Synthesis of *cis*-Aryl Cyclopropyl Sulfones

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Some new *cis*-1-(arylsulfonyl)-2-phenylcyclopropanes have been synthesized by the addition of arylthiocarbenes to styrene in presence of excess potassium *t*-butoxide at low temperatures. The (arylthio)cyclopropanes thus obtained are subsequently oxidized with 30% hydrogen peroxide in acetic acid to corresponding sulfones. The IR and PMR spectra of all these compounds were recorded. Their IR spectra displayed bands in the region 1033—1008 cm^{-1} which are considered to be the most characteristic of the cyclopropane ring. They have also exhibited bands in the region 850—820 cm^{-1} characteristic of *cis*-configuration. The PMR spectra gave complex multiplets in the region 1.4—3.1 ppm. A study of these chemical shifts for ring protons and other substituents reveals that all the substituents tend to cause protons *cis*-to them to appear at higher fields than those *trans*-to them. Thus the differences of the chemical shifts can be used as a criterion to distinguish between *cis*- and *trans*-1-(arylsulfonyl)-2-phenylcyclopropanes.

One of the important methods[1] of preparing cyclopropanes is by the utility of dimethylsulfoxonium methylide (I) and dimethylsulfonium methylide (II).[2] A wide variety of Michael acceptors have been explored with I and II. α,β-Unsaturated ketones, nitriles, isocyanides and nitro compounds gave good to excellent yields for the preparation of cyclopropanes.[3] The utility of II as a co-reactant with α,β-unsaturated sulfones for the synthesis of cyclopropyl sulfones[4-8] seemed to be stereoselective and the cyclopropane derivatives thus obtained appeared to have *trans*-configuration.

The reaction of carbenes, derivatives of bivalent carbon with carbon-carbon multiple bonds provides one of the important methods for the preparation of cyclopropane compounds. Schoellkopf *et al.*[9-13] reported the preparation of cyclopropanes by treating olefins with chloromethyl phenyl ether ($PhOCH_2Cl$) and chloromethyl phenyl sulfide ($PhSCH_2Cl$) through phenoxycarbene and phenylthiocarbene intermediates respectively. These reactions were considered to proceed stereospecifically *cis*.

Although the synthesis and study of quite a number of *trans*-1-(arylsulfonyl)-2-arylcyclopropanes are known,[4-8] there are no reports about the synthesis and study of corresponding *cis*-compounds in the literature except *cis*-1-(phenylsulfonyl)-2-phenylcyclopropane.[4] It was therefore felt that the preparation of *cis*-1-(arylsulfonyl)-2-arylcyclopropanes would be of quite interest and of significance.

Results and Discussion

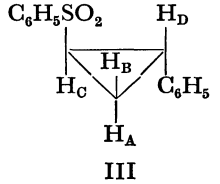
The first synthesis[14] of cyclopropyl sulfones was reported by α,γ-dehydrohalogenation of 3-chloropropyl sulfones. A few more cyclopropyl sulfones were reported according to various methods.[4,9,15,16] The synthesis of *cis*- and *trans*-1-(phenylsulfonyl)-2-phenylcyclopropane was reported first, by Truce and Badiger[4] in 1964.

A series of new *cis*-1-(arylsulfonyl)-2-phenylcyclopropanes (see Table 1) were synthesized by the addition of different aryl chloromethyl sulfides to excess of styrene at low temperature (−5 to −10 °C) in presence of excess potassium *t*-butoxide. The *cis*-1-(arylthio)-2-phenylcyclopropanes thus formed were subsequently oxidized with 30% hydrogen peroxide in acetic acid to obtain *cis*-1-(arylsulfonyl)-2-phenylcyclopropanes. Fairly high yields of *cis*-1-(arylsulfonyl)-2-phenylcyclopropanes have been obtained by refluxing for longer periods during the oxidation.

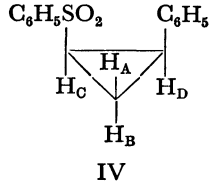
The IR spectra of most of these compounds showed medium to weak intensity bands in the region 1033—1008 cm^{-1} (see Table 2) which were considered to be the most characteristic of the cyclopropane deformation mode of the ring.[8,17-20] These compounds also displayed two high frequency bands in the region 3085—3060 cm^{-1} (ν CH_2 symmetric) and 3025—3000 cm^{-1} (ν CH_2 asymmetric) which in addition to the 1033—1008 cm^{-1} bands confirm the presence of cyclopropane ring system. All these compounds exhibited strong to medium intensity bands in the region 852—820 cm^{-1}, characteristic of *cis*-1-(arylsulfonyl)-2-phenylcyclopropanes.[21] These compounds have also exhibited very strong peaks characteristic of sulfonyl groups[22-25] in the regions 1342—1300 cm^{-1} and 1150—1136 cm^{-1}.

The PMR spectra of the compounds under present investigation exhibited complex multiplets in the region 1.40 to 2.45 ppm (methylene) and 2.36 to 3.12 ppm (methine) (see Table 3). The phenyl and arylsulfonyl groups showed signals in the regions 6.96 to 8.20 ppm. The chemical shifts data have been used[26-28] for the structural problems of cyclopropane derivatives. A study of the chemical shifts for ring protons and other substituent groups in cyclopropanes has indicated generally that all substituents tend to cause protons *cis*-to them to appear at higher fields than those *trans*-to them.

In the structure III both H_A and H_B are having substituents *cis*-to them. Hence H_A and H_B resonate at higher frequency with a small difference of chemical shifts between them, as is observed[7] in *trans*-1-(2-thienylsulfonyl)-2-phenylcyclopropane (H_A 1.50 ppm; H_B 1.89 ppm; H_C 2.77 ppm; H_D 2.89 ppm). Where

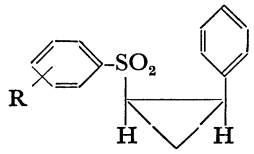


III



IV

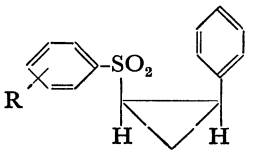
TABLE 1. *cis*-1-(ARYLSULFONYL)-2-PHENYLCYCLOPROPANES



S. No.	R	Yield/%	Mp/°C	Formula	Analysis (%) Calcd C	Calcd H	Found C	Found H
1.	H	88.5	65.5— 66[a]					
2.	*p*-Cl	78.6	90— 91	$C_{15}H_{13}ClO_2S$	61.53	4.47	61.40	4.58
3.	*p*-Br	80.3	109—110	$C_{15}H_{13}BrO_2S$	53.41	3.88	53.26	3.82
4.	*p*-CH_3	82.2	80— 81	$C_{16}H_{16}O_2S$	70.36	5.92	70.33	5.93
5.	*p*-OCH_3	86.1	114—115	$C_{16}H_{16}O_3S$	66.64	5.59	66.59	5.59
6.	*p*-NO_2	83.7	144—145	$C_{15}H_{13}NO_4S$	59.39	4.33	59.00	4.41
7.	3,4-Cl_2	78.1	95— 96	$C_{15}H_{13}Cl_2O_2S$	55.05	3.70	54.99	3.77

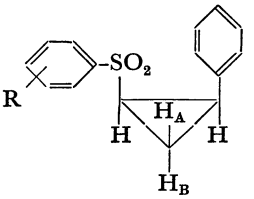
a) W. E. Truce and Badiger, *J. Org. Chem.*, **29**, 3277 (1964); report mp 67—68 °C, yield 83%.

TABLE 2. CHARACTERISTIC IR BANDS EXHIBITED BY



S. No.	R	ν CH_2 (cm^{-1}) 3100—3070 region	ν CH_2 (cm^{-1}) 3033—2955 region	Ring deformation (cm^{-1}) 1026 region	ν SO_2 (cm^{-1}) 1300 region	ν SO_2 (cm^{-1}) 1150 region	Absorption band at 848 (cm^{-1})
1.	H	—	3010(m)	1020(w)	1308(s)	1136(s)	835(m)
2.	*p*-Cl	3085(w)	3025(m)	1033(w)	1328(s)	1150(s)	830(s)
3.	*p*-Br	3060(w)	3000(w)	1030(w)	1300(s)	1140(s)	820(s)
4.	*p*-CH_3	—	3020(w)	1015(w)	1315(s)	1142(s)	850(m)
5.	*p*-OCH_3	—	3010(w)	1022(m)	1320(m)	1142(s)	842(m)
6.	*p*-NO_2	3084(w)	3020(w)	1008(w)	1342(s)	1140(s)	855(m)

TABLE 3. CHEMICAL SHIFTS OF



Solvent: $CDCl_3$, δ in ppm.

S. No.	R	Cyclopropyl CH_2(A)	Cyclopropyl CH_2(B)	Cyclopropyl CH	Aryl and arylsulfonyl
1.	H	1.42—1.64	2.00—2.24	2.36—2.88	6.97—7.58
2.	*p*-Cl	1.44—1.79	2.10—2.38	2.46—2.92	7.06—7.38
3.	*p*-Br	1.46—1.74	2.08—2.32	2.52—2.93	7.00—7.94
4.	*p*-CH_3	1.26—1.67	2.06—2.30	2.40—2.88	7.00—7.94
5.	*p*-OCH_3	1.42—1.72	2.00—2.27	2.52—2.90	6.72—6.86; 7.05—7.36
6.	*p*-NO_2	1.58—1.84	2.20—2.42	2.53—2.92	6.95—7.50; 8.02—8.20
7.	3,4-Cl_2	1.42—1.84	2.12—2.45	2.54—3.12	7.00—7.57

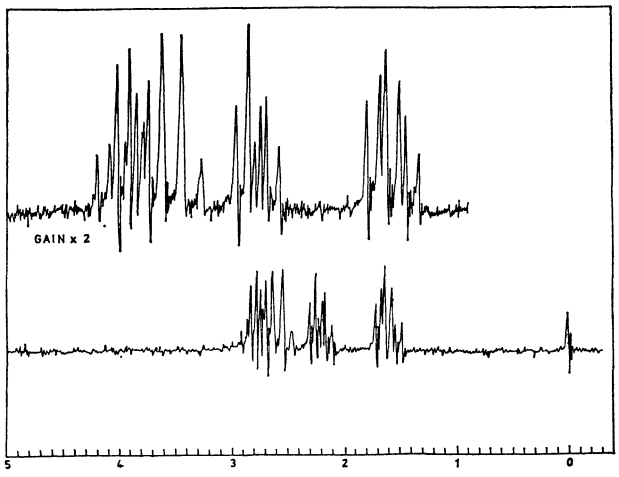


Fig. 1. 100 MHz ^1H NMR spectrum of **3** in the high field region (measured in $CDCl_3$).

as in IV H_A has substituents *cis*-to it but H_B is not having likewise. As a result of this, the chemical shift of H_A is observed at higher fields. There is a marked difference between chemical shifts of H_A and H_B in IV in comparison to III.

A representative spectra of these compounds in high field region in $CDCl_3$ is given in Fig. 1. Thus the chemical shifts data of ring protons of cyclopropane derivatives discussed above may be used as a criterion for the configurational assignments of *cis*- and *trans*-1-(arylsulfonyl)-2-phenylcyclopropanes.

The stereospecific synthesis adopted for these aryl cyclopropyl sulfones, IR and PMR spectral data, confirm that all these compounds are *cis*-isomers.

Experimental

All melting points were determined on a Mel-Temp apparatus and are uncorrected. The elemental analyses were performed by Dr. R. D. MacDonald, Australian Micro Analytical Service. The IR spectra were recorded on Perkin-Elmer model 257 in KBr discs. The PMR spectra were obtained at 100 MHz and on a Varian XL-100 spectrometer in deuteriochloroform using TMS as an internal reference. Chemical shifts were recorded in parts per million downfield from tetramethylsilane and IR frequencies in cm^{-1}.

Starting Materials. Styrene is obtained commercially and purified by distillation under reduced pressure.

Thiophenols. The arenesulfonyl chlorides were obtained by the chlorosulfonylation of the corresponding hydrocarbons as described by Huntress and Carten.[30] The arenesulfonyl chlorides were reduced to the corresponding thiophenols with zinc dust and dilute sulfuric acid. The procedure adopted was a modification of the method described by Vogel.[31] To a mixture of crushed ice and concentrated sulfuric acid the arenesulfonyl chloride was added with stirring. The zinc dust was added in portions as rapidly as possible to the cooled mixture without allowing the temperature to rise above 10 °C. The distillate obtained after the steam distillation of the mixture was extracted with ether. The product obtained after evaporation of ether was purified. Thiophenol: bp 168—169 °C, *p*-chlorothiophenol: mp 52—53 °C, *p*-bromothiophenol: mp 74—76 °C, *p*-thiocresol: bp 195—196 °C, *p*-methoxythiophenol: bp 225—227 °C, 3,4-dichlorothiophenol: bp 80—81 °C/8 mmHg. The *p*-nitrothiophenol: mp 73—74 °C, was prepared according to the procedure of Price and Stacy.[32]

Aryl Chloromethyl Sulfides: The aryl chloromethyl sulfides were prepared following the procedure of Francher.[33] A mixture of paraformaldehyde and benzene was taken in a conical flask and to this, concentrated hydrochloric acid was added rapidly with stirring. After a while, the mixture was kept at 40 °C and the appropriate thiol in benzene was added slowly. The resulting mixture was maintained slightly above 40 °C for 2 h. After removing the solvent the products were purified by distillation under reduced pressure. Phenyl chloromethyl sulfide: bp 109—110 °C/11 mmHg, *p*-chlorophenyl chloromethyl sulfide: bp 131—132 °C/12 mmHg, *p*-bromophenyl chloromethyl sulfide: bp 164—165 °C/18 mmHg, *p*-methoxyphenyl chloromethyl sulfide: bp 175—176 °C/20 mmHg, *p*-nitrophenyl chloromethyl sulfide: mp 54—55 °C, 3,4-dichlorophenyl chloromethyl sulfide: bp 144—145 °C/8 mmHg.

General Procedure for the Preparation of cis-*1-(Arylsulfonyl)-2-phenylcyclopropanes*: In a 250 ml three necked flask equipped with magnetic stirrer and fitted with a dropping funnel and calcium chloride guard tube was placed 25 ml of styrene. Small portions of potassium *t*-butoxide (5 g, 20% excess than 0.025 mol) was added with stirring to styrene at −5 to −10 °C. The aryl chloromethyl sulfide was added dropwise to the above mixture. After the complete addition the reaction mixture was stirred for 3 h and was diluted with water. The oily layer was separated and dried over anhydrous calcium chloride. It was then subjected to fractional distillation under reduced pressure and the product *cis*-1-(arylthio)-2-phenylcyclopropane was collected.

The sulfide (2.0 g) was dissolved in 20 ml of glacial acetic acid and 9 ml of 30% hydrogen peroxide was added to the mixture at ice-cold temperature. The mixture was refluxed for 25 to 48 h. It was then poured on to crushed ice and the solid separated was filtered off and dried. The product *cis*-1-(arylsulfonyl)-2-phenylcyclopropane was recrystallized from 2-propanol. The relevant data on the compounds synthesized are given in Table 1.

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