sultant solution was evaporated to a sirup under reduced pressure and the residual water was removed by repeated distillation with 100% ethanol under reduced pressure. The sirup was then dissolved in 40 ml. of hot methyl cellosolve (ethylene glycol monomethyl ether), filtered, nucleated and placed in an oven at 80° overnight. The crystalline material was filtered and washed with 100% ethanol; yield 6.7 g. (89%), m.p. 187–189° (cor.), $[\alpha]^{28}D$ −1.5° (initial, extrapolated) → +10.6° (final, *c* 4, water). The material was further purified by recrystallization from methyl cellosolve; yield 6.4 g. (95%), m.p. 190° (cor.), $[\alpha]^{25}D$ −3.0° (initial, extrapolated) → +10.5° (final, *c* 4, water). These constants were unchanged on further crystallization from this solvent or from ethanol effected by solution in minimal water and addition of warm 100% ethanol followed by crystallization at 60° (an ethyl alcoholate was not formed). The constants were likewise unaltered on standing under 95% ethanol (twice changed) for 1 week.

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Dibenzofuran-2-sulfonic and 3-Nitro-8-sulfonic Acids as Reagents for Amines and Amino Acids[1]

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Dibenzofuran-2-sulfonic acid, recently prepared in this Laboratory[2] is a strong acid and reacts with most amines to give stable salts. Simple salt formation from aqueous solution is much more convenient for preparation of derivatives than reactions commonly employed to identify amines such as acylation, quaternary base formation, etc. We have found that dibenzofuran-2-sulfonic acid (I) precipitates a large variety of amines and amino acids and that the salts formed are crystallizable solids having good melting points. The saturated solution of I in water is 4 *N* at 111° (99 g. of acid per 35 g. of water) and 0.34 *N* at 25°.

Since 3-nitrodibenzofuran has long been known,[3,4] it was expected that the sulfonic acid obtained from it would be an interesting and useful variant of compound I, and might have value in identifying amino compounds for which I was not suited. However, our expectations were not confirmed. The new compound, presumably the 3-nitro-8-sulfonic acid of dibenzofuran (compound II), was successfully prepared[5] but with difficulty, and it has none of the favorable crystallization characteristics of compound I. The free acid, II, appears to be very soluble in water from which it cannot be separated by usual crystallization methods. Crystallization from acetic acid however was satisfactory and gave the desired product in suitable purity. Despite its water solubility, II precipitates rapidly by salt formation with various amines, particularly aromatics. However, many of these only decomposed at high temperatures without showing characteristic melting points, hence have much less promise as derivatives than the salts from I.

The amino acid derivatives of dibenzofuran-2-sulfonic acid had been previously prepared and reported by Wendland and Smith.[6] We wish to add to those results the present observation that the neutral equivalents determined in alcoholic solution by the Foreman method[7] are highly reliable, with variations mostly ±1 from calculated and at worst only ±3. Thus this analytical procedure is most valuable in amino acid identifications. The salt of a monoamino monocarboxy acid titrates as a dibasic acid, a diamine monocarboxy acid as a tribasic acid, etc. The same titration can probably be applied also to the simple amine salts.

Experimental Part

Amino Salts of Dibenzofuran-2-sulfonic Acid.—The acid was prepared according to the method described in (2). The purified amine (1 to 2 g.) was mixed with sufficient water to effect solution, or for those amines of very slight solubility, an equivalent of hydrochloric acid was added. To the resulting solution was added the equivalent amount of a saturated solution of the sulfonic acid (about 0.34 *N* at room temp.). Most of the salts precipitated shortly at room temperature; after filtration they were recrystallized from boiling water, or from aqueous alcohol if the water solubility was very small.

The solubility of the salts was determined by preparing a measured volume of a saturated water solution, chilling at 0° overnight, and sampling. The filtrates (or supernatant fluid) were evaporated in tared bottles over sulfuric acid; from the weights of the residues the water solubilities were calculated. The results are assembled in Table I.

Amino compounds which failed to give the desired sulfonate salts were *p*-bromoaniline, *o*-nitroaniline, 2,4-dinitroaniline, 2,4-dinitrophenylhydrazine, 1-amino-2-naphthol-4-sulfonic acid, diphenylamine and sulfanilic acid. This group of compounds is of extremely feeble basicity, and at the same time are quite insoluble in water and in dilute hydrochloric acid.

Another group of amines, most of which are soluble in water, failed to give precipitates when treated with the aqueous saturated sulfonic acid. This group includes: 2-amino-1-butanol, 2-amino-2-methyl-1,3-propanediol, bis-(hydroxyethyl)-*n*-butylamine, hydroxyethylbutylamine, hydroxyethyldi-*n*-butylamine, bis-(hydroxyethyl)-phenylamine, hydroxylamine (note the various hydroxylated amines) and in addition methyl and ethyl amines, dimethyl, diethyl and diisopropyl amines, morpholine, nicotine, nicotinic acid, pyridine and α- and β-picolines. Concentrated solutions of methyl- and ethylamines added to saturated solutions of the sulfonic acid gave the result of precipitation at −5°, but the precipitates proved to be largely the free sulfonic acid. In another trial the anhydrous vapors of ethyl- and methylamines were distilled directly into the saturated acid solution, but no precipitates were formed at room temperature.

It appears that the low molecular weight aliphatic amines form extremely soluble salts with dibenzofuran sulfonic acid which cannot be crystallized—the result being the hydrolysis of the salt to a sufficient degree to precipitate the acid component. This behavior contrasts sharply with that of ammonia which yields a quite insoluble salt, although it precipitates slowly. (It should be noted here that Mitchell and Bryant[8] encountered similar difficulties in preparing picrates of the lower aliphatic amines, several of which had to be added to a solution of picric acid in anhydrous ether before the salt could be recovered.

Notable is the easy precipitation of urea from dilute solutions. Of the compounds related to urea, thiourea precipitated very slowly, and was contaminated by I from which it

(1) Taken in part from the M.S. dissertations of Rode (1948) and Meintzer (1951).

(2) R. Wendland, C. H. Smith and R. Muraca, THIS JOURNAL, **71**, 1593 (1949).

(3) W. Borsche and R. Bothe, *Ber.*, **41**, 1941 (1908).

(4) H. Gilman, W. Bywater and P. Parker, THIS JOURNAL, **57**, 885 (1935).

(5) 3-Nitro-8-dibenzofuransulfonic acid had been formed by W. Borsche and B. Schacke, *Ber.*, **56**, 2501 (1923). but was isolated by them only as the sodium or potassium salt which is much less soluble.

(6) R. T. Wendland and C. H. Smith, *Proc. No. Dak. Acad. Science*, **III**, 31 (1949).

(7) F. W. Foreman, *Biochem. J.*, **14**, 451 (1920).

(8) J. Mitchell and W. M. D. Bryant, THIS JOURNAL, **65**, 123 (1943).

TABLE I

AMINE SALTS OF DIBENZOFURAN-2-SULFONIC ACID[a]

Compound	M.p., °C.	Solubility, g./100 g. H_2O	Analytical values, % Sulfur (Parr) Calcd.	Sulfur (Parr) Found	Nitrogen (Dumas) Calcd.	Nitrogen (Dumas) Found
N,N-Dimethylaniline[b]	61–62	0.52	8.70	8.67	...	...
Tri-*n*-butylamine[c]	117–118	.4	7.40	7.09	3.23	3.42
N-Ethylaniline[d]	128–129	.6	8.68	8.56	3.79	3.70
N-Methylaniline	148–149	.6	9.02	9.22	3.94	4.11
Hexamethylenetetramine (tetra)	158–159	.3	11.32	11.33	...	...
Di-*n*-butylamine	164	.24	8.49	8.17	3.71	3.81
Di-isobutylamine	168	.30	8.49	8.30	3.71	3.80
Phenylhydrazine	193–194 dec.	.1	9.00	8.80	7.86	7.69
Quinoline[d]	195–196	.2	8.50	8.53	3.71	4.01
Diphenylguanidine	195–196	.1	6.98	6.57	9.14	9.06
Urea	203 [h]dec.	1.9	10.40	10.39	9.09	8.93
m-Toluidine	205–206	0.24	9.02	9.13	3.94	3.81
n-Butylamine	207–208	.8	9.98	9.60	4.36	4.58
8-Hydroxyquinoline (yellow)	207–208	.05	8.15	8.05	3.56	3.57
o-Aminodicyclohexyl[d,e,i]	213–255	.04	7.46	7.28	3.26	3.33
Cyclohexylamine[e]	214–216	.04	9.23	9.02	4.03	3.98
o-Phenylenediamine	225 [f]dec.	.3	9.00	8.82	7.86	7.91
o-Chloroaniline[e]	228–230	.24	8.53	8.60	3.73	3.86
p-Toluidine	232–234	.2	9.02	9.01	3.94	3.53
Dicyclohexylamine[e]	239–240	.05	7.46	7.42	3.26	3.67
p-Nitroaniline	240 dec.	.1	8.30	8.11	7.25	7.00
o-Toluidine	242–243 dec.	.14	9.02	9.26	3.94	3.79
β-Naphthylamine	245–246 dec.	.04	8.19	7.78	3.58	3.67
Sulfanilamide	245–246 dec.	.1	15.25	15.17	6.66	6.69
2,4-Diaminophenol (di)	250 dec.	.16	10.33	9.99	4.51	3.92[i]
m-Nitroaniline	250 dec.	.09	8.30	8.10	7.25	6.28[i]
Aniline	258–260	.23	9.39	9.40	4.10	3.93
α-Naphthylamine	260 [g]dec.	.1	8.19	7.84	3.58	3.74
Hydrazine (di)	260 dec.	.70	12.13	11.83	5.30	5.58
m-Phenylenediamine (di)	280–290 dec.	.20	10.60	10.70	4.63	4.26
p-Aminoacetanilide	Over 290	1.1	8.04	7.95	7.04	6.97
Benzidine (di)	Over 300	0.11	9.42	9.26	4.12	4.02
p-Phenylenediamine (di)	Stable to 305	.1	10.60	10.51	4.63	4.28
Ethylenediamine (di)	Stable to 305	.11	11.52	11.45	5.03	5.16
Ammonia	Over 310 dec.	1.87	...	...	5.26	5.21
Guanidine	Over 310	0.10	...	...	13.70	13.78
Semicarbazide[k]	205–215	Very sol.	...	...	13.00	4.80 ?

[a] All the salts formed are monosulfonates, unless designated by (di), (tri), etc. Melting points were taken with an enclosed thermometer and uncorrected. [b] The compound persistently forms an oil which requires low temperature and long standing to crystallize. [c] The salt separated as an oil which later crystallized. Recrystallization was from a saturated alcohol solution at 35°. [d] Tends to form an oil which slowly crystallizes. [e] The equivalent of aqueous sulfonic acid was added with vigorous shaking to the pure amine because latter would not readily dissolve in HCl. [f] Decomposition starts at 225° but the compound melts at 252–254°. [g] Decomposition starts at 260° (appar.) but compound melts at 285°. [h] The salt appears to melt and resolidify at 203°. There is no evidence of melting or charring up to 300°. [i] These salts gave consistently low Dumas nitrogen analyses due to excessive carbonization during combustion. [j] The large melting range could not be improved by repeated crystallization from aqueous alcohol. [k] The sulfonate salt was very soluble and on chilling seemed to become contaminated by coprecipitation of dibenzofuran-2-sulfonic acid. Its analysis was consistently low for nitrogen.

could not be separated; semicarbazide appeared to precipitate as the salt (very soluble) but its analysis was consistently bad; guanidine formed an extremely insoluble salt which was very high melting.

Preparation of 3-Nitrodibenzofuran-8-sulfonic Acid and Its Salts.—Dibenzofuran, recrystallized from 95% ethanol and melting at 87°, was nitrated in acetic acid solution by addition of concentrated nitric acid, using the procedure of Gilman.[4] The yellow 3-nitrodibenzofuran melting at 181° was submitted to sulfonation by action of concentrated sulfuric acid at 100° for a 30-minute period. Results of varying the ratio of sulfuric acid to 3-nitrodibenzofuran are shown in Table II.

Experiment 4 represents the conditions originally prescribed by Borsche and Schacke.[5] Smaller amounts of sulfuric acid than specified in expt. 1 were not suitable since then some of the nitro compound failed to dissolve. The conditions in 1 were adopted for all further production of the acid.

TABLE II

SULFONATION OF 3-NITRODIBENZOFURAN AT 100° FOR 30 MINUTES

	3-Nitro cpd., g.	96% Sulfuric acid G.	Mole	Yield of acid, g.	Per cent. of theory
1	10.0 (0.047 mole)	25.0	0.24	7.5	55.3
2	10.0	50.0	0.48	5.1	38.3
3	10.0	75.0	0.72	5.0	36.2
4	10.0	100.0	0.96	4.0	29.8

As the reaction proceeds the solution becomes bright orange colored: after about 15 minutes the 8-sulfonic acid begins to precipitate. It filters readily from the acid solution, redissolves in hot water and precipitates by chilling. However, this reprecipitated product is virtually unfilter-

TABLE III

3-NITRODIBENZOFURAN-8-SULFONIC ACID AND ITS AMINE SALTS

		Free acid	Salts of the free acid: 2 Aniline	3 *p*-Toluidine	4 *p*-Bromoaniline	5 Urea
M.p., °C.		Chars 240	258–260 dec.	250 dec.	258–266 dec.	Over 300 dec.
Neut. equiv.	Calcd.	293.2				
	Found	296.3, 296, 294.2				
N, %	Calcd.	4.78				
	Found	4.80, 5.0				
S, %	Calcd.	10.93	8.30	8.01	6.89	9.07
	Found	10.72	8.25	8.04	6.82	9.18
		10.62	8.40			

TABLE IV

AMINO ACID SALTS OF 3-NITRODIBENZOFURAN-8-SULFONIC ACID

Amino acid	M.p., °C.	Sulfur, % Calcd.	Found	
1-Arginine (di)[a]	235–236	8.43	7.98	*dl*-alanine, α-aminoisobutyric acid, *dl*-lysine, *dl*-methionine, *dl*-norleucine, *dl*-tryptophan[b] and *dl*-valine formed salts which decomposed without melting in the high range of 250–300°
Creatinine	258	7.89	7.82	
1-Cysteine	219	15.47	15.60	
1-Cystine (di)	215	15.50	15.70	
1-Histidine (di)	248	8.65	8.59	
dl-Iso-leucine	246	7.55	7.21	Glycine, aspartic and glutamic acids, tyrosine, proline and hydroxyproline, threonine, asparagine and serine all failed to precipitate from solution upon addition of the nitrosulfonic acid
dl-Phenyl-alanine	247	7.00	7.01	
l-Leucine	260–262 dec.	7.55	7.58	

[a] All salts were monosulfonates except those marked (di). [b] The tryptophan salt of the acid has a brilliant yellow coloration, which may have diagnostic significance; the others were nearly white or pale yellow.

able and very difficult to dry (indications being that it undergoes some hydrolysis of the sulfonic acid group due to the water present). Consequently the crude product was crystallized from glacial acetic acid. Three crystallizations gave a yellow product which could be dried suitably in a vacuum oven at 70°; it had no definite melting point but charred in the region of 240°. Of the analytical values the neutral equivalent seemed to be most reliable (calcd. 293; found 294 to 297).

This acid was tested as an agent for amines and amino acids, the procedure used being the same as given above. The results are given in Table III which lists properties of the free acid and its salts.

Although the analytical values for the acid itself leave something to be desired, the preparation and analysis of the four additional salts 2, 3, 4 and 5 (which crystallize nicely from ethanol) seem to confirm the constitution of the acid.

The acid is soluble in water, methyl and ethyl alcohols, and insoluble in ether, benzene and other non-polar solvents. It precipitates many metal ions from dilute aqueous solutions, *e.g.*, Ag^{+}, Cu^{+2}, Mg^{+2}, Ca^{+2}, Zn^{+2}, Al^{+3}, Pb^{+2}, Cr^{+3}, Mn^{+2}, Ni^{+2}, Fe^{+2}, Fe^{+3}, Co^{+2}, Sn^{+2} and Ba^{+2}. The sodium and potassium salts of the nitro acid seem to be more soluble than those from dibenzofuran-2-sulfuric acid itself, but quantitative studies were not made.

Although the ammonium salt of dibenzofuran-2-sulfonic acid is crystalline, the addition of ammonium hydroxide to an aqueous solution of 3-nitro acid gave a slimy stringy mass that resembled a thick soap curd. This curious behavior confirmed the considerable difference in solution characteristics of the two acids.

Twenty-four amino acids were tested for precipitability by 3-nitrodibenzofuran-8-sulfonic acid by the same procedure as given above. Table IV lists the results obtained on the salts.

Since the nitrosulfonic acid failed to precipitate nine of the twenty-four amino acids tested, and under the same conditions dibenzofuran-2-sulfonic acid failed in but three cases (7), the advantage of the latter is obvious.

Although the study of the 3-nitro acid was extended to other amines (salt of *n*-butylamine melted 264°, di-*n*-butylamine 167°, diphenylguanidine 225°) the salts formed in many cases showed decomposition without characteristic melting, hence offered little promise for inclusion in this particular study.

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2-Hydroxymethyl-5-hydroxy-6-acetyl-4-pyrone

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In a previous communication,[2] the attempted synthesis of 2-hydroxymethyl-5-hydroxy-6-acetyl-4-pyrone (6-acetylkojic acid) was reported, but a clean-cut reaction was not obtained and an erroneous conclusion as to the nature of the reaction product was made. This was pointed out by Hurd and Sims.[3] However, their confirmation of the fact that kojic acid does react with acetic anhydride under controlled conditions to form a dark mixture which solidifies only upon aging stimulated our further interest in this acetylation, for such behavior could not be attributed to kojic acid diacetate and can only be accounted for by the formation of other substances along with the

(1) The author wishes to acknowledge the financial assistance given this investigation by the Research Corporation. The kojic acid was furnished through the courtesy of the Corn Products Company.

(2) L. L. Woods, THIS JOURNAL, **70**, 2608 (1948).

(3) C. D. Hurd and R. J. Sims, *ibid.*, **71**, 2440 (1949).