## Dilithiation of 2-(Chloromethyl)-3-tosylpropene: Synthesis and Reactivity of a New Chlorinated Allyl Sulfone Dianion<sup>1</sup>

Carmen Nájera\* and José M. Sansano

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, 03080-Alicante, Spain

Abstract: Double lithiation of 2-(chloromethyl)-3-tosylpropene (4) with n-butyl-lithium at -90°C in the presence of DMPU leads to the dianion 5, which by reaction with deuterium oxide affords the corresponding 3,3-dideuteriated product 6. The alkylation reaction of dianion 5 gives mono and or 3,3-dialkylated products 11 and/or 7 or tosylated methylenecyclopropanes 8 depending on the reactivity of the alkylating agent, and by reaction with aldehydes or ketones as electrophiles tosylated 2,5-dihydrofurans 9 or 3-(tosylalkylidene)tetrahydrofurans 10 are, respectively, obtained.

 $\alpha$ -Lithio and  $\alpha, \alpha$ -dilithio sulfones are of great structural<sup>2</sup> and synthetic interest<sup>3</sup>. Especially useful are allyl sulfone monoanions, used for instance in the synthesis of vitamin A, retinoic acid derivatives and polyenes<sup>3</sup>, and allyl phenyl sulfone dianion<sup>4</sup> used in the synthesis of carba-prostacyclins<sup>4b</sup>. The dilithiation of allyl phenyl sulfone (1) presents a problem of regioselectivity since the double deprotonation gives either exclusively the  $\alpha, o$ -dianion 2 or the  $\alpha, \alpha$ -dianion 3, or a mixture of both depending on the temperature during the lithiation step (Scheme 1)<sup>4a</sup>. The reaction of the dianions 2 and or 3 with deuterium oxide or benzaldehyde affords the corresponding  $\alpha, o$ - and or  $\alpha, \alpha$ -disubstituted products. However, alkylation reaction takes place only at the  $\alpha$ -position independently of the structural nature of the dianion<sup>4</sup>. Here we described the regiospecific dilithiation of 2-(chloromethyl)-3-tosylpropene (4) to give a new chlorinated allyl sulfone dianion 5.



Scheme 1. i, Bu<sup>n</sup>Li.

The lithiation of 2-(chloromethyl)-3-tosylpropene (4)<sup>5</sup> with two equivalents of n-butyl-lithium in THF at -90°C in the presence of N,N'-dimethylpropyleneurea<sup>6</sup> (DMPU, two equivalents) over 15 min afforded the dianion 5. This intermediate is stable at -90°C for one hour and was chemically characterized by deuterolysis

with deuterium oxide affording the compound 6 in 72% yield (Scheme 2). The alkylation reaction gave mainly  $\alpha, \alpha$ -dialkylated products 7 in the case of very reactive alkylating agents (eg. dimethyl sulfate or allyl, benzyl and propargyl bromides), but with alkyl bromides or benzyl chloride tosylated methylenecyclopropanes 8<sup>7</sup> were exclusively obtained, even with a large excess of electrophile (Scheme 2 and Table 1). The  $\gamma$ -elimination of the alkylated monoanion 12 to give compounds 8b takes place between -30°C and room temperature.



Scheme 2. i, 2Bu<sup>a</sup>Li/DMPU/-90°C; ii, D<sub>2</sub>O; iii, R<sup>1</sup>Hal; iv, H<sub>3</sub>O<sup>+</sup>; v, R<sup>1</sup>R<sup>2</sup>CO.

When aldehydes were allowed to react with intermediate 5 at -90°C and the reaction temperature allowed to rise to 25°C, the corresponding tosylated 2,5-dihydrofurans  $9^8$  were obtained (Scheme 2 and Table 1). If the reaction with propanal was quenched with water at different temperatures, mixtures of compounds 9b and 15b (the latter as a mixture of diastereomers) were obtained and if deuterium oxide was added at -40°C a mixture of deuterated compounds 9b'and 15b' in *ca.* 1:3 molar ratio were isolated. It means that allylic monoanions of the type 13b and 14b are, respectively, the intermediates in the reaction of dianion 5 with aldehydes (Scheme 3). Only in the case of pivaldehyde, the functionalized (*E*)-2-tosyl-1,3-diene 16<sup>9</sup> was exclusively and stereoselectively obtained due to the  $\beta$ -elimination reaction of the corresponding intermediate of the type 13.



However, when ketones were used as electrophiles they reacted with dianion 5 at the less hindered  $\gamma$ -position to afford compounds 10 (Scheme 2 and Table 1). The cyclization process has been studied with 3-pentanone and the reaction mixture was also treated with deuterium oxide at -40°C. Under these reactions

Electrophile <sup>6</sup>	Product <sup>*</sup>			
	No.	R <sup>1</sup>	R <sup>2</sup>	Yield (%) <sup>c</sup>
Me <sub>2</sub> SO <sub>4</sub>	7a	Ме		47ª
CH <sub>2</sub> =CHCH <sub>2</sub> Br	7ь	CH <sub>2</sub> =CHCH <sub>2</sub>	1	46°
$CH = CCH_2Br$	7c	$CH \equiv CCH_2$		62
PhCH <sub>2</sub> Br	7d	PhCH <sub>2</sub>		38 <sup>r</sup>
I(CH <sub>2</sub> ) <sub>4</sub> I	7e	-(CH <sub>2</sub> ) <sub>4</sub> -		24
EtBr	8a	Et		54
Bu <sup>n</sup> Br	8b	Buª		45
Me <sub>3</sub> SiCH <sub>2</sub> Br	8c	Me <sub>3</sub> SiCH <sub>2</sub>		51
PhCH <sub>2</sub> Cl	8d	PhCH <sub>2</sub>		33
MeCHO	9a	Ме	н	62
EtCHO <sup>#</sup>	9b	Et	н	68
Pr <sup>i</sup> CHO <sup>s</sup>	- 9c	Pr <sup>i</sup>	Н	59
PhCHO	9d	Ph	H	67
Et <sub>2</sub> CO <sup>g</sup>	10a	Et	Et	52
PhCOMe	10b	Ph	Ме	61

Table 1. Reaction of Dilithiated 2-(Chloromethyl)-3-tosylpropene (5) with Electrophiles.

\* All products are pure and gave satisfactory spectral (IR, 300 MHz <sup>1</sup>H-NMR, 75 MHz <sup>13</sup>C-NMR and MS) and analytical data. <sup>b</sup> Two equivalents. <sup>c</sup> Isolated yield based on starting compound 4 after flash chromatography on silica gel. <sup>4</sup> 31% of compound 11a was also isolated. <sup>e</sup> 38% of compound 11b was also isolated. <sup>f</sup> 31% of compound 11d was also isolated. <sup>i</sup> 1.2 equivalents.

conditions compounds 10a' and 10a'' in ca. 3:7 molar ratio were isolated, these ratio increased to 1:50 if deuterolysis is carried out at -15°C. According to these results monoanions of the type 17 and 18 seem to be the intermediates in the reaction of dianion 5 with ketones, species 18 being the most stable thermodynamically (Scheme 4).



Scheme 3. i, EtCHO; ii,  $D_2O/-40$ °C.

The chlorine atom seems to play an important role in the structure of the dianion 5 and monoanions 12 and 14 by intramolecular complexation (CIPE effect)<sup>10</sup> between lithium and chlorine atoms<sup>11</sup>.



Scheme 4. i,  $Et_2CO$ ; ii,  $D_2O$ .

**Typical Procedure.** To a solution of compound  $4^5$  (98 mg, 0.40 mmol) and DMPU (0.11 ml, 0.88 mmol) in THF (3 ml) was added at -90°C under Ar, a 1.4 M solution of n-butyl-lithium (0.53 ml, 0.88 mmol) in hexane. After 15 min stirring at the same temperature the corresponding electrophile (see Table 1) was added. The mixture was stirred overnight allowing the temperature to rise to 25°C. The resulting solution was then hydrolyzed with a saturated aqueous solution of ammonium chloride and after extractive work-up the residue was purified by flash chromatography to afford compounds 6-11, 15 or 16.

## **REFERENCES AND NOTES**

1. Presented to GECOM XX, Reims, 1992, commun. no. 22.

- (a) Boche, G. Angew. Chem. 1989, 101, 286; Angew. Chem., Int. Ed. Engl. 1989, 28, 277. (b) Gais, H.-J.; Hellmann, G.; Günther, H.; López, F.; Lindner, H. J.; Braun, S. Angew. Chem. 1989, 101, 1061; Angew. Chem., Int. Ed. Engl. 1989, 28, 1025. (c) Gais, H.-J.; Hellmann, G.; Lindner, H. J. Angew. Chem. 1990, 102, 96; Angew. Chem., Int. Ed. Engl. 1990, 29, 100. (d) Gais, H.-J.; Müller, J.; Volhardt, J. J. Am. Chem. Soc. 1991, 113, 4002.
- (a) The Chemistry of Sulphones and Sulphoxides; Patai, S.; Rappoport, Z.; Stirling, C. Eds.; J. Wiley & Sons: Chichester 1988. (b) Schank, K. in Methoden der Organischen Chemie (Houben-Weyl); Thieme: Stuttgart, 1985, Vol. E/11.
- 4. (a) Volhardt, J.; Gais, H.-J.; Lukas, K. L. Angew. Chem. 1985, 97, 607; Angew. Chem. Int. Ed. Engl. 1985, 24, 610. (b) Gais, H.-J.; Ball, W. A.; Bund, J. Tetrahedron Lett. 1988, 29, 781. (c) Gais, H.-J.; Volhardt; J. Tetrahedron Lett. 1988, 29, 1529.
- 5. This reagent has been prepared from commercially available 3-chloro-2-(chloromethyl)propene by reaction with sodium *p*-toluenesulfinate in 78% yield: Nájera, C.; Sansano, J. M. Tetrahedron 1992, 48, 5179.
- 6. In the absence of DMPU the monolithium derivative is only formed. The corresponding monoanion of the phenylsulfonyl homologue has been described: Breuilles, P.; Uguen, D. Tetrahedron Lett. 1988, 29, 201.
- This type of tosylated methylenecyclopropanes has been used for the generation of methylenecyclopropene: (a) Billups, W. E.; Blakeney, A. J.; Chamberlain, W. T. J. Org. Chem. 1976, 41, 3771. (b) Roberts, S. W.; Stirling, C. J. M. J. Chem. Soc., Chem. Commun. 1991, 170.
- 8. For other approach to this type of tosylated 2,5-dihydrofurans see: Nájera, C.; Yus, M. J. Org. Chem. 1989, 54, 1491.
- 9. The stereochemistry was assigned by analogy with <sup>1</sup>H NMR data for this type of dienic sulfones: Cuvigny, T.; Hervé du Penhoat, C.; Julia, M. *Tetrahedron* 1986, 42, 5329.
- 10. Beak, P.; Meyers, A. I. Acc. Chem. Res. 1986, 19, 356.
- 11. We thank DGICYT, Spain (Project no. PB88-0287) for financial support. J. M. S. thanks also DGICYT for a predoctoral fellowship.

(Received in UK 13 August 1992)