CYCLOPROPANATION OF PHENYL STYRYL SULFONES WITH PHENACYLSULFONIUM YLIDES UNDER PHASE-TRANSFER CATALYSIS

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Cyclopropanation of substituted phenyl styryl sulfones **1** with dimethylsulfonium phenacylides was carried out by two different methods (under PTC catalysis with *in situ* generation of the ylides and by direct addition of ylides) to obtain a series of substituted 1-benzenesulfonyl-2-benzoyl-3-phenylcyclopropanes **2**. The PTC method was found to be more facile and efficient. The spectral data of cyclopropanes **2** are discussed.

Key words: Cyclopropanation; PTC catalysis; Sulfur ylides; Cyclopropanes; Antibacterial and antifungal activity.

Cyclopropanation of olefins is an important carbon–carbon bond forming reaction producing synthetically useful multifunctional molecules[1–4]. Although a number of methods have been developed over the years for such systems, cycloaddition of sulfur ylides to carbon–carbon double bonds is one of the important synthetic strategies[5]. Amongst non-stabilized and stabilized ylides, the former have been studied[6] to a greater extent than the latter. The stabilized ylides require an additional delocalization of charge in the transition state to undergo cycloaddition with Michael acceptors. The former can be generated *in situ* or prepared as stable ylide before adding to the activated double bonds[7]. However, these procedures require rigorous reaction conditions. The importance of phase transfer catalysis (PTC) in synthetic chemistry is well recognized[8]; it is an elegant and convenient method particularly useful for generating ylides from their stable salts[9,10]. In view of growing interest in the application of such processes, a variety of carbonyl activated alkenes have been used as substrates for cyclopropanation with carbonyl stabilized ylides[10–12]. On the other hand, there are less reports involving sulfonyl activated alkenes for a similar purpose[13,14].

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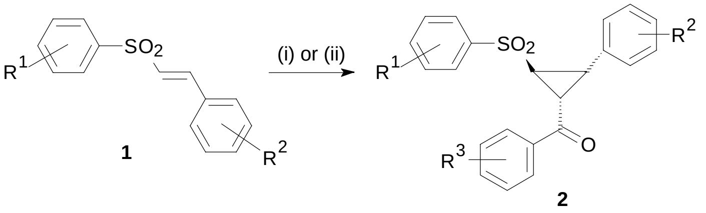
In the course of our sustained interest in the synthesis of cyclopropanoids under phase-transfer conditions, we report here on the synthesis of some new cyclopropanes. Thus, α,β-unsaturated sulfones **1** (refs[15,16]) have been cyclopropanated with stabilized ylides, phenacyldimethylsulfonium bromides[17,18] in the presence of benzyltriethylammonium chloride (BTEAC) as catalyst (method *A*, Scheme 1 and Table I). For comparison, the same substrates were also cyclopropanated by the direct addition of dimethylsulfonium phenacylide which is generated from the salt with alkali (method *B*). The yields of the products obtained under PTC are fairly high (70–82%) when compared to method *B* (55–65%) and method *B* requires longer reaction times (36–40 h) than method *A* (8–12 h). Moreover, the generation and preservation of the ylide can be avoided using the PTC method as it is generated *in situ* from the sulfonium salt. The ylide addition in this reaction is presumed to be stereoselective[14] since the relative configuration of the methine protons in **2** have been confirmed by their *J* values (Table II).

The IR spectra of **2** showed medium to strong bands in the regions 1 030–1 015 cm^{-1} confirming the presence of cyclopropane ring. Strong bands with varying intensities were also observed at 1 340–1 320 and 1 140–1 120 ($\nu(SO_2)$), 1 675–1 660 ($\nu(C=O)$), and 1 115–1 090 and 930–915 (*trans* geometry).

The ^1H NMR spectra of **2** showed an AMX pattern corresponding to the three methine protons of the cyclopropane moiety. As a result of vicinal couplings of these protons each appeared as a doublet of doublets. The influence of the different substituents on these (H_A, H_M and H_X) renders them to appear in different chemical environments[14]



1 and **2**	R^1	R^2	R^3	**1** and **2**	R^1	R^2	R^3
a	H	H	H	**g**	4-CH_3	4-CH_3	4-CH_3
b	H	H	4-OCH_3	**h**	4-OCH_3	4-OCH_3	H
c	H	H	4-Cl	**i**	4-OCH_3	4-OCH_3	4-OCH_3
d	H	4-Cl	4-CH_3	**j**	4-Cl	H	4-Cl
e	4-CH_3	H	4-Cl	**e**	4-Br	4-OCH_3	H
f	4-CH_3	4-CH_3	H	**k**	4-Br	2-Cl	H

(i) $R^3C_6H_4COCH_2S(CH_3)_2Br$; 50% aq. NaOH; BTEAC; CH_2Cl_2

(ii) $R^3C_6H_4COCH^-S^+(CH_3)_2$; benzene

SCHEME 1

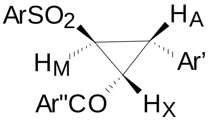
TABLE I
Physical data and IR data of compounds **2a–2l**

Compound	M.p., °C	Yield, %		Formula M.w.	Calculated/Found		IR spectrum, cm^{-1}		
		A	*B*		% C	% H	C=O	SO_2	ring deformation
2a	117–118	75	61	$C_{22}H_{18}O_3S$ 362.5	72.90 72.68	5.02 4.92	1 660	1 320, 1 440	1 020
2b	133–134	73	60	$C_{23}H_{20}O_4S$ 392.5	70.39 70.64	5.14 5.02	1 665	1 325, 1 130	1 015
2c	145–146	78	–	$C_{22}H_{17}ClO_3S$ 396.9	66.58 66.39	4.32 4.19	1 660	1 330, 1 120	1 025
2d	163–164	76	64	$C_{23}H_{19}ClO_3S$ 410.9	67.23 67.38	4.66 4.56	1 670	1 330, 1 125	1 030
2e	184–185	75	62	$C_{23}H_{19}ClO_3S$ 410.9	67.23 67.41	4.66 4.59	1 665	1 325, 1 130	1 030
2f	204–205	70	–	$C_{24}H_{22}O_3S$ 390.5	73.82 73.68	5.68 5.78	1 660	1 320, 1 125	1 025

TABLE I
(*Continued*)

Compound	M.p., °C	Yield, %		Formula M.w.	Calculated/Found		IR spectrum, cm^{-1}		
		A	*B*		% C	% H	C=O	SO_2	ring deformation
2g	221–222	72	58	$C_{25}H_{24}O_3S$ 404.5	74.23 74.06	5.98 6.06	1 660	1 325, 1 120	1 020
2h	216–217	74	–	$C_{24}H_{22}O_5S$ 422.5	68.23 68.00	5.25 5.33	1 665	1 320, 1 125	1 020
2i	229–230	77	55	$C_{25}H_{24}O_6S$ 452.5	66.36 66.18	5.35 5.24	1 665	1 320, 1 130	1 025
2j	241–242	82	65	$C_{22}H_{16}Cl_2O_3S$ 431.3	61.27 61.12	3.74 3.82	1 670	1 340, 1 125	1 030
2k	197–198	78	–	$C_{23}H_{19}BrO_4S$ 426.9	64.71 64.85	4.48 4.39	1 660	1 320, 1 120	1 025
2l	235–236	82	–	$C_{22}H_{16}BrClO_3S$ 475.8	55.54 55.38	3.39 3.32	1 675	1 330, 1 125	1 020

(see formula and Table II). The configuration of H_A, H_M and H_X of **2** may be assigned based on their *J* value as $J_{AM} = J_{MX} =$ *trans*; $J_{AX} =$ *cis*.



The ^{13}C NMR data of cyclopropane ring carbon atoms of compounds **2** are shown in Table III. The carbon attached directly to sulfonyl group (C-1) experiences higher deshielding effect than those adjacent to aroyl (C-3) and aryl (C-2) moieties and hence

TABLE II
^1H NMR spectral data of compounds **2a–2l**

Compound	H_A	H_M	H_X	Ar-H	Substituents	J_{AX}	J_{AM}	J_{MX}
2a	3.84	3.46	3.23	7.20–7.58 m, 15 H	–	10.10	5.61	6.02
2b	3.80	3.42	3.28	7.18–7.62 m, 14 H	3.84 (Ar-OCH_3)	10.12	5.60	6.03
2c	3.94	3.48	3.26	7.15–7.57 m, 14 H	–	10.13	5.62	6.05
2d	3.96	3.40	3.28	7.11–7.62 m, 13 H	2.38 (Ar-CH_3)	10.12	5.63	6.04
2e	3.84	3.45	3.24	7.02–7.48 m, 13 H	2.40 (Ar-CH_3)	10.12	5.62	6.03
2f	3.81	3.42	3.25	7.00–7.56 m, 13 H	2.40 (Ar-CH_3) 2.46 (SO_2Ar-CH_3)	10.13	5.60	6.05
2g	3.82	3.45	3.23	6.98–7.42 m, 12 H	2.38 (Ar-CH_3) 2.42 (COAr-CH_3) 2.43 (SO_2Ar-CH_3)	10.12	5.61	6.05
2h	3.79	3.45	3.22	7.22–7.65 m, 13 H	3.80 (Ar-OCH_3) 3.92 (SO_2Ar-OCH_3)	10.11	5.61	6.04
2i	3.78	3.44	3.27	7.01–7.48 m, 12 H	3.76 (Ar-OCH_3) 3.85 (COAr-OCH_3) 3.89 (SO_2Ar-OCH_3)	10.10	5.60	6.03
2j	3.99	3.50	3.30	7.13–7.58 m, 13 H	–	10.14	5.64	6.05
2k	3.95	3.43	3.32	7.05–7.60 m, 13 H	3.88 (Ar-OCH_3)	10.10	5.63	6.04
2l	3.98	3.47	3.35	7.10–7.54 m, 13 H	–	10.13	5.63	6.05

there exists a difference in their δ_C values[14]. The ^{13}C chemical shift value of 192 corresponds to the carbonyl carbon. The mass spectra (70 eV) of **2a**, **2b**, **2d** and **2j** exhibited low intense molecular ions at *m/z* 362, 392, 410 and 430, respectively, confirming their chemical composition. Elimination of SO_2 from the molecular ion and expulsion of CO from the base peak are some of the salient features observed. Benzoyl cation (*m/z* 105) formed by an α-cleavage process of the molecular ion appeared as the base peak of the spectrum.

Several compounds of this series showed in the first preliminary semiquantitative antimicrobial activity tests by the paper disc method[19] a promissing activity against several strains of bacteria and fungi. Further detailed studies of biological activity of these compounds are in progress.

EXPERIMENTAL

Melting points were determined on a Mel–Temp apparatus and are uncorrected. The IR spectra (wavenumbers in cm^{-1}) were recorded on a Perkin–Elmer grating infrared spectrophotometer model 337 in KBr pellets. ^1H NMR spectra were recorded in $CDCl_3$ on Bruker spectrometer operating at 500 or 200 MHz and ^{13}C NMR spectra at 125 or 50 MHz with TMS as an internal standard, chemical shifts are given in ppm (δ-scale), coupling constants *J* in Hz. The mass spectra were recorded on a Finnigan Mat 1210 B double focussing mass spectrometer. Microanalyses were obtained from the Regional Sophisticated Instrumentaion Centre, Punjab University, Chandigarh.

TABLE III
^{13}C NMR spectral data of compounds **2a–2l**

Compound	C-1	C-2	C-3	C-4	Substituents
2a	38.84	29.46	37.43	192.44	–
2b	38.43	29.39	37.38	192.36	53.94 (Ar-OCH_3)
2c	38.89	29.61	37.37	192.55	–
2d	38.96	29.75	37.37	192.73	20.85 (Ar-CH_3)
2e	38.54	29.63	37.29	192.75	19.99 (Ar-CH_3)
2f	38.74	29.39	37.08	192.24	21.34 (Ar-CH_3); 21.43 (SO_2Ar-CH_3)
2g	38.89	29.54	37.45	191.93	21.38 (Ar-CH_3); 21.46 (COAr-CH_3); 21.52 (SO_2Ar-CH_3)
2h	38.85	29.40	37.26	192.61	54.08 (Ar-OCH_3); 55.10 (SO_2Ar-OCH_3)
2i	37.95	30.02	38.11	191.65	55.02 (Ar-OCH_3); 55.40 (COAr-OCH_3); 55.48 (SO_2Ar-OCH_3)
2j	38.98	29.63	37.35	192.75	–
2k	39.02	29.94	38.05	192.93	54.58 (Ar-OCH_3)
2l	39.15	30.20	37.94	192.78	–

General Procedure for the Preparation of the Substituted 1-Benzenesulfonyl-2-benzoyl-3-phenylcyclopropanes **2**

Method A: A mixture of **1** (5 mmol), phenacyldimethylsulfonium bromide (6 mmol) and methylene chloride (40 ml) was stirred with 50% aqueous NaOH (20 ml) until a clear two-phase system was obtained and to this benzyltriethylammonium chloride (BTEAC) 500 mg was added. The stirring was continued for 8–12 h at room temperature. The progress of the reaction was monitored with TLC. After completion of the reaction, the reaction mixture was diluted with water. The organic layer was separated, washed with water and brine and dried over anhydrous Na_2SO_4. When the solvent was evaporated a syrupy substance was formed which was filtered through a silica gel column (9–10 g, hexane–ethyl acetate, 3 : 2) to get pure **2**.

Method B: The cycloaddition was carried out by refluxing a solution of **1** (5 mmol) and dimethylsulfonium phenacylide (6 mmol) in dry benzene or toluene (20 ml) for 36–40 h. After completion of the reaction, the solvent was removed under reduced pressure. The resultant crude product was filtered through a silica gel column (9–10 g, hexane–ethyl acetate, 3 : 2) to obtain pure **2**.

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