_2 column. Elution with a mixture of hexane and ethyl acetate (20:1) provided **4f** in 86% yield.

4f: colorless oil; ^1H nmr (CDCl_3) δ 7.75-7.20 (m, 10H), 4.20 (t, $J = 7.3$ Hz, 2H), 3.60 (br s, 1H), 3.21 (t, $J = 7.3$ Hz, 2H); ms, m/z (relative intensity) 285 (M^+ , 77), 176 (100), 167 (21), 148 (33), 84 (27); ir (neat) 3250, 3000, 1640 cm^{-1} . The product (**5d**) and (**5e**) was obtained in a same manner. **5d**: white solid; mp 129-130 $^\circ\text{C}$; ^1H nmr (CDCl_3) δ 7.60-7.20 (m, 10H), 5.20 (s, 1H), 4.35 (br s, 1H), 3.67 (m, 4H); ms, m/z (relative intensity) 268 (M^+ , 100), 159 (7); ir (KBr) 3200, 3000, 1580 cm^{-1} . **5e**: white solid; mp 31-33 $^\circ\text{C}$; ^1H nmr (CDCl_3) δ 7.70-7.20 (m, 10H), 5.05 (s, 1H), 4.25 (m, 2H), 3.95 (m, 2H); ms, m/z (relative intensity) 269 (M^+ , 44), 160 (48), 132(100), 117(27), 91(37); ir (KBr) 2900, 1650, 1160, 980 cm^{-1} .

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7. Spectroscopic data of **4h** and **6h** are as follows. **4h** : white solid ; mp 64-65 °C ; ¹H nmr (CDCl₃) δ 7.50-7.05 (m, 10H), 4.10 (m, 4H), 1.85 (m, 4H) ; ms, m/z (relative intensity) 298 (M⁺, 34), 199 (27), 166 (75), 161(66), 121(100), 105(78) ; ir (KBr) 2900, 1580, 1470, 1260, 1100 cm⁻¹. **6h** : colorless oil ; ¹H nmr (CDCl₃) δ 7.60-7.10 (m, 10H), 4.15 (t, J = 6.3 Hz, 2H), 3.55 (t, J = 6.2 Hz, 2H), 1.75 (s, 1H), 1.70-1.40 (m, 4H) ; ms, m/z (relative intensity) 318 (M⁺, 35), 226 (97), 199 (96), 165 (100), 121 (98) ; ir (neat) 3300, 1465, 1425, 1060, 740 cm⁻¹.
8. Spectroscopic data of **8c** and **8d** are as follows. **8c** : yellowish oil ; ¹H nmr (CDCl₃) δ 7.80-7.20 (m, 15H), 6.00 (s, 1H) ; ms, m/z (relative intensity) 316 (M⁺, 100), 236 (25), 210 (63), 165 (32) ; ir (neat) 3250, 2900, 1580, 1440, 1260 cm⁻¹. **8d** : yellowish oil ; ¹H nmr (CDCl₃) δ 7.75-7.15 (m, 14H), 5.62 (s, 1H) ; ms, m/z (relative intensity) 317 (M⁺, 5), 209 (29), 208 (100), 180 (7) ; ir (neat) 3000, 1650, 1160, 980 cm⁻¹.
9. Spectroscopic data of **7e** and **8e** are as follows. **7e** : yellowish oil ; ¹H nmr (CDCl₃) δ 11.50 (br s, 1H), 7.78-7.10 (m, 14H) ; ms, m/z (relative intensity) 333 (M⁺, 100), 240 (25), 165 (42) ; ir (neat) 3450, 1450, 1330, 1160, 720 cm⁻¹. **8e** : yellowish solid ; mp 83-84 °C ; ¹H nmr (CDCl₃) δ 8.10-7.10 (m, 14H), 5.95 (s, 1H) ; ms, m/z (relative intensity) 333 (M⁺, 100), 240 (83), 165 (32) ; ir (KBr) 3000, 1580, 1495, 1150, 770 cm⁻¹.
10. Spectroscopic data of **9** and **10** are as follows. **9** : colorless oil ; ¹H nmr (CDCl₃) δ 7.80-7.05 (m, 10H), 5.10-4.70 (m, 1H), 4.60-4.20 (m, 2H), 3.90-3.60(m, 2H) ; ms, m/z (relative intensity) 300 (M⁺, 55), 199 (45), 165 (47), 121 (100) ; ir (neat) 3450, 1490, 1160, 760 cm⁻¹. **10** : colorless oil ; ¹H nmr (CDCl₃) δ 7.80-7.10 (m, 10H), 4.90-4.70 (m, 1H), 4.50-4.10 (m, 4H) ; ms, m/z (relative intensity) 300 (M⁺, 35), 199 (100), 165 (15), 121 (21) ; ir (neat) 3450, 1580, 1450, 750, 700 cm⁻¹.

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