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Synthesis with Sulfones (n°XXX) * : Stereoselective Synthesis of Arenesulfonyl-1,3-dienes.

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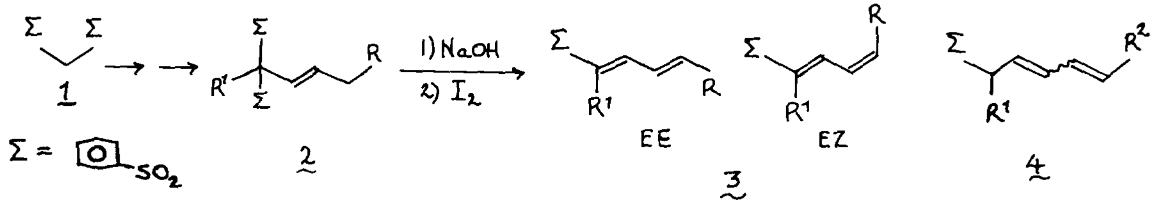
Summary : *Basic treatment of allylic 1,1-disulfones gives 1-arenesulfonyl 1,3-dienes. Condensation of aldehydes with lithiated allylic sulfones and in situ acetylation of the alkoxide thus formed followed by basic elimination of acetic acid leads to EE 2-arenesulfonyl 1,3-dienes. Good to very good stereoselectivity can be achieved.*

In a new way to prepare Z olefins, recently described, acetoxysulfones (threo and erythro) are formed by condensation of aldehydes with metalated sulfones ; acetic acid is eliminated to give E vinylic sulfones (1) which in turn are converted into Z olefins by stereospecific hydrogenolysis with sodium dithionite (2). The preceding letter describes another way to carry out the stereospecific hydrogenolysis (3). It was clearly desirable to examine whether this could be extended to the stereoselective synthesis of 1,3-dienic systems, particularly the E,Z dienes which are both of special importance and not so easy to prepare in a convenient way (4).

We first tried to use 1-arenesulfonyl 1,3-dienes 3 as intermediates. Allylic 1,1-disulfones 2, now readily available from 1,1-bisbenzenesulfonylmethane 1 (5), are a convenient starting material due to their high melting points.



As shown in Table 1, elimination of arenesulfinic acid took place with sodium hydroxide in t-butanol/benzene (or toluene) to give the desired arenesulfonyl dienes. The yields were not optimized. It might be preferable to accept incomplete conversion since too vigorous conditions led to isomerisation to the allylic 3,5-diene sulfones (7) 4 when R was greater than methyl.

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* Synthesis with sulfones (n°XXIX) see reference 3.

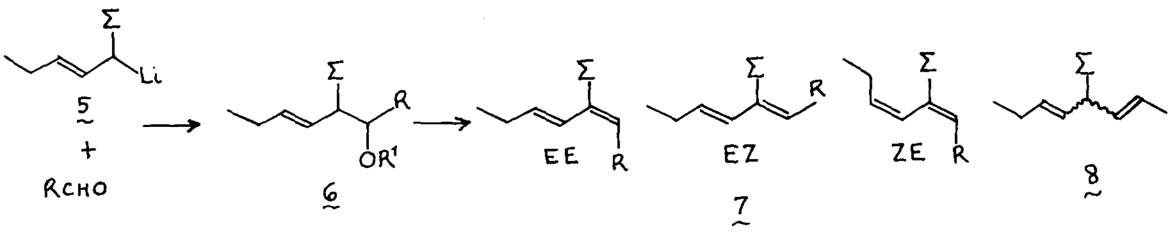
Initial elimination of arenesulfinic acid affords mixtures of 3EE and 3EZ which vary from 50/50 to 30/70. Upon treatment with iodine (9) the stereochemical composition is about 85/15, 3EE to 3EZ.

Table 1 : Basic 1,4 elimination of benzenesulfinic acid from 1,1-bisbenzenesulfonyl 2-alkenes with sodium hydroxide followed by iodine equilibration (9). (80 mg of NaOH powder, 10ml of solvent, and 0.30g of 3A molecular sieves per mmol).

Entry	2		°C	Time	Solvents	2[a]	3[b]	Isomeric %[c]		4
	R^1	R		h	(%volume)	(Yield%)	(Yield%)	3EE	3EZ	(Yield%)
1	CH_3	H	80	8	tBuOH-benzene (50) (50)	23	65			
2	"	CH_3	95	4	tBuOH-toluene (50) (50)	23	77	84	16	
3	"	nC_4H_9	105	7	"	17	31	85	15	36
4[d]	"	"	100	1	"	78	15	85	15	2

[a] 2 and 3 are easily separated by vacuum flash chromatography (6) [b] isolated pure, entries 1-2 ; as a mixture of 3 and 4, entries 3-4 [c] HPLC and NMR ^{1}H 250 MHz analysis. [d] 32 mg-NaOH powder.

The synthesis of 2-benzenesulfonyl-1,3-dienes 7 was next investigated. The readily available E 1-benzenesulfonyl 2-pentene 5 was treated first with n-butyllithium and then with aldehydes, the reaction mixture being quenched with acetic anhydride. The acetoxysulfones 6 were formed in satisfactory yields as a mixture of diastereoisomers, Table 2. These were then exposed to the basic conditions used in the synthesis of E vinylic sulfones (1). Elimination of acetic acid occurred with formation of the dienesulfone 7, Table 3.



Powdered sodium hydroxide in dioxane or preferably in ether gave the best results as regards yields and stereochemistry. This was about 90-93% EE and 7-10% EZ. Other basic conditions were tried with less satisfactory results. For instance sodium ethoxide in ethanol gave a 67% yield of diene 7 (85% EE, 15% EZ) and 31% of the bis allylic sulfone

Table 2 : Condensation of 1-lithio 1-benzenesulfonyl 2-pentene with aldehydes.

Entry	5 %Z [a]	RCHO R	R^1	6 Yield [b] %	Number of Diastereoisomers	threo/erythro	Minor Products
5	2	C_2H_5	Ac	79	2	57/43	5 (5-7%)
6	0.3	nC_6H_{13}	"	78	2	"	5
7	18	"	"	50	4	c	d

[a] HPLC analysis (± 0.5) [b] NMR ^{1}H 90MHz contains 5-7% of unreacted 5 [c] not determined [d] notable amount of unidentified sulfones

Table 3 : Conversion of the acetoxy(tosyloxy)sulfones 6 into 2-benzenesulfonyl 1,3-dienes 7

Entry	5 %Z [a]	6 [b] R	R^1	Base (equiv.)	Solvent	Time h	Yield %	7 Isomeric Distribution% [e] EE	EZ	ZE	Minor Products
8	2	C_2H_5	Ac	NaOH (2)	dioxane	4	51 [c]	90	10		
9	0.5	nC_6H_{13}	"	" (4)	"	2½	50 [c]	93	7		
10	"	"	"	" (2)	ether	6	78 [d]	93	7		
11	"	"	"	NaOEt (5)	ethanol	1	61 [d]	85	15		8 (31%)
12	18	"	"	NaOH (2)	dioxane	6	65 [d]	79	10	11	
13	0.5	"	Ts	NaOH (2)	dioxane	2	78 [d]	12	88		

[a] HPLC [b] diastereoisomeric mixture 57/43 threo/erythro except for entries 12 (4 diastereoisomers) and 13 (threo only) [c] yield from 5 [d] yield from 6 [e] NMR ^{1}H 250MHz for ZE isomer (±2%) ; otherwise HPLC analysis ± 0.5%.

8 $R^2=nC_5H_{11}$.

The second route thus gives more stereoselective results. It is possible to increase the stereoisomeric purity of diene 7 by simple flash chromatography (11) ; by this technique the EE and EZ isomers were separated to yield each isomer pure (99.5%).

Thanks are due to the CNRS (LA32 and A.T.P. "Messagers chimiques").

Notes and References.

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8) 3 EE R=nBu, R^1=Me and 3 EZ R=nBu, R^1=Me were separated by preparative HPLC and identified by NMR ^1H 250MHz analysis. ($CDCl_3$ + TMS) : 3dEE 0.93(t,7,3H) ; 1.2 to 1.5(m,4H) ; 1.94(s,3H) ; 2.25(m,2H) ; 6.3(m,2H) ; 7.36(d,10.3,1H) ; 7.5 to 8(m,-5H)-double irradiation gives J=15.8 Hz for -HC=CH- ; 3dEZ 0.94(t,7,3H) ; 1.2 to 1.6(m,4H) ; 1.94(s,3H) ; 2.37(m,2H) ; 5.95 to 6.1(m,1H) ; 6.1 to 6.35(t,11.2,-1H) ; 7.5 to 8(m,6H)- double irradiation gives J=11.2 Hz for -HC=CH-.

U.V. Spectra (MeOH) : 3EE ϵ_{max}=23460 at λ_{max}=260nm and for HPLC analysis (silica gel column) ϵ_{265}=22290 ; 3EZ ϵ_{max}=17510 at λ_{max}=262nm ; ϵ_{265}=17040.

HPLC analysis were carried out on a Dupont 850 Liquid Chromatograph with the U.V. spectrophotometer set at λ=265nm (column-Zorbax Sil 4.6mmx25cm ; flow 1.2 cm^3/min.; P 150 bars). Ethylacetate and isooctane were the solvents in the proportions 5/95 for 3 and 3/97 for 7.
Diene sulfones 3 (and to a lesser degree 7) are fragile and must be conserved in solution preferably at low temperature.

9) J.J. Burger, T.B.R.A. Chen, E.R. de Waard and H.O. Huisman, Tetrahedron, 36, 723 (1980). The modified iodine equilibration is as follows : 1mmol of 3 and 0.5 mmol of iodine were dissolved in 40 ml of ether. The solution was stirred for 45 minutes at room temperature followed by extractive work up (washings with saturated aqueous $Na_2S_2O_3$ and water). 3 was recovered quantitatively and the stereochemical composition was found to be 85-88% EE and 12-15% EZ.

10) NMR ^1H spectra for dienesulfones 7, R=nHex are as follows : 7EE 0.75 to 1.06(m,-6H) ; 1.13 to 1.72(m,8H) ; 1.85 to 2.43(m,4H) ; 5.68 to 6.16(m,2H) ; 6.87(t,-J=7.7,1H) ; 7.28 to 7.89(m,5H) , double irradiation gives J=16.5 Hz for -HC=CH- ; 7EZ 0.78 to 1.12(m,6H) ; 1.12 to 1.77(m,8H) ; 2.09 (quintuplet, J=4.8,2H), 2.52 to 2.82(m,2H) ; 5.79(dt,J_1=15, J_2=6,5,1H) ; 6.02 to 6.29(m,2H) ; 7.33 to 7.92-(m,5H) ; 7EE + 7ZE 0.54(t,J=5,0.3H) ; 0.81 to 0.99(m,5.7H) ; 1.08 to 1.70(m,-8.2H) ; 2.08(quintuplet, J=7, 1.8H), 2.29(q,J=7.5,2H) ; 5.68 to 6.08(m,2H) ; 6.94-(m$\sim$q, J=7.5,1H) ; 7.48 to 7.66(m,3H) ; 7.87(dc,J=7,2H) double irradiation gives J=16.5Hz for 90% -CH=CH-(lower field) J=11.2 for 10% -CH=CH- (higher field).
U.V. Spectra (MeOH) 7EE ϵ_{max}=17200 at λ_{max}=224nm ; ϵ_{265} =2870
7EZ ϵ_{max} =18100 at λ_{max} =222nm ; ϵ_{265} =6190.

11) W.C. Still, M. Kahn and A. Mitra, J. Org. Chem., 43, 2923 (1978).

12) Satisfactory (±0.3% on C, H and S) microanalysis were obtained for all dienic sulfones.

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