

2-Dibenzofuransulfonamides*

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The synthesis of 2-dibenzofuransulfonamide and of a number of its N-substituted derivatives is reported. These substances are readily accessible from dibenzofuran.

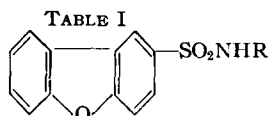


EXPERIMENTAL

ALTHOUGH 2-dibenzofuransulfonic acid is readily prepared by sulfonation of dibenzofuran (1, 2), no 2-dibenzofuransulfonamides are known. The synthesis of 3-dibenzofuransulfonamide has, however, been reported (3). Since polycyclic sulfonamides may be pharmaceutically interesting, the synthesis of several representative 2-dibenzofuransulfonamides (listed in Table I) has now been carried out by permitting ammonia or the appropriate amine to react with 2-dibenzofuransulfonyl chloride. The latter, in turn, was conveniently obtained by the rapid interaction of free 2-dibenzofuransulfonic acid with phosphorus pentachloride in the presence of phosphorus oxychloride. A previous preparation of 2-dibenzofuransulfonyl chloride involved treatment of sodium 2-dibenzofuransulfonate with phosphorus oxychloride at 165–180° for a period of six hours (2). The direct chlorosulfonation of dibenzofuran to 2-dibenzofuransulfonyl chloride is largely vitiated by the ease with which dibenzofuran is disulfonated when allowed to react with a twofold molar quantity of chlorosulfonic acid. The introduction of a chlorosulfonyl group generally requires at least two moles of chlorosulfonic acid per mole of aromatic reactant.

2-Dibenzofuransulfonyl Chloride.—Dibenzofuran was converted to 2-dibenzofuransulfonic acid by means of concentrated sulfuric acid (1). When a mixture consisting of 20.0 Gm. of the anhydrous sulfonic acid, 32.5 Gm. of phosphorus pentachloride, and 45 cc. of phosphorus oxychloride was warmed, a vigorous reaction occurred with evolution of hydrogen chloride. The reaction mixture was refluxed for a few minutes, ice-cooled, and poured on 700 Gm. of ice. The lower layer of phosphorus oxychloride, in which the sulfonyl chloride was dissolved, was attacked only very slowly by the ice water on stirring. However, when the interface was left undisturbed for awhile so that the heat evolved by the slow hydrolysis of phosphorus oxychloride was permitted to produce a local temperature rise at the interface, then the hydrolysis quite suddenly became rapid and much heat was generated. At the first sign of this rapid hydrolysis the mixture was vigorously stirred and more ice was added if necessary. The 2-dibenzofuransulfonyl chloride precipitated as a white solid; it weighed 18.3 Gm. (85% crude yield) after being dried *in vacuo* and was used without purification for the preparation of the sulfonamides.

2-Dibenzofuransulfonamides.—The sulfonamides with $R = \text{H}$, CH_3 , and C_2H_5 resulted from the reaction of 2-dibenzofuransulfonyl chloride with excess quantities of aqueous 33% ammonia, 25% methylamine, and 33% ethylamine. The sulfonamides were filtered at 60–70° to avoid possible contamination by ammonium or amine 2-dibenzo-



R	Formula	Analysis, % ^a								M. P. °C. d.
		Carbon		Hydrogen		Nitrogen ^b		Sulfur ^c		
		Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	
H	C ₁₂ H ₉ NO ₃ S	58.29	58.41	3.67	3.41	5.67	5.50	12.97	13.21	236-7
CH ₃	C ₁₃ H ₁₁ NO ₃ S	59.75	59.98	4.25	4.20	5.36	5.48	12.27	12.00	133
C ₂ H ₅	C ₁₄ H ₁₃ NO ₃ S	61.07	61.21	4.76	4.55	5.09	5.10	11.64	11.93	148.5
C ₆ H ₅	C ₁₈ H ₁₃ NO ₃ S	66.86	66.79	4.05	4.07	4.33	4.51	9.91	9.95	180.5
2-pyridyl	C ₁₇ H ₁₂ N ₂ O ₃ S	62.95	63.00	3.73	3.86	8.64	8.57	9.88	9.55	242-3

^a Performed by W. Manser, Zurich, Switzerland.

^b By the micro-Dumas method.

^c By the method of W. Zimmermann, *cf.* Grant, J., "Quantitative Organic Microanalysis Based on the Methods of F. Pregl," 5th English Edition, J. & A. Churchill Ltd., London, 1951, pp. 132–137.

^d Uncorrected.

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furansulfonates, which are of low water solubility (4). The yields were almost quantitative. For the recrystallization 75% ethanol was used when R was H, 60% ethanol when R was CH_3 or C_2H_5 . 2-Dibenzofuransulfonanilide was obtained by adding the sulfonyl chloride to an excess of aniline and

briefly heating to 100°. Dilute hydrochloric acid was then added and the sulfonamide was filtered (yield 93%). It was recrystallized from 70% ethanol. N-(2'-pyridyl)-2-dibenzofuransulfonamide was formed by the reaction of 2-dibenzofuran-sulfonyl chloride with 2-aminopyridine in pyridine solution. The product precipitated on dilution of the reaction mixture with water and was recrystallized from 75% ethanol.

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The Liquid-Liquid Countercurrent Separation of a Menthol-Menthyl Acetate Mixture*

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AS A PRELUDE TO the use of a continuous multistage liquid-liquid countercurrent extractor for fractionation of volatile oils, it seemed desirable to employ a simple funnel assembly in making initial investigations on the applicability of the general countercurrent distribution method to these systems. The results of such a study, as applied to separation of a mixture of menthol and menthyl acetate, are presented in this paper.

Up to the present time, studies on the separation, isolation, and purification of volatile oil components have utilized mainly the principles of fractional distillation and crystallization. These methods have serious limitations particularly when the boiling points of individual components are very close, when the compounds are thermolabile, or when the compounds are liquid at room temperature and not readily amenable to purification by crystallization. Countercurrent distribution is free of these limitations since separation of compounds by this technique requires only a rational choice of immiscible solvents so that the partition coefficients of the respective compounds are reasonably different.

The theory and application of this type of separation are well known and are described in a number of conveniently accessible sources (1, 2).

By a derivation similar to that of Craig (1), an equation can be derived for calculating the fraction, $T_{n,r}$, of substance present in the r th stage for n transfers in a countercurrent distribution assembly:

$$T_{n,r} = \frac{n!}{r!(n-r)!} X^{n-r} Y^r \quad (1)$$

where,

$$X = \frac{KR}{KR + 1}$$

$$Y = \frac{1}{KR + 1}$$

and where,

K = partition coefficient, and

$R = \frac{\text{volume of upper phase}}{\text{volume of lower phase}}$

The data which follow describe the agreement between experimental results and the theoretical predictions of Eq. 1, on the system under study.

EXPERIMENTAL AND RESULTS

It can be shown that the most efficient separation of two compounds by countercurrent distribution between two immiscible liquid phases of equal volumes is effected when the K value of the one compound is equal to the reciprocal of the other (1). The composition of the methanol-water phase which would satisfy this condition when partitioned against petroleum ether (Skellysolve-A) is illustrated in the data of Fig. 1. Thus a methanol-water composition of 90.5/9.5 (v/v) was utilized for this study.

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