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A CONVENIENT METHOD FOR THE PREPARATION OF α-ALKYLATED VINYLIC SULFONES AND THEIR CONVERSION TO ALLYLIC SULFONES

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2-Pyrrolidinoalkyl p-tolyl sulfones, which were readily available by the addition of pyrrolidine to vinylic or allylic sulfones, were converted to the corresponding α-alkylated vinylic sulfones through α-alkylation followed by elimination of pyrrolidino group. Some of the α-alkylated vinylic sulfones were further transformed to the corresponding allylic sulfones.

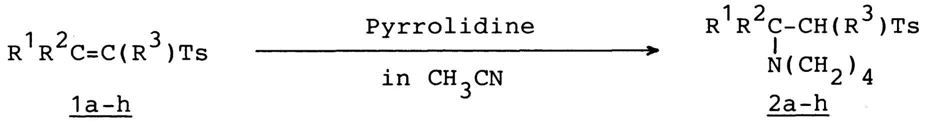
In connection with our studies on the reaction of allylic sulfones,[1-5] we herein report a facile method for the preparation of α-alkylated vinylic sulfones and their transformation to the corresponding allylic sulfones.

It is well known that various kinds of nucleophiles add to vinylic sulfones.[6] We therefore tried to apply this reaction for protection of carbon-carbon double bond of vinylic sulfones in their α-alkylation. β-Methoxy-, β-phenylthio-, and β-dialkylaminoethyl p-tolyl sulfones were prepared and their α-alkylation was examined via lithiation. In conclusion, it was found that dialkylamino group is most suitable for the protection of the double bond because β-elimination reaction takes place in other cases. The results for addition of pyrrolidine to vinylic or allylic sulfones (1) were shown in Table 1. The addition to allylic sulfones (1b, 1e) seems to proceed through the corresponding vinylic sulfones which are formed in the equilibrium under basic conditions.[7]

α-Alkylation of the β-pyrrolidinoalkyl p-tolyl sulfones (2) thus prepared was carried out in the usual way with butyllithium and alkyl halides as shown in Table 2. The subsequent elimination of pyrrolidino group to give the vinylic sulfones (14 - 24) was generally achieved by oxidation to N-oxide with m-chloroperbenzoic acid (MCPBA) in the presence of sodium hydrogencarbonate in dichloromethane at room temperature. The elimination was also possible by treating the quaternary salt formed from β-pyrrolidinoalkyl p-tolyl sulfone (the case of 3 is shown in Table) and methyl iodide with triethylamine. The results are summarized in Table 3. It is noted that the E- and Z-isomers' ratios of the resulting vinylic sulfones (19 - 23) are parallel to the diastereomeric ratios of the starting β-pyrrolidinoalkyl p-tolyl sulfones (8 - 12).

The conversion of vinylic sulfones (15 - 17) to the corresponding allylic sulfones (25 - 27) was next examined. O'Conner and Lyness have reported that the equilibrium between 1-methanesulfonyl-1-hexene (28) and 1-methanesulfonyl-2-hexene

Table 1. Addition of Pyrrolidine to Vinylic or Allylic Sulfones

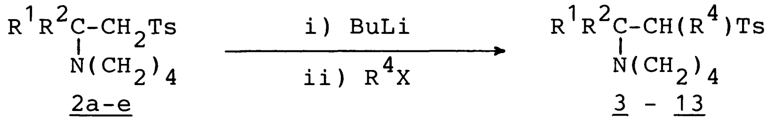


$$\underset{\text{1a-h}}{R^1R^2C{=}C(R^3)Ts} \xrightarrow[\text{in } CH_3CN]{\text{Pyrrolidine}} \underset{\text{2a-h}}{R^1R^2\underset{N(CH_2)_4}{\underset{|}{C}}\text{-}CH(R^3)Ts}$$

Substrate 1a-h		Pyrrolidine equiv.	Additive (equiv.)	Temp	Time	Yield/% a) 2a-h	Mp/°C b)
1a	$H_2C{=}CHTs$	1.2	-	r.t.	28 h	2a,quant.	65.5-66.0
1b	$H_2C{=}CHCH_2Ts$	3.0	-	r.t.	17 h	2b,quant.	56.0
1c	n-BuCH=CHTs	3.0	-	r.t.	2 d	2c, 81	45.0
1d	PhCH=CHTs	10	DBU (1.0)	r.t.	1 d	2d,quant.	101-102
1e	$H_2C{=}C(CH_3)CH_2Ts$	10	DBU (10)	50 °C	53 h	2e, 90	71.0
1f	$H_2C{=}C(CH_2Ph)Ts$	10	-	60 °C	12 h	2f,quant.	96.0-97.0
1g	$H_2C{=}C(CH_3)Ts$	10	DBU (1.0)	reflux	6 h	2g,quant.	60.5-61.0
1h	$H_2C{=}C(n\text{-}Bu)Ts$	10	DBU (1.0)	reflux	9 h	2h, 93	oil

a) All compounds gave satisfactory spectral data and combustion analyses for C, H, and N. b) Recrystallized from hexane.

Table 2. Alkylation of β-Pyrrolidinoalkyl p-Tolyl Sulfones

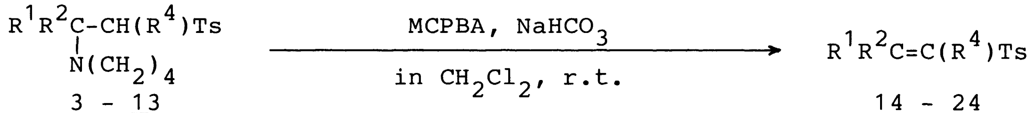


$$\underset{\text{2a-e}}{R^1R^2\underset{N(CH_2)_4}{\underset{|}{C}}\text{-}CH_2Ts} \xrightarrow[\text{ii) } R^4X]{\text{i) BuLi}} \underset{\text{3 - 13}}{R^1R^2\underset{N(CH_2)_4}{\underset{|}{C}}\text{-}CH(R^4)Ts}$$

	Substrate R^1	R^2	R^{4}X (equiv.)	Temp/°C	Yield/% a) 3 - 13
2a	H	H	CH_3I (2)	- 72 ⟶ - 40	3, 87 b)
2a	H	H	$CH_3(CH_2)_2I$ (1.2) c)	- 72 (1 h)	4, 87 d)
2a	H	H	$CH_3(CH_2)_3I$ (1.2) c)	- 72 (1 h)	5, 87 e)
2a	H	H	$CH_3(CH_2)_7I$ (1.2) c)	- 72 (1 h)	6, 92 e)
2a	H	H	$PhCH_2Br$ (1.05) f)	- 72 (1 h)	7, 90 g)
2b	H	CH_3	CH_3I (1.2) c)	- 72 (1 h)	8, 95 e,h)
2b	H	CH_3	$PhCH_2Br$ (1.2) c)	- 72 (1 h)	9, 94 e,h)
2c	H	$CH_3(CH_2)_3$	CH_3I (1.1) i)	- 72 (1 h)	10, 93 e,h)
2d	H	Ph	CH_3I (1.2) c)	- 72 (1 h)	11, 92 e,h)
2d	H	Ph	$PhCH_2Br$ (1.1) j)	- 72 (1 h)	12, 74 e,h)
2e	CH_3	CH_3	CH_3I (1.3) c)	- 72 (1 h)	13, 91 e)

a) All compounds gave satisfactory spectral data. b) Mp was consistent with that of 2g. c) 5 equiv. of HMPA was added. d) Mp 57-58 °C. e) oil. f) 2 equiv. of HMPA was added. g) Mp was consistent with that of 2f. h) Mixture of diastereoisomers. Their ratios were determined by 400 MHz ^{1}H-NMR spectra as follows: 7/3 (8), 2/3 (9), 5/3 (10), 2/3 (11), and 7/6 (12). i) 1.5 equiv. j) 0.5 equiv. of HMPA was added.

Table 3. Preparation of α-Alkylated Vinylic Sulfones



$$\underset{\underset{\textstyle N(CH_2)_4}{|}}{R^1R^2C}\text{-}CH(R^4)Ts \xrightarrow[\text{in } CH_2Cl_2,\ \text{r.t.}]{\text{MCPBA, NaHCO}_3} R^1R^2C{=}C(R^4)Ts$$

3 - 13 → 14 - 24

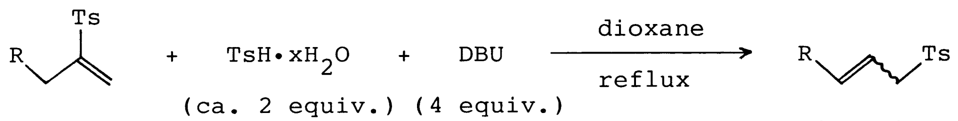
	Substrate R^1	R^2	R^4	Yield/%[a] (Time)		Substrate R^1	R^2	R^4	Yield/%[a] (Time)
3	H	H	CH_3	14, 83[b] (b)	9	H	CH_3	$PhCH_2$	20, 94[d] (2 d)
4	H	H	$CH_3(CH_2)_2$	15, 90 (2 d)	10	H	$CH_3(CH_2)_3$	CH_3	21, 94[d] (21 h)
5	H	H	$CH_3(CH_2)_3$	16, 81 (15 h)	11	H	Ph	CH_3	22, 92[d] (40 h)
6	H	H	$CH_3(CH_2)_7$	17, 95 (1 d)	12,	H	Ph	$PhCH_2$	23, 100[d] (17 h)
7	H	H	$PhCH_2$	18, 95[c] (13 h)	13,	CH_3	CH_3	CH_3	24, 86[e] (30 h)
8	H	CH_3	CH_3	19, 92[d] (65 h)					

a) All compounds gave satisfactory spectral data. b) After quaternarization with methyl iodide (5 equiv.) in CH_2Cl_2 at room temperature for 43 h, treated with Et_3N (5 equiv.) in CH_3CN (r.t., 12 h + 60 °C, 11 h). Mp 55.0 - 56.0°C (from hexane). c) Mp 52.0 - 52.5 °C. d) Mixture of E- and Z-isomers. Their ratios (E/Z) were determined by 400 MHz ^1H-NMR spectra as follows: 70/30 (19), 37/63 (20), 63/37 (21), 42/58 (22), and 55/45 (23). e) Mp 67.0 °C (from hexane).

(29) under basic conditions (t-BuOK in t-BuOH at room temperature) almost completely shifts to 29.[7] Therefore, if 2-tosyl-1-alkenes (15 - 17) can be transformed to the corresponding 1-tosyl-1-alkenes (30), the above conversion must be possible. This was successfully achieved through addition-elimination reaction of p-toluenesulfinic acid (TsH) toward 2-tosyl-1-alkenes (15 - 17) to give 30 followed by rearrangement to allylic sulfones (25 - 27) under basic conditions by treating 15 - 17 with TsH and DBU in refluxing dioxane as shown in Table 4. Ultimately it was revealed that β-pyrrolidinoethyl p-tolyl sulfone (2a) is a useful and stable crystalline reagent for the preparation of two carbon homologated allylic sulfones from alkyl halides.

A typical experimental procedure is described for the transformation of tosylethene (1a) to 1-tosyl-2-decene (27) via 2-tosyl-1-decene (17) in the following: (i) Addition of Pyrrolidine to 1a —— A mixed solution of 1a (182 mg, 1 mmol) and pyrrolidine (100 μl, 1.2 mmol) in acetonitrile (1 ml) was allowed to stand for 28 h at room temperature. The progress of the reaction was monitored by TLC. After replacing the solvent by ethyl acetate, the solution was washed with brine and dried over Na_2SO_4. The residue obtained by evaporation of the solvent was subjected to a preparative TLC (SiO_2, hexane/AcOEt/Et_3N=20/20/1) to isolate 2-pyrrolidino-1-tosylethane (2a) in quantitative yield (253 mg). Pure sample for elemental analysis was obtained by recrystallization from hexane. Calcd (Found): C 61.63 (61.49), H 7.56 (7.68), N, 5.53 (5.33). (ii) α-Alkylation of 2a —— To a mixed solution of 2a (101 mg, 0.4 mmol) and HMPA (350 μl, 2 mmol) in THF (4 ml) was added 1.05 equivalent of butyllithium (hexane solution) at - 72 °C under nitrogen. After stirring for 30 min, a THF solution (0.5 ml) of octyl iodide (87 μl, 0.48 mmol) was added at - 72 °C. The reaction mixture was quenched by the

Table 4. Conversion of 2-Tosyl-1-alkenes to Allylic Sulfones



15 - 17 25 - 27

	Substrate R	Reaction time h	Yield/% 25 - 27$^{a)}$	E/Z
15	CH_3CH_2	5	25, 95	81/19
16	$CH_3(CH_2)_2$	4.5	26, 94	81/19
17	$CH_3(CH_2)_6$	4	27, 94	79/21

a) All compounds gave satisfactory spectral data.

addition of methanol (2 ml) at - 72°C after 1 h. After work-up in a usual way, 1-pyrrolidino-2-tosyldecane (6) was isolated as an oil by a preparative TLC (SiO_2, hexane/AcOEt/Et_3N=100/20/0.1) in 92% yield (135 mg). Its structure was confirmed by IR, 400 MHz ^{1}H-NMR, and mass (M^+, 365) spectra. (iii) Oxidative Elimination of Pyrrolidino Group —— A CH_2Cl_2 solution (4.5 ml) of MCPBA (69 mg, 0.28 mmol) was added dropwise to a heterogenious mixture of 6 (73 mg, 0.2 mmol) and solid $NaHCO_3$ (34 mg, 0.4 mmol) in CH_2Cl_2 (1.5 ml) with vigorous stirring. After stirring for 1 day, the reaction mixture was quenched by the addition of solid $NaHSO_3$ followed by replacement of the solvent by ethyl acetate. After washing twice with water and drying over Na_2SO_4, 17 was separated as an oil by a preparative TLC (SiO_2, hexane/AcOEt=5/1) in 95% yield (56 mg). IR, 400 MHz ^{1}H-NMR, and mass (M^+, 294) spectra were satisfactory. (iv) Conversion of Vinylic Sulfone (17) to Allylic Sulfone (27) —— A mixed solution of 17 (88 mg, 0.3 mmol), p-toluenesulfinic acid (TsH•xH_2O, x=ca.1, 104 mg, ca. 0.6 mmol) , and DBU (180 µl, 1.2 mmol) in dioxane (2 ml) was refluxed for 4 h. After work-up in a usual manner, 1-tosyl-2-decene was isolated by a preparative TLC (SiO_2, hexane/AcOEt=8/1) in 94% yield (83 mg). The oily product gave the satisfactory IR, 400 MHz ^{1}H-NMR, and mass (M^+, 294) spectra.

Further work is in progress to elucidate the scope and limitation of the present synthetic method in our laboratory.

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