to stock 100% sulfuric acid to obtain the maximum freezing point.

In the run with aniline the reaction mixture was neutralized, steam distilled, and titrated with nitrite to determine the combined sulfonation products. No detectable amount of aminobenzenesulfonic acid could be found, but the fact that the curves of aniline, methylaniline, and isopropylaniline have lower limiting slopes than the curve of dimethylaniline suggests that some sulfonation took place.

Summary

In contrast to dimethylaniline, which may be sulfonated selectively in the *meta* position at low temperature with fuming sulfuric acid, aniline yields a mixture of products in which the *ortho-para* isomers predominate. Evidence is presented that the difference in behavior is due to the formation of a molecular addition complex between aniline and sulfur trioxide which carries no electrical charge.

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[CONTRIBUTION FROM THE DEPARTAMENTO DE QUIMICA, FACULDADE DE FILOSOFIA, UNIVERSIDADE DE SÃO PAULO, BRAZIL]

The Configuration of Sulfoxides. Mixed Crystals of Sulfoxides with Sulfones

BY HEINRICH RHEINBOLDT AND ERNESTO GIESBRECHT

In 1926 Strecker and Spitaler[1] showed that dimethyl sulfoxide and sulfone, diethyl sulfoxide and sulfone, as well as di-*n*-propyl sulfoxide and sulfone, have, in pairs, practically the same value of molecular refraction with the result of an identical refraction equivalent for the groups $SO^{=}$ and $SO_2^{=}$ in such sulfoxides and sulfones.

On the basis of the relation existing between the molecular refraction and the real volume of the molecules arose the idea that perhaps corresponding sulfoxides and sulfones, in general, could be isomorphous if the valency angle in the sulfur atom would not be too divergent because of the different nature of the two organic substituents.

We investigated, therefore, by the thermal analysis method, the binary systems of a series of symmetrically substituted sulfoxides and sulfones of the general formulas R_2SO and R_2SO_2 comprising the following very different types where the substituted group R was as follows

1. $CH_2(CH_2)_2CH_3$
2. $CH_2(CH_2)_{14}CH_3$
3. CH_2CH_2OH
4. $CH_2C_6H_5$
5. $CH_2C_6H_4NO_2$-*p*
6. $CH_2CH_2C_6H_5$
7. C_6H_5
8. $C_6H_4CH_3$-*p*
9. C_6H_4Br-*p*
10. $C_6H_4OCH_3$-*p*

In every case we found the formation of continuous series of mixed crystals. The systems of the compounds 1, 3, 4, 5 (Fig. 1) show a mixed crystal series of the type I, and the ones of the compounds 2, 6, 7, 8, 9, 10 (Fig. 2) a series of the type III of Bakhuis-Roozeboom's classification.[2]

On the contrary, sulfides do not give mixed crystals either with the pertaining sulfoxides or with the sulfones. This was proved by the binary systems of dibenzyl sulfide and bis-*p*-bromophenyl sulfide with the corresponding sulfoxides and sulfones.

This finding indicates that these pairs of sulfoxides and sulfones must have the same steric configuration.

In the sulfones the tetrahedral configuration seems sufficiently established. Electron diffraction measurements on dimethyl sulfone gave results that were best explained by the tetrahedral configuration of the molecule.[3]

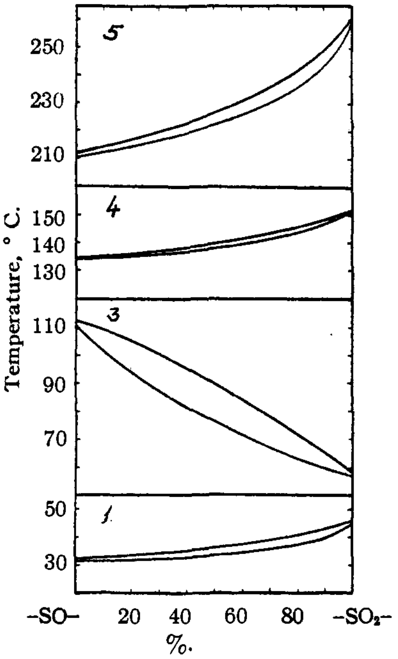

Fig. 1.—Binary systems of sulfoxides and sulfones with mixed crystals series of type I.

Determinations of the dipole moments for dimethyl sulfone in the vapor-phase,[4] and for diethyl sulfone,[5] diphenyl sulfone[6,7] and derivatives[7] in solution demonstrated a tetrahedral arrangement of the four valence bonds.

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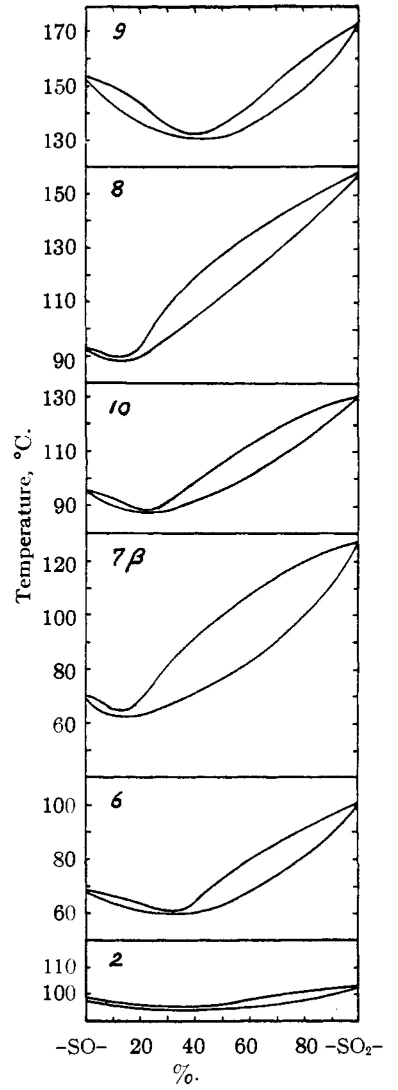

Fig. 2.—Binary systems of sulfoxides and sulfones with mixed crystals series of type III.

In the sulfoxides, electric dipole moment measurements of diphenyl sulfoxide[6,8,9] and derivatives[7,9] and of dibenzyl sulfoxide[8] showed that, contrary to the configuration of ketones, the oxygen atom is not found in the same plane with the sulfur atom and the two other groups linked to it. This fact in itself allows to explain the resolubility of asymmetrically substituted sulfoxides in optically active forms[10] by attributing to the molecules the configuration of a trilateral pyramid with the sulfur atom in any one of the vertices. However, on the basis of the octet theory, in combination with the parachor values which indicate a bond different from the one of the double covalent bond between the sulfur and oxygen atom (semipolar bond),[11] was constructed a model of an asymmetric sulfur atom, in which is located an unshared electron pair in the fourth vertex of the tetrahedron.[12]

Thus it was possible to show the parallelism, as far as their electronic configuration is concerned, between the sulfoxides and the radicals of sulfonium salts. This hypothesis, however, was not shared by everyone[7,8] and even recently uncertain and strange ideas concerning the relation between the configuration of sulfoxides and sulfones were discussed.[13]

The formation of continuous mixed crystals series of sulfoxides with sulfones seems to us an experimental support of the tetrahedral configuration of the sulfoxides in the assumption that it will be proved in the case of the sulfones.

Experimental

The phase diagrams, liquid-solid, of the binary systems were elaborated with our "thaw-melting point method."[14]

The series of the thawing points (th. p.) of the mixtures of the components progressively varied giving the **solidus** curve and the series of the melting points, the **liquidus** curve of the systems. If the contrary is not indicated, all mixtures of the components were prepared by common, complete and homogeneous melting and the solidified masses closely ground in a agate mortar. The temperatures were determined with short and standardized thermometers, accurate to ±0.1°, each covering a range of 50°. All percentages indicated are by weight.

Experiments 4, 7b/11 and 12 are credited to Mr. Hercules Vieira de Campos.

Binary Systems

1. **bis-*n*-Butyl Sulfoxide and Sulfone.**—The sulfoxide was prepared by oxidation of the sulfide (b. p. 188–189°) with nitric acid (density 1.3) at 0°. By recrystallization from petroleum ether needles with m. p. 32.6° were obtained; reported m. p. 32°.[15,16]

The sulfone was obtained by oxidation, at room temperature, of the sulfide dissolved in glacial acetic acid, with a solution of potassium permanganate in bi-normal sulfuric acid. The raw product (94%, m. p. 39–42°) gave after repeated recrystallizations from a mixture of methanol and water, large brilliant plates with m. p. 46.0°; reported m. p. 43°,[16] 43.5°,[15,17] 44°.[18] Continuous series of mixed crystals of type I.

TABLE I

Sulfoxide, %	Th. p., °C.	M. p., °C.	Sulfoxide, %	Th. p., °C.	M. p., °C.
0.0	45.2	46.0	58.2	33.0	36.3
10.2	39.2	42.9	70.8	32.6	35.1
19.8	37.5	40.4	88.8	32.0	34.0
32.2	35.7	39.1	95.6	32.0	33.2
45.2	34.3	37.4	100.0	31.8	32.6

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2. **bis-*n*-Hexadecyl Sulfoxide and Sulfone.**—The sulfoxide was prepared by oxidation of dicetyl sulfide [recrystallized from a mixture of carbon disulfide and chloroform (1:2), m. p. 61.3°[19]] with nitric acid (density 1.3) at 25°. The reaction was completed by heating for a short time to 60°. The raw product (77%, m. p. *ca.* 90°) was dissolved in hot dioxane, treated with charcoal and the brilliant plates separated from the cooled solution were repeatedly recrystallized from carbon tetrachloride: m. p. 98.8°; reported m. p. 97–98°.[20]

The sulfone was prepared by oxidation of the sulfide dissolved in glacial acetic acid, with 30% hydrogen peroxide at 90°. The yellowish raw product (98%, th. p. 94°, m. p. 96°) was treated with charcoal in hot dioxane, and the colorless plates obtained from this solution were many times recrystallized from chloroform; m. p. 103.4°, reported m. p. 100–100.5°.[20] Continuous mixed crystal series of type III; minimum at 60% sulfoxide and 95°.

TABLE II

Sulf-oxide, %	Th. p., °C.	M. p., °C.	Sulf-oxide, %	Th. p., °C.	M. p., °C.
0.0	102.3	103.4	69.7	94.1	96.0
5.1	100.7	102.8	74.1	94.3	96.2
14.9	98.8	101.8	88.0	95.1	97.2
31.4	96.3	99.8	95.3	96.2	98.1
46.1	95.0	97.0	100.0	97.9	98.9
59.8	93.9	95.5			

3. **bis-β-Hydroxyethyl Sulfoxide and Sulfone.**—The sulfoxide was prepared by oxidation of thiodiglycol dissolved in acetone, with 30% hydrogen peroxide at −20°, and the reaction completed at 0°. The raw product (70%, th. p. 108°, m. p. 110°) separated in form of needles from the solution concentrated under reduced pressure, was repeatedly recrystallized from a mixture of ethanol and chloroform (1:9). White needles were obtained with m. p. 112.3°; reported m. p. 110–111°,[21] 111°,[22] 111–112°,[23] 112–113° (cor.).[24]

The sulfone was obtained by the action of 30% hydrogen peroxide on the sulfide in acetone at 25°, and the reaction completed by heating for a short time. The raw product (90%, m. p. 56–57°) was repeatedly recrystallized from a mixture of ethanol and chloroform (1:9), giving small, brilliant needles of silky aspect, with m. p. 58.1°; reported m. p. 57–58°.[23] Continuous series of mixed crystals of type I.

TABLE III

Sulf-oxide, %	Th. p., °C.	M. p., °C.	Sulf-oxide %	Th. p., °C.	M. p., °C.
0.0	57.3	58.1	61.3	81.8	96.1
5.1	58.1	62.1	78.6	93.5	104.2
19.7	63.4	72.3	94.6	106.0	111.0
41.9	72.0	85.9	100.0	111.0	112.3

4. **Di-benzyl Sulfoxide and Sulfone.**—The compounds were prepared by oxidation of the sulfide with 30% hydrogen peroxide in glacial acetic acid, the sulfoxide at 10° and the sulfone at 95°, and recrystallized from ethanol. The melting points correspond to the numerous indications of the literature which give to the sulfoxide from 130 to 135° and to the sulfone from 149 to 153°. Continuous series of mixed crystals of type I.

TABLE IV

Sulf-oxide, %	Th. p., °C.	M. p., °C.	Sulf-oxide, %	Th. p., °C.	M. p., °C.
0.0	151.0	151.7	49.7	137.7	139.8
6.3	148.5	149.8	69.4	135.3	136.9
10.5	146.8	148.1	85.7	134.4	135.4
28.1	141.5	143.9	94.0	134.0	135.0
38.4	139.1	141.5	100.0	134.0	134.8

5. **bis-*p*-Nitrobenzyl Sulfoxide and Sulfone.**—The sulfoxide: To a solution of 3 g. of the sulfide (m. p. 158.2–159.0° from benzene; reported 158–159°,[25] 159°[25a]) in 120 cc. of 80% acetic acid heated to 60° was added under stirring a saturated aqueous solution of 0.75 g. of chromium trioxide and this heated to 60–70° during twenty minutes. The solution after cooling was poured into water and the sulfoxide (88%) was separated having a m. p. *ca.* 200°. Recrystallized from ethanol, small needles, lightly yellowish were obtained with m. p. 212.0°. Fichter and Wenk[26] give the m. p. 208–210° for the sulfoxide prepared by anodic oxidation of the sulfide. Heated slightly over the melting point, the substance decomposes with a pronounced odor of sulfur dioxide.

bis-*p*-Nitrobenzyl sulfone was obtained by oxidation of the sulfide with 30% hydrogen peroxide in glacial acetic acid at 90°. The raw product (95%, m. p. *ca.* 256°) was purified by repeated recrystallizations from 80% acetic acid. Small needles, slightly yellowish were obtained with m. p. 260.5°; reported m. p. 260°.[27]

Because of the thermal decomposition of the sulfoxide, the mixtures were prepared by close grinding of the components in an agate mortar. In order to have a control, the mixture with 54.6% of sulfoxide was heated to incipient melting and after that closely ground. In the determinations of all the melting points of the system no decomposition was ever shown. Continuous series of mixed crystals of type I.

TABLE V

Sulf-oxide, %	Th. p., °C.	M. p., °C.	Sulf-oxide, %	Th. p., °C.	M. p., °C.
0.0	259.4	260.5	54.6	221.3	224.6
6.9	245.7	252.0	61.0	218.8	222.1
14.3	239.1	245.0	74.5	215.1	218.0
28.3	232.0	235.3	92.5	211.6	213.8
45.2	225.1	228.2	100.0	211.0	212.0

6. **bis-2-Phenylethyl Sulfoxide and Sulfone.**—bis-2-Phenylethyl sulfide was prepared by adding 40 g. of 2-phenylethyl chloride (b. p. 187–188° (698 mm.), reported b. p. 194–195° (705 mm.)[28]) was added at 30° under stirring to a solution of potassium sulfide, prepared from 18 g. of potassium sulfide, in 400 cc. of ethanol. It was heated for one hour under reflux. Then it was extracted with ether, the extracts washed with water and dried with sodium sulfate. After separation of the ether by distillation it remained a yellowish oil with penetrating odor, which did not crystallize at −12°. Distillation in vacuum gave a colorless liquid with slight odor which distilled under 2 mm. at 187° but did not crystallize. Transformed into the addition compound with mercury chloride (colorless needles of m. p. 101.0°) and this decomposed by boiling with water, an oil was obtained which, kept for two days at 0°, solidified and gave, after repeated recrystallizations from 80% ethanol, small colorless and odorless needles with m. p. 92.2°; reported m. p. 92°.[28]

The sulfoxide was prepared by adding to a solution of 7

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[19] Reported m. p. 57.5°, Friedau, *Ann.*, **83**, 16 (1862); 57–58° B. A. Hunter, *C. A.*, **36**, 4474 (1942).

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[25] W. J. Horn, THIS JOURNAL, **43**, 2610 (1921).

[25a] O. Fischer, *Ber.*, **28**, 1338 (1895).

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g. of the sulfide in 100 cc. of ether, cooled at −20°, under energetic stirring, and in small portions, a solution of 5.5 g. of monoperphthalic acid in 300 cc. of ether. The mixture was kept at 0° for twenty-four hours. After separation of the ether by distillation, the residue was extracted with 100 cc. of hot chloroform. The phthalic acid was filtered, and the chloroform separated by distillation. The ramanescent oil crystallized at 0° after two hours. The raw product (7.4 g., m. p. 56–60°) repeatedly recrystallized from petroleum ether (50–60°) gave lamellar plates with m. p. 69.0°. The substance was soluble at room temperature in the majority of the ordinary solvents, slightly soluble in petroleum ether and insoluble in water.

Anal.[29] Calcd. for $C_{16}H_{18}OS$: (0.1520 g. used 0.1073 g. of monoperphthalic acid) 0.1071 g.

The same sulfoxide was obtained by oxidation of the crystallized sulfide with chromium trioxide. To a solution of 1.0 g. of the sulfide in 5 cc. of 80% acetic acid heated to 60° was added in small portions under vigorous stirring 0.2 g. of chromium trioxide in 2 cc. of water. The mixture was heated for twenty minutes at 60–70° and after cooling poured into iced water; kept for two days at 0° the resultant oil crystallized completely. The raw product (99%, m. p. 60–62°) repeatedly recrystallized from petroleum ether (50–60°), gave brilliant colorless plates with m. p. 69.1°. Mixed melting point of equal parts with the previous product gave m. p. 68.1–69.1°.

The sulfone was prepared by oxidation of the sulfide, dissolved in glacial acetic acid, with 30% hydrogen peroxide at 90°. The raw product (97%, m. p. 92–94°) repeatedly recrystallized from ethanol, presented brilliant colorless plates. It was soluble in chloroform, acetone, acetic acid, benzene, all at room temperature, and in hot methanol and ethanol; slightly soluble in ether, insoluble in water; m. p. 100.6°, reported m. p. 101°.[28] Continuous mixed crystal series of type III; minimum at 60.5° and 68% sulfoxide.

TABLE VI

Sulf-oxide, %	Th. p., °C.	M. p., °C.	Sulf-oxide, %	Th. p., °C.	M. p., °C.
0.0	99.8	100.6	71.1	60.0	61.4
4.6	95.0	98.7	75.6	60.1	62.5
14.7	85.2	94.1	84.9	62.4	65.1
28.9	74.1	87.0	89.5	63.4	66.1
45.1	65.0	75.6	94.8	65.6	67.7
57.6	61.1	66.8	100.0	68.3	69.0
64.6	59.9	61.9			

7. Diphenyl Sulfoxide and Sulfone: (a) With β-Form of Diphenyl Sulfone.—The sulfoxide was prepared by oxidation of the sulfide with chromium trioxide in 80% acetic acid at 70°. The raw product (83%, m. p. *ca.* 66°) was recrystallized from petroleum ether (50–60°) and then from ethanol. It formed small colorless plates with m. p. 69.6–70.4° corresponding to the numerous indications of the literature which give melting points from 67–69° to 71–72°. The β-form of the sulfone, prepared by oxidation of the sulfide with 30% hydrogen peroxide at 90°, was obtained according to the indications of Mikeska, Farinacci and Bogert.[30]

TABLE VIIa

Sulf-oxide, %	Th. p., °C.	M. p., °C.	Sulf-oxide, %	Th. p., °C.	M. p., °C.
0.0	127.0	127.8	78.9	63.1	70.8
14.2	106.9	121.4	84.1	62.8	66.0
29.6	90.5	113.5	89.0	63.0	65.5
39.7	82.4	107.2	93.1	63.9	67.1
50.0	76.2	100.0	95.6	65.1	69.0
65.3	68.2	87.1	100.0	69.6	70.4
74.6	64.6	76.8			

The mixtures of the substances were prepared by close grinding of the components in an agate mortar. Continuous series of mixed crystals of type III; minimum: 63.5° and 86% sulfoxide.

(b) With α-Form of Diphenyl Sulfone.—Both compounds were prepared by oxidation of the sulfide with 30% hydrogen peroxide in glacial acetic acid—the sulfoxide at room temperature and the sulfone at 90°—and recrystallized from ethanol. Continuous series of mixed crystals of type III with minimum at 62.5°, and 86% sulfoxide.

TABLE VIIb

Sulf-oxide, %	Th. p., °C.	M. p., °C.	Sulf-oxide, %	Th. p., °C.	M. p., °C.
0.0	124.4	125.0	83.1	62.1	67.0
5.8	115.0	124.1	88.2	61.7	65.4
12.3	105.0	121.0	90.2	62.4	66.1
30.0	85.0	112.0	93.7	63.4	69.0
55.1	68.9	95.0	95.6	65.0	69.8
69.5	64.1	83.6	100.0	69.7	70.5

The same result was obtained by close grinding of the components in an agate mortar.

8. bis-*p*-Tolyl Sulfoxide and Sulfone.—The sulfoxide was prepared according to the indication of Parker,[31] by the reaction of toluene with thionyl chloride in the presence of aluminum chloride. The raw product, after treating with charcoal in petroleum ether, was repeatedly recrystallized from petroleum ether (50–60°) and gave colorless needles with m. p. 93.0°. Reported melting point was 92°.[31] It was easily soluble in the ordinary solvents, slightly soluble in petroleum ether, insoluble in water.

The sulfone was prepared by oxidation of the sulfoxide with 30% hydrogen peroxide in glacial acetic acid at 90°. The raw product (99%, m. p. *ca.* 150°) was many times recrystallized from ethanol, giving brilliant colorless plates with m. p. 158.1°. Reported melting points are 155–156°,[32] 156–157°,[33] 156.0–158.0°,[34] 157°,[35] 157–158°[36,37] and 158°.[31,38,39] Continuous mixed crystal series of type III; minimum at 89.0° and 88% sulfoxide.

TABLE VIII

Sulf-oxide, %	Th. p., °C.	M. p., °C.	Sulf-oxide, %	Th. p., °C.	M. p., °C.
0.0	157.3	158.1	71.7	95.2	105.2
10.8	145.9	152.8	75.1	92.6	100.1
25.6	132.1	144.5	81.9	88.8	91.0
36.5	123.1	137.7	87.7	88.3	89.6
45.7	115.6	131.0	91.5	88.8	90.5
58.4	105.0	120.8	95.0	89.7	91.8
65.0	100.2	113.5	100.0	92.1	93.0

9. bis-*p*-Bromophenyl Sulfoxide and Sulfone.—The sulfoxide was obtained by oxidation of the sulfide obtained by bromination of diphenyl sulfide in glacial acetic acid. After recrystallizations from ethanol, the substance

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(29) Method of H. Böhme, *Ber.*, **70**, 379 (1937).

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(39) H. Meyer and R. Grim, *Ann.*, **433**, 327 (1923).

had a m. p. 112.4°.[40] To a solution of 3 g. of sulfide in 50 cc. of 80% acetic acid at 60° was added a saturated aqueous solution of 0.64 g. of chromium trioxide. It was heated for twenty minutes, then poured into iced water. The raw product (90%, m. p. 148–150°) was separated and purified by repeated recrystallizations from petroleum ether (70–80°), giving small colorless crystals with m. p. 153.4°. Reported melting points were 152°,[41] 153°.[42]

The sulfone was prepared by oxidation of the sulfide with 30% hydrogen peroxide in glacial acetic acid at 90°. The raw product (99%, m. p. *ca.* 170°) was repeatedly recrystallized from ethanol, giving small colorless needles with m. p. 172.1°. Reported melting points were 168°,[43,44] 170°,[42] 170.0–171.0°[45] and 172°.[46,47,48,49] Continuous mixed crystals series of type III; minimum at 61% sulfoxide and 131.5°.

TABLE IX

Sulfoxide, %	Th. p., °C.	M. p., °C.	Sulfoxide, %	Th. p., °C.	M. p., °C.
0.0	171.1	172.1	53.3	131.5	134.9
9.9	158.8	167.1	59.6	130.6	133.0
18.6	149.8	161.3	64.8	131.7	134.1
25.0	144.2	155.5	69.4	132.3	135.4
34.7	138.5	146.7	79.7	136.6	143.6
41.5	134.4	141.6	88.1	141.5	149.0
48.8	132.3	137.8	100.0	152.4	153.4

10. **bis-*p*-Methoxyphenyl Sulfoxide and Sulfone.**—The sulfoxide was obtained by oxidation of the sulfide with chromium trioxide. The sulfide was prepared from anisole and thionyl chloride in contact with aluminum chloride. It distilled at 212–213° (10 mm.) and after many recrystallizations from ethanol gave small colorless needles with m. p. 46.0°. Reported melting points were 43–44°,[50] 45–46°[51] and 46°.[52] To a solution of 6 g. of the sulfide in 50 cc. of 80% acetic acid at 60° was added a saturated aqueous solution of 1.8 g. of chromium trioxide. The mixture was heated for twenty minutes at 60–70°, then poured after cooling into iced water. The raw product (81%, m. p. *ca.* 90°) was repeatedly recrystallized from petroleum ether (50–60°) and dried at 75° and 2 mm. Minute brilliant colorless crystals with m. p. 95.8° were obtained. Reported melting points were 93–94°,[53] and 96°.[52,54,55,56]

The sulfone was obtained by oxidation of the sulfide with 30% hydrogen peroxide in glacial acetic acid at 90°. The raw product (99%, m. p. 124–126°) was treated with charcoal in ethanol and many times recrystallized from ethanol. Small flat needles with m. p. 130.2° were obtained. Reported melting points were 120°,[52] 129°,[53,57] 129–130°,[58] 130°[59] and 130.4°.[50] Continuous mixed crystals series were of type III; minimum at 77% sulfoxide and 87.3°.

TABLE X

Sulfoxide, %	Th. p., °C.	M. p., °C.	Sulfoxide, %	Th. p., °C.	M. p., °C.
0.0	129.6	130.2	72.1	88.2	90.4
8.9	122.7	128.0	76.4	87.2	87.9
26.3	110.1	120.1	82.1	87.9	89.4
33.6	105.5	116.0	85.8	88.6	91.1
50.3	95.6	105.8	90.1	89.5	92.7
61.2	91.2	97.9	100.0	94.8	95.8
64.0	90.1	95.3			

11. **Dibenzyl Sulfide and Sulfoxide.**—Simple eutectic system without formation of mixed crystals; eutectic point at 48° and *ca.* 3% sulfoxide.

TABLE XI

Sulfoxide, %	Th. p., °C.	M. p., °C.	Sulfoxide, %	Th. p., °C.	M. p., °C.
0.0	48.5	49.1	49.5	48.0	111.9
3.8	47.9	49.2	59.5	48.1	117.8
8.9	48.0	66.9	77.5	47.9	126.2
16.9	47.8	81.7	95.0	48.0	133.0
32.2	48.1	98.8	100.0	134.0	134.8

12. **Dibenzyl Sulfide and Sulfone.**—Simple eutectic system without mixed crystals; eutectic point at 48.3° and *ca.* 1% sulfone.

TABLE XII

Sulfone, %	Th. p., °C.	M. p., °C.	Sulfone, %	Th. p., °C.	M. p., °C.
0.0	48.5	49.1	48.7	48.4	130.0
3.3	48.3	66.1	65.6	48.4	139.0
5.1	48.3	74.0	81.4	48.3	145.8
12.7	48.4	92.3	93.2	48.3	149.9
29.1	48.3	113.6	100.0	151.0	151.7

13. **bis-*p*-Bromophenyl Sulfide and Sulfoxide.**—Simple eutectic system without mixed crystals; eutectic point at 17% sulfoxide and 97°.

TABLE XIII

Sulfoxide, %	Th. p., °C.	M. p., °C.	Sulfoxide, %	Th. p., °C.	M. p., °C.
0.0	111.8	112.4	41.8	97.0	122.2
4.6	97.0	110.5	51.9	97.1	129.5
9.5	97.0	107.5	65.3	97.1	138.1
13.0	97.0	104.0	75.5	97.1	144.2
25.9	97.0	108.6	90.2	97.2	150.7
			100.0	152.4	153.4

14. **bis-*p*-Bromophenyl Sulfide and Sulfone.**—Simple eutectic system without mixed crystals; eutectic point at 16% sulfone and 98.4°.

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(59) J. Annaheim, *Ann.*, **172**, 46 (1874).

TABLE XIV

Sulfone %	Th. p., °C.	M. p., °C.	Sulfone, %	Th. p., °C.	M. p., °C.
0.0	111.8	112.4	49.8	98.4	135.0
5.0	98.4	109.1	66.0	98.4	149.8
13.7	98.4	101.4	74.4	98.4	156.2
23.9	98.6	108.3	88.7	98.5	166.3
30.2	98.5	116.1	100.0	171.1	172.1
40.9	98.5	127.1			

Summary

1. The determination of solid–liquid phase diagrams in ten pairs of symmetrically substituted sulfoxides and sulfones showed the formation of continuous series of mixed crystals.

2. Sulfides do not form mixed crystals with sulfoxides or sulfones in the wide ranges studied.

3. These results prove that sulfoxides and sulfones have the same steric configuration. Attributing to the sulfones a tetrahedral configuration the same applies also to the sulfoxides. This confirms the most accepted hypothesis concerning the electronic structure of the sulfoxides.

4. This study is being continued specially in regard to the asymmetrically substituted compounds.

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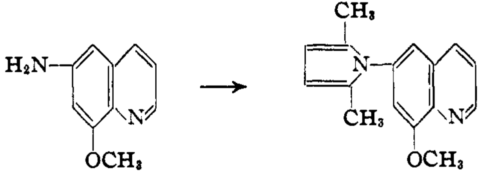
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE[1]]

Some Isomeric (Methoxy)-(2,5-dimethylpyrryl-1)-quinolines

BY HENRY GILMAN AND LAWRENCE FULLHART

In a study[1] of 2,5-dimethylpyrryl-1 derivatives in experimental avian malaria, it was shown that 6-methoxy-8-(2,5-dimethylpyrryl-1)-quinoline has significant activity. This suggested an examination of some isomers. The following five isomers have been prepared and are now described: 6-methoxy-5-(2,5-dimethylpyrryl-1), 8-methoxy-5-(2,5-dimethylpyrryl-1), 2-methoxy-6-(2,5-dimethylpyrryl-1), 7-methoxy-8-(2,5-dimethylpyrryl-1) and 8-methoxy-6-(2,5-dimethylpyrryl-1). The final step in the synthesis of these compounds was a condensation of a methoxy-amino quinoline with acetonylacetone, and this reaction is represented by the following preparation of 8-methoxy-6-(2,5-dimethylpyrryl-1)-quinoline, an isomer in which the methoxy and basic groups have been transposed with respect to the active type already described.[1,2]

$H_3COCH_2CH_2COCH_3$ +



Of the five isomers prepared, the only one which showed activity was 8-methoxy-6-(2,5-dimethylpyrryl-1)-quinoline. However, the activity of this compound in experimental avian malaria was appreciably less than that of 6-methoxy-8-(2,5-dimethylpyrryl-1)-quinoline.

Experimental

Synthesis of (Methoxy)-(2,5-dimethylpyrryl-1)-quinolines.—The pyrryl-quinolines were formed, in essential accordance with the general procedure of Hazelwood, Hughes and Lions,[3] by condensing the amino-quinoline with acetonylacetone.

As a rule, a mixture of the aminomethoxyquinoline and the acetonylacetone in 10 cc. of 95% ethanol and 1 cc. of glacial acetic acid was refluxed for three hours. The solution was then poured upon crushed ice, and the solid which precipitated was crystallized from an appropriate solvent. In the condensation of 6-amino-8-methoxyquinoline with acetonylacetone, two drops of 1:1 hydrochloric acid was used in place of the usual 1 cc. of glacial acetic acid. In the preparation of 7-methoxy-8-(2,5-dimethylpyrryl-1)-quinoline, the solution was allowed to stand overnight during which time the compound crystallized out. Table I contains the data on these preparations. Methanol was the solvent.

TABLE I

(METHOXY)-(2,5-DIMETHYLPYRRYL-1)-QUINOLINES

Amino-methoxy-quinoline	Mole × 100	$(CH_3COCH_2—)_2$ mole × 100	Product Yield, %	Product M. p., °C.	N Anal, % Found[a]
5-NH_2-6-CH_3O	1.72	2.62	70	125–127	10.93
5-NH_2-8-CH_3O	0.57	1.75	80	155–156	11.14
6-NH_2-2-CH_3O	2.8	4.39	85	88–89	10.96
6-NH_2-8-CH_3O	1.7	5.26	57.5	161–164	11.44
8-NH_2-7-CH_3O[b]	2.87	5.0	96	141–142	11.21

[a] Calcd., N, 11.11.

[b] Ethyl alcohol was the solvent.

Nitro- and Aminoquinolines.—We used concentrated nitric acid in the preparation of 5-nitro-6-methoxyquinoline.[4] To 15.9 g. (0.1 mole) of 6-methoxyquinoline cooled to 0° was added slowly with stirring 50 g. of concentrated sulfuric acid. Then to the solution of the sulfate was added dropwise 50 g. of concd. nitric acid, keeping the solution at 0°. The temperature was allowed to rise to that of the room and then to 40° where it was held for ten hours. After pouring the mixture upon crushed ice, neutralizing with 30% sodium hydroxide, and crystallizing from ethanol there was obtained 19 g. (91%) of compound melting at 104–105°. The nitro compound was reduced to the corresponding amine by the method of Jacobs and Heidelberger.[4b]

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[1] Gilman, Stuckwisch and Nobis, THIS JOURNAL, **68**, 326 (1946).

[2] See also, Gilman, Tolman, Yeoman, Woods, Shirley and Avakian, *ibid.*, **68**, 426 (1946), for some types containing the 2,5-dimethylpyrryl and the trifluoromethyl groups.

[3] Hazelwood, Hughes and Lions, *J. Proc. Roy. Soc., N. S. Wales*, **71**, 92 (1937).

[4] (a) Decker and Engler, *Ber.*, **42**, 1739 (1909); (b) Jacobs and Heidelberger, THIS JOURNAL, **42**, 2285 (1920).