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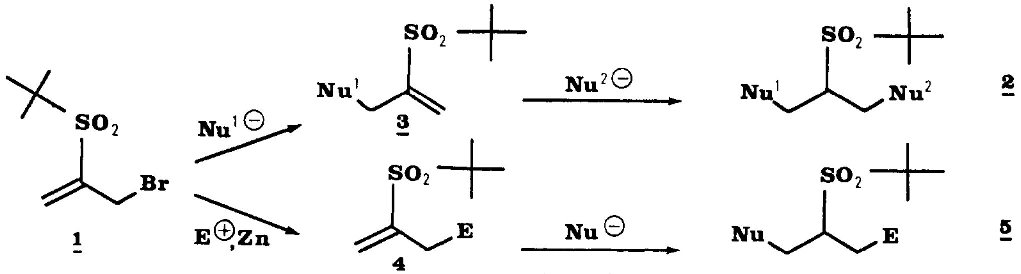
3-Bromo-2-(tert-butylsulfonyl)-1-propene.A multi-coupling reagent.
Part 2. <1>

P. AUVRAY, P. KNOCHEL* and J.F. NORMANT
Laboratoire de chimie des organo-éléments, tour 44-45
4, place Jussieu 75230 Paris Cédex 05 France

Summary :

3-bromo-2-(tert-butylsulfonyl)-1-propene **1** *reacts in good yields with various electrophiles (aldehydes, ketones, nitriles and alkynes) in the presence of zinc metal to give unsaturated sulfones of type* **4**. *These compounds can further react with soft or hard nucleophiles (alkyl-, vinyl-, aryllithium compounds, a nitroparaffin or dimethylmalonate) to yield highly functionnalized sulfones of type* **5** *which can be readily transformed into enones or into a dienone. Thus sulfone* **1** *is a versatile multi-coupling reagent which is synthetically equivalent to the* $a^2/a^{2'}$ *synthon* **8** *and to the* $d^2/a^{2'}$ *synthons* **9** *and* **10**.



Scheme 1

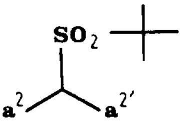
We recently reported <1> that the easily available 3-bromo-2-(tert-butylsulfonyl)-1-propene **1** could react stepwise with two different nucleophiles Nu^1 and Nu^2 to give sulfones of type **2** in high yields (see scheme 1). The nucleophile Nu^1 can be of high reactivity (alkyl-, vinyl-, aryl- Grignard derivatives and alkynyllithiums) as well as of moderate reactivity (lithium ketone or ester enolates, indolylmagnesium bromide and lithium thiolate). A lithium cuprate chosen as nucleophile Nu^2 allows the intermediate unsaturated sulfone **3** to contain other functional groups (such as an ester). Sulfone **1** is thus an efficient $a^2/a^{2'}$ multi-coupling <2,3> reagent.

We now report that the same reagent **1** can act as $d^2/a^{2'}$ multi-coupling reagent : in the presence of zinc, bromo-sulfone **1** reacts under our previously described <4,5> Barbier conditions with a variety of electrophiles such as aldehydes, ketones, nitriles and even alkynes to furnish functionnalized unsaturated sulfones of type **4**. These sulfones **4** can again react with a number of nucleophiles Nu to give the highly functionnalized sulfones of type **5** (see scheme 1). Table 1 shows that aldehydes and ketones react uniformly well and furnish the corresponding β-hydroxy-vinylsulfones **4a**-**4h** in high yields. With enones only 1, 2 addition is observed (see compounds **4g** and **4h** of table 1). Nitriles lead to the β-keto-vinylsulfones **4i**-**4k** in acceptable yields (see table 2). Hydrolysis of the intermediate imine requires a treatment with ≃1N HCl (0.5 h, 0°) at the end of the reaction . Only activated alkynes like trimethylsilyl propargyl ether lead to the desired diene **4l** in good yield (74%, see table 3) . In the case of hexyne, the reaction is too sluggish and the corresponding diene **4n** is obtained in low yield (side products like the dimer of sulfone **1** are also formed;compare with ref.4).

The unsaturated sulfones **4** easily give sulfones of type **5** (see scheme 1) in good yields if they are treated with hard nucleophiles like alkyl-, aryl- or vinyllithium derivatives (2 equiv. of RLi at -80°; 15 min) as well as with soft nucleophiles like 2-nitropropane <8> or dimethylmalonate <9> (4 equiv.) in the presence of 1,8-diazabicyclo [5. 4. 0] undec-7-ene (DBU) (1 equiv. ; 12 h. ; 25°). Some of these Michael-additions can be highly diastereoselective (see table 4).

The functionnalized sulfones **5** can be transformed easily in sulfur free compounds by successive oxidation with 3 equiv. of pyridinium chlorochromate (PCC) in CH_2Cl_2(1 equiv. AcONa; 15-20 h. at 25°) leading to the ketones **6a-6b** which readily eliminate tert-$BuSO_2H$ by treatment with 1.1 equiv. of DBU in CH_2Cl_2 (25° ; 0.25-1 h.) ; see scheme 2. This reaction proceeds under mild conditions and can even be used for the synthesis of a dienone : thus oxidation of sulfone **5e** and successive elimination of tert-$BuSO_2H$ and HNO_2<10> lead to the dienone **7c** in 90% yield (see scheme 3).

We have thus demonstrated that sulfone **1** is an efficient multi-coupling reagent which corresponds to the $a^2/a^{2'}$ synthon **8** (see ref. <1>) and the $d^2/a^{2'}$ synthons **9** and **10** :



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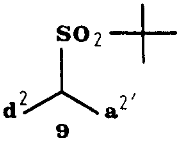

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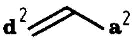

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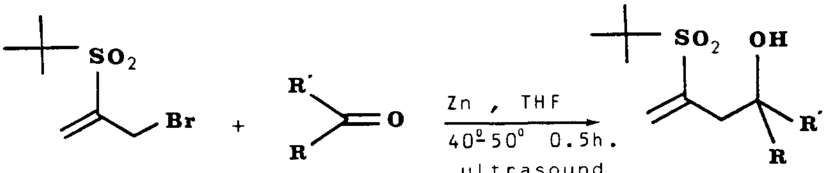
The highly functionnalized sulfones obtained by our method should find many applications. Some sulfones of type **4** are nice precursors for cyclisation reactions. These developpements will be reported shortly.

Acknowledgements :

We thank the Vieille Montagne Company for a generous gift of zinc of high purity , the CNRS for financial support (UA 473) and the Rhône Poulenc Company for a grant to one of us.

Table 1 <6>

Products of type **4** obtained by the reaction of sulfone **1** with aldehydes and ketones in the presence of dibromoethane activated zinc (45°-50°; 0. 5 h. in THF) under Barbier conditions <7>.



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4a-4h

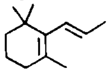
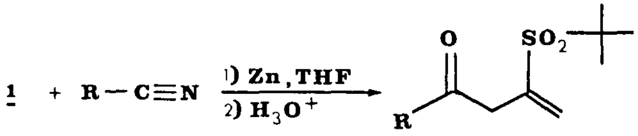
	R	R'	m.p. (°)	yield (%)		R	R'	m.p. (°)	yield (%)
4a	Pent	H	25	90	**4e**	Pent	Pent	51	82
4b	tert-Bu	H	83	85	**4f**	Me	Ph	127	86
4c	Ph	H	97	90	**4g**		Me	87	83
4d	Et	Et	61	68	**4h**	$-(CH_2)_3-CH=CH-$		81	80

Table 2 <6>

Products of type **4** obtained by the reaction of sulfone **1** with nitriles in the presence of zinc under Barbier conditions <7>.

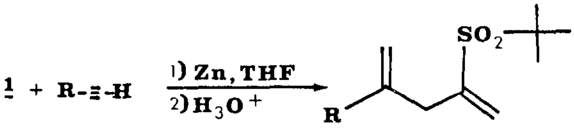


4i-4k

	R	m.p. (°)	yield (%)
4i	Pr	51	64
4j	Pent	49	70
4k	Cyclohexyl	23	65

Table 3 <6>

Products of type **4** obtained by the reaction of sulfone **1** with alkynes in the presence of zinc under Barbier conditions <7>.



4l-4n

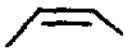
	R	m.p. (°)	yield (%)
4l	$-CH_2OSiMe_3$ (a)	34	74
4m	$-(CH_2)_2OSiMe_3$ (a)	oil	46
4n	Bu	oil	20

(a) This compound is isolated as an alcohol (Hydrolysis with 1N HCl , 0° , 0. 5 h.)

Table 4 <6>

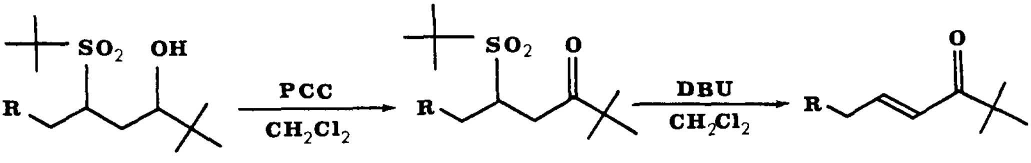
Products **5a-5f** obtained by adding a nucleophile Nu to an unsaturated sulfone of type **4**.

5a-5f

	R	R'	Nu	d.r.(a)	yield(%)
5a	Ph	Me	n-BuLi	57:43	88
5b	t-Bu	H	 Li	>95:5	81
5c	t-Bu	H	PhLi	90:10	93
5d	t-Bu	H	Et  Li	>95:5	90
5e	t-Bu	H	$(CH_3)_2CHNO_2$	68:32 (b)	90
5f	t-Bu	H	$CH_2(CO_2Me)_2$	95:5 (c)	86

(a) The diastereoisomeric ratio (d.r.) is determined by ^{13}C or ^{1}H-NMR .
(b) m.p. of **5e** : 123-132°.
(c) m.p. of **5f** : 93°.

Scheme 2 <6>

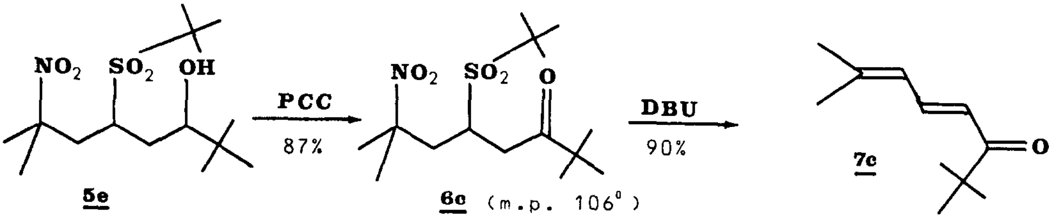


5c : R=Ph
5d : R=(Z)-3-Hexenyl

6a : R=Ph ; 87%
6b : R=(Z)-3-Hexenyl ; 88%

7a : R=Ph ; 93%
7b : R=(Z)-3-Hexenyl ; 90%

Scheme 3 :



5e

6c (m.p. 106°)

7c

References and notes :

<1> Part 1. P. KNOCHEL and J. F. NORMANT, Tetrahedron Lett. **26**, 425 (1985).

<2> D. SEEBACH Ang. Chem. **91** , 259 (1979); Ang. Chem. Int. Ed. Engl. **18**, 239 (1979)

<3> P. KNOCHEL and D. SEEBACH , Tetrahedron Lett. **23** , 3897 (1982)

<4> P. KNOCHEL and J. F. NORMANT , Tetrahedron Lett. **25** , 1475 (1984)

<5> P. KNOCHEL and J. F. NORMANT , Tetrahedron Lett. **25** , 4383 (1984)

<6> The given yields are those of flash chromatographically purified materials. All spectroscopic data (I.R., ^{1}H-NMR and ^{13}C-NMR) are compatible with the shown structure.

<7> For a typical procedure see a similar Barbier reaction reported in reference <5>.

<8> The presence of a free β-hydroxy group in the unsaturated sulfone seems to enhance the rate of the addition reaction. Thus the reaction of 2-tertbutylsulfonyl-4-methyl-pentene with an excess of 2-nitropropane and one equivalent of DBU at 25° needs more than 50 hours and 2-tertbutylsulfonyl-4,4-dimethyl-pentene gives no reaction even after 12 hours at 120° . For the addition of nitroparaffins to α,β-unsaturated sulfoxides and sulfones see :
G. D. BUCKLEY, J. L. CHARLISH and J. D. ROSE J. Chem. Soc , 1514 (1947)
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N. ONO, A. KAMIMURA and A. KATJI Synthesis , 226 (1984)

<9> Under our conditions (excess of malonate), $(R(SO_2tBu)CH\text{-}CH_2)_2C(COOMe)_2$, resulting from diaddition, is never observed , compare with :
W. TRUCE and E. WELLISH , J. Am. Chem. Soc **74** , 2881 (1952)

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