Pergamon

Tetrahedron Letters 39 (1998) 5827–5830

TETRAHEDRON LETTERS

Claisen Rearrangement of γ-Hydroxyvinyl Sulfones *via* Ketene Acetal Derivatives. A New Entry to Functionalized (2E,4E)-Alkadienoic Esters.

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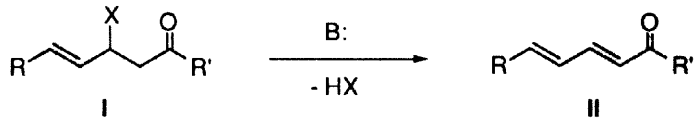
Received 7 April 1998; revised 26 May 1998; accepted 1 June 1998

Abstract: In situ prepared ketene acetals of γ-hydroxyvinyl sulfones undergo a Claisen rearrangement affording 3-phenylsulfonyl esters.These compounds are converted to (2E,4E)-dienoic esters by a base-assisted elimination of benzenesulfinic acid.

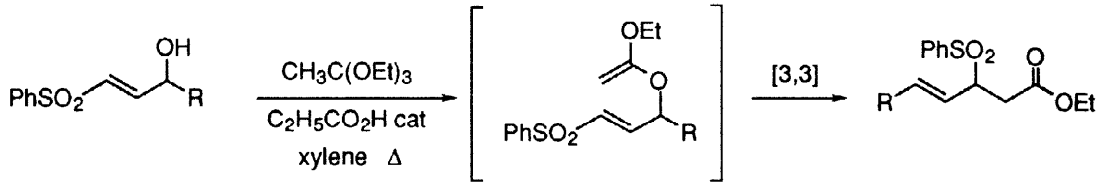
Dienoic acid derivatives occupy a prominent position in synthesis because of their frequent occurrence in many targets of biological relevance[1] and utility as synthetic intermediates. The large number of synthetic methods that are currently available for their preparation, testifies to the growing interest in this class of compounds. Early protocols mainly involved Wittig-type reactions[2] but later on other useful preparations of dienoic acid derivatives became available taking advantage of some recently developed methodologies.[3] The base-assisted elimination of stabilized anionic frameworks from unsaturated substrates represents a viable route to stereodefined diene systems (Scheme 1). Suitable precursors for this synthetic strategy are allyl acetates,[4] β-acetoxy sulfones,[5] and adducts of 2-phenylsulfonyl 1,3 dienes.[6]



I II

Scheme 1 X = OAc, $PhSO_2$ R' = OR", NR_2

We describe here a practical method for the preparation of compounds of type **I** through a Claisen rearrangement of ketene acetal derivatives of γ-hydroxyvinyl sulfones **1** (Scheme 2).



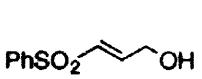
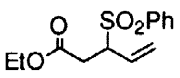
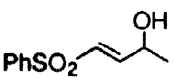
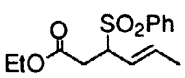
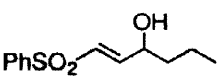
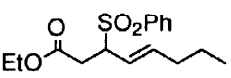
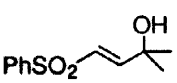
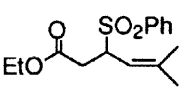
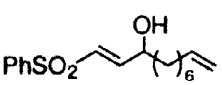
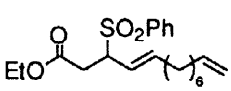
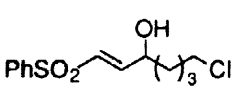
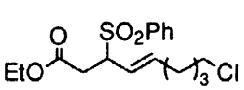
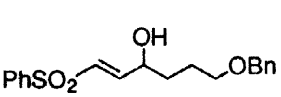
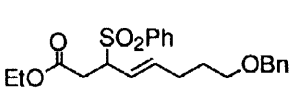
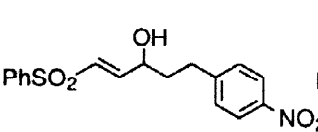
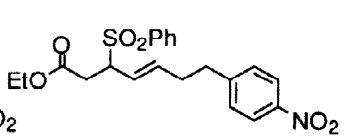
1 **2** **3**

Scheme 2

PII: S0040-4039(98)01151-4

Functionalized sulfones **1** can be readily prepared from aldehydes using the procedure by Dominguez and Carretero[7] and then treated with triethyl orthoacetate in xylene at reflux.[8] The intermediate ketene acetals **2** undergo a [3,3] sigmatropic shift[9] that leads to 3-phenylsulfonyl ester derivatives **3** (Table 1).

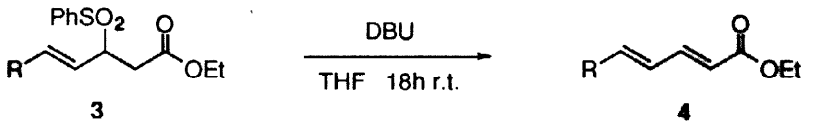
Table 1. Claisen rearrangement of hydroxy sulfones **1**

Entry	Hydroxy sulfone 1	Sulfonyl ester 3	Reaction time h	Yield[a] %
a			5	65
b			2	72
c			2.5	76
d			18	78[b]
e			2	85
f			2	81
g			1.5	75
h			2.5	89

a. Yields of pure, isolated products. b. Yield based on recovered **1d** (48% conversion)

The stereochemistry of the newly formed double bond has been established to be (E) from the large coupling constant between the olefinic protons (J=15.4 Hz).[10] The rearrangement usually takes place in 2 hours with two interesting exceptions (Table 1). Primary vinyl alcohol **1a** (entry a) reacts in 5 hours affording the corresponding ester **3a** in relative low yield (65%). The observed deceleration in the reaction rate is probably due to the lack of substituents at C-3 as pointed out in some recent studies.[11] On the other hand, tertiary vinyl alcohol **1d** is not completely converted into **3d** (entry d, Table 1) even after prolonged reaction times. The recovery of starting vinyl sulfone **1d** indicates that the ketene acetal formation is considerably slowed down by the steric crowding around the hydroxy group.[12] The yields of products **3** obtained after purification by column chromatography on silica gel are usually satisfactory especially for functionalized substrates (entries e-h, Table 1).

The subsequent elimination process has been tested using several base/solvent couples but the best results were obtained using DBU in THF at room temperature (Scheme 3).

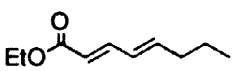
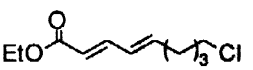
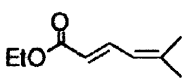
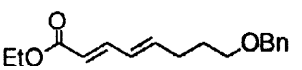
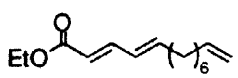
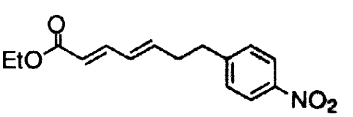


3 4

Scheme 3

The dienoic ester derivatives were recovered in good yield after solvent evaporation and quick filtration on silica gel (Table 2). The stereochemistry of dienoic products **4** was found to be (2E,4E)[13]; the amount of the (2Z,4E) isomer was negligible by ^{1}H-NMR analysis.

Table 2. Synthesis of (2E,4E)-dienoic esters using DBU in THF.

entry	ester 3	dienoic ester 4	yield %	entry	ester 3	dienoic ester 4	yield %
1	c		75	4	f		94
2	d		78	5	g		89
3	e		85	6	h		93

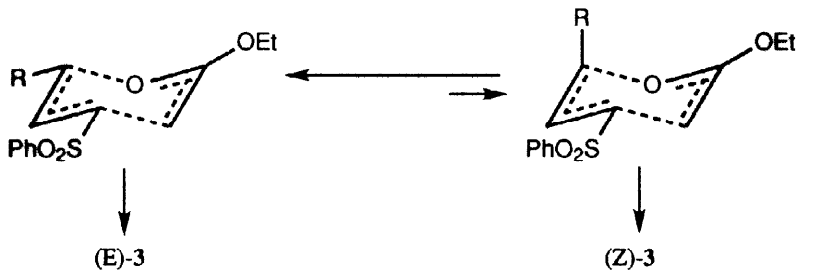
In conclusion, a two step synthesis of functionalized dienoic esters starting from γ-hydroxyvinyl sulfones has been devised.[14] Vinyl sulfones **1** are converted into the corresponding ketene acetals that undergo a Claisen rearrangement to 3-phenylsulfonyl esters **3**. Compounds **3** undergoes a base assisted elimination of benzenesulfinic acid which stereoselectively afford (2E,4E)-dienoic esters **4**. Synthetic applications of this new procedure to the preparation of biologically active compounds is currently under study in our laboratory.

Acknowledgments. Work carried out in the framework of the National Project "Stereoselezione in Sintesi Organica.Metodologie e Applicazioni" supported by the Ministero della Ricerca Scientifica e Tecnologica, Rome, and by the University of Camerino.

References and Notes

1. For some recent examples see: Tanaka, M.; Nara, F.; Suzuki-Konakai, K.; Hosoya, T.; Ogita, T. *J. Am. Chem. Soc.* **1997**, *119*, 7871; b) Millar, J. G.; *Tetrahedron Lett.* **1997**, *38*, 7971; c) Gurjar, M.K.; Chakrabarti, A.; Venkateswara Rao, B.; Kumar, P. *Tetrahedron Lett.* **1997**, *38*, 6885; d) Kerr, R. G.; Lawry, J. *Tetrahedron Lett.* **1996**, *37*, 8306.
2. a) Review: Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863; b) Vedejs, E.; Engler, D. A. *Tetrahedron Lett.* **1977**, 1241; c) Huang, Y; Shen, Y.; Zheng, J.; Zhang, S. *Synthesis* **1985**, 57.

3. *Cross couplings:* a) Abarbri, M.; Parrain, J-L.; Cintrat, J-L.; Duchene, A. *Synthesis* **1996**, 82; b) Lu, X.; Huang, X.; Ma, S. *Tetrahedron Lett.* **1992**, *33*, 2535; c) Mitsudo, T.; Zhang, S-W.; Kondo, T.; Watanabe, Y. *Tetrahedron Lett.* **1992**, *33*, 341; *Isomerizations:* d) Ma, D.; Lu, X. *Tetrahedron* **1990**, *46*, 3189 and 6919; *Carbonylations:* e) Imada, H.; Alper, H. *J. Org. Chem.* **1996**, *61*, 6766; f) Huh, K.; Orita, A.; Alper, H. *J. Org. Chem.* **1993**,*58*, 6956; *Condensations:* g) Herscovici, J.; Boumaiza, L.; Antonakis, K. *Tetrahedron Lett.* **1991**, *32*, 1791; *Homologations:* h) Bernabeu, M. C.; Chinchilla, R.; Najera, C. *Tetrahedron Lett.* **1995**, *36*, 3901; i) Lewis, N.; McKen, P. W.; Taylor, R. K. J. *Synlett* **1991**, 898.
4. Trost, B. M.; Lautens, M.; Peterson, B. *Tetrahedron Lett.* **1983**, *24*, 4525.
5. Mandai, T.; Moriyama, T.; Tsujimoto, K.; Kawada, M.; Otera, J. *Tetrahedron Lett.* **1986**, *27*, 603.
6. Plobeck, N.; Backvall, J. E. *J. Org. Chem.* **1991**, *56*, 4508.
7. a) Dominguez, E.; Carretero, J. C. *Tetrahedron* **1990**, *46*, 7197; b) Trost, B. M.; Grese, T. A. *J. Org. Chem.* **1991**,*46*, 3189; for a recent synthetic application of γ-oxygenated vinyl sulfones see: c) Alonso, I.; Carretero, J. C.; Garrido, J. L.; Magro, V.; Pedregal, C. *J. Org. Chem.* **1997**, *62*, 5682.
8. Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T-T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.
9. Reviews: a) Wipf, P. *Claisen Rearrangement in Comprehensive Organic Synthesis* Trost, B. M.; Fleming, I.; Paquette, L. A. Eds. Pergamon Oxford, 1991, Vol. 5, p. 827; b) Ziegler, F. E. *Chem Rev.* **1988**, *88*, 1423; c) Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975**, *22*, 1.
10. The observed preference for the E stereoisomer is probably a consequence of a chair-like transition state in which the substituents occupy a pseudo-equatorial orientation.



11. a) Burrows, C. J.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 6984; b) Aviyente, V.; Yoo, H. N.; Houk, K. N. *J. Org. Chem.* **1997**, *62*, 6121.
12. Welch, J. T.; Eswarakrishnan, S.*J. Org. Chem.* **1985**, *50*, 5909.
13. A coupling constant J= 15.3 Hz has been observed for the C-2 proton.
14. *Typical experimental procedures: Claisen rearrangement* : Vinyl sulfone **1** (2 mmol) was suspended in xylene (8 mL) and then triethyl orthoacetate (0.65g, 4 mmol) was added. A catalytic amount of propanoic acid (2 drops) was added and the suspension was heated at reflux for the indicated time (see Table 1). After evaporation of the solvent at reduced pressure, the crude ester **3** was purified by column chromatography. Compound **3f**: oil, IR (ν_{MAX}/cm^{-1}) : 1735, 1630, 1307, 1085; ^{1}H-NMR (300MHz, $CDCl_3$) δ : 1.19 (3H, t, *J* 6.5 Hz), 1.33-1.45 (2H, m), 1.54-1.70 (2H, m), 1.92-2.08 (2H, m), 2.61 (1H, dd, *J* 9.9, 16 Hz), 3.11 (1H, dd, *J* 4.3, 16 Hz), 3.46 (2H, t, *J* 6.3 Hz), 3.98-4.09 (1H, m), 4.11 (2H, q, *J* 7.2 Hz), 5.32 (1H, dd, *J* 8.5, 15.3 Hz), 5.48 (1H, dt, *J* 6.2, 15.3 Hz), 7.51-7.70 (3H, m), 7.80-7.95 (2H, m); *m/z* : 313 (M^+ - C_2H_5O), 217, 171, 135, 93, 77. Compound **3g**: oil, IR (ν_{MAX}/cm^{-1}) : 1738, 1635, 1307, 1085; ^{1}H-NMR ($CDCl_3$) δ : 1.22 (3H, t, *J* 7.1Hz), 1.52-1.71 (2H, m), 2.01-2.16 (2H, m), 2.59 (1H, dd, *J* 10, 15.8 Hz), 3.10 (1H, dd, *J* 4.3, 15.8 Hz), 3.36 (2H, t, *J* 6.4 Hz), 4.02 (1H, dd, *J* 4.3, 8.6 Hz), 4.10 (2H, q, *J* 7.0 Hz), 4.46 (2H, s), 5.30 (1H, dd, *J* 8.5, 15.4 Hz), 5.50 (1H, dt, *J* 6.4, 15.4 Hz), 7.28-7.38 (3H, m), 7.48-7.66 (5H, m), 7.78-7.86 (2H, m); *m/z* : 313 (M^+ - C_2H_5O- $C_6H_5SO_2$),184, 141, 91, 77.
Base assisted elimination: Phenylsulfonyl ester **3** (1 mmol) was dissolved in dry THF (6 mL) and then DBU (1.2 mmol) was added at room temperature. After stirring for 18 hours, the solvent was removed under reduced pressure and the crude product was quickly filtered on a short pad of silica gel (hexane-ethyl acetate 95:5). Compound **4f** : oil, IR (ν_{MAX}/cm^{-1}) : 1720, 1640; ^{1}H-NMR (300MHz, $CDCl_3$) δ : 1.28 (3H, t, *J* 7.1 Hz), 1.55-1.68 (2H, m), 1.70-1.89 (2H, m), 2.14-2.25 (2H, m), 3.54 (2H, t, *J* 6.3 Hz), 4.19 (2H, q, *J* 7.1 Hz), 5.22 (1H, d, *J* 15.3 Hz), 5.95-6.28 (2H, m), 7.26 (1H, dd, *J* 10.0, 15.3 Hz); *m/z* : 216 (M^+), 171, 143, 125, 97. Compound **4h** : mp 66°C, IR (ν_{MAX}/cm^{-1}) (KBr) : 1720, 1650; ^{1}H-NMR ($CDCl_3$) δ : 1.29 (3H, t, *J* 7.2 Hz), 2.45-2.60 (2H, m), 2.87 (2H, t, *J* 7.3 Hz), 4.19 (2H, q, *J* 7.2 Hz), 5.79 (1H, d, *J* 15.4 Hz), 6.00-6.25 (2H, m), 7.21 (1H, dd, *J* 9.8, 15.4 Hz), 7.32 (2H, d,*J* 8.7 Hz), 8.15 (2H, d, *J* 8.7 Hz); *m/z* : 275 (M^+), 230, 201, 139, 111, 67.