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AN EASY SYNTHESIS OF THE 2-PHENYLSULFONYL-SUBSTITUTED ALLYLIC BROMIDES AND ACETATES AND THEIR REACTIVITY TOWARDS NUCLEOPHILES

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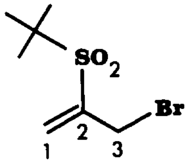
<u>Summary</u> - The reaction of phenyl vinyl sulfone with various aldehydes in the presence of a catalytic amount of DABCO furnishes in good yields the corresponding 2-phenylsulfonyl-substituted alcohols 5a-5e which can be easily converted into their acetates 2a-2b or into their allylically rearranged bromides 3a-3d. These reagents, in turn, react with nucleophiles (ketone enolates and cuprates) with an allylic rearrangement (S_N2' mechanism) to give the functionalized unsaturated sulfones 6a-g and 7a-g. A palladium catalyzed reaction allows a stereo-controlled transformation of the sulfone 6b into the (Z,Z) skipped 1,4-diene 8.



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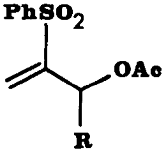
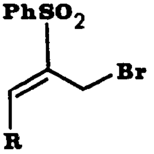


2a : R=CH_3
2b : R=C_3H_7

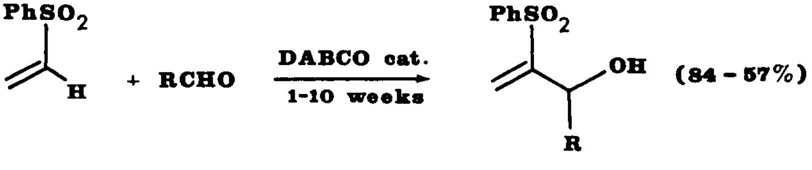


3a : R=CH_3
3b : R=C_3H_7
3c : R=C_4H_9
3d : R=isoC_4H_9

Recently[1,2] we have demonstrated that the easily available 3-bromo-2-tert-butyl-sulfonyl-1-propene 1 is a versatile multi-coupling reagent[3]. It reacts with various nucleophiles[1] (amines, thiolates, ketone and ester enolates, aryl-, alkenyl- alkynyl- and alkyl magnesium or lithium reagents) or with electrophiles[2] (aldehydes, ketones, nitriles, alkynes) in the presence of zinc, leading to functionalized unsaturated sulfones which can undergo further useful transformations[4,5]. The synthetic potential of the reagent 1 would be further enhanced if substituents could be introduced at the positions 1 or 3 of the sulfone 1.

We report now the synthesis of the reagents of type 2 or 3 and their reactivity[6]. We have found that a slow reaction occurs at 25° between the phenyl vinylsulfone 4 and various aldehydes in the presence of a catalytic amount of 1,4-diazabicyclo [2.2.2] octane (DABCO)[7,8] to give the allylic alcohols 5a-5e in good yields (see scheme 1 and table 1).

<u>Scheme 1</u> -



4 5a - 5e

Table 1 - **Synthesis of the allylic alcohols 5a-5e by the reaction of the phenyl vinylsulfone 4 with aldehydes in the presence of a catalytic amount of DABCO**[8,9]

RCHO	Product	Reaction time (weeks)	Yield %
CH_3CHO	5a	2	84
PrCHO	5b	4	75
BuCHO	5c	10	79
iso-BuCHO	5d	11	81
PhCHO	5e	3	57

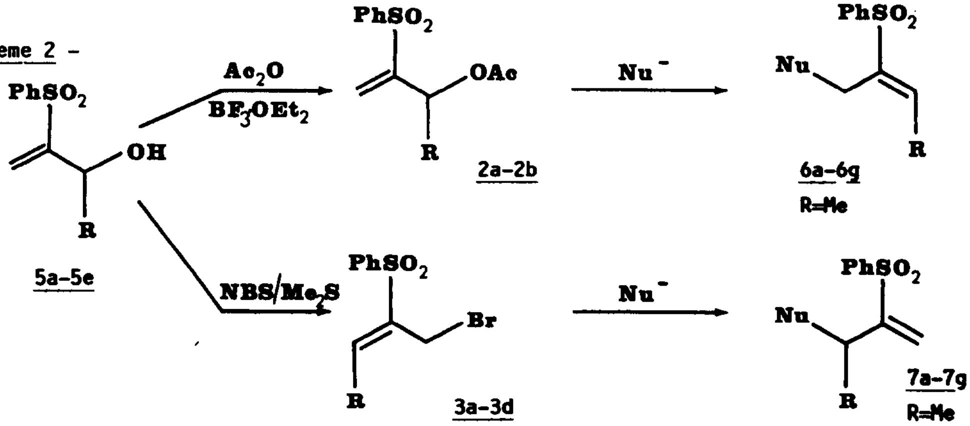
Table 2 - **Synthesis of the 2-phenylsulfonyl allylic acetates and bromides (respectively 2a-2b and 3a-3c) from the alcohols 5a, 5b and 5d**[9]

Alcohol 5	Method^a	Product	Yield %
5a	A	2a	94
5a	B	3a	85^b
5b	A	2b	95
5b	B	3b	87^b
5c	B	3c	87^b
5d	B	3d	82^b

a/ Method A : excess of Ac_2O, 1 drop of $BF_3.OEt_2$; 0°, 5min ; method B : 1.2 equiv. of MeSMe ; 1.1 equiv. of NBS, CH_2Cl_2, 12hr at 25° ; b/ 100%-(E)-isomer.

The alcohols 5a-5c can be converted into the corresponding acetates 2a-2b (excess Ac_2O ; $BF_3.OEt_2$ cat ; 5 min ; 0°)[10] or into the allylic rearranged isomerically pure (E)-bromides 3a-3d (1.2 equiv. of Me_2S ; 1.1 equiv. of N-bromosuccinimide (NBS) in CH_2Cl_2, 12hr at 25°)[11] in high yields (see scheme 2 and table 2). These allylic acetates and bromides react regioselectively with carbon nucleophiles (ketone enolates or lithium aryl-, alkenyl- and alkyl- cyanocuprates[12]) to give the S_N2' substitution products respectively of type 6 and 7 (see scheme 2 and table 3). The S_N2' regioisomer is usually highly favored, even in the case of the bromide 3a which bears a methyl substituent at the allylic position[14,15].

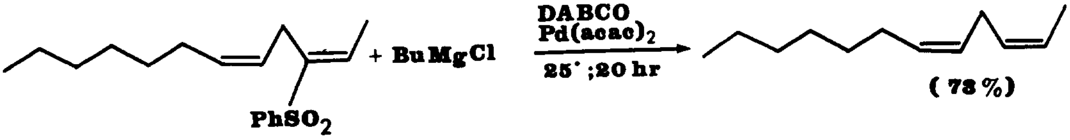
Scheme 2 -



However in the case of the hindered lithium tert-butyl cyanocuprate, the formation of the S_N2 product is also observed (see entry 10 of table 3). Also the (Z)-lithium octenyl cyanocuprate gives under our standard conditions[13] a mixture of the S_N2' and S_N2 type products (50:50) but the addition of 2 equiv. of $BF_3.OEt_2$[16] increases the S_N2'/S_N2 ratio to (90:10) ; see entry 4 of table 3). The vinylic sulfones of type 6 are all isomerically pure (E isomer).

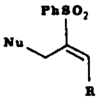
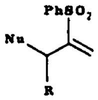
The unsaturated sulfones of type 6 and 7 can be readily transformed in sulfur free compounds. For example, treatment of the isomerically pure (2E, 5Z) dienyl-sulfone 6b with 1.8 equiv. of butylmagnesium chloride in THF in the presence of catalytic amounts of $Pd(acac)_2$ and DABCO[17] (25°, 20hr) allows a short synthesis of the (2Z,5Z) dodecadiene 8 in 73% yield and excellent isomeric purity ($\geq$ 99%) ; see scheme 3.

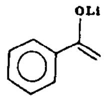
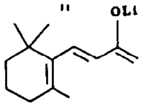
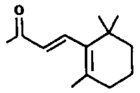
Scheme 3 -



6b

8

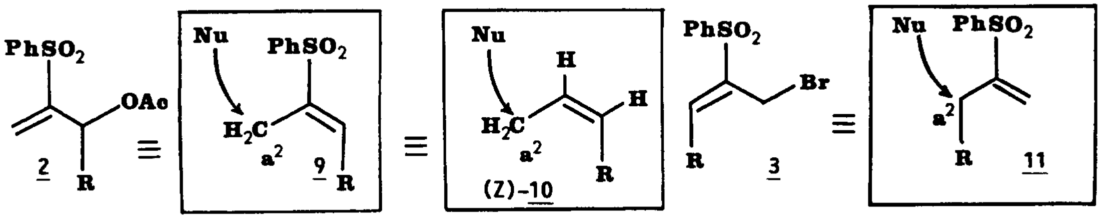
Table 3 - Synthesis of unsaturated sulfones of type 6 :  and 7 :  according to scheme 2[9,13]

Entry	Substrate	Nucleophile (Nu-Met)	Reactions conditions		Product of type 6 or of type 7	Yield %
			temp.	time(hr)		
1	2a	BuCuCNLi	-60° → -15°	1 [a]	6a:Nu=Bu-	82
2	3a	BuCuCNLi	-60°	0.5[a]	7a: "	89
3	2a	(Z)-C_6H_{13}-CH=CH-CuCNLi	-15°	1.5	6b:Nu=(Z)-C_6H_{13}-CH=CH-	78
4	3a	(Z)-C_6H_{13}-CH=CH-CuCNLi	-60° → -10°	2	7b: "	77[b]
5	2a	PhCuCNLi	-60° → -45°	1	6c:Nu=Ph-	84
6	3a	PhCuCNLi	-60°	0.25	7c: "	96
7	2a	cyclo-C_6H_{11}-CuCNMgCl	-80° → -30°	2	6d:Nu=cyclo-C_6H_{11}-	95
8	3a	cyclo-C_6H_{11}-CuCNMgCl	-60°	1	7d: "	94
9	2a	tert-BuCuCNLi	-60° → -45°	2.2	6e:Nu=tert-Bu	98
10	3a	tert-BuCuCNLi	-60°	0.25	7e: "	35[c]
11	2a	 OLi	-60° → -10°	2.5	6f:Nu=$PhCOCH_2$-	80
12	3a	"	-60° → -10°	2.5	7f: "	56
13	2a	 OLi	-60° → -25°	3.5	6g:Nu=  O	89
14	3a	"	-60° → -20°	1.5	7g: "	78

a/ In this case ether is used as solvent ; b/ 10% of the S_N2 product (6b) are also isolated ; without $BF_3.OEt_2$ a 50:50 ratio of 6b and 7b is obtained ; c/ 65% of the S_N2 product 6e are also isolated.

The reagents of type 2 and 3 are thus synthetically equivalent to the regioisomeric a^2 allylic synthons respectively 9, 10 and 11 ; see scheme 4.

Scheme 4 -



Further aspects of the reactivity of the sulfones 2 and 3 are currently investigated in our laboratory (see the following publication).

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References and Notes :

1. P. Knochel and J.F. Normant, Tetrahedron Lett. 26, 425 (1985)
2. P. Auvray, P. Knochel and J.F. Normant, Tetrahedron Lett. 26, 2329 (1985)
3. P. Knochel and D. Seebach, Tetrahedron Lett. 23, 3897 (1982)
4. P. Auvray, P. Knochel and J.F. Normant, Tetrahedron Lett. 26, 4455 (1985)
5. P. Knochel and J.F. Normant, J. Organomet. Chem. (1986), in press
6. For the reactivity of bromides of type 3 towards electrophiles, see the following publication
7. a/ R. Oda, T. Kawabata and S. Tanimoto, Tetrahedron Lett. 1653 (1964) ; b/ K. Morita, Z. Suzuki and H. Hirose, Bull. Chem. Soc. Japan, 2815 (1968) ; c/ A.B. Baylis and M.E. Hillman, German Patent 2155113 (May 1972) ; C.A. 77, 34174q (1972) ; d/ S.E. Drewes and N.D. Emslie, J. Chem. Soc. Perkin Trans. 1, 2079 (1982) ; e/ P. Perlmutter and C.C. Teo, Tetrahedron Lett. 25, 5951 (1984) ; f/ H.M.R. Hoffmann and J. Rabe, J. Org. Chem. 50, 3849 (1985) g/ O. Basavaiah and V.V.L. Gowriswari, Tetrahedron Lett. 27, 2031 (1986)
8. In a typical reaction, 3g (17.8mmol) of the phenyl vinylsulfone 4 and 0.2g (1.78mmol) of DABCO are dissolved in 5ml of acetaldehyde. After 2 weeks at 25°, the aldehyde excess is evaporated and a flash-chromatographic purification of the remaining oil gives 3.18g (84%) of the pure alcohol 5a
9. The given yields are those of flash chromatographically purified materials. All the spectroscopic datas (I.R., ^{1}H-NMR and ^{13}C-NMR) are compatible with the shown structure.
10. D. Seebach, G. Calderari and P. Knochel, Tetrahedron 41, 4861 (1985)
11. E.J. Corey, C.U. Kim and M. Takeda, Tetrahedron Lett. 4339 (1972) ; see also ref. 7f.
12. J.P. Gorlier, L. Hamon, J. Levisalles and J. Wagnon, J. Chem. Soc. Chem. Commun. 88 (1973) ; L. Hamon and J. Levisalles, J. Organomet. chem. 251, 133 (1983)
13. In a typical reaction, 8.5mmol of an ethereal solution of phenyllithium (1.16N) is slowly added at -80° to a stirred suspension of 376mg (4.2mmol) of CuCN in 20ml THF. After 30min. stirring at -30°, a solution of 508mg (2mmol) of the acetate 2a in 2ml of THF is slowly added at -80° to the cyanocuprate solution. The temperature is allowed to raise to -45° in 1 hour and the reaction mixture is quenched with 20ml of an NH_4Clsolution. After the usual work-up and a flash-chromatographic purification, 455mg (83.6%) of the pure sulfone 6c is obtained.
14. The corresponding 2-nitro substituted allylic pivalates show even higher S_N2' selectivity : see ref. 10
15. High regio- and diastereo- selectivity has been observed in 5-membered analogous 2-phenylsulfonyl- substituted allylic compounds : R.E. Donaldson, J.C. Saddler, S. Byrn, A.T. Mc Kenzie and P.L. Fuchs, J. Org. Chem. 48, 2167 (1983) ; D.K. Hutchinson and P.L. Fuchs, J. Amer. Chem. Soc. 107, 6137 (1985) ; D.K. Hutchinson, S.A. Hardinger and P.L. Fuchs, Tetrahedron Lett. 27, 1425 (1986)
16. K. Maruyama and Y. Yamamoto, J. Amer. Chem. Soc. 99, 8068 (1977)
17. J.L. Favre and M. Julia, Tetrahedron Lett. 24, 4311 (1983).

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