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Formation of symmetrical alkenes by homocoupling of metallated sulfones under nickel catalysis

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Summary — Allylic sulfones undergo a coupling reaction with organometallic compounds (Mg or Li) not only with copper catalysts but also with iron or nickel salts. With γ,γ-disubstituted allylic sulfones and also saturated aliphatic sulfones, however, another reaction was observed whereby two molecules of the starting sulfone are coupled to give symmetrical alkenes. The scope of this reaction was investigated.

sulfone / nickel / homocoupling / alkene

Résumé — **Formation d'alcènes symétriques par couplage de sulfones métallées en présence de sels de nickel.** *Le couplage des sulfones allyliques avec les organomagnésiens ou lithiens est catalysé par les sels de fer ou de nickel. En revanche avec les sulfones allyliques γγ-disubstituées, on observe la formation des alcènes symétriques. Le domaine d'application de cette réaction, qui n'est pas limitée aux seules sulfones allyliques, a été étudié.*

sulfone / nickel / homocouplage / alcène

Introduction

The sulfonyl group has proved to be a very useful auxiliary group in organic synthesis due to the easy deprotonation in the α position and the nucleophilic properties of the resulting carbanion [1]. Towards the end of the syntheses the auxiliary group must be removed. This is generally achieved by hydrogenolysis or less frequently by base-promoted elimination [1]. Neither method leads to a modification of the carbon skeleton. On the other hand, substitution of the sulfonyl moiety with an organometallic compound simultaneously achieves desulfonylation and extension of the carbon chain. However such a substitution is not easy and requires activation. α-Alkoxy and to a lesser extent α-alkylthio sulfones are prone to direct displacement of the sulfonyl group [1c, d] but ordinary sulfones are not. This is why the possibility of transition metal activation for such processes has been investigated by our group and others.

In the case of vinylic sulfones it has proved possible to carry out the substitution of the sulfonyl group with Grignards under nickel or preferably iron catalysis [2]. This stands out in contrast with the catalysis with copper salts which led to Michael-type addition [3]. Vinylic halides undergo substitution by Grignard reagents under catalysis by nickel, iron, copper or other metals [4].

Cross-coupling of allylic sulfones with organometallic reagents

A number of allylic residues can be substituted by various nucleophiles under transition metal catalysis [4]. With allylic halides, the reaction involves formation of π-allylic complexes. Hydrogenolysis due to β-hydride elimination in the transition metal organometallic can be observed with the so-called 'reducing' Grignard reagents. The transition metal promoted substitution of the sulfonyl group in allylic sulfones with Grignard derivatives is very typical. With non-reducing reagents such as phenylmagnesium bromide, iron salts are very efficient catalysts compared to nickel and copper analogs. This is shown in table I where the phenylation of phenyl allyl **1** and *tert*-butyl allyl sulfones **1a** in the presence of various metal salts is reported. When alkyl Grignard reagents such as hexylmagnesium bromide were used, the yield of non-1-ene obtained upon iron catalysis dramatically dropped to 10% with 1% $Fe(DBM)_3$ and no more than 25% with 10% $Fe(DBM)_3$. Formation of hexene by β-hydride elimination was observed. The use of copper salts was now rewarding and cross-coupling reactions between various allylic sulfones and alkyl or allyl Grignard reagents in the presence of catalytic amount of cupric acetylacetonate were successfully performed [5a]. Organocopper and cuprate reagents are more stable than the corresponding iron or nickel derivatives toward β-hydride elimination [4]. The

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Table I. Reaction of allyl phenyl sulfone **1** and allyl *tert*-butyl sulfone **1a** with PhMgBr (1.5 equiv) in the presence of various catalysts (in THF, 20 h, 10 °C).

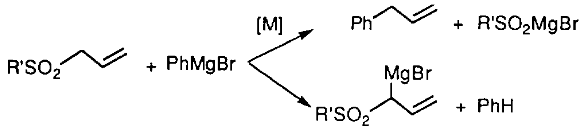
$$R'SO_2\text{-}CH_2\text{-}CH{=}CH_2 + Ph\text{-}MgBr \xrightarrow{[M]} Ph\text{-}CH_2\text{-}CH{=}CH_2 + R'SO_2\text{-}MgBr$$

Run	*Sulfone*	*Catalyst*	*Allylbenzene (%)*	*Starting sulfone (%)*
1	**1**	None	0	88
2		1% Fe(acac)$_3$	82	–
3		1% Fe(DBM)$_3$^{b}	88	–
4		1% Cu(acac)$_2$	13	70
5		10% Cu(acac)$_2$	35	51
6		1% Ni(acac)$_2$	20	75
7		10% Ni(acac)$_2$	100 (80:17:3)^a	0
8	**1a**	1% Fe(acac)$_3$	81 (79:18:3)^a	–
9		1% Fe(DBM)$_3$^{b}	87 (97:3:0)^a	–
10		1% Cu(acac)$_2$	6	80
11		1% Ni(acac)$_2$	53	35

[a] Under the reaction conditions allyl benzene was partially isomerized: (allylbenzene/(*E*) propenyl benzene/(*Z*) propenyl benzene); [b] DBM for dibenzoylmethanato.

substitution of the sulfonyl group of allylic sulfones with stable enolates under palladium catalysis [5b] has been described.

Without transition metal, no coupling was observed; only metallation took place as shown by the yellow color [6]. In the experiment reported as run 5 in table I, the medium was quenched with D_2O and beside the expected allylbenzene (35% yield), monodeuterated sulfone was recovered. There is apparently a competition between metallation [7] and substitution.

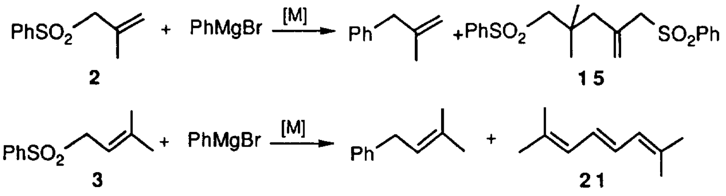


Increasing the reaction time did not improve the yield of coupled product whereas increasing the amount of catalyst did. This can be easily understood since the competition between the deprotonation and the substitution (both reactions being irreversible) cannot be influenced by the time of reaction but depends on the amount of catalyst, as expected.

The results observed with the *tert*-butyl sulfone are very similar to those obtained with the phenyl sulfone, although *tert*-butyl sulfones are less acidic than phenyl sulfones by two pK_a units [7]. Substitution of the allyl group of phenyl sulfones by methyl groups in the γ position led to a strong decrease in the yield of coupled product; with 1% Fe (DBM)$_3$ the yields are for allyl (88%), (*p*-tolyl) pent-2-enyl (72%) α/γ = (*E*) 68:32, methallyl (68%), prenyl (10%) α/γ = 98:2. On the other hand, α-substitution by two methyl groups led to 84% condensation, mainly (96:4) in the γ position. The methallyl **2** and prenyl **3** sulfones are compared more extensively in table II.

Substitution of the allylic residue in the sulfone greatly affected the yield of coupling product. With methallyl phenyl sulfone, the yield of methallyl benzene was still acceptable with nickel or preferably iron catalysis. Another product **15** was isolated. This dimer had also been obtained when phenyl isobutenyl sulfone was treated with phenylmagnesium bromide without transition metal salts [2a] and results from a Michael-type

Table II. Reaction of methallyl phenyl sulfone **2** and phenyl prenyl sulfone **3** with PhMgBr in THF (1.5 equiv; conditions A: 20 h, 20 °C; B: 6 h, 65 °C).



Sulfone	*Catalyst*	*Conditions*	*Coupling (%)*	*Starting sulfone (%)*	*Other products*
Methallyl	None	A	0	80	**15** 20%
	10% Cu(acac)$_2$	A	42	48	
	1% Ni(acac)$_2$	A	7	21	**15** 45%
	10% Ni(acac)$_2$	A	60	12	**15** 16%
	1% Fe(DBM)$_3$	A	68	18	
Prenyl	10% Ni(acac)$_2$	A	5	40	**21** 12%
	1% Fe(DBM)$_3$	A	10	78	–
	1% Ni(acac)$_2$	B	3	29	**21** 45%
	10% Ni(acac)$_2$	B	6–10	15	**21** 35%
	1% Fe(DBM)$_3$	B	10	70	–
	1% Ni(acac)$_2$	B^a			**21** 80%

[a] The sulfone was first metalled with *i*-PrMgBr (1.0 equiv) at −78 °C and warmed to 20 °C; Ni(acac)$_2$ was added and the mixture refluxed for 10 h.

addition of the methallylic anion through its less hindered carbon to the vinylic sulfone obtained upon basic equilibration of the allylic sulfone.

Reaction of phenyl magnesium bromide with phenyl prenyl sulfone **3** led to a very poor yield of prenylbenzene but to sizeable amounts of a hydrocarbon which proved to be 2,7-dimethylocta-2,4,6-triene **21**.

It is obvious that the triene **21** has been formed from two molecules of sulfone **3** whereas the phenyl residue of the Grignard derivative has not been attached. It was reasoned that this reagent had only performed the metallation of the sulfone and that the sulfonyl prenyl carbanion had undergone this interesting coupling reaction. The PhMgBr solution was therefore added to the sulfone at −78 °C and the temperature was allowed to reach room temperature before the addition of nickel acetylacetonate. The orange solution was then refluxed for 6 h; the yield of triene reached 64%. When *n*-BuMgBr or *i*-PrMgBr were used under the same reaction conditions the yield was 80%.

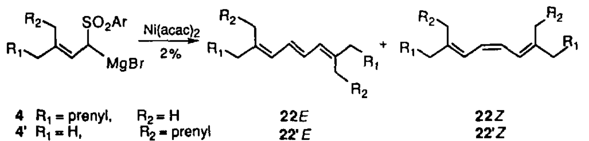
The formation of symmetrical alkenes by homocoupling of two molecules of a suitable precursor has been observed in carbene or carbenoid chemistry [8], or in the McMurry reaction [9] of carbonyl derivatives.

The formation of these alkenes by a catalytic coupling of sulfones, readily available from alkyl halides, could be of interest compared with oxidation into carbonyl derivatives and stoichiometric reduction of these. A preliminary communication has been published [10].

Homocoupling of metallated isoprenoid sulfones

The scope of the reaction was then investigated with isoprenologous C_{10} sulfones: *p*-tolyl geranyl **4** and neryl **4′** sulfones. They should lead to the C_{20} pentaenes **22** and **22′**. These hydrocarbons have been obtained previously by unsymmetrical coupling of C_{10} aldehydes with phosphonium salts [11] or phosphine oxides [12] or sulfonyl carbanions [13] followed by reductive elimination [14]. The configuration of the double bonds present in the starting materials was retained. The new central double bond was usually a mixture of (*E*) and (*Z*) isomers [11]. Sometimes the (*E*) isomer predominated [12b, 13]. The (*Z*) isomer has also been obtained by semihydrogenation of the corresponding acetylene derivative [13b].

When geranyl *p*-tolyl sulfone **4** or neryl *p*-tolyl sulfone **4′** were treated with *i*-PrMgBr followed by $Ni(acac)_2$ in refluxing THF, the expected pentaenes were formed in 65 and 55% (isolated) yields respectively. The yields measured by UV spectrometry were decidedly higher. The ^{13}C NMR spectra showed that the configuration of the double bonds already present in the starting material was retained whereas the newly formed one was about *E*/*Z* = 50:50 as in the Wittig synthesis.

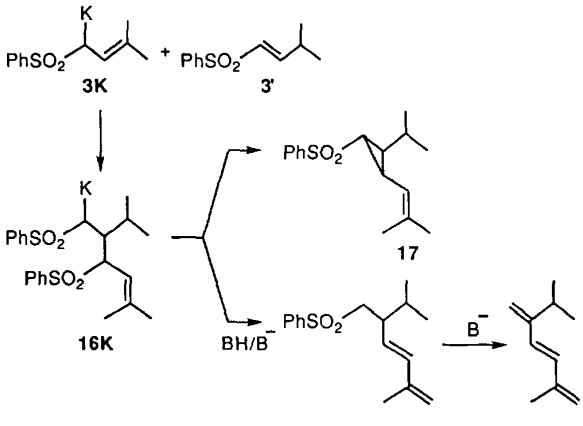


4 R1 = prenyl, R2 = H 22*E* 22*Z*
4′ R1 = H, R2 = prenyl 22′*E* 22′*Z*
5 R1 = farnesyl, R2 = H 23*E* 23*Z*

(*E*,*E*)-Geranylgeraniol was converted into the corresponding chloride which on treatment with sodium benzenesulfinate gave (*E*,*E*)-geranylgeranyl phenylsulfone **5**. When treated as above this gave phytoene **23** [9, 15] in 74% isolated yield. These results show that the new reaction can be of use for the preparation of symmetrical polyene hydrocarbons of the carotenoid series.

Further investigation of the reaction conditions with phenyl prenyl sulfone **3** showed that $NiCl_2$ or $NiCl_2(PPh_3)_2$ were equivalent to $Ni(acac)_2$ at 65 °C, but the reaction at 20 °C was much slower; $NiCl_2(dppe)$ was very much less efficient.

Metallation of phenyl prenyl sulfone **3** with *n*-BuLi instead of a Grignard reagent followed by treatment with $Ni(acac)_2$ led to a slightly decreased yield (58%). Potassium *tert*-butoxide (1 equiv) led to a different reaction. In the presence or absence of nickel, the C10 sulfones **17** (25%) and **18** (26%) were formed, together with triene **20** (20%) after 18 h at room temperature. When KH (0.5 equiv) was used to generate the potassium derivative of prenyl sulfone, disulfone **16** (27%) was isolated. Apparently, isomerization of sulfone **3** has produced some of the isomeric α-vinylic sulfone **3′** which underwent Michael addition with the conjugate base of sulfone **3**. The disulfone **16** thus formed would be an intermediate in the formation of sulfones **17** and **18** and triene **20** under basic conditions.



Related results have been obtained by treatment of allylic sulfones with sodium hydroxide in liquid ammonia [15b].

Homocoupling of metallated benzyl phenyl sulfone

Refluxing sulfone **6** with *i*-PrMgBr and 2% $Ni(acac)_2$ for 6 h, gave 50% stilbene (*E*/*Z* = 80:20) with 50% unchanged sulfone; addition of more catalyst and further refluxing led to a 70% yield.

However when sulfone **6** was metallated with *n*-butyllithium, only 12% stilbene (*E*/*Z* = 65:35) was obtained, the main product being now 1,2,3-triphenylcyclopropane (60%) of *trans* configuration. A small amount of 1,2,3-triphenylpropene was also formed. This