[Contribution from the Department of Chemistry, Purdue University]

PREPARATION OF CYCLOALKYL ALKYL SULFONES

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The preparation of cycloalkyl sulfones has received relatively little attention in the past (1–6). Of the various methods used to prepare alkyl sulfones, the two most common procedures are the oxidation of sulfides and the alkylation of sulfinates. The latter method involves the reaction of an alkali or silver sulfinate with an alkylating agent such as an alkyl halide, sulfate, or an activated aromatic halide.

The present work describes the preparation of a series of cyclohexyl and cyclopentyl sulfones by the alkylation of sodium cycloalkanesulfinates. Only cyclobutyl methyl sulfone was prepared in the cyclobutyl series; sodium methanesulfinate was alkylated with cyclobutyl bromide in 6.0% yield.

Chlorosulfonation of cyclohexane (7) with sulfuryl chloride in the presence of benzene, a catalytic amount of pyridine, and irradiation gave a 45.4% yield of cyclohexanesulfonyl chloride. Cyclopentanesulfonyl chloride was synthesized from cyclopentane by the same procedure. The yields were 45.3% and 53.8% for two runs. Although cyclobutanesulfonyl chloride was not to be used in this work (due to a lack of substantial quantities of cyclobutane), it was of interest to see if this compound could be prepared by the chlorosulfonation procedure. Cyclobutane, when treated with sulfuryl chloride under the conditions described above, gave a 46.6% yield of cyclobutanesulfonyl chloride.

Cyclohexanesulfonyl chloride and cyclopentanesulfonyl chloride were reduced (8) to the corresponding sodium sulfinates in 42.8% and 56.5% yields, respectively. The sulfinates were treated with various alkylating agents in ethanol to give the cycloalkyl sulfones.

It was of interest to study the action of *tert*-butyl bromide on sodium cyclohexanesulfinate and sodium cyclopentanesulfinate. Posner (9) claimed to have prepared *tert*-amyl phenyl sulfone by the reaction of sodium benzenesulfinate with *tert*-amyl bromide. Every attempt by Ipatieff and coworkers (10) to synthesize *tert*-alkyl phenyl sulfones by this method led to the isolation of benzenesulfinic acid and diphenyl disulfide. It was pointed out (10) that the "sulfone" obtained by Posner (9) was probably benzenesulfinic acid.

The reaction of *tert*-butyl bromide with sodium cyclohexanesulfinate in ethanol gave dicyclohexyl disulfide. Proof of structure of the disulfide was accomplished in the following manner:

$$(C_6H_{11}S)_2 \xrightarrow[AcOH]{Cl_2,H_2O} C_6H_{11}SO_2Cl \xrightarrow{NH_4OH} C_6H_{11}SO_2NH_2.$$

The melting point of the sulfonamide was not depressed by an authentic sample. Similar results were obtained with sodium cyclopentanesulfinate and *tert*-butyl bromide.

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Sulfinic acids have been known to disproportionate[2] when heated to give thiosulfonates (11). The latter compounds can be converted, when heated in the presence of water, to disulfides (12). The first step in the reaction of sodium cyclohexanesulfinate (also cyclopentanesulfinate) with *tert*-butyl bromide probably was the dehydrohalogenation of the bromide to give isobutylene, sodium bromide, and cyclohexanesulfinic acid. The sulfinic acid was then converted, as explained above, to the disulfide.

EXPERIMENTAL[3]

Cyclohexanesulfonyl chloride. Cyclohexane (5 moles) was chlorosulfonated (7) to give 207 g. (45.4%) of cyclohexanesulfonyl chloride, b.p. 108.0–109.5° (4 mm.), n_D^{20} 1.4970; lit. (12a), b.p. 122–123° (14 mm.), n_D^{21} 1.4970.

By adding dry ammonia to a small amount of cyclohexanesulfonyl chloride dissolved in ether, the *sulfonamide* was prepared. Recrystallization from 60–70° petroleum ether gave a solid, m.p. 94.0–95.0°, lit. (12a), m.p. 94–95°.

Sodium cyclohexanesulfinate. The procedure employed for the preparation of sodium *p*-toluenesulfinate (8) was used to synthesize this compound. Starting with 80 g. (0.44 mole) of cyclohexanesulfonyl chloride, the yield was 32 g., 42.8%.

The *S-benzylthiuronium salt* was prepared and was recrystallized from water, m.p. 143°.

Anal. Calc'd for $C_{14}H_{22}N_2O_2S_2$: N, 8.91. Found: N, 8.89.

Cyclopentanesulfonyl chloride. A mixture of 350 g. (5.0 moles) of cyclopentane, 390 g. of benzene, and a catalytic amount of pyridine was treated with 335 g. (2.5 moles) of sulfuryl chloride in the presence of light furnished by two 200-watt lamps. Three hours was needed for the addition of the sulfuryl chloride to the mixture. The excess cyclopentane and benzene were removed and distillation of the residue gave 190 g. (45.3%) of cyclopentanesulfonyl chloride, b.p. 71–73° (2 mm.), 91° (5 mm.), 99° (7 mm.), 104.5–105.0° (9 mm.), n_D^{20} 1.4910 A duplicate run gave a 53.8% yield.

Anal. Calc'd for $C_5H_9ClO_2S$: C, 35.62; H, 5.38.

Found: C, 35.60; H, 5.48.

Treatment of the sulfonyl chloride with aniline in benzene gave *cyclopentanesulfonanilide*; recrystallized from 60–70° petroleum ether, m.p. 89–90°; lit. (4), m.p. 89.5–90.5°.

Sodium cyclopentanesulfinate. Cyclopentanesulfonyl chloride (194 g., 1.15 moles) was reduced (8) to give 102 g. (56.5%) of sodium cyclopentanesulfinate.

The *S-benzylthiuronium salt* was prepared and was recrystallized from dilute ethanol, m.p. 168°. It was necessary to preheat the melting point bath to 163° to avoid decomposition of the salt.

Anal. Calc'd for $C_{13}H_{20}N_2O_2S_2$: N, 9.33. Found: N, 10.08.

Cyclobutanesulfonyl chloride. Cyclobutane (14 g., 0.25 mole), benzene (19.5 g., 0.25 mole), and four drops of pyridine were placed in a 50-ml., three-neck flask equipped with a separatory-funnel, Dry Ice condenser, and thermometer. The mixture was irradiated with two 200-watt lamps placed one inch from the flask. Sulfuryl chloride (16.75 g., 0.125 mole) was added gradually and the evolution of hydrogen chloride began within 20 minutes. The temperature of the reaction never rose above 40°. Distillation of the mixture gave 9 g. (46.6%) of cyclobutanesulfonyl chloride, b.p. 67.5–68.0° (5 mm.), n_D^{20} 1.4603.

Anal. Calc'd for $C_4H_7ClO_2S$.: C, 31.07; H, 4.56.

Found: C, 31.18; H, 4.62.

Alkylation of the sulfinates: General procedure. A solution of the sodium cycloalkane-

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[2] von Braun and Weissback, *Ber.*, **63**, 2836 (1930), worked with cyclohexanesulfinic acid and observed the following reaction:

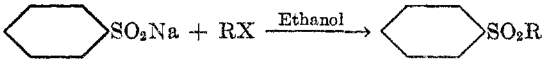
$$3\ C_6H_{11}SO_2H \xrightarrow[100°]{N_2\ \text{atm.}} C_6H_{11}SO_2SC_6H_{11} + C_6H_{11}SO_3H + H_2O.$$

[3] All melting points are uncorrected.

sulfinate, the alkylating agent, and absolute ethanol was refluxed for a certain length of time. The hot solution was then filtered to remove the sodium halide which had formed during the reaction and the filtrate was heated on a steam-bath to evaporate the ethanol. Water was added and the resulting mixture was extracted with chloroform or carbon tetrachloride. The solvent was then removed and the residue was either distilled or recrystallized or both. Unreacted sulfinate was recovered from the aqueous layer.

TABLE I

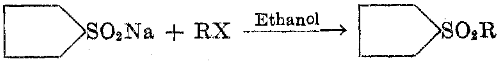
PREPARATION OF THE CYCLOHEXYL SULFONES



SULFINATE (moles)	RX	MOLES	ETHANOL (ml.)	REFLUX TIME (hrs.)	SULFONE	
					Conversion, %	Yield, %
0.0588	Methyl iodide	0.36	150	140	72.5	82.5
.0294	Ethyl bromide	.183	75	48	32.9	58.7
.0294	Propyl bromide	.03	75	48	46.6	46.6
.0588	Isopropyl bromide	.36	200	72	26.8	40.7
.0294	Butyl bromide	.03	75	48	33.4	33.4
.0059	Benzyl chloride	.044	20	20	35.9	35.9
.0588	Cyclohexyl bromide	.30	200	96	6.4	10.9
.0588	Cyclopentyl bromide	.03	200	96	30.9	30.9

TABLE II

PREPARATION OF THE CYCLOPENTYL SULFONES



SULFINATE (moles)	RX	MOLES	ETHANOL (ml.)	REFLUX TIME (hrs.)	SULFONE	
					Conversion, %	Yield, %
0.10	Methyl iodide	0.50	200	96	58.7	61.2
.10	Ethyl bromide	.50	200	96	25.9	35.0
.10	Propyl bromide	.50	200	96	40.3	55.0
.10	Butyl bromide	.50	200	96	56.7	71.4
.10	Benzyl chloride	.50	240	72	49.1	49.1
.10	Cyclopentyl bromide	.20	200	72	20.0	20.0

Cyclobutyl methyl sulfone. A mixture of 10 g. (0.074 mole) of cyclobutyl bromide (13), 20 g. (0.196 mole) of sodium methanesulfinate, and 50 ml. of absolute ethanol was refluxed for 72 hours. Ethanol was evaporated, water was added, and the mixture was extracted with chloroform. Distillation of the product, after removal of chloroform, gave cyclobutyl methyl sulfone (0.6 g., 6.05%); b.p. 117° (4 mm.), n_{D}^{20} 1.4752.

Anal. Calc'd for $C_5H_{10}O_2S$: C, 44.76; H, 7.51.

Found: C, 44.71; H, 7.38.

Reaction of tert-butyl bromide with sodium cyclohexanesulfinate. Sodium cyclohexanesulfinate (68 g., 0.4 mole), 82.2 g. (0.6 mole) of *tert*-butyl bromide, and 400 ml. of absolute ethanol were refluxed for 72 hours. Sodium bromide was filtered off and the ethanol was evaporated. Water was added and the mixture was extracted with carbon tetrachloride. The aqueous layer yielded 38.5 g. of organic salts. Distillation of the product, after removal of carbon tetrachloride, gave 11.0 g. of a liquid (presumed to be dicyclohexyl disulfide) boiling at 136–138° (2.5 mm.). This material was redistilled, b.p. 128–129° (1.5 mm.), n_D^{20} 1.5450.

Anal. Calc'd for $C_{12}H_{22}S_2$: C, 62.56; H, 9.63.

Found: C, 62.49; H, 9.69.

TABLE III

Cyclohexyl Sulfones

SULFONE	B.P., °C.	MM.	n_D^{20}	M.P., °C.	FORMULA	ANALYSES C Calc'd	ANALYSES C Found	ANALYSES H Calc'd	ANALYSES H Found
Cyclohexyl methyl	119–120[a]	2	1.4920		$C_7H_{14}O_2S$	51.85	51.60	8.70	8.80
Cyclohexyl ethyl				35–37[b, c]	$C_8H_{16}O_2S$	54.51	54.48	9.15	9.02
Cyclohexyl propyl				50–51[b]	$C_9H_{18}O_2S$	56.80	56.77	9.53	9.50
Cyclohexyl isopropyl				40.5–41.0[d]	$C_9H_{18}O_2S$	56.80	56.80	9.53	9.45
Butyl cyclohexyl	164–165 191.5	5 16	1.4850	19[e]	$C_{10}H_{20}O_2S$	58.79	58.65	9.87	9.96
Benzyl cyclohexyl				104.5–105.0[f]	$C_{13}H_{18}O_2S$	65.50	65.55	7.61	7.49
Dicyclohexyl				130–132[g]	$C_{12}H_{22}O_2S$	62.57	62.70	9.63	9.70
Cyclohexyl cyclopentyl				71–72[d]	$C_{11}H_{20}O_2S$	61.07	61.10	9.32	9.18

[a] Barnard, Fabian, and Koch, *J. Chem. Soc.*, 2442 (1949), report b.p. 94.5–95.0° (0.05 mm.), n_D^{20} 1.4918. [b] Recrystallized from 3:1 mixture of low-boiling petroleum ether and diethyl ether. [c] Bloomfield *J. Chem. Soc.*, 1547 (1947) reports m.p. 34°., [d] Recrystallized from low-boiling petroleum ether. [e] Freezing point. [f] Recrystallized from absolute ethanol. [g] Borsche and Lange, *Ber.*, **38**, 2768 (1905) report m.p. 132.0–132.5°.

TABLE IV

Cyclopentyl Sulfones

SULFONE	B.P., °C.	MM.	n_D^{20}	M.P., °C.	FORMULA	ANALYSES C Calc'd	ANALYSES C Found	ANALYSES H Calc'd	ANALYSES H Found
Cyclopentyl methyl	116–117	2	1.4867		$C_6H_{12}O_2S$	48.62	48.60	8.16	8.03
Cyclopentyl ethyl				47–48[a]	$C_7H_{14}O_2S$	51.85	51.95	8.70	8.73
Cyclopentyl propyl	125.0–125.5	3	1.4839		$C_8H_{16}O_2S$	54.51	54.55	9.15	9.24
Butyl cyclopentyl	129	2	1.4812		$C_9H_{18}O_2S$	56.80	57.00	9.53	9.61
Benzyl cyclopentyl				85–86[a]	$C_{12}H_{16}O_2S$	64.26	64.60	7.19	7.32
Dicyclopentyl				68–70[a]	$C_{10}H_{18}O_2S$	59.36	59.60	8.97	8.98

[a] Recrystallized from 60–70° petroleum ether.

A solution of 1.65 g. of this liquid, 1.75 g. of water, and 20 ml. of glacial acetic acid was treated with chlorine until the color of the solution became yellow. Considerable heat was liberated. The solution was poured on ice and extracted with ether. The ethereal solution was washed with dilute sodium bisulfite solution, dilute sodium bicarbonate solution, water, and was dried over sodium sulfate. Distillation gave 0.7 g. of cyclohexanesulfonyl chloride, b.p. 72–73° (1.5 mm.), n_D^{20} 1.4978. Treatment of this sulfonyl chloride with aqueous ammonia gave the *sulfonamide*, m.p. 95.0–95.5°. The melting point was not depressed by an authentic sample.

Reaction of tert-butyl bromide with sodium cyclopentanesulfinate. A solution of 46.5 g. (0.3 mole) of sodium cyclopentanesulfinate, 82.2 g. (0.6 mole) *tert*-butyl bromide, and 500 ml. of absolute ethanol was refluxed for 77 hours. A considerable amount of isobutylene, identified as the dibromide, was collected in a trap attached to the system and cooled with a Dry Ice-acetone bath. Sodium bromide was filtered off when the reaction was over and the ethanol was evaporated. Water was added, and the mixture was extracted with carbon tetrachloride. The aqueous layer yielded 25.0 g. of organic salts. Distillation of the product, after removal of carbon tetrachloride, gave 4.0 g. of impure dicyclopentyl disulfide, b.p. 105.5–106.0° (1.5 mm.), n_D^{20} 1.5400. The material was redistilled, b.p. 110.5° (3.0 mm.), n_D^{20} 1.5361.

Anal. Calc'd for $C_{10}H_{18}S_2$: C, 59.33; H, 8.96.
Found: C, 60.49; H, 8.44.

A pure sample of dicyclopentyl disulfide prepared from cyclopentanesulfonyl chloride and hydriodic acid (14) had a refractive index at 20° of 1.5470.

A portion of the impure disulfide, dissolved in glacial acetic acid and water, was treated with chlorine. The resulting sulfonyl chloride was not isolated but was converted directly to cyclopentanesulfonanilide, m.p. 89.5–90.0°. The melting point was not depressed by an authentic sample.

SUMMARY

A series of cyclohexyl and cyclopentyl sulfones was prepared by the alkylation of the sodium cycloalkanesulfinates, *i.e.*, $C_6H_{11}SO_2R$ (where R is methyl, ethyl, propyl, isopropyl, butyl, benzyl, cyclohexyl, and cyclopentyl) and $C_5H_9SO_2R$ (where R is methyl, ethyl, propyl, butyl, benzyl, and cyclopentyl). Cyclobutyl methyl sulfone was synthesized by the action of cyclobutyl bromide on sodium methanesulfinate. With the exception of cyclohexyl methyl sulfone, cyclohexyl ethyl sulfone, and dicyclohexyl sulfone, the compounds prepared have not been previously reported.

The reaction of *tert*-butyl bromide with sodium cyclohexanesulfinate and sodium cyclopentanesulfinate gave dicyclohexyl disulfide and dicyclopentyl disulfide respectively.

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