Tetrahedron Letters, Vol. 34, No. 18, pp. 2945-2948, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

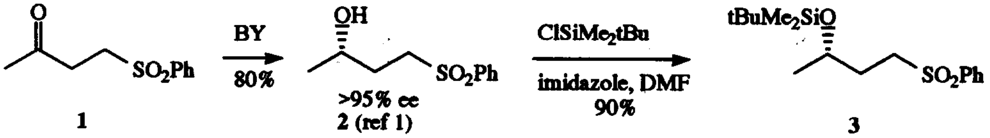
Preparation of Lactones with Several Ring Sizes *via* the Same Intermediate

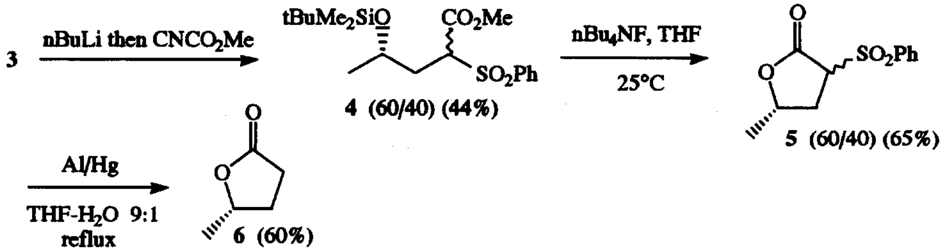
Sylvie Robin
Laboratoire des Carbocycles, associé au CNRS, Bât. 420, Université de Paris Sud,
91405 ORSAY, France

François Huet *
Laboratoire de Synthèse Organique, associé au CNRS, Faculté des Sciences, BP 535,
Université du Maine, 72017 Le Mans, France

Abstract : Several lactones were prepared from (S)-1-(phenylsulfonyl)-3-butanol **2** by cyclization of alkylation products of its silyl derivative **3** with electrophilic reagents bearing a functional group.

We recently showed that several hydroxy-sulfones could be obtained by microbiological reductions of keto-sulfones (e.g. **2** from **1** by baker's yeast reduction).[1] We anticipated[2,3] that lactones could be prepared *via* reduction product **2** by alkylation of the corresponding dianion with the appropriate electrophilic reagent followed by cyclization. However several attempts in such alkylations failed or led to bad results. Therefore we tried to do the same *via* monoanion of the corresponding silyl derivative **3**.[4] Alkylation with methyl cyanoformate[5] led to the expected product **4** in moderate yield as a mixture of two diastereomers in a 60/40 ratio. Desilylation [4] and reduction [6,7] gave lactone **6**.[8]



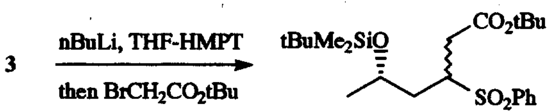


4 (60/40) (44%)

5 (60/40) (65%)

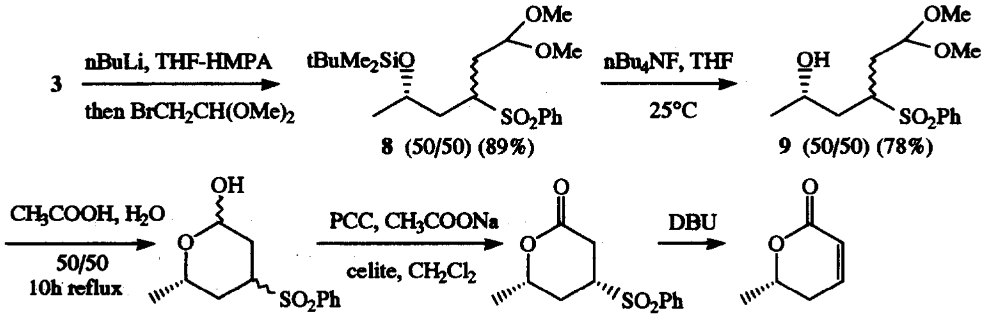
6 (60%)
$[\alpha]_D$ -27.7 (c 1.89, CH_2Cl_2)
ee>95% (^1H NMR with Eu(hfc)$_3$)

Afterwards we tried to prepare lactones **11** and **12** through the alkylation product of **3** with tertiobutyl bromoacetate. Unfortunately the reaction led to 24% only of isolated **7** along with several unidentified products and a small amount of phenylsulfinic acid elimination product from **7**.



7 (24%)

Therefore we used bromoacetaldehyde dimethyl acetal as an alkylating agent and obtained **8** in high yield as a 50/50 diastereomeric mixture. Desacetalisation led to lactol **10** as a mixture of several isomers. Oxidation^{9,10} only gave one lactone, presumably the cis product **11**. This assignment was deduced from ^1H NMR coupling constants (H_4 : 11.7, 3.3 Hz ; H_6 : 11.5, 2.6 Hz). This unexpected stereochemical result leads to assumption that epimerization occured either at the desacetalisation step or at the oxidation step. Elimination of sulfinic acid with 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU)^{1,3} led to lactone **12**.^{3,11}



8 (50/50) (89%)

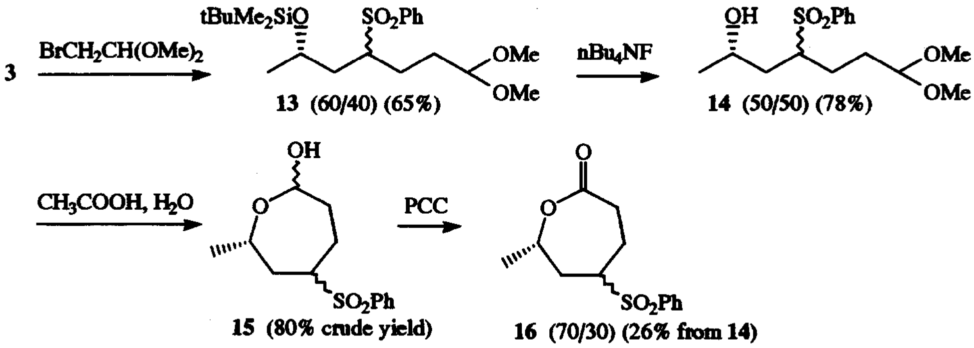
9 (50/50) (78%)

10 (76%)

11 (74%)
$[\alpha]_D$ +16 (c 1, $CHCl_3$)
mp 109.2°C

12 (80%)
$[\alpha]_D$ +212 (c 0.3, $CHCl_3$)
ee>95% (^1H NMR with Eu(hfc)$_3$)

Alkylation of 3 with 3-bromopropionaldehyde dimethyl acetal gave compound **13** as a 60/40 diastereomeric mixture. Subsequent desilylation then hydrolysis yielded lactol **15** which was unstable in the presence of silica gel and was not purified. Oxidation gave lactone **16** in 26% yield from **14** as a diastereomeric mixture. Both isomers could be separated by column chromatography on silica gel. These seven membered ring lactones (5R,7S)-**16** and (5S,7S)-**16** were thus obtained in moderate yield but in rather simple experimental conditions. The configuration of both isomers could not be assigned.



Our results show that several lactones are obtained in high enantiomeric excess from compound 1 which is easily available. They also suggest alternatives to circumvent difficulties in several alkylation reactions.

References and Notes

1) Robin, S. ; Huet, F. ; Fauve, A. ; Veschambre, H. *Tetrahedron Asymmetry*, in press.

2) Sato, T. ; Okumura, Y. ; Itai, J. ; Fujisawa, T. *Chem. Lett.*, **1988**, 1537-1540 ; Tanikaga, R. ; Hosoya, K. ; Kaji, A. *Synthesis*, **1987**, 389-390 ; Kozikowski, A.P. ; Mugrave, B.B. ; Li, C.S. ; Felder, L. *Tetrahedron Lett.*, **1986**, *27*, 4817-4820.

3) Gopalan,A.S. ; Jacobs, H.K. *Tetrahedron Lett.,* **1990**, *31*, 5575-5578.

4) Corey, E.J. ; Venkateswarlu, A. *J. Amer. Chem. Soc.*, **1972**, *94*, 6190-6191.

5) nBuLi in hexane (3.6 mmol) was added at -78°C under argon to a stirred solution of 3 (3.3 mmol) in THF (6 mL). The reaction mixture was allowed to warm up to 0°C, stirred 1 h at 0°C and cooled again to -78°C. HMPA (3 mmol) and $CNCO_2Me$ (3.3 mmol) were added at -78°C and the reaction mixture was allowed to warm up slowly to room temperature and stand at this temperature overnight. Hydrolysis, extraction and column chromatography on silica gel led to **4**. Componds **8** and **13** were obtained similarly.

6) Corey, E.J. ; Chaykovsky, M. *J. Amer. Chem. Soc.*, **1964**, *86*, 1639-1640.

7) Aluminium amalgam (L.F. Fieser, M. Fieser, Reagents for Organic Synthesis, Vol. 1, J. Wiley and Sons, Inc. New-York London Sydney, 1967, 20) was added to a solution of **5** in the mixture THF/H_2O 90/10 and reaction mixture was heated to reflux for 1 h. Cooling, filtration, drying, evaporation and column chromatography on silica gel led to **6**.

8) Barbier, P. ; Benezra, C. *J. Med. Chem.*, **1982**, *25*, 943-946 ; Uematsu, T. ; Matsuo, N. ; Sanemitsu, Y. *Agric. Biol. Chem.*, **1984**, *48*, 2477-2481 ; Soai, K. ; Yokoyama, S. ; Hayasaka, T. ; Ebihara, K. *Chem. Lett.*, **1988**, 843-846 ; Ohta, T. ; Miyake, T. ; Seido, N. ; Kumobayashi, H. ; Akutagawa, S. ; Takaya, H. *Tetrahedron Lett.*, **1992**, *33*, 635-638.

9) Corey, E.J. ; Suggs, J.W. *Tetrahedron Lett.*, **1975**, 2647-2650 ; Kurth, M.J. ; O' Brien, M.J. ; Hope, H. ; Yanuck, M. *J. Org. Chem.*, **1985**, *50*, 2626-2632 ; Wadsworth, D.H. ; Geer, S.M. ; Detty, M.R. *J. Org. Chem.*, **1987**, *52*, 3662-3668.

10) Pyridinium chlorochromate (4 mmol), anhydrous sodium acetate (2 mmol), celite (1.5 g) and CH_2Cl_2 (8 mL) were strongly stirred then a solution of lactol **10** (1 mmol) in CH_2Cl_2 (2 mL) was added. Reaction mixture was stirred at room temperature (~ 2 h) then at 40°C (~ 24 h depending on TLC monitoring). Filtration through a pad of florisil, evaporation and column chromatography on silica gel led to **11**. Compound **16** was obtained similarly.

11) Kuhn, R. ; Kum, K. *Chem. Ber.*, **1962**, *95*, 2009-2011 ; Procter, G. ; Russell, A.T. ; Murphy, P.J. ; Tan, T.S. ; Mather, A.N. *Tetrahedron*, **1988**, *44*, 3953-3973.

(Received in France 9 February 1993; accepted 11 March 1993)