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Regio- and Stereoselective Synthesis of (E)- and (Z)-Allylsulfones from Aldehydes and Alkynes

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Several (E)- and (Z)-1-p-toluenesulfonyl(=tosyl)-2-alkenes, allylsulfones, were regio- and stereoselectively prepared from aldehydes and alkynes, respectively, in good yields by application of the results of our previous investigation on "syn-effect" and iodosulfonization.

Allylsulfones are useful synthetic intermediates because of the ability of the sulfonyl group to generate an adjacent carbanion and to act as a leaving group in substitution and elimination reactions.[1)] We have been investigating the preparation and the reactions of allylsulfones[2)] and the related vinylsulfones[3)] to extend the synthetic utility of such sulfones.

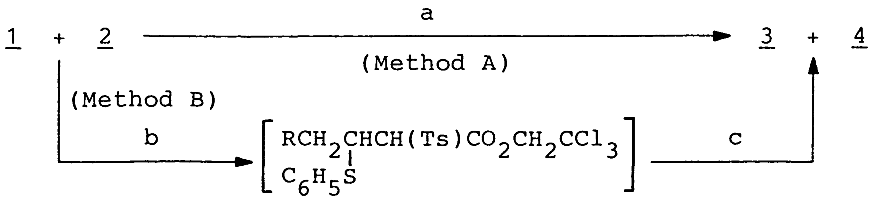
In the previous papers,[3a,b)] we reported the regio- and stereoselective synthesis of (E)- and (Z)-vinylsulfones and their conversion to the corresponding allylsulfones under mild basic conditions, and it was found that α-substituted vinylsulfones and (Z)-vinylsulfones gave exclusively the corresponding (E)-allylsulfones,[3a,b)] probably due to the steric congestion which precludes the possibility of a stabilizing syn interaction, "syn-effect",[4)] between the α- and δ-position as being pointed out by Block et al.,[4d)] while (E)-vinylsulfones preferentially afford (Z)-allylsulfones as kinetically-controlled products. These facts prompted us to develop the regio- and stereoselective synthesis of (E)-allylsulfones from aldehydes according to the following scheme, since our previous method employing sulfonylmethylphosphonate afforded the mixture of (E)- and (Z)-isomers.[3a)] Ts in the scheme means tosyl ($p\text{-}CH_3C_6H_4SO_2\text{-}$) group.

$$\underset{\underline{1}}{\mathrm{RCH_2CHO}} + \underset{\underline{2}}{\mathrm{TsCH_2CO_2CH_2CCl_3}} \xrightarrow[-\,\mathrm{H_2O}]{} \underset{\underline{3}}{\mathrm{RCH_2CH{=}C(Ts)CO_2CH_2CCl_3}} \xrightarrow{\text{base}}$$

$$\underset{\underline{4}}{\mathrm{RCH{=}CHCH(Ts)CO_2CH_2CCl_3}} \xrightarrow{\mathrm{Zn/H^+}} \underset{\underline{5}}{[\mathrm{RCH{=}CHCH(Ts)CO_2H}]} \xrightarrow[-\mathrm{CO_2}]{} \underset{\underline{6}}{\mathrm{RCH{=}CHCH_2Ts}}$$

An attempt to prepare vinylsulfone (3) from aldehyde (1) and 2,2,2-trichloroethyl tosylacetate (2) by the general Knoevenagel condensation[5)] resulted in the formation of unseparable mixture of 3 and allylsulfone (4) as an oil (Method A in Table 1). The improved method B,[3c)] via the formation of sulfide (7) followed by the oxidation with Oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) in two phases ($CH_2Cl_2/H_2O$) using a phase transfer catalyst, afforded also the mixture of 3 as major product and 4 as minor one in better yield except the case of Run 11 than that by the method A as shown in Table 1. The mixture of 3 and 4 thus prepared was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in CH_3CN at room temperature to convert to (E)-4 in the similar manner described in the previous papers.[3a,b,d] The reductive deprotection of 2,2,2-trichloroethyl ester (4) with Zn/aq. AcOH and the subsequent decarboxylation at high temperature in DMSO afforded the expected (E)-allylsulfones (6a-f) in good yields as shown in Table 2.

On the other hand, the preparation of (Z)-allylsulfones (11) was achieved according to the scheme illustrated on the next page starting from alkynes (7) through propargylsulfone derivatives (10) followed by the hydrogenation catalyzed by Pd-$BaSO_4$ (Table 3). One carbon homologative Method B using chloromethyl p-tolyl sulfide was inferior to Method A via iodosulfonization



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(a) piperidine in AcOH, 25 °C, see Table 1 (Method A). (b) C_6H_5SH (1.1 equiv.), piperidine (0.1 equiv.), r.t., see Table 1 (Method B) for solvent and Time t_1. (c) Oxone (2 equiv.), Bu_4NHSO_4 (0.3 equiv.) in CH_2Cl_2/H_2O (4/3), r.t., Time t_2.

Table 1. The Knoevenagel Condensation of Aldehydes (1) with 2

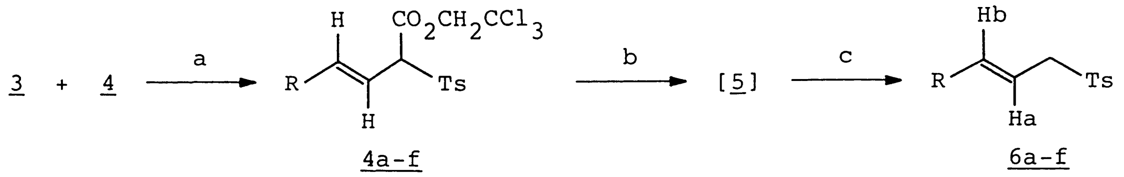
Method A

Run	1a-f (equiv.)	piperidine (equiv.)	Time/d	Yield of 3 + 4/%	Ratio[a] of 3/4
1	1a, CH_3CH_2CHO (1.2)	0.1	1	70	66/34
2	1b, $CH_3(CH_2)_4CHO$ (1.1)	0.2	4.5	78	47/53
3	1c, $CH_3(CH_2)_8CHO$ (1.1)	0.2	7	63	39/61
4	1d, $CH_3(CH_2)_{10}CHO$ (1.1)	0.1	2	60[b]	53/47
5	1e, $C_6H_5(CH_2)_2CHO$ (1.1)	0.2	4.5	88	46/54
6	1f, $(CH_3)_2CHCH_2CHO$ (1.2)	0.2	1	97	93/7

Method B

Run	1a-e (equiv.)	solvent	Time t_1	Time t_2	Yield of 3 + 4/%	Ratio[a] of 3/4
7	1a (1.1)	CH_3CN	overnight	7 d	84[c]	94/6
8	1b (1.2)	CH_3CN	6 h	4 d	96	85/15
9	1c (1.2)	$(ClCH_2)_2$	2 d[d]	10 d[e]	75	100/0
10	1d (1.2)	CH_2Cl_2	4 d	7 d	86	98/2
11	1e (1.2)	CH_3CN	6 h	4 d	82	81/19

a) Determined by 400 MHz ^1H-NMR spectra. b) Solidified. c) 3a, Mp 82.5-83.0 °C (from i-PrOH). d) Refluxed with 0.3 equiv. of piperidine. e) In $MeOH/H_2O$ (2/1).



(a) DBU (2 equiv.) in CH_3CN, r.t., 1 h, then HCl/MeOH. (b) Zn (3 equiv.) in 80% AcOH, r.t., Time t_1. (c) AcOH (2 equiv.) in DMSO, 100°C, Time t_2.

Table 2. Preparation of (E)-Allylsulfones (6) via 4

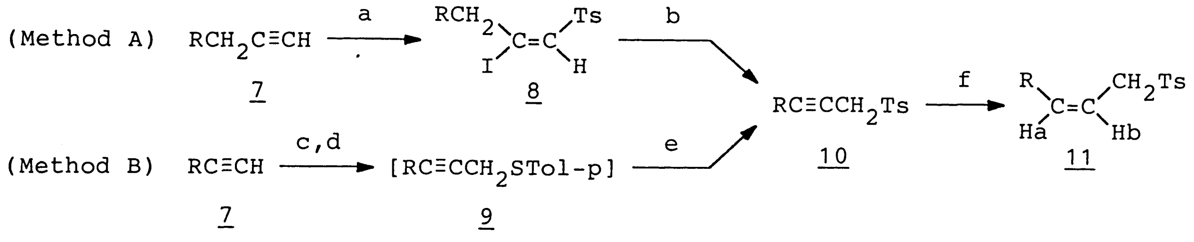
Run	R	Ratio[a)] of 3/4	Yield of 4a-f[b)]/%	t_1/h	t_2/h	Yield of 6a-f[b)]/%	^{J}Ha-Hb of 6/Hz
1	CH_3	66/34	4a, 78	3	2	6a, 82	15.3
2	$CH_3(CH_2)_3$	85/15	4b, 84	7	3.5	6b, 89	15.3
3	$CH_3(CH_2)_7$	100/0	4c, 86	6	9[c)]	6c, 94	15.3
4	$CH_3(CH_2)_9$	53/47	4d, 96[d)]	8	3	6d, 79[e)]	15.3
5	$C_6H_5CH_2$	81/19	4e, 93	4	4	6e, 87	15.3
6	$(CH_3)_2CH$	93/7	4f, 98	overnight	5	6f, 85	15.6

a) Ratios of 3/4 of the starting materials used. b) All the products were oil except 4d and 6d and gave the satisfactory spectral data. (Z)-Isomers of 4 and 6 were not detected by 400 MHz ^{1}H-NMR spectra. c) Refluxed in xylene. d) 4d, Mp 33-34 °C (crude). e) 6d, Mp 48.7-49.0 °C (from i-PrOH).

of 7 in some respects, namely yields, a stench of the sulfide and the necessity of precaution to air and moisture for the Grignard reagent.

Though the mechanism for the conversion of 8 to 10 with triethylamine is still ambiguous, the fact that 1-tosyl-1-alkyne (12, R=$C_6H_5CH_2$) was isolated in low yield (29%) when 8h was treated with DBU (1.1 equiv.) as a base in CH_3CN at 0 °C for 10 min seems to suggest that it proceeds through the reaction pathway A shown on the next page.

Now, both (E)- and (Z)-allylsulfones have come available. Not only are these compounds useful as building blocks in organic synthesis, but also they will be helpful for the stereochemical investigation including ours on the "syn-effect".[3a,b,d)]

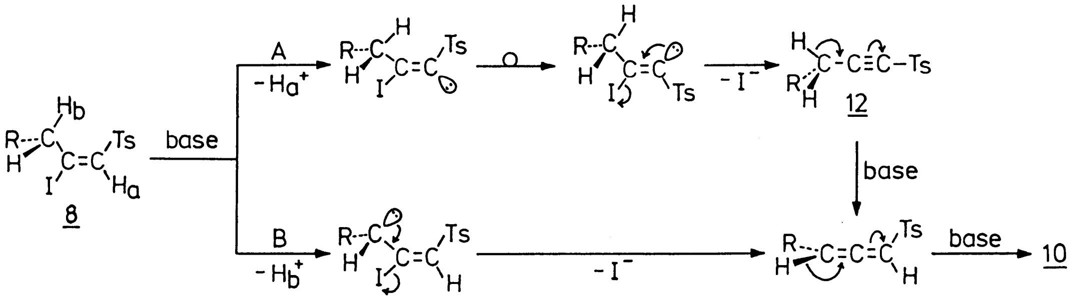


(a) p-$TolSO_2Na \cdot 4H_2O$ (1.5 equiv.) and I_2 (1 equiv.) in $AcOEt/H_2O$ (2/1), r.t., 24 h. (b) Et_3N (5 equiv.) in CH_3CN, see conditions in Table 3. (c) EtMgBr (1.2 equiv.) in ether, reflux, 3 h. (d) p-$TolSCH_2Cl$ (1.3 equiv.) in ether, reflux, overnight. (e) Oxone (3 equiv.) in $MeOH/H_2O$ (2/1), r.t., 4 h. (f) H_2/Pd-$BaSO_4$ (5 mol%) in MeOH, 25 °C, T h in Table 3.

Table 3. Preparation of (Z)-Allylsufones (11) via 10

Run	7a-i, R	Method	Yield of 8a-i^a)/%	Conditions	Yield of 10a-i^a)/%	T/h	Yield of 11a-i^a)/%	^{J}Ha-Hb of 11/Hz
1	7a, CH_3CH_2	A	8a, 88	50 °C, 1 d	10a, 95	3.0$^{b)}$	11a, 89$^{c)}$	10.7
2	7b, $CH_3(CH_2)_2$	A	8b, 95	50 °C, 1 d	10b, 94	0.5	11b, 91	10.7
3	〃	B			10b, 63	〃	〃	〃
4	7c, $CH_3(CH_2)_3$	B			10c, 47	1.0	11c, 92	10.7
5	7d, $CH_3(CH_2)_4$	A	8d, 92	50°C, 2.5 d	10d, 89	0.5	11d, 94	10.7
6	7e, $CH_3(CH_2)_5$	B			10e, 53	1.0	11e, 97	10.7
7	7f, $CH_3(CH_2)_7$	A	8f, 79	50 °C, 2 d	10f, 92	4.0	11f, 94	10.7
8	7g, $CH_3(CH_2)_8$	B			10g, 62	2.0	11g, 93	10.7
9	7h, $C_6H_5CH_2$	A	8h, 75	r.t., 3 d	10h, 87$^{d)}$	1.0	11h, 93	9.6
10	7i, $C_6H_5(CH_2)_2$	B			10i, 72$^{e)}$	1.0	11i, 96$^{f)}$	10.7

a) All the products except 10h,i were oil and gave the satisfactory spectral data. (E)-Isomers of 11 were not detected by 400 MHz ^{1}H-NMR spectra. b) At 0 °C. c) Contaminated with a small amount of 10a. d) Mp 78-80 °C (from i-PrOH). e) Mp 57-58 °C (from i-PrOH). f) 1 mol% of Pd-BaSO$_4$ was used.



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