Pergamon

Tetrahedron Letters, Vol. 36, No. 6, pp. 923-926, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(94)02373-5

A Facile Synthesis of 2, 4-Disubstituted Furans from β-Hydroxy Sulfones.

Jin Hang Jung, Jae Wook Lee[1], Dong Young Oh*

Department of Chemistry, Korea Advanced Institute of Science and Technology,
373-1 Kusung-Dong, Yusung-Gu, Taejon, 305-701 Korea.

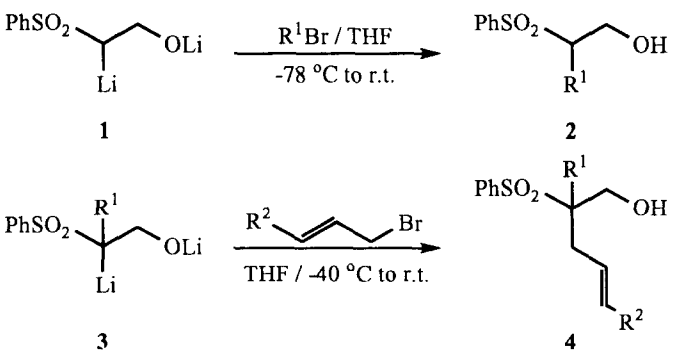
Abstract A convenient synthetic approach to 2,4-disubstituted furans **6** from 2-(phenylsulfonyl)ethan-1-ol is described.

Since many furans exist in nature and some of them exhibit interesting biological activities, a number of synthetic method have been developed.[2] But 2,4-disubstituted furans are difficult to prepare.[3]

Broadly applicable methods for the preparation of 2,4-disubstituted furans involve the substitution of initial furan ring[4] or ring formation from acyclic precursors.[5,6] We report herein a facile preparation of 2,4-disubstituted furans from β-hydroxy sulfones **4**.

β-Hydroxy sulfones are useful synthetic intermediates because of the ability of the sulfonyl group to generate an adjacent carbanion and to act as a leaving group in elimination reaction. An example of the furan synthesis using β-hydroxy sulfones is in the literature, but therein furans were obtained through palladium(II)-catalyzed intramolecular cyclization, followed by acid-catalyzed aromatization of 2-sulfonyl 3- and 4-alkenyl alcohol derivatives.[6]

Scheme 1



Recently we have developed methods for the halocyclization of the compounds having double bond and sulfonyl group[7,8]. In the course of investigation on electrophilic cyclization to functionalized alkenes, we have found that β-hydroxy sulfones act as the precursor of furan derivatives.

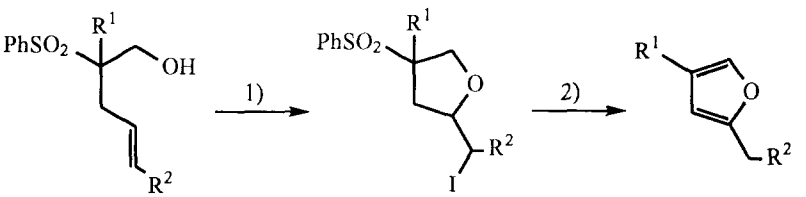
Table 1. Preparation of β-Hydroxy Sulfones **4**.

Entry	R^1	R^2	Adduct	Yield (%)[a]
a	$PhCH_2$	H	**4a**	78
b	$PhCH_2$	CH_3	**4b**	65
c	$PhCH_2$	Ph	**4c**	67
d	Hexyl	H	**4d**	80
e	Hexyl	Ph	**4e**	62

[a]Isolated yield based on 2-(Phenylsulfonyl)ethan-1-ol

The required β-hydroxy sulfones **4** easily prepared by two step reactions; alkylation and allylation of 2-(phenylsulfonyl)ethan-1-ol. (Scheme 1) The dianion **1** of 2-(phenylsulfonyl)ethan-1-ol generated on treatment with 2.2 equiv. of n-BuLi in THF is highly reactive toward alkyl halides.[9] Thus, treatment of dianion **1** with alkyl halides give the corresponding β-hydroxy sulfones **2**. Alternatively, treatment of the dianion **3** generated from β-hydroxy sulfones **2** and 2.2 equiv. of n-BuLi with allylic bromides gave the corresponding β-hydroxy sulfones **4**. The results are summarized in the Table 1.

Scheme 2



4 **5** **6**

Condition : 1) 1.5 equiv. $NaHCO_3$, 3.3 equiv. I_2 in THF-H_2O (2:1 vol) at r.t. 1 h

2) 5 equiv. t-BuOK in THF at 0°C 30 min

The reaction of **4** with 1.5 equiv. of $NaHCO_3$ and 3.3 equiv. of I_2 in THF - H_2O (2:1 vol) at room temperature afforded tetrahydrofurans **5**. We found that this reaction rate was quite dependent on the amount of iodine. This reaction could be accelerated by using excess iodine, it may be shown that molecular complex between aromatic ring and iodine was formed by noncovalent interaction.[10] So we used 3.3 equiv. of I_2 in this reaction, and obtained tetrahydrofurans **5** quantitatively. We did not have to isolate the cis- and trans- isomers of **5**, because the diastereomers afforded same furan **6**. After usual work-up, crude mixture of **5** was almost pure, so no more purification step was needed. Tetrahydrofuran **5** then treated with 5 equiv. of t-BuOK in THF at 0°C, and 2,4-disubstituted furans **6** were obtained in good yield.[11] (Scheme 2, Table 2)

Table 2. Preparation of 2,4-Disubstituted Furans **6** from β-Hydroxy Sulfone **4**

entry	R^1	R^2	Product	Yield (%)[a]
a	$PhCH_2$	H	**6a**	75
b	$PhCH_2$	CH_3	**6b**	80
c	$PhCH_2$	Ph	**6c**	77
d	Hexyl	H	**6d**	89
e	Hexyl	Ph	**6e**	81

[a]Isolated yield based on **4**.

In summary, we have developed a new method for the preparation of 2, 4-disubstituted furans from β-hydroxy sulfones **4**. We obtained 2, 4-disubstituted furans in good yields via I_2-induced cyclization, followed by base-catalyzed aromatization of β-hydroxy sulfones **4**. The synthetic application using this methodology is in progress.

References and Notes

1. Recent address ; R & D center, Dae Woong Pharm. Co. Ltd., Sung Nam, 461-120, Korea
2. a) Shikrishna, A.; Sunderbabu, G. *Chem. Lett.*, **1988**, 371
   b) Wakabayashi, Y.; Fukuda, Y.; Shirakami, H.; Utimoto, K.; Nozaki, H. *Tetrahedron*, **1985**, *41*, 3655

c) Wynberg, H.; Wiersum, U. E. *J. Chem. Soc., Chem. Commun.*, **1990**, 460

d) Minami, I.; Yuhhara, M.; Watanabe, H.; Tsuji, J. *J. Organomet. Chem.*, **1987**, *334*, 225

e) Kosugi, M.; Takano, I.; Hishino, I.; migita, T. *J. Chem. Soc., Chem. Commun.*, **1983**, 989

3. Nielman, J.A.; Keay, B. A. *Tetrahedron Lett.*, **1994**, *35*, 5335
4. a) Chiarello, J.; Joullie, M. *Tetrahedron*, **1988**, *44*, 41

b) Nolan, S. M.; Cohen, T. *J. Org. Chem.*, **1981**, *46*, 2473

5. a) Bosshard, P.; Eugster, C. H.: *Adv.Hetero. Chem.*, **1966**, *7*, 378

b) Dean, F. M. *Adv.Hetero. Chem.*, **1982**, *30*, 168

c) Dean, F. M. *Adv.Hetero. Chem.*, **1982**, *31*, 238

d) Sargent, M. V.; Dean, F. M. Furans and their Benzo Derivatives: Reactivity, Synthesis and Applications. In *Comp. Hetero. Chem.*, **1982**, *3*, 599

6. Igarashi, S.; Haruta, Y.; Ozawa, M.; Nishide, Y.; Kinoshita, H.; Inomata, K. *Chem. Lett.*, **1989**, 737
7. Lee, J. W.; Oh, D. Y. *Heterocycles*, **1990**, *31*, 1417
8. Lee, J. W.; Jung, J. H.; Oh, D. Y. *Bull. Korean Chem. Soc.*, **1994** in print
9. Julia, M.; Uguen, D. *Bull. Soc. Chim. Fr.*, **1976**, 519
10. Munoz, J. J.; Morales, R.; Martinez, J. L.; Jones, J. A. *J. Org. Chem.*, **1990**, *55*, 1122.
11. Typical Procedure : **6a** ; To a mixture of **4a** (1 mmol) in THF - H_2O (4 ml : 2 ml) at r.t. was added $NaHCO_3$(1.5 mmol) and I_2 (3.3 mmol). After stirring the mixture for 1 hour, sat. $Na_2S_2O_3$ was added, and the solution was extracted with $CHCl_3$. The combined extract was washed with sat. $Na_2S_2O_3$, water and brine. Drying over anhydrous $MgSO_4$ and evaporation of the solvent gave almost pure crude product **5a**, then a solution of ^tBuOK(5 mmol) in 6 ml of THF was added to a solution of crude product **5a** in 4 ml of THF at 0^oC under N_2. After 30 min, the usual work-up was perfomed. Purification by column chromatography on silica gel was accomplished.; **4-Benzyl-2-methylfuran(6a):** ^{1}H-NMR ($CDCl_3$) δ 2.23 (s, 3H), 3.72(s, 2H), 5.83(s, 1H), 7.06(s, 1H), 7.25(m, 5H) ; IR (film) 3028, 2918, 1609, 1553, 1495, 1264, 1118, 920, 718; Mass, m/z(%) 172(M^+, 15.1), 128(100), 129(91.5), 115(90.7)

(*Received in Japan* 16 *September* 1994; *revised* 18 *November* 1994; *accepted* 30 *November* 1994)