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Tosylated Lithium 2-(Lithiomethyl)-2-propen-1-olate: a γ-Alkoxide Allyl Sulfone Anion in Organic Synthesis

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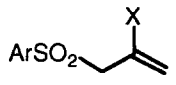
Abstract: Dilithiated 2-(tosylmethyl)-2-propen-1-ol (**6**) functioned as a nucleophile at the α-position of the allylic anion in reactions with deuterium oxide, alkyl halides, and aldehydes, and in conjugate additions to α,β-unsaturated carbonyl compounds. With nitro-olefins conjugate addition occurred at the γ-position of the allylic anion. The hydroxy ester derived by reaction with *tert*-butyl bromoacetate was converted into a variety of synthetically useful dienic and β,γ-unsaturated δ-lactones. The reductive detosylation of some of the hydroxy sulfones with sodium amalgam was also studied.

INTRODUCTION

Allylic carbanions derived from allyl sulfones are excellent allylic intermediates for regioselective carbon-carbon bond formation reacting at the α-position. They have been used in the synthesis of many natural products, specially terpenoids[1]. Mono-[2-8] and di-lithium[6b] derivatives of functionalized allyl sulfones of the type **1** (X=OR[2], SPh[2], SO_2Ph[2], $CONR_2$[3]), **2**[4], **3**[5], and **4** (X=Cl[6], $SiMe_3$[7], Br[8]) are also useful multicoupling reagents specially in annelation reactions[2b,3b,5,6b,d,7,8a,c]. In connection with our studies on the synthesis[9] and reactivity of γ-functionalized allyl sulfones with isobutene structure of the type **4** as mono-[6c] and di-lithium[6b,d]



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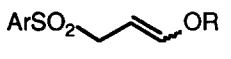

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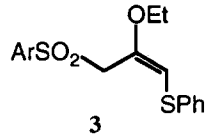

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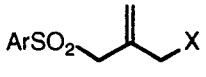

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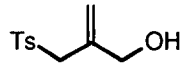


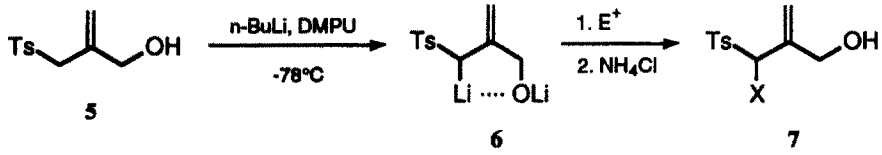
5

derivatives we were interested in the anion derived from 2-(tosylmethyl)-2-propen-1-ol (**5**)[9]. Very recently, the analogous phenylsulfonyl alcohol has been lithiated with LDA and the Michael addition of the corresponding anion to nitroolefins has been studied[8b]. We describe here our independent findings about the preparation,

reactivity and synthetic applications of the anion derived from tosylated methallyl alcohol **5**.

RESULTS AND DISCUSSION

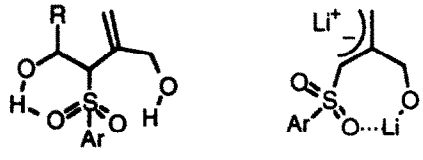
The treatment of 2-(tosylmethyl)-2-propen-1-ol (**5**)[10] with n-butyllithium (2 equiv.) at -78°C in THF in the presence of *N,N'*-dimethylpropyleneurea[12] (DMPU, 2 equiv.) for 15 min led to the formation of the corresponding dianion **6**. This intermediate was chemically characterized by deuterolysis with deuterium oxide to afford compound **7a** in 90% yield and with 78% of deuterium incorporation (MS) (Scheme 1 and Table 1). When a solution of intermediate **6** was allowed to rise to room temperature and deuterium oxide was added, 53% yield and 63% of deuterium was obtained. Reactions of intermediate **6** with other electrophiles, such as alkyl halides and aldehydes, took place at the α-sulfonyl position of the allylic anion to give compounds **7b-k** (Scheme 1 and Table 1). In the case of aldehydes 1,4-diols **7i-k** were obtained as mixture of diastereoisomers[13] (Table 1).



5 **6** **7**

Scheme 1

1,4-Diols **7i-k** were reluctant to cyclize to the corresponding methylenetetrahydrofurans under a number of different dehydration conditions (TsOH/PhMe, $BF_3{\cdot}OEt_2/CH_2Cl_2$, 6N HCl/THF or TFA/THF, under reflux). This behaviour may be rationalized by hydrogen bonding between hydroxy and SO_2 groups leading to conformation A. This type of intramolecular chelation has been also proposed by Ghera et al.[8b] for the anion (B) (Ar = phenyl), which is analogous to **6**, to explain the regio- and stereo-chemical outcomes in the reaction with nitroolefins (see *infra*).



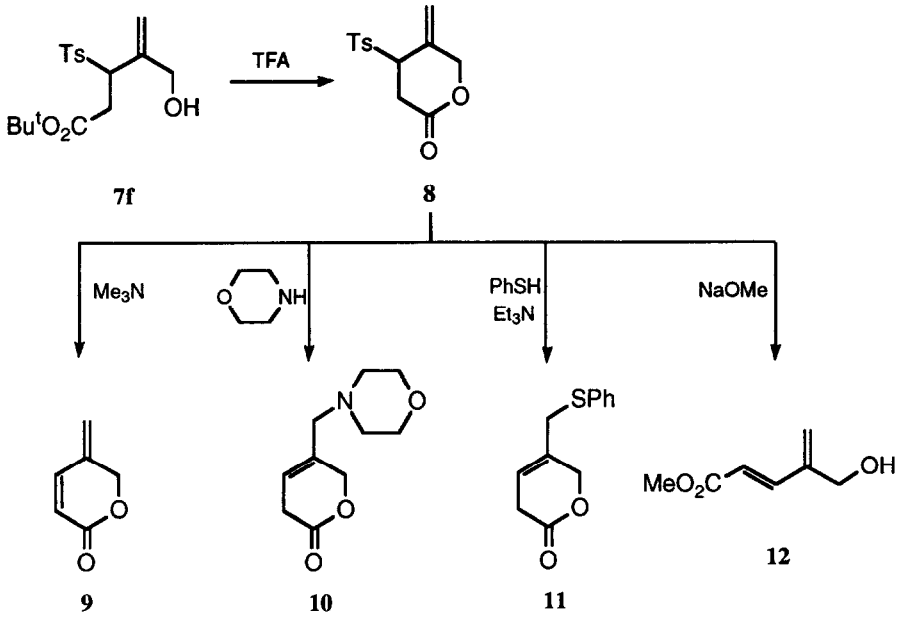
A **B**

Compound **7f**, obtained by reaction of intermediate **6** with *tert*-butyl bromoacetate, was transformed into δ-lactone **8** (89%) by treatment with 30% trifluoroacetic acid (TFA) under reflux for 2 h. This δ-lactone **8** was a convenient precursor to the new 5-methylene-2-penten-5-olide (**9**), which was obtained by reaction of compound **8** with an excess of trimethylamine in dichloromethane (Scheme 2 and Table 2). The δ-lactone **8** reacted with heteronucleophiles such as morpholine or thiophenol, in the presence of triethylamine, to furnish

Table 1. Reaction of Intermediate **6** with Electrophiles

Electrophile	Product			
	no.	X	yield (%)[a]	mp (°C)[b] or R_f[c]
D_2O	**7a**	D	90	83-84
MeI	**7b**	Me	70	0.48
CH_2=$CHCH_2Br$	**7c**	CH_2=$CHCH_2$	65	0.71
HC≡CCH_2Br	**7d**	HC≡CCH_2	51	0.72
n-BuI	**7e**	n-Bu	40	0.59
t-BuO_2CCH_2Br	**7f**	*t*-BuO_2CCH_2	90	79-80
Me_3SiCH_2Br	**7g**	Me_3SiCH_2	72	0.88
$PhCH_2Br$	**7h**	$PhCH_2$	55	0.76
EtCHO	**7i**	EtCHOH	90	0.42[d,e]
i-PrCHO	**7j**	i-PrCHOH	63	0.53[f]/0.48[e,g]
PhCHO	**7k**	PhCHOH	52	0.55/0.61[e,g]

[a] Isolated yield after flash chromatography (silica gel) based on starting alcohol **5**. [b] From hexane/ether. [c] For oils, in ether. [d] *Erythro/threo*: 3/1. [e] Deduced from ^1H NMR. [f] Mp 109-110°C. [g] *Erythro/threo*: 2/1.



Scheme 2

the β,γ-unsaturated δ-lactones **10** or **11**, respectively (Scheme 2 and Table 2). These lactones are probably formed by the 1,6-Michael addition of the nucleophile to the *in situ* formed pyrone **9** under kinetic reaction conditions[15]. Accordingly, the reaction of isolated pyrone **9** with morpholine or thiophenol and trimethylamine in dichloromethane yielded the same β,γ-unsaturated δ-lactones **10** or **11**, respectively (Table 2). When sodium methoxide was used as base, δ-lactone **8** underwent β-elimination of *p*-toluenesulfinic acid and ring opening to give stereoselectively the dienic hydroxyester **12** (Scheme 2 and Table 2).

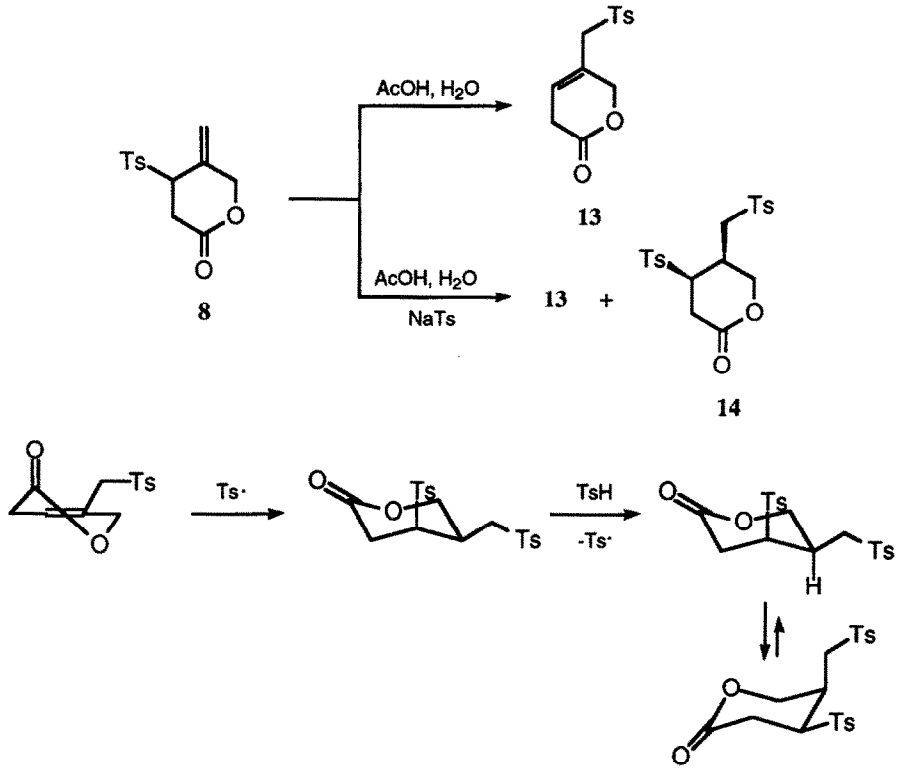
Lactone **8** suffered typical allyl sulfone 1,3-rearrangement[16] when it was treated with a mixture of acetic acid/water (3/2) under reflux for 1 d to lead to the formation of δ-lactone **13** (45% yield) by the dissociation-recombination mechanism involving an ion pair intermediate[16]. If this reaction was carried out in the presence of a seven fold excess of sodium *p*-toluenesulfinate under reflux for 4h a *ca.* 1/1 mixture of lactones **13** and **14** (74% overall yield) was obtained, probably through a radical chain mechanism involving the tosyl radical[16] (Scheme 3). The *cis* configuration of lactone **14** has been deduced from ^{1}H NMR spectrum, which showed two coupling constants of 7.2 and 7.8 Hz between the methylene and the methine protons at the α- and β-position of the carbonyl group, respectively. Due to the values of 5.3 and 3.9 Hz of the coupling constants between the methylene and the methine protons at the α- and β-position of the oxygen, we could conclude that the tosyl and tosylmethyl groups in compound **14** are at the equatorial and axial position, respectively. The obtained *cis* stereochemistry for product **14** is in agreement with the addition of the tosyl radical to the double bond of compound **13** at the axial position as in the case of the radical iodosulphonylation reaction of cyclohexene[17].

Table 2. Synthesis of Compounds **9-12**

Starting δ-lactone	Reaction conditions			Product		
	reagent	solvent	time (h)	no.	yield (%)[a]	R_f[b]
8	Me_3N	CH_2Cl_2	1	**9**	90	0.57
8	morpholine	THF	1	**10**	65	0.56
8	PhSH, Et_3N	CH_2Cl_2	4.5	**11**	60	0.72
8	NaOMe	MeOH	1	**12**	72	0.63
9	morpholine	CH_2Cl_2	1.5	**10**	73	0.56
9	PhSH, Me_3N	CH_2Cl_2	6	**11**	80	0.72

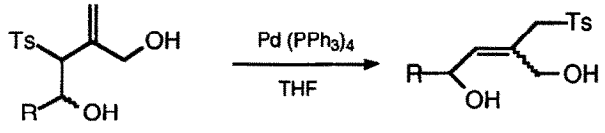
[a] Isolated yield of crude pure compounds (>93%, GLC), based on starting δ-lactone. [b] Ether.

Rearrangement of lactone **8** to give **13** did not take place on treatment with tetrakis(triphenylphosphine)-palladium(0) (10 mol %) in boiling toluene[18]. However, diols **7i** and **7j** underwent palladium(0)-catalysed



Scheme 3

isomerization in refluxing THF (2 and 3 d, respectively) to give compounds **15i** and **15j**, respectively. These isomerized diols were isolated as mixture of *Z/E* diastereoisomers in 1/5 ratio in the case of **15i** (73% yield) and only as the *E*-isomer for compound **15j** (40% yield) (Scheme 4). The stereochemistry was deduced from chemical shifts values for the olefinic protons in compounds **15** in comparison with lactone **13**.



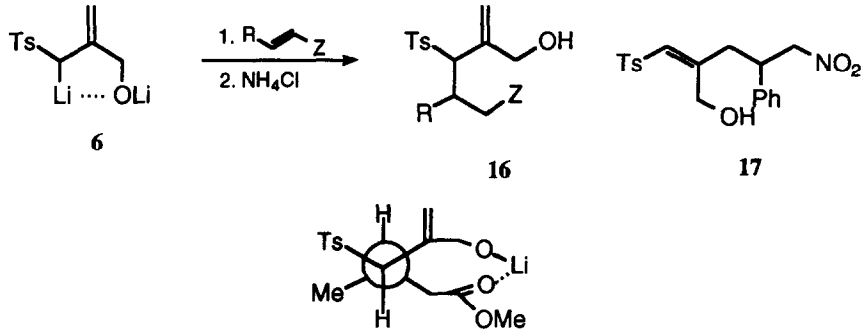
7i , R=Et
7j , R=i-Pr

15i (73%)
15j (40%)

Scheme 4

The Michael addition of dianion **6** to α,β-unsaturated carbonyl compounds led only α-addition products **16a-c**, whereas with β-nitrostyrene the γ-addition compound **17** was the exclusive product, which was

obtained regio- and stereo-selectively (Scheme 5 and Table 3). The regio- and stereo-chemistry of compound **17** is in agreement with structure **B**[8b] for dianion **6** (see *supra*) and seemed to be a consequence of the hard-hard interaction between the nitroolefin and the allylic anion[19]. The addition of dianion **6** took place in 1h at -78°C, in the case of β-nitrostyrene, and between -78 and -40°C for α,β-unsaturated ketones or ester. In the case of methyl crotonate the 1,4-addition was also steroselective and compound **16c** was obtained with *threo* configuration[20], probably due to the formation of the most stable transition state which afforded structure **C** favoured by chelation of the lithium alkoxide and the ester groups.

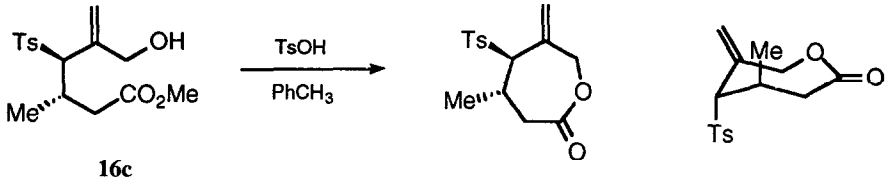


6 **16** **17**

C

Scheme 5

The stereochemistry of compound **16c** was demostrated by means of ^1H NMR NOE experiments with the ε-lactone **18**, which was obtained by heating hydroxyester **16c** with *p*-toluenesulfonic acid under toluene reflux for 2 d (70% yield) (Scheme 6). Caprolactone **18** shows also a small coupling constant for methine protons in the β and γ positions, which was consistent with the conformation in which the tosyl and the methyl groups are axially orientated, probably owing to a 1,3-allylic strain for the tosyl group in an equatorial orientation. The axial position for the methyl group is also in agreement with the coupling constants (6.0 and 1.7 Hz) between the methine and the methylene protons in β- and α-position, respectively.



16c **18**

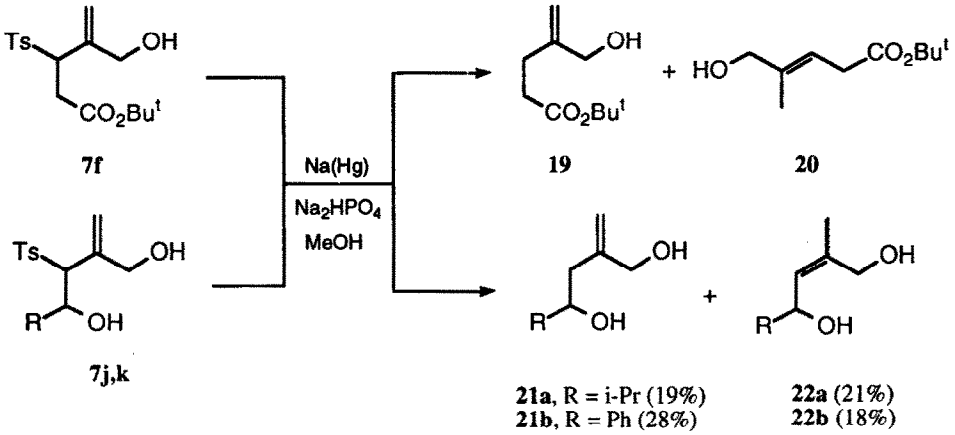
Scheme 6

Table 3. Michael Addition of Dianion **6** to Electrophilic Olefins

No.	R	Z	yield(%)[a]	R_f[b]
16a	H	$COCH_3$	42	0.20
16b	H	$COCH_2CH_3$	61	0.38
16c	CH_3	CO_2CH_3	66	0.49
17	Ph	NO_2	70	0.72

[a] Based on alcohol **5** after flash chromatography (silica gel). [b] Ether.

Finally, we have studied the reductive desulfonylation of representative compounds **7** with sodium amalgam in methanol buffered by Na_2HPO_4[21]. In the case of compound **7f** a mixture of exo and endo unsaturated alcohols **19** and **20** in *ca.* 1/1 molar ratio was obtained (65% yield) (Scheme 7). The *E*-stereochemistry of hydroxy-ester **20** was deduced by NOE experiments. Diols **7j** and **7k** were reduced in 48 and 58% overall yield (after flash chromatography), respectively, to give the expected exo and endo unsaturated diols **21** and **22** in *ca.* 1/1 molar ratio and also compounds **23a** (8%) and **24** (12%), respectively. In these cases all reduced products could be separated by chromatography. Dienic alcohol **23a** was formed through a Julia olefination reaction[22] and alcohol **24**[23] arose, probably, from the 1,4-reduction of the intermediate dienic alcohol **23b**. Compounds **22** were also obtained as mixtures of *Z/E* diastereomers in *ca.* 1/1 molar ratio (Scheme 7).



Scheme 7

We conclude that the allylic anion **6** derived from γ-tosylated methallyl alcohol **5** is a good functionalized organolithium compound[24] for the regioselective alkylation at the α-position with alkyl halides, aldehydes and α,β-unsaturated carbonyl compounds and it can be used for the synthesis of different substituted unsaturated δ-lactones.

EXPERIMENTAL PART

General. See reference 6d.

Synthesis of 2-(Tosylmethyl)-2-propen-1-ol (5)[9]. The reaction of 2-(chloromethyl)-3-tosylpropene with $NaNO_2$ in DMSO[9] can be carried out to prepare 1 g of compound **5**. For more than 5 mmol scale the procedure was carried out by hydrolysis[11] of 2-(tosylmethyl)-2-propenyl acetate, prepared from 2-(chloromethyl)- 3-tosylpropene (97%)[9], as follows: to a solution of 2-(tosylmethyl)-2-propenyl acetate (2.68 g, 10 mmol) in methanol (5 mL) was added 3M HCl (1.5 mL) and the resulting mixture was stirred at rt for 1 d. Then, the solvent was evaporated (15 Torr) and the residue was dissolved in water (10 mL) and extracted with ether (3x20 mL). The organic layer was dried (Na_2SO_4) and evaporated (15 Torr) to give crude product **5**, which was recrystallized to afford 2.03 g of pure compound **5** (90%) as white crystals.

Reaction of Lithium 2-(Lithiomethyl)-2-propen-1-olate (6) with Electrophiles. Synthesis of Compounds 7, 16 and 17. General Procedure. To a solution of 2-(tosylmethyl)-2-propen-1-ol (**5**) (98 mg, 0.43 mmol) and DMPU (0.116 mL, 0.95 mmol) in dry THF (3 mL) cooled at -78°C was added a 1.6 M solution of n-butyllithium (0.6 mL, 0.95 mmol) in hexanes. After 15 min strirring, the corresponding electrophile was added (1.2 mmol) and the reaction mixture was warmed up to -40°C (in the case of D_2O and β-nitrostyrene the temperature was kept at -78°C for 1 h, in the case of n-butyl iodide was warmed up to -15°C). The reaction mixture was hydrolyzed with a saturated aqueous solution of ammonium chloride and extracted with ether (3x20 mL). The organic layer was dried (Na_2SO_4) and evaporated and the residue was purified by column chromatography (silica gel, hexane/ether) and/or recrystallization to afford compounds **7**, **16** and **17**. Yields and physical data are included in Tables 1 and 3, spectral and analytical data follow.

***2-(1-Tosyl-1-deuteriomethyl)-2-propen-1-ol* (7a)**: ν (KBr) 3480 (OH), 3050, 1630, 880 (C=CH), 1290 and 1140 cm^{-1} (SO_2); δ_H 2.44 (s, 3H, CH_3Ar), 2.71 (br. s, 1H, OH), 3.87 (s, 1H, CHD), 4.19 (s, 2H, CH_2O), 4.93, 5.33 (2s, 2H, CH_2=C), 7.35 and 7.76 (2d, *J*=8.1 Hz, 4H, ArH); δ_C 21.60 (CH_3Ar), 59.79 (t, *J*=22.1 Hz, CHD), 64.99 (CH_2O), 120.41 (C=CH_2), 128.77, 129.72, 135.16, 136.49 and 144.92 (ArC, *C*=CH_2); *m/z* 228 (*M*$^+$+1, 14%), 211 (*M*$^+$+1-H_2O, 100), 157 (71), 147 (31), 139 (34) and 73 (22) (Found: C, 58.24; H, 5.57; S, 14.20. Calcd. for $C_{11}H_{13}DO_3S$: C, 58.11; H, 5.70; S, 14.20%).

***2-(1-Tosylethyl)-2-propen-1-ol* (7b)**[25]: ν 3500 (OH), 3050, 1630, 815 (C=CH), 1290 and 1140 cm^{-1} (SO_2); δ_H 1.45 (d, *J*=7.2 Hz, 3H, CH_3CS), 2.40 (br. s, 1H, OH), 2.45 (s, 3H, CH_3Ar), 3.94 (q, *J*=7.2 Hz, 1H, CHS), 4.14, 4.23 (2dd, *J*=13.7, 2.7 Hz, 2H, CH_2OH), 5.11, 5.42 (2s, 2H, CH_2=C), 7.35 and 7.74 (2d, *J*=8.1 Hz, 4H, ArH); δ_C 14.47 (CH_3CS), 21.62 (CH_3Ar), 62.33 (CS), 65.56 (CH_2O), 118.51, 141.84 (C=CH_2), 129.34, 129.54, 133.59 and 144.87 (ArC); *m/z* 241 (*M*$^+$+1, 14%), 223 (*M*$^+$+1-

H_2O, 76), 185 (32), 159 (39), 157 (100), 139 (82), 125 (27), 93 (10), 85 (79), 69 (40) and 67 (65).

2-Methylene-3-tosyl-5-hexen-1-ol **(7c)**: ν 3490 (OH), 3070, 1640, 810 (C=CH), 1300 and 1145 cm-1 (SO_2); δ_H 2.5–2.60 (m with s at 2.45, 4H, OH, CH_3Ar), 2.55, 2.77 (2m, 2H, CH_2CS), 3.80 (dd, *J*=11.6 and 3.9 Hz, 1H, CHS), 4.00, 4.09 (2d, *J*=14.0 Hz, CH_2O), 5.04 (m, 2H, CH_2CH), 5.13, 5.48 (2s, 2H, CH_2=C), 5.59 (m, 1H, C*H*=CH_2), 7.34 and 7.74 (2d, *J*=8.4 Hz, 4H, ArH); δ_C 21.59 (*C*H_3Ar), 32.40 (*C*H_2CS), 65.76 (CH_2OH), 66.80 (CHS), 118.46, 119.15 (2xC=*C*H_2), 133.80 (*C*H=CH_2), 139.51 (*C*=CH_2), 129.29, 129.58, 132.58 and 144.97 (ArC); *m/z* 267 (*M*+-1, 14%), 223 (*M*+-1-H_2O, 28), 185 (25), 157 (100), 139 (68), 111 (49), 110 (10) , 109 (19).

2-Methylene-3-tosyl-5-hexyn-1-ol **(7d)**: ν 3500 (OH), 3300, 2120 (C≡CH), 3100, 1640, 820 (C=CH), 1300 and 1145 cm-1 (SO_2); δ_H 1.96 (t, *J*=2.7 Hz, 1H, C≡CH), 2.27 (br. s, 1H, OH), 2.38 (s, 3H, CH_3Ar), 2.77 (ddd, *J*=16.7, 11.3, 2.7 Hz, 1H of CH_2CH), 2.89 (ddd, *J*=16.7, 4.5, 2.7 Hz, 1H of CH_2CH), 3,97 (dd, *J*=11.3, 4.5 Hz, 1H, CHS), 4.13, 4.14 (2dd, *J*=13.7, 2.5 Hz, 2H, CH_2OH), 5.17, 5.46 (2s, 2H, CH_2=C), 7.28 and 7.67 (2d, *J*=8.1 Hz, 4H, ArH); δ_C 19.01 (*C*H_2CS), 21.59 (*C*H_3Ar), 65.27 (CHS), 66.67 (CH_2O), 70.87, 78.82 (C≡C), 119.47, 139.30 (C=CH_2), 129.26, 129.73, 133.56 and 145.32 (ArC); *m/z* 265 (*M*+-1, 14%), 247 (*M*+-1-H_2O, 38), 185 (24), 157 (47), 139 (100), 109 (70) and 105 (12).

2-(1-Tosylpentyl)-2-propen-1-ol **(7e)**[25]: ν 3500 (OH), 3100, 1630, 820 (C=CH), 1290 and 1140 cm-1 (SO_2); δ_H 0.75 (t, *J*=6.6 Hz, 3H, CH_3CH_2), 1.17 (m, 4H, CH_2CH_2CH_3) 1.74, 1.90 (2m, 2H, CH_2CS), 2.35-2.50 (m with s at 2.37, 4H, OH and CH_3Ar), 3.64 (dd, *J*=11.7, 3.3 Hz, 1H, CHS), 3.97, 4.08 (2d, *J*=13.8 Hz, 2H, CH_2OH), 5.03, 5.38 (2s, 2H, CH_2=C), 7.26 and 7.66 (2d, *J*=8.1 Hz, 4H, ArH); δ_C 13.60 (*C*H_3CH_2), 21.57 (*C*H_3Ar), 22.17, 27.56, 28.47 [(*C*H_2)$_3$CH_3], 65.73 (CH_2OH), 67.53 (CHS), 118.56, 140.12 (C=CH_2), 129.25, 129.47, 134.02 and 144.74 (ArC); *m/z* 283 (*M*+-1, 8%), 265 (*M*+-1-H_2O, 14), 185 (15), 157 (46), 139 (42) and 109 (100).

tert-*Butyl 5-Hydroxy-4-methylene-3-tosyl-pentenoate* **(7f)**: ν (KBr) 3530 (OH), 3060, 1640, 890 (C=CH), 1730 (C=O), 1290 and 1140 cm-1 (SO_2); δ_H 1.31 [s, 9H, $(CH_3)_3C$], 2.24 (br. s, 1H, OH), 2.37 (s, 3H, CH_3Ar), 2.74 (dd, *J*=16.6, 11.5 Hz, 1H of CH_2CO), 2.92 (dd, *J*=16.6, 4.3 Hz, 1H of CH_2CO), 3.92, 4.01 (2dd, *J*=13.5, 5.5 Hz, 2H, CH_2OH), 4.14 (dd, *J*=11.5, 4.3 Hz, 1H, CHS), 5.07, 5.36 (2s, 2H, CH_2=C), 7.26 and 7.66 (2d, *J*=8.3 Hz, 4H, ArH); δ_C 21.58 (*C*H_3Ar), 27.84 (3x*C*H_3C), 34.87 (*C*H_2CO_2), 62.43 (CS), 66.04 (CH_2OH), 82.11 (CH_3CO), 118.37, 140.82 (C=CH_2), 129.34, 129.66, 133.58, 145.16 (ArC) and 169.13 (C=O); *m/z* 341 (*M*+-1, 0.4%), 285 (16), 267 (83), 249 (30), 185 (19), 157 (15), 139 (100) and 111 (36) (Found: C, 59.80; H, 7.10; S, 9.30. Calcd. for $C_{17}H_{24}O_5S$: C, 60.00; H, 7.06; S, 9.41%).

2-[1-Tosyl-2-(trimethylsilyl)ethyl]-2-propen-1-ol **(7g)**[6c].

2-[1-Tosyl-2-phenylethyl]-2-propen-1-ol **(7h)**: ν 3480 (OH), 3020, 3080, 1640, 820 (C=CH),

1290 and 1140 cm^{-1} (SO_2); δ_H 1.73 (br. s, 1H, OH), 2.45 (s, 3H, CH_3Ar), 3.03 (dd, *J*= 13.6, 12.1 Hz, 1H, of CH_2Ph), 3.42 (dd, *J*= 13.6, 3.5 Hz, 1H of CH_2Ph), 3.71, 3.83 (2d, *J*= 13.8 Hz, 2H, CH_2OH), 4.04 (dd, *J*=12.1, 3.5 Hz, 1H, CHS), 5.34, 5.45 (2s, 2H, CH_2=C), 7.14-7.24 (m, 5H, Ph), 7.35 and 7.79 (2d, *J*= 8.3 Hz, 4H, ArH); δ_C 21.60 (CH_3Ar), 34.50 (CH_2Ph), 66.3 (CH_2O), 67.80 (CHS), 119.30 (C=CH_2) 126.8, 128.50, 129.00, 129.30, 129.70, 134.20, 136.40, 139.60 and 145.00 (ArC and CH_2=*C*); *m/z* 317 (*M*$^+$+1, 2%), 299 (*M*$^+$+1-H_2O, 13), 185 (15), 161 (10), 159 (13), 157 (100), 144 (13), 143 (99) and 139 (23).

erythro/threo-*2-Methylene-3-tosyl-hexane-1,4-diol* **(7i)**: ν 3600-3200 (OH), 3100, 1640, 880 (C=CH), 1290 and 1140 cm^{-1} (SO_2); δ_H *(erythro)* 0.84 (t, *J*= 7.4 Hz, 3H, CH_3CH_2), 1.40, 1.52 (2m, 2H, CH_2CH_3), 2.37 (s, 3H, CH_3Ar), 3.05, 3.68 (2br. s, 2H, 2xOH), 3.66 (d, *J*= 2.5 Hz, 1H, CHS), 3.93, 4.13 (2d, *J* =13.7 Hz, CH_2OH), 4.20 (m, 1H, CHO), 5.26, 5.39 (2s, 2H, CH_2=C), 7.27 and 7.66 (2d, *J*=8.1 Hz, 4H, ArH); δ_H *(threo)* 0.87 (t, *J*=7.4 Hz, 3H, CH_3CH_2), 1.40, 1.52 (2m, 2H, CH_2CH_3), 2.36 (s, 3H, CH_3Ar), 3.05, 3.68 (2br. s, 2H, 2xOH), 3.74 (d, *J*= 9.1 Hz, 1H, CHS), 4.00 (m, 2H, CH_2OH), 4.15 (m, 1H, CHO), 4.93, 5.32 (2s, 2H, CH_2C), 7.29 and 7.67 (2d, *J*= 8.1 Hz, 4H, ArH); δ_C *(erythro)* 10.15 (CH_3CH_2), 21.65 (CH_3Ar), 27.63 (CH_2CH_3), 65.60 (CH_2O), 70.10 (CHS), 71.93 (CHO), 123.77, 137.48 (C=CH_2), 128.76, 129.81, 134.65 and 145.21 (ArC); δ_C *(threo)* 9.38 (CH_3CH_2), 21.65 (CH_3Ar), 27.29 (CH_2CH_3), 65.76 (CH_2O), 71.41 (CHS), 72.87 (CHO), 119.52, 139.61 (C=CH_2), 128.76, 129.21, 135.29 and 145.21 (ArC); *m/z* 285 (*M*$^+$+1, 3%), 267 (17), 209 (19), 185 (10), 157 (30), 139 (24), 111 (100) and 93 (12).

erythro/threo-*5-Methyl-2-methylene-3-tosyl-hexane-1,4-diol* **(7j)**: ν 3600-3200 (OH), 3100, 1640, 880 (C=CH), 1290 and 1140 cm^{-1} (SO_2); δ_H *(erythro)* 0.79, 1.00 [2d, *J*=6.6 Hz, 6H, $(CH_3)_2CH$], 1.83 [m, 1H, $CH(CH_3)_2$], 2.45 (s, 3H, CH_3Ar), 3.19 (br. s, 1H, CH_2OH), 3.77 (d, *J*= 2.6 Hz, 1H, CHO*H*), 3.92 (d, *J*=2.0 Hz, 1H, CHS), 3.98 (m, 1H, *C*HOH), 4.08 (dd, *J* =13.4, 4.8 Hz, 1H of CH_2OH), 4.27 (dd, *J* =13.4, 2.6 Hz, 1H of CH_2OH), 5.30, 5.46 (2s, 2H, CH_2=C), 7.35 and 7.74 (2d, *J*=8.1 Hz, 4H, ArH); δ_H *(threo)* 0.82, 1.00 [2d, *J*=6.9 Hz, 6H, $(CH_3)_2CH$], 1.82 [m, 1H, $CH(CH_3)_2$] , 2.23 (m, 1H, CH_2OH), 2.45 (s, 3H, CH_3Ar), 3.52 (d, *J*= 2.5 Hz, 1H, CHO*H*), 3.90 (d, *J*=9.9Hz, 1H, CHS), 4.10, 4.17 (2m, 2H, CH_2OH), 4.90, 5.40 (2s, 2H, CH_2=C), 7.34 and 7.75 (2d, *J*= 8.1 Hz, 4H, ArH); δ_C *(erythro)* 18.66, 19.03 [$(CH_3)_2CH$)], 21.59 (CH_3Ar), 31.44 [$CH(CH_3)_2$], 65.06 (CH_2O), 70.80 (CHS), 74.01 (CHO), 124.05, 137.85 (C=CH_2), 128.71, 129.70, 134.53 and 145.07 (ArC); δ_C *(threo)* 18.66, 19.03 [$(CH_3)_2CH$)], 21.67 (CH_3Ar), 29.98 [$CH(CH_3)_2$], 65.40 (CH_2O), 72.04 (CHS), 73.83 (CHO), 119.88, 139.61 (C=CH_2), 129.28, 129.52, 134.62 and 145.12 (ArC); *m/z* 299 (*M*$^+$+1, 3%), 281 (*M*$^+$+1-H_2O, 7), 157 (15), 139 (11), 125 (100) and 73 (43) (Found: C, 60.66; H, 7.46; S, 10.66. Calcd. for $C_{15}H_{22}O_4S$: C, 60.40; H, 7.38; S, 10.74%).

erythro/threo-*2-Methylene-4-phenyl-3-tosyl-butane-1,4-diol* **(7k)**: ν 3470 (OH), 3035, 1640, 880 (C=CH), 1290 and 1140 cm^{-1} (SO_2); δ_H *(erythro)* 2.36 (s, 3H, CH_3Ar), 2.64 (br. s, 2H, 2xOH),

3.49 (dd, *J*=13.0, 5.5 Hz, 1H of CH_2OH), 3.58 (dd, *J*=13.0, 5.0 Hz, 1H of CH_2OH), 3.89 (d, *J*=3.0 Hz, 1H, CHS), 5.37, 5.59 (2s, 2H, CH_2=C), 5.48 (d, *J*=3.0 Hz, 1H, CHO), 7.15 (s, 5H, Ph), 7.22 and 7.65 (2d, *J*=8.2 Hz, 4H, ArH); δ_H *(threo)* 2.35 (s, 3H, CH_3Ar), 2.64 (br. s, 2H, 2xOH), 3.25, 3.38 (2d, *J*=14.0 Hz, 2H, CH_2OH), 4.04 (d, *J*=10.1 Hz, 1H, CHS), 5.09, 5.15 (2s, 2H, CH_2=C), 5.22 (d, *J*= 10.1 Hz, 1H, CHOH), 7.16 (s, 5H, Ph), 7.24 and 7.70 (2d, *J*= 8.2 Hz, 4H, ArH); δ_C *(erythro)* 21.69 (CH_3Ar), 65.93 (CH_2O), 72.11 (CHS), 74.16 (CHO), 119.69 , 127.64, 128.34, 129.28, 129.48, 129.65, 135.01, 136.48, 139.47 and 145.12 (C=C, ArC); δ_C *(threo)* 21.56 (CH_3Ar), 66.58 (CH_2O), 70.42 (CHS), 71.59 (CHO), 122.17, 125.99, 127.83, 128.18, 128.80, 129.69, 134.59, 136.12, 139.33 and 145.09 (C=C, ArC); *m/z* 333 (M^++1, 0.2%), 316 (M^++1-H_2O, 5), 227 (13), 209 (284), 175 (51), 159 (39), 157 (38), 143 (33), 139 (37), 107 (100) and 79(11).

7-Hydroxy-6-methylene-5-tosylheptan-2-one **(16a)**: ν 3480 (OH), 3080, 1640, 840 (C=CH), 1700 (C=O), 1290 and 1140 cm^{-1} (SO_2); δ_H 2.02, 2.23 (2m, 2H CH_2CS), 2.08 (s, 3H, CH_3CO), 2.41-2.54 (m with s at 2.44, 5H, CH_2CO and CH_3Ar), 2.60 (br. s, 1H, OH), 3.84 (dd, *J*=10.9, 4.4 Hz, CHS), 4.07 (s, 2H, CH_2OH), 5.12, 5.46 (2s, 2H, CH_2=C), 7.34 and 7.74 (2d, *J*=8.1 Hz, 4H, ArH); δ_C 21.57 (CH_3Ar), 22.48 (CH_2CS), 29.80 (CH_3CO), 39.77 (CH_2CO), 65.72 (CH_2OH), 65.76 (CHS), 118.88, 140.02 ($C=CH_2$), 129.22, 129.56, 133.85, 144.89 (ArC) and 207.34 (C=O); *m/z* 297 (M^++1,<1%), 279 (34), 157 (12), 141 (100), 123 (43) and 81 (18).

8-Hydroxy-7-methylene-6-tosyloctan-3-one **(16b)**: ν 3480 (OH), 3010, 1610, 880 (C=CH), 1700 (C=O), 1290 and 1140 cm^{-1} (SO_2); δ_H 0.99 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 2.00, 2.26 (2m, 2H, CH_2CS), 2.35 (q, *J*= 7.3 Hz, 2H, CH_2CH_3), 2.40-2.51 (m with s at 2.45, 5H, CH_2CH_2CO, CH_3Ar), 2.65 (br. s, 1H, OH), 3.85 (dd, *J*= 10.9, 4.4 Hz, 1H, CHS), 4.07 (s, 2H, CH_2OH), 5.12, 5.48 (2s, 2H, CH_2=C), 7.34 and 7.74 (2d, *J*= 8.1 Hz, 4H, ArH); δ_C 7.61 (CH_3CH_2), 21.57 (CH_3Ar), 22.53 (CH_2CS), 35.76, 38.42 [$(CH_2)_2CO$], 65.74 (CH_2OH), 65.85 (CHS), 118.86, 140.02 ($C=CH_2$), 129.21, 129.56, 133.86, 144.88 (ArC) and 210.14 (C=O); *m/z* 311 (M^++1, 1%), 293 (23), 155 (100), 139 (48), 137 (43) and 81 (19).

threo-*Methyl 6-Hydroxy-3-methyl-5-methylene-4-tosylhexanoate* **(16c)**[25]: ν 3490 (OH), 3080, 1640, 880 (C=CH), 1720 (C=O), 1290 and 1140 cm^{-1} (SO_2); δ_H 1.20 (d, *J*= 6.7 Hz, 3H, CH_3CH), 1.90 (br s, 1H, OH), 2.27 (dd, *J*=15.4, 6.6 Hz, 1H of CH_2CO), 2.44 (s, 3H, CH_3Ar), 2.75 (m, 1H, $CHCH_3$), 2.85 (dd, *J*=15.4, 3.9 Hz, 1H of CH_2CO), 3.66 (s, 3H, CH_3O), 3.70 (d, *J*=9.1 Hz, 1H, CHS), 3.77 (m, 2H, CH_2OH), 5.44, 5.46 (2s, 2H, CH_2=C), 7.32 and 7.72 (2d, *J*= 8.2 Hz, 4H, ArH); δ_C 19.00 (CH_3CH), 21.54 (CH_3Ar), 31.09 ($CHCH_3$), 38.36 (CH_2CO), 51.63 (CH_3O), 66.52 (CH_2OH), 69.87 (CHS), 119.20, 140.23 ($C=CH_2$), 129.03, 129.47, 135.64, 144.67 (ArC) and 172.82 (C=O); *m/z* 327 (M^++1, 3%), 309 (40), 295 (25), 171 (100), 139 (62) and 97 (40).

(Z)-*5-Nitro-4-phenyl-2-(tosylmethylene)-heptan-1-ol* **(17)**[25]: ν 3480 (OH), 3080, 1650, 800

(C=CH), 1550, 1380 (NO_2), 1290 and 1140 cm^{-1} (SO_2); δ_H 2.35 (br. s, 1H, OH), 2.44 (s, 3H, CH_3Ar), 2.54 (dd, *J*=13.5, 9.8 Hz, 1H of CH_2CHPh), 2.74 (m, 1H of CH_2CHPh), 3.77 (m, 1H, C*H*Ph), 4.46 (m, 2H, CH_2OH), 4.58 (dd, *J*= 7.5, 2.0 Hz, 2H, CH_2N), 5.95 (s, 1H, CHS), 7.05-7.29 (m, 7H, Ph and 2H of *p*-TolH) and 7.53 (d, *J*=8.2 Hz, 2H of *p*-TolH); δ_C 21.63 (*C*H_3Ar), 39.73 (*C*H_2C), 42.27 (*C*HPh), 59.70 (CH_2OH), 79.70 (CH_2N), 127.00, 127.39, 128.02, 129.09, 129.89, 130.16, 137.49, 137.94, 144.55 and 153.80 (C=CH, ArC); *m/z* 376 (*M*$^+$+1, 11%), 358 (18), 202 (56), 157 (43), 155 (100), 141 (31), 139 (35) and 91 (11).

Synthesis of 4-Methylene-3-tosylpentanolide (8). A solution of compound **7f** (350 mg, 1.3 mmol) in 30% trifluoroacetic acid (3 mL) was heated under reflux for 2 h. The cooled reaction mixture was poured into water and extracted with ether (3x20 mL). The organic layer was dried (Na_2SO_4), evaporated (15 Torr) and the resulting residue was recrystallized from hexane/ether to give 244 mg of lactone **8** as white crystals (89%): mp 109-110°C; ν (KBr) 3080, 1640, 835 (C=CH), 1750 (C=O), 1300 and 1140 cm^{-1} (SO_2); δ_H 2.40 (s, 3H, CH_3Ar), 2.71 (dd, *J*=16.5, 7.4 Hz, 1H of CH_2CO), 3.02 (dd, *J*=16.5, 7.9 Hz, 1H of CH_2CO), 4.11 (m, 1H, CHS), 4.51, 4.73 (2d, *J*=12.8 Hz, CH_2O), 5.33, 5.49 (2s, 2H, CH_2=C), 7.32 and 7.68 (2d, *J*=8.2 Hz, 4H, ArH); δ_C 21.67 (*C*H_3Ar), 29.96 (*C*H_2CO), 60.63 (CHS), 70.79 (CH_2OH), 123.20, 130.52 (C=CH_2), 129.34, 130.08, 132.63, 145.92 (ArC) and 168.25 (C=O); *m/z* 266 (*M*+, 0.5%), 155 (13), 111 (100), 92 (15), 91 (66), 83 (11), 67 (42), 65 (43), 53 (14), 51 (16) and 41 (44) (Found: C, 58.50; H, 5.40; S, 11.90. Calcd. for $C_{13}H_{14}O_4S$: C, 58.65; H, 5.26; S, 12.03%).

Reaction of 4-Methylene-3-tosylpentanolide (8) with Nucleophiles. General Procedure. To a solution of compound **8** (146 mg, 0.55 mmol) in the suitable solvent (see Table 2), cooled at 0°C, was added dropwise the corresponding nucleophile (2 equiv.). The reaction mixture was stirred for 5 min at 0°C and then at room temperature for the time indicated in Table 2. Then, a saturated aqueous solution of NaCl (3 mL) was added and the resulting mixture was extracted with ether (3x20 mL), dried (Na_2SO_4) and evaporated (15 Torr) yielding crude pure compounds **9-12** (>95%, GLC). These compounds decomposed in the purification by flash cromatography (silica gel, hexane/AcOEt) except compound **11.** Yields and physical data are included in Table 2, spectral and analytical data follow.

***4-Methylene-2-penten-5-olide* (9)**: ν 3030, 1580, 820 (C=CH) and 1710 cm^{-1} (C=O); δ_H 4.92 (m, 2H, CH_2O), 5.31 (m, 2H, CH_2=C), 5.88 and 7.02 (2d, *J*=9.7 Hz, 2H, CH=CH); δ_C 69.76 (CH_2O), 118.52, 134.75 (CH_2=C), 119.56, 143.37 (CH=CH) and 163.13 (C=O); *m/z* 110 (*M*+, 51%), 82 (100), 81 (60), 54 (17), 53 (77), 52 (67), 51 (36), 50 (35) (Found: *M*+ 110.037001. Calcd. for $C_6H_6O_2$, 110.036780).

***4-(Morpholinomethyl)-3-penten-5-olide* (10)**: ν 3040, 1650, 830 (C=CH) and 1730 cm^{-1} (C=O); δ_H 2.38 (t, *J*=4.5 Hz, 4H, 2xCH_2CH_2O), 2.98 (s, 2H, CCH_2N), 3.09 (s, 2H, CH_2CO), 3.68 (t, *J*=4.5 Hz, 4H, 2xCH_2CH_2O) and 4.89 (br. s, 1H, CH=C); δ_C 30.00 (*C*H_2CO), 53.42 (CH_2CH_2N), 60.92 (CCH_2N), 66.81 (*C*H_2CH_2N), 70.25 (CCH_2O), 119.32 (*C*H=C), 131.57 (CH=*C*) and 169.22 (C=O); *m/z* 197 (*M*+, 20%), 149 (100), 139 (12), 119 (28), 111 (12), 110 (13), 105 (16), 100 (11), 97 (10), 91 (44), 87 (22), 82

(22), 81 (18), 71 (57), 56 (34), 55 (23), 54 (24), 43 (40), 41 (44) (Found: M^+ 197.106384. Calcd. for $C_{10}H_{15}NO_3$, 197.105194).

4-(Phenylthiomethyl)-3-penten-5-olide **(11)**[25]: ν 3040, 1590, 890 (C=CH) and 1730 cm^{-1} (C=O); δ_H 2.96 (d, *J*=1.2 Hz, 2H, CH_2CO), 3.51 (s, 2H, CH_2S), 4.90 (s, 2H, CH_2O), 5.51 (br. s, 1H, CH=C) and 7.18-7.50 (m, 5H, PhH); δ_C 29.94 (CH_2CO), 37.05 (CH_2S), 69.78 (CH_2O), 119.48, 130.02 (CH=C), 127.30, 128.91, 128.93 and 131.14 (Ph); *m/z* 220 (M^+, 19%), 123 (59), 111 (22), 110 (66), 109 (100), 108 (18), 83 (13), 82 (42), 81 (43), 78 (12), 77 (32), 69 (39), 67 (35), 66 (16), 65 (87), 63 (18), 58 (12), 54 (17), 53 (96), 52 (30), 51 (75), 50 (46), 44 (39) and 41 (84).

(E)-*Methyl 5-Hydroxy-4-methylene-2-pentenoate* **(12)**[25]: ν 3370 (OH), 3060, 1630, 850 (C=CH) and 1700 cm^{-1} (C=O); δ_H 1.62 (br. s, 1H, OH), 3.77 (s, 3H, CH_3O), 4.36 (s, 2H,CH_2OH), 5.53, 5.65 (2s, 2H, CH_2=C), 5.99 and 7.34 (2d, *J*=16.2 Hz, 2H, CH=CH); δ_C 51.69 (CH_3O), 62.30 (CH_2O), 118.33, 143.82 (CH=CH), 122.98, 143.40 (CH_2=C) and 167.34 (C=O); *m/z* 142 (M^+, 14%), 111 (35), 84 (22), 82 (100), 81 (35), 55 (37), 53 (27), 51 (24) and 41 (11).

Reaction of 4-Methylene-2-pentenolide (9) with Nucleophiles. General Procedure. Reactions were carried out as in the case of compound **8**, starting from pyrone **9** (40 mg, 0.36 mmol) using the reaction conditions indicated in Table 2, to lead to compounds **10** and **11**.

Rearrangements of 4-Methylene-3-tosylpentanolide (8). A solution of lactone **8** (53 mg, 0.20 mmol) in a mixture of acetic acid/water (3/2, 2.5 mL) was stirred at 110°C for 1 d. The reaction mixture was cooled at rt and extracted with ether (3x10 mL), the organic layer was washed successively with water and brine, dried (Na_2SO_4) and evaporated (15 Torr). The residue was purified by flash chromatography (silica gel, hexane/AcOEt) to give 24 mg of lactone **13** (45%). When the same reaction was carried out in the presence of sodium *p*-toluenesulfinate (300 mg, *ca.* 1.5 mmol) for 4 h, a mixture of compounds **13** and **14** were obtained. They were separated by flash chromatography (hexane/ether) yielding 21 mg of compound **13** and 11 mg of compound **14** (74% overall yield), which were recrystallized separately from hexane/CH_2Cl_2.

4-(Tosylmethyl)-3-penten-5-olide **(13)**: mp 94-95 °C; ν (Nujol) 1720 (C=O), 1300 and 1140 cm^{-1} (SO_2); δ_H 2.46 (s, 3H, CH_3Ar), 3.06 (m, 2H, CH_2CO), 3.83 (s, 2H, CH_2S), 4.93 (br. s, 2H, CH_2O), 5.66 (br. s, 1H, CH=C), 7.37 and 7.74 (2d, *J*=8.1 Hz, 4H, ArH); δ_C 21.50 (CH_3Ar), 30.40 (CH_2CO), 59.80 (CH_2S), 70.00 (CH_2O), 123.43 (C=CH), 145.30 (CH=C), 126.60, 128.12, 129.85, 134.50, (ArC) and 167.90 (C=O); *m/z* 266 (M^+, 1%), 155 (9), 139(11), 111(100), 91 (61), 82 (22), 67 (39), 53 (29) and 41 (38) (Found: C, 58.50; H, 5.30; S, 12.30. Calcd. for $C_{13}H_{14}O_4S$: C, 58.65; H, 5.26; S, 12.03%).

cis-*3-Tosyl-4-(tosylmethyl)-5-pentanolide* **(14)**: mp 182-183°C; ν (KBr) 1740 (C=O), 1300 and 1140 cm^{-1} (SO_2); δ_H 2.49 (s, 6H, 2xCH_3Ar), 2.74 (dd, *J*=16.5, 7.5 Hz, 1H of CH_2CO), 2.89 (dd, *J*=16.5, 7.5 Hz, 1H of CH_2CO), 3.12 (m, 1H, $CHCH_2O$), 3.28 (dd, *J*=14.3, 5.2 Hz, 1H of CH_2S), 3.35 (dd, *J*= 14.3, 7.7 Hz, 1H of CH_2S), 3.67 (td, *J*=7.5, 5.5 Hz, 1H, CHS), 4.46 (dd, *J*=12.3, 5.3 Hz, 1H of CH_2O), 4.56 (dd, *J*=12.3, 3.9 Hz, 1H of CH_2O), 7.41 (m, 4H, ArH), 7.73 and 7.80 (2d, *J*= 8.3 Hz, 4H, ArH); δ_C

21.72, 21.76 (2xCH_3Ar), 28.64 ($CHCH_2S$), 29.50 (CH_2CO), 56.76 (CH_2S), 58.93 (CHS), 67.76 (CH_2O), 128.09, 129.21, 130.22, 130.41, 132.34, 135.68, 145.64, 146.24 (ArC) and 168.11 (C=O); *m/z* 422 (*M*+, <0.1%), 267 (15), 155 (29), 139 (35), 111 (25), 97 (190), 91 (100), 81 (24), 67 (16), 65 (47) and 52 (33) (Found: C, 56.77; H, 5.26; S, 15.25. Calcd. for $C_{20}H_{22}O_6S_2$: C, 56.87; H, 5.21; S, 15.17%).

Rearrangements of Compounds 7. Synthesis of Products 15. General Procedure. A mixture of diol **7i** or **7j** (0.18 mmol) and $Pd[(PPh_3)]_4$ (21 mg, 0.018 mmol) in dry THF (3 mL) was heated under reflux for 2 or 3 d, respectively. Then, the suspension was cooled at room temperature, filtered off and to the filtrate was added brine (10 mL) and extracted with ether (2x10 mL). The organic layer was dried (Na_2SO_4) and evaporated (15 Torr) and the residue was purified by flash chromatography (silica gel, hexane/ether) followed by recrystallization to give compounds **15**.

(Z,E)-2-(Tosylmethyl)-2-hexene-1,4-diol **(15i)**: mp 134-135°C (hexane/ether); ν 3560 (OH), 3040, 1680 (C=CH), 1240 and 1150 cm^{-1} (SO_2); δ_H 0.73, 0.81 (2t, *J*=7.5 Hz, 3H, CH_3CH_2), 1.18-1.57 (m, 2H, CH_2CH_3), 1.89, 2.87 (2br. s, 2H, 2xOH), 2.37, 2.39 (2s, 3H, CH_3Ar), 3.6-4.26 (m, 5H, CH_2O, CHO CH_2S), 5.20 (d, *J*=8.3 Hz, 1H, *Z*-CH=C), 5.83 (d, *J*=8.7 Hz, 1H, *E*-CH=C) and 7.29-7.75 (m, 4H, ArH); δ_C 9.41, 9.67 (CH_3CH_2), 21.60, 21.63 (CH_3Ar), 29.34, 29.66 (CH_2CH_3), 55.44, 60.09, 62.10, 66.41 (CH_2S, CH_2O), 68.64, 69.20 (CHO), 128.17, 128.27, 128.46, 128.59, 129.79, 130.05, 135.00, 135.97, 138.64, 141.11, 145.00 and 145.36 (ArC, CH=C); *m/z* 266 (M^+-H_2O, 3%), 255 (4), 201 (23), 199 (22), 183 (26), 157 (44), 152 (17), 139 (46), 129 (24), 111 (53), 92 (27), 91 (95), 81 (53), 77 (66), 71 (16), 65 (46), 63 (16), 57 (100), 53 (20), 51 (51), 43 (28) and 41 (34) (Found: C, 58.95; H, 7.11; S, 11.34. Calcd. for $C_{14}H_{20}O_4S$: C, 59.15; H, 7.04; S, 11.27%).

(E)-5-Methyl-2-(tosylmethyl)-2-hexene-1,4-diol **(15j)**: mp 96-97°C (hexane/ether); ν 3700-3100 (OH), 3020, 1650 (C=CH), 1290 and 1140 cm^{-1} (SO_2); δ_H 0.78, 0.90 [2d, *J*=6.7 Hz, 6H, $(CH_3)_2CH$], 1.66 [m, 1H, $CH(CH_3)_2$], 2.11, 2.70 (2br. s, 2H, 2xOH), 2.40 (s, 3H, CH_3Ar), 3.86-4.05 (m, 5H, CH_2S, CH_2O, CHO), 5.90 (d, *J*=8.5 Hz, 1H, CH=C), 7.32 and 7.76 (2d, *J*=8.1 Hz, 4H, ArH); δ_C 18.11, 18.27 [$(CH_3)_2CH$], 21.67 (CH_3Ar), 33.43 [$CH(CH_3)_2$], 55.54 (CH_2S), 66.68 (CH_2O), 72.94 (CHO), 128.17, 128.78, 130.08, 136.12, 137.70 and 145.37 (ArC, CH=C); *m/z* 280 (M^+-H_2O, 1%), 262 (2), 255 (26), 237 (10), 157 (100), 139 (58), 92 (12), 91 (39), 81 (29), 65 (12), 43 (18) and 41 (14) (Found: C, 60.00; H, 7.56; S, 10.50. Calcd. for $C_{15}H_{22}O_4S$: C, 60.40; H, 7.38; S, 10.74%).

Synthesis of *trans*-3-Methyl-5-methylene-4-tosylhexanolide (18). A mixture of ester **17c** (65 mg, 0.20 mmol) and *p*-toluenesulfonic acid (52 mg, 0.28 mmol) was dissolved in toluene (3 mL) and heated under reflux for 2 d. Then, the reaction mixture was dissolved in ether (30 mL), washed successively with water, a saturated solution of aqueous $NaHCO_3$ (10 mL) and brine. The organic layer was dried (Na_2SO_4) and evaporated (15 Torr) and the resulting residue was purified by flash chromatography (silica gel, hexane/ether) affording 41 mg of compound **18** (70%): mp 177-178°C (hexane/ether); ν (KBr) 3030, 1630, 880 (C=CH), 1730 (C=O), 1290 and 1140 cm^{-1} (SO_2); δ_H 1.06 (d, *J*=7.2 Hz, 3H, CH_3CH), 2.44 (s, 3H, CH_3Ar), 2.62 (dd, *J*=14.5, 6.0 Hz, 1H of CH_2CO), 3.05 (m, 1H, $CHCH_3$), 3.78 (dd, *J*=14.5, 1.7 Hz, 1H of CH_2CO),

4.38, 5.37 (2d, *J*=13.0 Hz, 2H, CH_2O), 4.89, 5.47 (2s, 2H, CH_2=C), 7.33 and 7.67 (2d, *J*= 8.2 Hz, 4H, ArH); δ_C 18.53 (*C*H_3CH), 21.66 (*C*H_3Ar), 25.52 (*C*HCH$_3$), 36.53 (*C*H_2CO), 67.91 (CH_2O), 74.18 (CHS), 128.81, 129.70, 130.86, 132.96, 133.59, 145.27 (C=C, ArC) and 172.88 (C=O); *m/z* 295 (*M*+1, 0.2%), 294 (*M*+, 0.1), 139 (39), 97 (100), 91 (37), 79 (18), 77 (14), 67 (27), 65 (25) and 55 (18) (Found: C, 61.22; H, 6.12; S, 10.88. Calcd. for $C_{15}H_{18}O_4S$: C, 61.15; H, 6.20; S, 10.93%).

Reduction of Compounds 7 with Sodium Amalgam. General Procedure. To a suspension of anhydrous Na_2HPO_4 (251 mg, 1.75 mmol) and *ca.* 6% sodium amalgam (1.70 g, 4.4 mmol) in dry methanol (5 mL) was dropped at 0°C a solution of the corresponding sulphone (0.44 mmol) in methanol (1.5 mL). The reaction mixture was stirred at room temperature until the reduction was complete (monitored by TLC and GLC). Then, the reaction mixture was hydrolyzed with water and extracted with dichloromethane (3x15 mL). The organic layer was dried (Na_2SO_4), concentrated in vacuo (15 Torr) and the residue was purified by flash chromatography (silica gel, hexane/ether) and/or recrystallized to yield compounds **19-24**. Compounds **19** and **20** could not be separated. Yields are included in the text, physical, spectroscopic and analytical data follow.

tert-*Butyl* *5-Hydroxy-4-methylene-pentenoate* **(19)**: ν 3400 (OH), 3030, 1645, 840 (C=CH) and 1720 cm^{-1} (C=O); δ_H 1.38 [s, 9H, $(CH_3)_3C$], 2.35 (br. s, 1H, OH), 2.33 (m, 4H, $CH_2CH_2CO_2$), 3.97 (s, 2H, C*H*$_2$OH), 4.80 and 4.98 (2s, 2H, CH_2=C); δ_C 27.80 (*C*H_2CH_2CO), 28.00 [(*C*H_3)C], 34.42 (*C*H_2CO), 68.32 (CH_2OH), 110.11 (*C*H_2=C), 147.62 (CH_2=*C*) and 172.7 (C=O); *m/z* 130 (*M*$^+$-Bu^t, 4%), 57 (100), 43 (26) and 41 (31).

tert-*Butyl* *5-Hydroxy-4-methyl-3-pentenoate* **(20)**: ν 3400 (OH), 3030, 1645, 840 (C=CH) and 1720 cm^{-1} (C=O); δ_H 1.37 [s, 9H, $(CH_3)_3C$], 1.60 (s, 3H, CH_3C=C), 2.35 (br. s, 1H, OH), 2.93 (d, *J*=7.1 Hz, 2H, CH_2CO), 4.01 (s, 2H, C*H*$_2$OH) and 5.51 (tq, *J*=7.1, 2.7 Hz, 1H, CH=C); δ_C 28.00 [(*C*H_3)$_3$C], 31.14 (*C*H_3C=C), 33.83 (*C*H_2CO), 65.90 (CH_2O),117.61 (*C*H=C), 138.22 (CH=*C*) and 171.4 (C=O); *m/z* 153 (*M*$^+$-H_2O,-CH_3, 1%), 113 (34), 112 (55), 84 (31), 71 (25), 67 (17), 57 (100), 56 (21), 43 (31) and 41 (51).

5-Methyl-2-methylene-hexane-1,4-diol **(21a)**: R_f 0.68 (ether); ν 3700-3000 (OH), 3040, 1640 and 880 cm^{-1} (C=CH); δ_H 0.87, 0.89 [2d, *J*=6.8 Hz, 6H, (C*H*$_3$)$_2$CH], 1.65 [dheptet, *J*=6.8, 5.5 Hz, 1H, $(CH_3)_2$C*H*], 2.07 (dd, *J*=14.1, 9.8 Hz, 1H of C*H*$_2$CHO), 2.30 (dd, *J*=14.1, 1.8 Hz, 1H of C*H*$_2$CHO), 2.46 (br. s, 2H, 2xOH), 3.43 (ddd, *J*=9.8, 5.5, 1.8 Hz, 1H, CHO), 4.04 (s, 2H, CH_2O), 4.91 and 5.07 (2s, 2H, CH_2=C); δ_C 17.56, 18.61 [(*C*H_3)$_2$CH], 33.70 [*C*H(CH$_3$)$_2$], 38.69 (*C*H_2CHO), 66.42 (CH_2O), 75.65 (CHO), 113.86 (*C*H_2=C) and 146.60 (*C*=CH_2); *m/z* 101 (*M*$^+$-Pr^i, 4%), 83 (42), 73 (63), 72 (66), 71 (10), 57 (41), 56 (16), 55 (98), 54 (49), 53 (20), 45 (17), 44 (15), 43 (95), 42 (16) and 41 (100) (Found: *M*$^+$-H_2O 126.105159. Calcd. for $C_8H_{14}O$, 126.104465).

2-Methylene-4-phenylbutane-1,4-diol **(21b)**: R_f 0.72 (ether); mp 88-89°C (hexane/ether); ν (KBr) 3700-3100 (OH), 3080, 1660 and 880 cm^{-1} (C=CH); δ_H 1.62 (br. s, 1H, OH), 2.46 (m, 2H, C*H*$_2$CH), 2.70 (br. s 1H, OH), 4.04 (s, 2H, CH_2O), 4.76 (dd, *J*=8.5, 4.4 Hz, 1H, CHO), 4.91, 5.08 (2s, 2H,

CH_2=C), 7.19 and 7.32 (2m, 5H, ArH); δ_C 44.10 (*C*H_2CH), 66.42 (CH_2O), 73.61 (CHO), 114.8 (*C*H_2=C), 125.70, 127.62, 128.41, 144.00 and 145.52 (*C*=CH_2, ArC); *m/z* 178 (*M*+, 1%), 107 (100), 79 (50) and 77 (28) (Found: *M*+-H_2O 160.088850. Calcd. for $C_{11}H_{12}O$, 160.088815).

(Z,E)-*2,5-Dimethyl-2-hexene-1,4-diol* **(22a)**[25]: R_f 0.57 (ether); ν 3700-3100 (OH), 3040, 1640 and 880 cm^{-1} (C=CH); δ_H 0.80, 0.81 [2d, *J*=6.8 Hz, 6H, (C*H*$_3$)$_2$CH], 0.89, 0.90 [2d, *J*=6.7 Hz, 6H, (C*H*$_3$)$_2$CH], 1.20, 1.80 (2br. s, 2H, 2xOH), 1.65 (d, *J*=1.2 Hz, 3H, *E*-CH_3C), 1.77 (d, *J*= 1.4 Hz, 3H, *Z*-CH_3C), 3.92, 4.24 (2d, *J*=12.6 Hz, 2H, CH_2O), 3.97 (s, 2H, CH_2O), 4.05 (m, 2H, 2xCHO), 5.30 (dq, *J*=8.5, 1.2 Hz, 1H, *Z*-CH=C) and 5.40 (dq, *J*=8.4, 1.4 Hz, 1H, *E*-CH=C) ; δ_C 14.16 (*C*H_3CH), 18.04, 18.15 [(*C*H_3)$_2$CH], 21.83 (*C*H_3CH), 34.11, 34.34 [(CH$_3$)$_2$*C*H], 61.92, 68.01 (CH_2O), 72.83, 73.18 (CHO), 126.24, 129.33 (*C*H=C), 138.20 and 138.84 (*C*=CH); *m/z* 126 (*M*+-H_2O, 1%), 101 (23), 83 (38), 71 (15), 57 (16), 55 (91), 53 (13), 43 (100) and 41 (73).

(Z)-*2-Methyl-4-phenyl-2-butene-1,4-diol* **(22b)**: R_f 0.72 (ether); mp 115-116°C (hexane/ether); ν 3700-3100 (OH), 3030, 1660 and 820 cm^{-1} (C=CH); δ_H 0.89, 1.25 (2br. s, 2H, 2xOH), 1.83 (s, 3H, CH_3C), 4.01 (s, 2H, CH_2O), 5.50-5.56 (m, 2H, CHO, CH=C) and 7.26-7.36 (m, 5H, ArH); δ_C 14.09 (*C*H_3C), 62.06 (CH_2O), 70.39 (CHO), 125.80, 127.54, 128.56, 130.55, 137.56 and 143.70 (C=C, ArC); *m/z* 160 (*M*+-H_2O, 68%), 145 (53), 132 (60), 116 (49), 91 (100) and 77 (33) (Found: C, 74.15; H, 7.88. Calcd. for $C_{11}H_{14}O_2$: C, 74.16; H, 7.87%)[26].

(E)-*2-Methyl-4-phenyl-2-butene-1,4-diol* **(22b)**: R_f 0.72 (ether); mp 115-116°C (hexane/ether); ν 3700-3100 (OH), 3030, 1660 and 820 cm^{-1} (C=CH); δ_H 1.54 (br. s, 2H, 2xOH), 1.78 (s, 3H, CH_3C), 3.95 (s, 2H, CH_2O), 5.45 (d, *J*=8.7 Hz, 1H, CHO), 5.65 (dq, *J*=8.7, 1.5 Hz, 1H, CH=C) and 7.18-7.38 (m, 5H, ArH); δ_C 14.11 (*C*H_3C), 68.12 (CH_2O), 71.11 (CHO), 127.14, 128.12, 128.81, 129.32, 137.84 and 145.71 (C=CH, ArC); *m/z* 160 (*M*+-H_2O, 68%), 145 (51), 132 (57), 116 (47), 91 (100), 77 (28) and 51 (32)[26].

(E)-*5-Methyl-2-methylene-3-hexen-1-ol* **(23a)**: R_f 0.83 (ether); ν 3700-3100 (OH), 3060, 1630 and 960 cm^{-1} (C=CH); δ_H 0.80, 0.96 [2d, *J*=6.7 Hz, 6H, (C*H*$_3$)$_2$CH)], 1.65 (br. s, 1H, OH), 2.25 [m, 1H, C*H*(CH$_3$)$_2$], 4.25 (d, *J*=5.0 Hz, 2H, CH_2O), 4.98, 5.08 (2s, 2H, CH_2=C), 5.66 (dd, *J*= 16.1, 6.8 Hz, 1H, CHC*H*=CH) and 5.97 (d, *J*= 16.1 Hz, 1H, CC*H*=CH); δ_C 18.22, 18.26 [(*C*H$_3$)$_2$CH], 31.39 [(CH$_3$)$_2$*C*H], 63.03 (CH_2O), 113.11 (*C*H_2=C), 125.47, 136.70 and 137.79 (*C*=CH_2 and CH=CH); *m/z* 101 (*M*+-Pr^i, 12%), 86 (10), 84 (15), 59 (48), 58 (17), 49 (22) and 43 (100).

(E/Z)-*2-Methyl-4-phenyl-2-buten-1-ol* **(24)**[23]: R_f 0.80 (ether); ν 3600-3100 (OH), 3050, 1610 and 880 cm^{-1} (C=CH); δ_H 1.40 (br. s, 2H, 2xOH, *E*+*Z*), 1.79 (s, 3H, CH_3C, *E*), 1.85 (br. s, 3H, CH_3C, *Z*), 3.40 (m, 4H, 2xC*H*$_2$CH, *E*+*Z*), 4.05 (s, 2H, CH_2O, *E*), 4.25 (s, 2H, CH_2O, *Z*), 5.52 (m, 1H, CH=C, *Z*), 5.62 (m, 1H, CH=C, *E*) and 7.16-7.38 (m, 5H, ArH, *E*+*Z*); δ_C 13.79 (CH_3, *E*), 21.34 (CH_3, *Z*), 33.80 (*C*H_2CH, *Z*), 33.91 (*C*H_2CH, *E*), 61.63 (CH_2O, *Z*), 68.78 (CH_2O, *E*), 124.67 (*E*+*Z*), 126.50 (*Z*), 128.33 (*E*+*Z*), 128.45 (*E*+*Z*), 135.35 (*Z*), 135.68 (*E*) and 140.95 (*Z*+*E*) (ArC, C=CH); *m/z* 162 (*M*+, 21%), 131

(100), 129 (32), 128 (13), 115 (18), 104 (22), 92 (13), 91 (54), 78 (10), 77 (16), 71 (13), 65 (15), 51 (14) and 43 (12).

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24. For a review on functionalized organolithium compounds, see: Nájera, C.; Yus, M. *Trends in Organic Chemistry* **1991**, *2*, 155-181.
25. High resolution mass spectrum corresponding to M^+ could not be obtained.
26. Elemental analysis was carried out for the mixture of both diastereomers of **22b**.

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