60–70 nm shorter wavelength. In the nmr spectra, protons on the carbocyclic ring of **1** absorbed energy at a higher magnetic field than do the corresponding protons on **2** and **3**. The absorption due to the proton at C-2 on **1** is shifted 4.0 ppm upfield with respect to that of the proton at C-3 on **2**. All these facts speak for the nonaromatic character of **1** and for the assigned structure.

The compound **1** was synthesized under conditions comparable to those reported earlier for the preparation of quinoxaline 1,4-dioxides from BFO.[1] Further, the color of **1** in solution approximates that observed during the course of more typical reactions which lead to fully aromatic compounds. It follows that 2,3-dihydroquinoxaline 1,4-dioxides are likely intermediates in the reaction between BFO and enamines; also, this same possibility cannot be ignored in considering intermediates in the reaction between BFO and carbanions.[3]

Experimental Section

2-Dimethylamino-2,3-dihydro-3,3-dimethylquinoxaline 1,4-Dioxide (1).—A stirred solution of 13.6 g (0.1 mol) of BFO in 100 ml of $CHCl_3$ was treated dropwise over a period of 30 min with a solution of 9.9 g (0.1 mol) of *N,N*-dimethylisobutenylamine[2] in 50 ml of $CHCl_3$. During the addition the temperature rose spontaneously but slowly to 37° and the reaction solution turned deep red. The temperature remained at 37° for 15 min and then dropped slowly to room temperature. The reaction mixture was allowed to stand overnight. The $CHCl_3$ was evaporated under reduced pressure, and the dark-red residue was eluted by C_6H_6–$CHCl_3$ (1:1) on a column of Florisil to afford 12 g of a dark crystalline substance which was recrystallized from Me_2CO–C_6H_{14} to give garnet-colored crystals, yield 4.5 g, mp 119–123°. Two further recrystallizations furnished an analytically pure sample of **1**: yield 3.5 g (15%); mp 135–137°; uv max (H_2O) 251 nm (ε 17,200), 482 (9320); nmr (CCl_4) δ 1.49 (s, 3, *trans*-3-CH_3), 1.52 (s, 3, *cis*-3-CH_3), 2.34 (s, 6, NCH_3), 4.20 (s, 1, 2 H), 6.6–6.9 (m, 2), 7.2–7.5 (m, 2); mass spectrum (70 eV) *m/e* (rel intensity) 235 (6), 192 (11), 177 (14), 99 (100), 84 (83).

Anal. Calcd for $C_{12}H_{17}N_3O_2$: C, 61.3; H, 7.3; N, 17.9. Found: C, 61.2; H, 7.1; N, 18.0.

2-Dimethylaminoquinoxaline 1,4-Dioxide (2).—In a reaction vessel equipped with a reflux condenser, a stirred solution of 1.36 g (0.01 mol) of BFO in 50 ml of $CHCl_3$ was treated dropwise over a period of 2 min with 1.14 g (0.01 mol) of *N,N,N',N'*-tetramethyl-1,1-vinylidenediamine.[4] The temperature rose spontaneously to the boiling point of the mixture and after 5 min began to fall. When the reaction mixture was at room temperature a yellow crystalline precipitate formed. The crude product was recrystallized from $CHCl_3$–C_6H_{14} to give 1.1 g (54%) of **2**, mp 177–180°. One further recrystallization afforded the analytical sample: mp 178–180°; uv max (MeOH) 239 nm (sh, ε 10,300), 279 (24,800), 305 (sh, 9340), 354 (8500), 422 (6200); nmr ($CDCl_3$) δ 3.20 (s, 6, NCH_3), 7.84 (m, 2), 8.20 (s, 1), 8.40 (m, 2).

Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.5; H, 5.4; N, 20.5. Found: C, 58.3; H, 5.2; N, 20.4.

2-Dimethylamino-3-methylquinoxaline 1,4-dioxide (3) was prepared from *N,N,N',N'*-tetramethyl-1,1-propenylidenediamine[4] in a manner similar to that described above: yield 39%; mp 124–127° (Me_2CO–C_6H_{14}); uv max (H_2O) 240 nm (ε 20,000), 276 (16,200), 310 (8500), 341 (sh, 9250), 352 (10,900), 411 (5000); nmr ($CDCl_3$) δ 2.70 (s, 3, CCH_3), 3.06 (s, 6, NCH_3), 7.72 (m, 2), 8.48 (m, 2).

Anal. Calcd for $C_{11}H_{13}N_3O_2$: C, 60.3; H, 6.0; N, 19.1. Found: C, 60.3; H, 5.9; N, 19.2.

Registry No.—**1**, 29086-42-8; **2**, 29086-43-9; **3**, 29086-44-0.

(3) (a) C. H. Issidorides and M. J. Haddadin, *J. Org. Chem.*, **31**, 4067 (1966); (b) K. Ley, F. Seng, U. Eholzer, R. Nast, and R. Schubart, *Angew. Chem., Int. Ed. Engl.*, **8**, 596 (1969).

(4) H. Bredereck, F. Effenberger, and H. P. Beyerlin, *Chem. Ber.*, **97**, 3081 (1964).

Acknowledgment.—The technical assistance of Mr. David A. Johnson was a valuable asset to the completion of this work. Also, I would like to express my appreciation to Professor Hans Muxfeldt for helpful advice.

Preparation of Substituted 1,2-Benzoisothiazolin-3-one 1,1-Dioxides (*o*-Benzoic Sulfimides)

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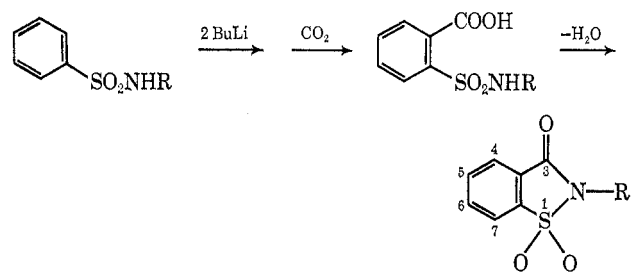
Received November 27, 1970

Ortho lithiation of *N*-methyl- and *N*-phenylbenzenesulfonamides followed by carbonation and cyclization has previously been reported[1] to produce *N*-methyl- and *N*-phenyl-1,2-benzoisothiazolin-3-one 1,1-dioxide (Ia,b), in 49 and 22% yields, respectively (Scheme I).

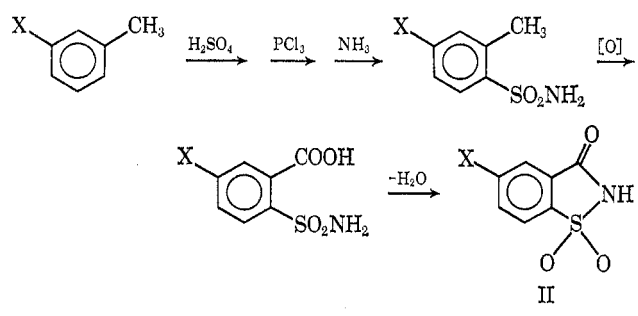
SCHEME I



Ia, R = CH_3
b, R = C_6H_5

In connection with another study, fairly large quantities of certain 5-substituted 2*H*-1,2-benzoisothiazolin-3-one 1,1-dioxides (*i.e.*, 5-substituted *o*-benzoic sulfimides) (II) were required. The multistep preparation of a few such compounds has been reported (Scheme II)

SCHEME II



II

utilizing vigorous oxidation of *o*-toluenesulfonamides. The latter compounds are obtained *via* sulfonation of a substituted toluene, and cyclodehydration of the *o*-sulfamoylbenzoic acid gives II. The reported procedures did not appear promising, however, since

(1) H. Watanabe, R. Gay, and C. R. Hauser, *J. Org. Chem.*, **33**, 900 (1968).

TABLE I

SUBSTITUTED *N-tert*-BUTYLARYLSULFONAMIDES[a]

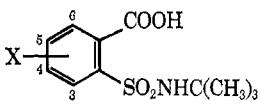
$ArSO_2NHC(CH_3)_3$

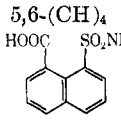
Ar	Registry no.	Yield, %	Mp, °C	Crystn[b] solvent	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
C_6H_5	2512-24-5	94	78–80		$C_{10}H_{15}NO_2S$	56.31	7.09	6.57	56.34	7.06	6.73
$4\text{-}CH_3C_6H_4$	2849-81-2	97	111–114	E	$C_{11}H_{17}NO_2S$	58.11	7.54	6.16	58.36	7.59	5.90
$4\text{-}ClC_6H_4$	29083-03-2	74	119–121	E	$C_{10}H_{14}ClNO_2S$	48.48	5.69	5.65	48.46	5.69	5.61
$4\text{-}CH_3OC_6H_4$	2849-81-2	55	102–104	E	$C_{11}H_{17}NO_3S$	54.29	7.04	5.76	54.05	7.17	5.46
$4\text{-}FC_6H_4$	29083-05-4	97	87–89	I	$C_{10}H_{14}FNO_2S$	51.93	6.10	6.06	51.71	6.18	5.83
2-Naphthyl	24293-49-0	81	146–148	E	$C_{14}H_{17}NO_2S$	63.84	6.51	5.32	63.78	6.62	5.12
1-Naphthyl	29083-07-6	96	149–151	E	$C_{14}H_{17}NO_2S$	63.84	6.51	5.32	63.68	6.33	5.30

[a] Prepared from the corresponding arylsulfonyl chloride and *tert*-butylamine as illustrated in the Experimental Section for *N-tert*-butylbenzenesulfonamide. [b] E = ethanol; I = isopropyl alcohol.

TABLE II

SUBSTITUTED 2-(*N-tert*-BUTYLSULFAMOYL)BENZOIC ACIDS[a]



X	Registry no.	Yield, %	Mp, °C (dec)	Crystn[b] solvent	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
H	29104-99-2	48	105–107	B–H	$C_{11}H_{15}NO_4S$	51.34	5.88	5.44	51.35	5.96	5.60
$5\text{-}CH_3$	29083-08-7	28	149–151	EA–H	$C_{12}H_{17}NO_4S$	53.11	6.32	5.16	53.27	6.48	4.90
5-Cl	29083-09-8	25[c]	145–147	E	$C_{11}H_{14}ClNO_4S$	45.28	4.84	4.80	45.42	5.00	4.59
$5\text{-}OCH_3$	29083-10-1	27	165–168	E	$C_{12}H_{17}NO_5S$	50.16	5.96	4.87	49.79	6.03	4.76
5-F	29083-11-2	35	143–146	H	$C_{11}H_{14}FNO_4S$	48.10	5.13	5.09	47.88	5.09	5.38
5,6-$(CH)_4$	29083-12-3	30	173–176	B	$C_{15}H_{17}NO_4S$[d]	62.40[d]	5.85	4.05	61.98	5.80	3.93
	29083-13-4	14	214–216	E–H	$C_{15}H_{17}NO_4S$	58.60	5.58	4.56	58.40	5.65	4.52

[a] Prepared from the corresponding *N-tert*-butylarylsulfonamide using *n*-butyllithium and carbon dioxide as illustrated in the Experimental Section for 5-methyl-2-(*N-tert*-butylsulfamoyl)benzoic acid. [b] EA = ethyl acetate; H = hexane; E = ether; B = benzene. [c] Better yields were obtained when the reaction was carried out at −60° and powdered carbon dioxide was added to the dilithio salt. [d] Obtained as a 0.5 benzene solvate after drying at room temperature under vacuum.

yields were either not reported or very low[2–4] or difficulties were encountered with purification of the final products.[5] Other methods for preparing *o*-benzoic sulfimides are equally difficult or require several-step procedures.[6,7]

The method of Hauser[1] for preparing I appeared attractive for preparing compounds of type II *if* an R group could be found which could be easily replaced by a hydrogen atom in the final product. An R group is necessary for the reaction with butyllithium since primary arylsulfonamides (*e.g.*, benzenesulfonamide) failed to metalate in the ortho position.

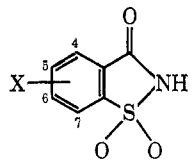
The benzyl group was found to be unsatisfactory as the R group. Preparation of 2-benzyl-5-methyl-1,2-benzoisothiazolin-3-one 1,1-dioxide (**8**) from *N*-benzyl-*p*-toluenesulfonamide proceeded smoothly in two steps (see Experimental Section); however, no conditions could be found for debenzylating **8**. Unsuccessful debenzylation attempts, resulting in the recovery of unchanged **8**, included the use of hydrogen and palladium or platinum in a variety of solvents, as well as hydrobromic acid in acetic acid and aqueous hydrochloric acid in ethanol. Similar failures resulted from repeated attempts to debenzylate the known[8] 2-benzyl-1,2-benzoisothiazolin-3-one 1,1-dioxide.

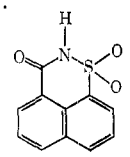
On the other hand, a *tert*-butyl substituent proved to be admirably suited as a protecting group in the preparation of II (Scheme I, R = *tert*-butyl). Ortho lithiation and carbonation of *N-tert*-butylarylsulfonamides (Table I) produced the desired substituted 2-(*N-tert*-butylsulfamoyl)benzoic acids (Table II). The latter compounds were smoothly cyclized *and* dealkylated in one step by polyphosphoric acid to give the desired substituted 1,2-benzoisothiazolin-3-one 1,1-dioxides, **1–5** (Table III). Application of the same reaction sequence to 2- and 1-(*N-tert*-butyl)naphthalenesulfonamides gave products carbonated at the 1 and 8 positions, respectively, which in turn produced the previously known **6** (1,2-dehydro-1-oxonaphth[1,2-*d*]-isothiazole 3,3-dioxide) and **7** (2,3-dihydro-3-oxonaphtho[1,8-*de*]-1,2-thiazine 1,1-dioxide) (Table III), respectively. Functional groups sensitive to *n*-butyllithium could not be employed. Thus, when 4-bromo-*N*-(*tert*-butyl)benzenesulfonamide was used in this method, complete debromination occurred to give *o*-benzoic sulfimide ("saccharin") as the final product in high yield. 4-Chloro-*N*-(*tert*-butyl)benzenesulfon-

(2) W. Noyes, *Amer. Chem. J.*, **8**, 167 (1886).
(3) R. DeRoode, *ibid.*, **13**, 217 (1891).
(4) G. Hamor and B. Reavlin, *J. Pharm. Sci.*, **56**, 135 (1967).
(5) C. Whitehead, J. Traverso, J. Bell, and P. Willard, *J. Med. Chem.*, **10**, 844 (1967).
(6) R. Ponci, T. Vitali, F. Mossini, and L. Amoretti, *Farmaco, Ed. Sci.*, **22**, 991 (1967).
(7) E. Muller Ed., "Methoden der Organischen Chemie," Georg Thieme Verlag, Stuttgart, 1955, p 626.
(8) H. Eckenroth and G. Koerppen, *Chem. Ber.*, **29**, 1048 (1896).

TABLE III

SUBSTITUTED 1,2-BENZOISOTHIAZOLIN-3-ONE 1,1-DIOXIDES[a]



No.	X	Yield, %	Mp, °C	Crystn[b] solvent	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
1	H[c]	51	225–227[c]	E							
2	5-CH_3	57	203–205		$C_8H_7NO_3S$	48.72	3.58	7.10	48.73	3.65	6.95
3	5-Cl	34	212–215		$C_7H_4ClNO_3S$	38.63	1.84	6.44	38.69	1.91	6.21
4	5-OCH_3	53	237–239[d]	E	$C_8H_7NO_4S$	45.04	3.31	6.57	45.05	3.44	6.45
5	5-F	23	218–220	Et	$C_7H_4FNO_3S$	41.79	2.00	6.96	41.82	2.02	6.85
6	4,5-$(CH)_4$	39	244–247[e]	I	$C_{11}H_7NO_3S$	56.64	3.03	6.01	56.40	2.97	5.92
7		62	267–269[e]	I	$C_{11}H_7NO_3S$	56.64	3.03	6.01	56.45	3.04	5.94

[a] Prepared from the corresponding substituted 2-(*N*-*tert*-butylsulfamoyl)benzoic acid and polyphosphoric acid as illustrated in the Experimental Section for compound **2**. [b] E = ethanol, Et = ether, I = isopropyl alcohol; where no solvent is indicated, product was obtained analytically pure from the reaction. [c] "Saccharin," lit. mp 225–228°, mmp 225–227°. [d] R. D. Haworth and A. Lapworth, *J. Chem. Soc.*, **125**, 1306 (1924), report mp 242°. [e] H. Kaufmann and H. Zobel, *Chem. Ber.*, **55B**, 1499 (1922), report mp 244° for **6** and mp 265° for compound **7**.

amide gave improved yields of ortho-carbonated product when the reaction was carried out at −60°. Except for these restrictions, the method appears to be a versatile, superior technique, even on fairly large scale, for converting arylsulfonyl chlorides to substituted 1,2-benzoisothiazolin-3-one 1,1-dioxides.

Experimental Section[9]

Arylsulfonyl chlorides were purchased from either Eastman Chemical Co. or Aldrich Chemical Co. and used as received. *n*-Butyllithium in hexane was purchased from Foote Chemical Co.

***N*-*tert*-Butylbenzenesulfonamide.**—To a stirred solution of 32.9 g (0.45 mol) of *tert*-butylamine in 75 ml of dry chloroform at 0° was slowly added a solution of 26.5 g (0.15 mol) of benzenesulfonyl chloride in 100 ml of chloroform. The cooling bath was removed and the suspension was stirred 1 hr at room temperature. After 1 hr at reflux, the suspension was cooled and washed successively with 200-ml portions of 3 *N* hydrochloric acid and then water (twice). The chloroform layer was dried (Na_2SO_4) and evaporated to give 30 g (94%) of analytically pure product, mp 77–80°. See Table I.

5-Methyl-2-(*N*-*tert*-butylsulfamoyl)benzoic Acid.—To 13.6 g (0.060 mol) of *N*-*tert*-butyl-*p*-toluenesulfonamide in 400 ml of dry tetrahydrofuran at 0° in a thoroughly dried three-necked round-bottom flask was added 120 ml (0.18 mol) of 1.6 *M* *n*-butyllithium in hexane. After 10 min at 0° the reaction was stirred for 1–2 hr at room temperature (samples of the reaction were carbonated, and thin layer chromatography on Eastman chromagram sheets, Type 6060, using benzene–5% acetic acid as eluent was employed to follow the course of these reactions). Carbon dioxide was then bubbled through the reaction for 0.5 hr[10] followed by the addition of 200 ml of water and 40 ml of 12 *N* HCl. After evaporation (reduced pressure, minimum heat applied) to one-half volumn, chloroform extracts of the residual mixture were dried over $CaSO_4$. Evaporation of solvent and recrystallization (see Table II) gave the product, mp 149–151° dec.

5-Methyl-1,2-benzoisothiazolin-3-one 1,1-Dioxide (2).—A yellow suspension of 0.50 g (0.019 mol) of 5-methyl-2-(*N*-*tert*-butylsulfamoyl)benzoic acid in 20 ml of polyphosphoric acid was heated (steam bath) for 15 min while mixing manually with a spatula. The thick syrup was poured (hot) in a thin stream onto an excess of crushed ice which was vigorously stirred. Filtration of the solid and a thorough wash with water gave 0.21 g (57%) of analytically pure product: mp 203–205° (see Table III); nmr (DMSO-d_6) τ 7.49 (s, 3, CH_3), 3.33 (broad, 1, NH, exchanges in D_2O), 2.2–1.8 (m, 3, aromatic protons).

2-Benzyl-5-methyl-1,2-benzoisothiazolin-3-one 1,1-Dioxide (8).—This compound was prepared from *N*-benzyl-*p*-toluenesulfonamide [mp 113–115° (lit.[11] mp 115–116°)] by the lithiation–carbonation procedure described above. The resultant semicrystalline material, after infrared spectral comparison to authentic 2-(*N*-benzylsulfamoyl)-5-methylbenzoic acid (**9**) (see below), was found to be suitable for use in the next step.

A solution of the above semisolid in 500 ml of benzene containing 50 mg of *p*-toluenesulfonic acid was refluxed for 3 hr. After evaporation of all solvent and recrystallization from ethanol, there was obtained 3.7 g (37%) of **8**: mp 133–135°; nmr (DMSO-d_6) τ 7.48 (s, 3, CH_3), 5.07 (s, 2, CH_2), 1.7–2.7 (m, 8, aromatic protons).

Anal. Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.88. Found: C, 62.77; H, 4.71; N, 4.85.

2-(*N*-Benzylsulfamoyl)-5-methylbenzoic Acid (9).—A suspension of compound **8** in concentrated ammonium hydroxide was heated in a steel pressure vessel at 125° for 2 hr. After cooling to 0°, careful acidification (hydrochloric acid) gave a quantitative yield of **9**, mp 154–157°. An infrared spectrum was virtually identical with that of the semisolid obtained above from the action of butyllithium–carbon dioxide on *N*-benzyl-*p*-toluenesulfonamide.

Anal. Calcd for $C_{15}H_{15}NO_4S$: C, 59.0; H, 4.95; N, 4.60. Found: C, 58.58; H, 5.00; N, 4.80.

Registry No.—**1**, 81-07-2; **2**, 29083-15-5; **3**, 29083-16-7; **4**, 29083-17-8; **5**, 29083-18-9; **6**, 29083-19-0; **7**, 29083-20-3; **8**, 29083-21-4; **9**, 29083-22-5.

Acknowledgment.—The author is grateful to Messrs. Harold Ramus, Paul Kelbaugh, and Nelson Treadway, Jr., for their assistance in the synthetic work and to Dr. R. V. Kasubick for determining conditions for large-scale preparations.

(9) Melting points were determined in a Thomas-Hoover capillary melting point apparatus and are uncorrected. Nmr spectra were obtained on a Varian Associates A-60 spectrometer with tetramethylsilane as an internal standard. Yields reported are for single experiments; no attempts were made to maximize yields in any particular reaction.

(10) A faster method involved pouring the reaction onto a suspension of solid carbon dioxide in ether.

(11) S. Wawzonek and D. Meyer, *J. Amer. Chem. Soc.*, **76**, 2918 (1954).