

## A CONDENSED SYNTHESIS OF DIHYDRO-3(2H)-FURANONE

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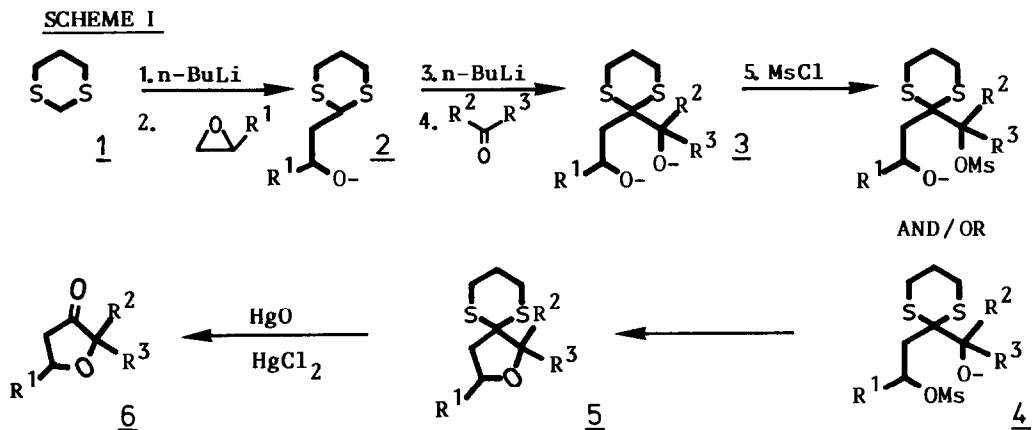
**Abstract:** A straight forward synthesis of dihydro-3(2H)-furanone is described. An attempted preparation of the oxetan-3-one precursor **10** by this method gave, instead, the ring enlargement product **11**.

The molecules of dihydro-3(2H)-furanone and 3(2H)-furanone have been found to increasingly play an important part in the structural features of quite a number of natural products varying from the simple **bullatenone** to the complex **eremantholides**, the latest example being the 2-methyl-3(2H)-furanone dimer isolated from red marine algae.<sup>1</sup> Consequently, several synthetic methods for the construction of the 3(2H)-furanone moiety have lately appeared in the literature, including, for example, the hydration and cyclisation of acetylenic ketone<sup>2</sup> and diol<sup>3</sup>, the hydrolysis and cyclisation of isoxazolines<sup>4</sup>, and the acid catalysed cyclisation-dehydration of hydroxy-1,3-diketone.<sup>5</sup> Here it is also interesting to note that the resistance towards base catalysed cyclisation of the  $\alpha'$ -hydroxy- $\alpha, \beta$ -unsaturated ketone to the corresponding dihydrofuranone was in fact one of the factors which led to the introduction of the rules for ring closure by Baldwin.<sup>6</sup>

In this communication we would like to present a most simple and efficient synthesis of dihydro-3(2H)-furanones, which, we believe, should provide synthetic chemists with a very versatile alternative to the existing methods.

Consecutive **one-pot** conventional treatment of sublimed 1,3-dithiane **1** in THF solution with equimolar *n*-butyllithium, epoxide, *n*-butyllithium, carbonyl compound, and finally methanesulfonyl chloride furnished the corresponding acetal **5** which, after hydrolysis ( $\text{HgO}$ ,  $\text{HgCl}_2$ )<sup>7</sup>, gave the dihydrofuranone **6**. The course of the reaction can be rationalised as in **SCHEME I**, and preparation examples are given in **TABLE**.

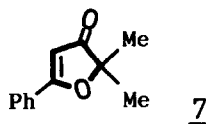
We have monitored the reaction sequence shown in **SCHEME I** and have isolated the reaction intermediates **2** and **3** as the corresponding alcohols. Also, as indicated in **TABLE**, where two isomers were possible (entries iv-vi) the reaction was found to yield both isomers in almost equal amounts, which assessment was evident from the nmr spectra of **5** and **6**. Actual separation of isomers was best performed with the dialcohol derived from **3** by using PLC (silica gel; 70% chloroform in hexane). Thus, two pure isomers of the final product **6** were obtained.



			% 5	% 6
i.	R <sup>1</sup> = H	R <sup>2</sup> = Me, R <sup>3</sup> = H	61	57
ii.	R <sup>1</sup> = H	R <sup>2</sup> = Ph, R <sup>3</sup> = H	67	59
iii.	R <sup>1</sup> = H	R <sup>2</sup> = 4-OMe-C <sub>6</sub> H <sub>4</sub> , R <sup>3</sup> = H	70	56
iv.	R <sup>1</sup> = Me	R <sup>2</sup> = Ph, R <sup>3</sup> = H	68 <sup>a</sup>	59 <sup>a</sup>
v.	R <sup>1</sup> = Ph	R <sup>2</sup> = 4-OMe-C <sub>6</sub> H <sub>4</sub> , R <sup>3</sup> = H	71 <sup>a</sup>	60 <sup>a</sup>
vi.	R <sup>1</sup> = Ph	R <sup>2</sup> = Me, R <sup>3</sup> = H	67 <sup>a</sup>	52 <sup>a</sup>
vii.	R <sup>1</sup> = Ph	R <sup>2</sup> = R <sup>3</sup> = Me	56	49 <sup>b</sup>

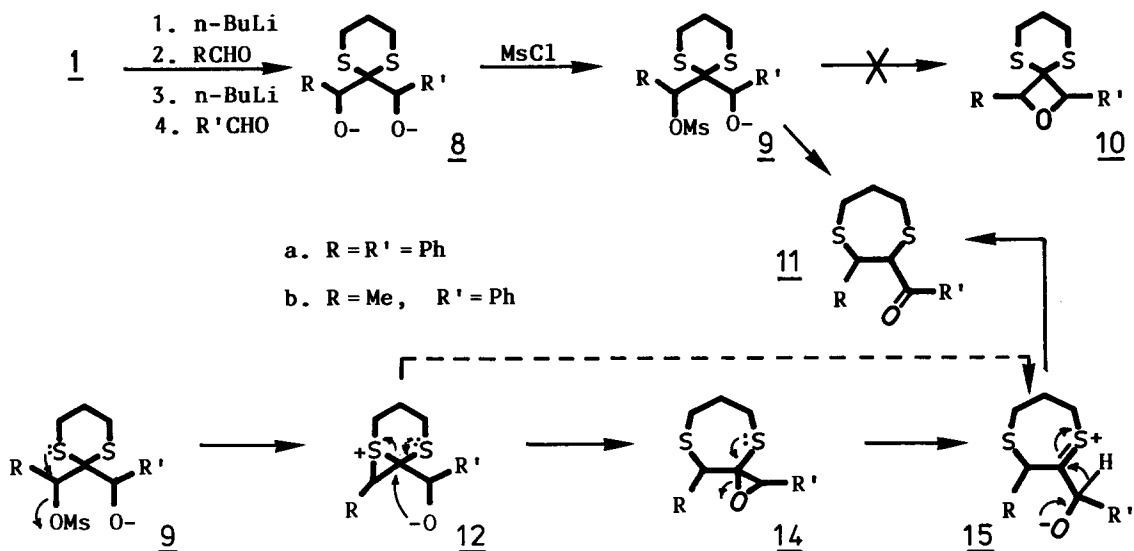
<sup>a</sup> two (*cis*-, *trans*-) isomers.      <sup>b</sup> see Text.

Interestingly, hydrolysis of 5-vii (R<sup>2</sup> = R<sup>3</sup> = Me) gave, instead of 6-vii, an oxidised material with physical properties identical to that of the reported bullatenone 7.<sup>2</sup>



Having prepared various dihydrofuranones it was recognised that appropriate modification should lead to the oxetan-3-one system. However, no trace of the four membered ring ether **10** could be detected when the dialkoxide **8** was treated with one equivalent of methanesulfonyl chloride and the mixture left stirring overnight at 0° or at room temperature<sup>8</sup>, but instead, a ring expansion product **11** was isolated in fair yield.<sup>9</sup> It is believed that the reaction path involves a series of neighbouring group participation reactions as shown in **SCHEME II**. It should also be pointed out that, in this reaction, where R and R' are not equivalent only one product was obtained.

### SCHEME II



Although the present method fails to give the oxetan-3-one precursor **10** it provides a swift and straight forward synthesis of dihydro-3(2H)-furanone. The method appears to be general and should be applied to a wide variety of substrates.

### Preparation of 5. A typical procedure.

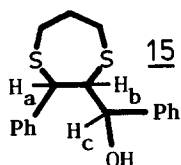
To a -78° solution of 1,3-dithiane (361 mg, 3.0 mmole) in THF (30 ml) was added 1.43 molar n-butyllithium in n-hexane (2.1 ml, 3.0 mmole) and the solution left stirring at 0° for 30 min after which it was cooled to -78°, then 2 molar propylene oxide in THF (1.5 ml, 3.0 mmole) was added and the mixture then stirred at 0° for 30 min. The whole sequence above was then repeated again but employing an equimolar amount of benzaldehyde instead of propylene oxide, after which the above reaction mixture was cooled to -78° and methanesulfonyl chloride (0.38 ml, 3 mmole) was added and the solution left stirring at 0° for 6 hr. Work up with saturated ammonium chloride solution followed by purification of the crude product by PLC (silica gel: 15% chloroform in hexane

as eluant) gave **5-iv** (544 mg, 68%) as a mixture of two isomers in almost equal amount. As indicated in Text, each isomer can be obtained in the pure state by separating the isomeric dialcohols derived from **3-iv** followed by cyclisation.

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#### References :

1. W. Parker, R.A. Raphael, D.I. Wilkinson, *J. Chem. Soc.*, 1958, 3871; P.W. Le Quesne, M.D. Menachery, M.P. Pastore, C.J. Kelly, T.F. Brennan, K.D. Onan, R.F. Raffauf, C.M. Weeks, *J. Org. Chem.*, 1982, **47**, 1519; A.S. Martin, J. Rovirosa, O. Munoz, M.H.M. Chen, R.D. Guneratne, J. Clardy, *Tetrahedron Lett.*, 1983, **24**, 4063.
2. R.F.W. Jackson, R.A. Raphael, *J. Chem. Soc. Perkin Trans.I*, 1984, 535.
3. H. Saimoto, T. Hiyama, H. Nozaki, *J. Amer. Chem. Soc.*, 1981, **103**, 4975; T. Hiyama, M. Shinoda, H. Saimoto, H. Nozaki, *Heterocycles*, 1981, **15**, 263.
4. S.H. Andersen, K.K. Sharma, K.B.G. Torrsell, *Tetrahedron*, 1983, **39**, 2241; D.P. Curran, D.H. Singleton, *Tetrahedron Lett.*, 1983, **24**, 2079.
5. A.B. Smith, III, P.A. Levenberg, P.J. Jerris, R.M. Scarborough, Jr., P.M. Wovkulich, *J. Amer. Chem. Soc.*, 1981, **103**, 1501.
6. J.E. Baldwin, *J. Chem. Soc. Chem. Commun.*, 1976, 734. In contrast acid catalysed cyclisation of  $\alpha'$ -hydroxy- $\alpha,\beta$ -unsaturated ketone takes place readily and has frequently been used to synthesise dihydro-3(2H)-furanone; for example see A.E. Guthrie, J.E. Semple, M.M. Joulie, *J. Org. Chem.*, 1982, **47**, 2369.
7. A.P. Kozikowski, Y.Y. Chen, *J. Org. Chem.*, 1980, **45**, 2236.
8. Compound **8** was also isolated as the corresponding alcohol.
9.  $^1\text{H}$  NMR (in  $\text{CDCl}_3$ ) of **11 a** (61% purified yield);  $\delta$  1.98-2.45 (m, 2H), 2.94-3.25 (m, 4H), 4.64, 4.85 (AB system,  $J = 10$  Hz, 2H), 7.20 (broad s, 5H), 7.25-7.55 (m, 3H), 7.58-7.87 (m, 2H). **11 b** (58%);  $\delta$  1.24 (d,  $J = 7$  Hz, 3H), 1.86-2.33 (m, 2H), 2.78-3.05 (m, 4H), 3.51 (dq,  $J = 7, 10$  Hz, 1H), 4.10 (d,  $J = 10$  Hz, 1H), 7.20-7.63 (m, 3H), 7.78-7.97 (m, 2H).



Structure **11 a** has been further proved by its reaction with  $\text{NaBH}_4$  to give a single isomer of the corresponding alcohol **15** (76%).

$^1\text{H}$  NMR (in  $\text{CDCl}_3$ ) of **15**;  $\delta$  1.80-2.20 (m, 2H), 2.64 (d,  $J = 4$  Hz, 1H, disappeared with  $\text{D}_2\text{O}$ , OH), 2.80-3.17 (m, 4H), 3.47 (dd,  $J = 4, 8$  Hz, 1H,  $\text{H}_b$ ), 4.20 (d,  $J = 8$  Hz, 1H,  $\text{H}_a$ ), 4.70 (t,  $J = 4$  Hz, 1H,  $\text{H}_c$ , collapsed to a doublet,  $J = 4$  Hz, with  $\text{D}_2\text{O}$ ), 7.27 (s, 5H), 7.37 (s, 5H). An example of ring expansion of 1,3-dithiane

has recently been reported, see C.G. Francisco, R. Freire, R. Hernandez, J.A. Salazar, E. Suarez, *Tetrahedron Lett.*, 1984, **25**, 1621.

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