TABLE I
TERTIARY AMINO ALCOHOL HYDROCHLORIDES

$(C_6H_5)_2$—C(OH)—R·HCl

R	Yield, %	M.p.,[a] °C.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
$CH_2CH_2CH_2N$⟨ring⟩	51	223–224[b]	$C_{21}H_{28}ClNO$	72.92	8.16	4.05	72.75	8.15	4.33
$CH_2CH_2CH_2N(CH_3)_2$	55	204–206[c]	$C_{18}H_{24}ClNO$	70.69	7.91	4.58	70.64	8.05	4.64
$CH_2CH_2CH_2N$⟨ring⟩$N-CH_3$	60	143–144[d]	$C_{21}H_{28}N_2O$	77.74	8.69	8.63	77.60	8.45	8.50
$CH_2CH_2N(C_2H_5)_2$	53	202–204[e]	$C_{19}H_{26}ClNO$	71.43	8.19	4.38	71.46	8.08	4.69

[a] Melting points are corrected. [b] A. Marxer [*Helv. Chim. Acta*, **24**, 209E (1941)] reports m.p. 212–214°. [c] W. J. Croxall and J. W. Dawson [U. S. Patent 2,584,429] report m.p. 122–123.5° for the base. A sample of base obtained from hydrochloride salt had m.p. 121–123°. [d] Analyzed as the free base. A sample converted to the hydrochloride salt had m.p. 233–234°. H. E. Zaugg, R. J. Michaels, H. J. Glenn, L. R. Swett, M. Freifelder, G. R. Stone, and A. W. Weston [*J. Am. Chem. Soc.*, **80**, 2763 (1958)] report m.p. 232–233°. [e] D. W. Adamson [British Patents 624,118, 627,139 (1949)] reports m.p. 202–203°.

it can be alkylated with methyl iodide to give diphenylmethylcarbinol. In 1928, Wooster[2] showed that although this alkylation proceeded very slowly in benzene or ether, the reaction occurred very rapidly in liquid ammonia and a good yield of the desired product could be obtained. He was unsuccessful in his attempts to extend the reaction to aryl halides. Although it was not recognized at the time, Frey[3] had accomplished such an alkylation when he isolated triphenylcarbinol from his attempt to prepare benzophenone by the reaction of bromobenzene with diethyl oxalate and sodium. This product undoubtedly arose from the reaction of bromobenzene with the disodio derivative of benzophenone.

More recently Hamrick and Hauser[4] prepared the disodio derivative of benzophenone in liquid ammonia and reacted it with benzyl chloride and benzhydryl chloride to give 1,1,2-triphenylethanol and 1,1,2,2-tetraphenylethanol, respectively, in good yield.

The benzophenone disodio derivative has recently[5] been utilized for the preparation of cyclic ethers by the following reactions.

$$Ph_2C(Na)ONa + (CH_2)_nX_2 \longrightarrow Ph_2C\begin{matrix}O\\|\\(CH_2)_n\end{matrix}O + 2NaX$$

$n = 1, 2, 3, 4$

We have found that alkylation of the disodio derivative of benzophenone with aminoalkyl halides provides a convenient method for preparing a variety of amino alcohols, many of which are obtained in low yields by other procedures. The synthesis is outlined below.

$$Ph_2C{=}O \xrightarrow[2Na]{NH_3} Ph_2C(Na)ONa + RCl \xrightarrow[H_2O]{} Ph_2C(R)OH$$

The yields and properties of compounds which we have prepared by this procedure are shown in Table I.

(2) C. B. Wooster, *J. Am. Chem. Soc.*, **50**, 1388 (1928).
(3) H. Frey, *Chem. Ber.*, **28**, 2514 (1895).
(4) P. J. Hamrick, Jr., and C. R. Hauser, *J. Am. Chem. Soc.*, **81**, 493 (1959).
(5) D. V. Ioffe, *Zh. Obshch. Khim.*, **34**, 3900 (1964).

Experimental Section

General Procedure.—To approximately 2000 ml. of liquid ammonia cooled in a Dry Ice–isopropyl alcohol bath was added with stirring during 15 min. 48 g. (2 g.-atoms) of sodium. After 45 min. a solution of 182 g. (1.0 mole) of benzophenone in 500 ml. of ether was added during 30 min. After an additional 45 min., a solution of 1 mole of the aminoalkyl chloride in 500 ml. of ether was slowly added. The mixture was stirred for 1 hr., during which time it went from blue-black to pea green. Next the ammonia was evaporated with the aid of a water bath, and then 750 ml. of water was added while a nitrogen atmosphere was maintained. The reaction mixture set to a solid cake and 1000 ml. of benzene was added to facilitate stirring. Two clear layers formed and the organic phase was separated, washed three times with water, and dried. The dry solution was acidified with isopropyl alcohol containing 10% hydrogen chloride; the amino alcohol hydrochloride was separated by filtration. The crude product was obtained in yields of 70–90% and was purified by recrystallization from isopropyl or ethyl alcohol.

The Synthesis of 2,1,3-Benzothiadiazine 2,2-Dioxides and 1,2,3-Benzoxathiazine 2,2-Dioxides

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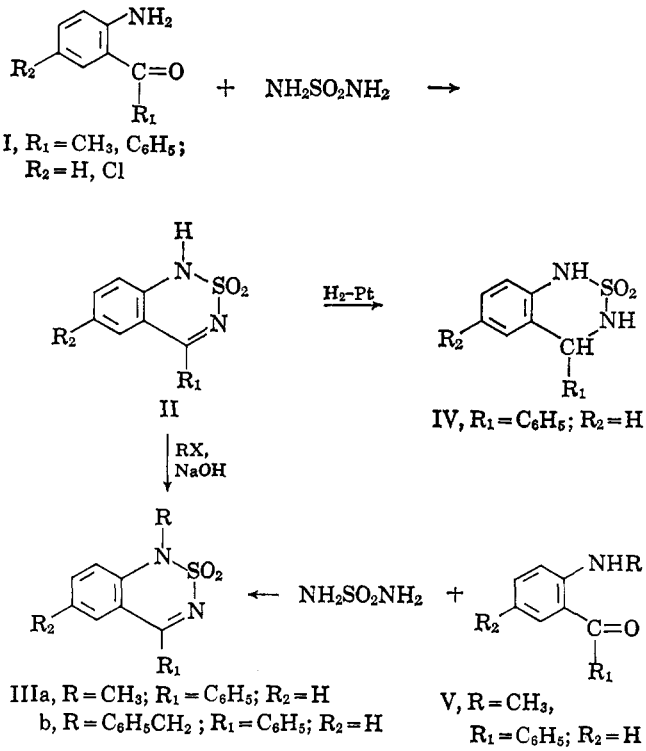
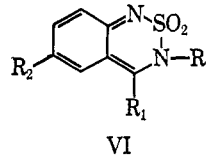
As a continuation of work underway in these laboratories[1] on the preparation of new heterocyclic systems based on sulfamide[2] as a starting material, we have investigated the reaction of sulfamide with *o*-aminobenzophenones and *o*-aminoacetophenones. We have found that simply fusing the amino ketones I with an excess of sulfamide at about 140° followed by heating at 180–190° affords good yields of 1H-2,1,3-benzothiadiazine 2,2-dioxides (II), a previously unreported heterocyclic system.[3]

(1) J. B. Wright, *J. Org. Chem.*, **29**, 1905 (1964).
(2) Obtained from General Chemical Division, Allied Chemical Corp.
(3) 1H-2,1,3-Benzothiadiazin-4-(3H)-one 2,2-dioxides have been reported recently: J. R. Geigy A-G., German Patent 1,120,456 (1962); E. Cohen and B. Klarberg, *J. Am. Chem. Soc.*, **84**, 1994 (1962).



One of the compounds of the type II that was prepared (where R_1 = C_6H_5 and R_2 = H) was found to alkylate readily in the presence of sodium hydroxide using methyl iodide and benzyl chloride to give the corresponding 1-methyl and 1-benzyl derivatives (IIIa and IIIb). The possibility existed that alkylation in these cases could have taken place at the 3-nitrogen to form a compound of type VI. However, it was



VI

shown that in the case of methylation the 1-substituted product was formed since the same product was formed by treatment of N-methyl-*o*-aminobenzophenone (V, R = CH_3, R_1 = C_6H_5, R_2 = H) with sulfamide. The position of benzylation is assigned the 1-position because of its analogy to the position of methylation.

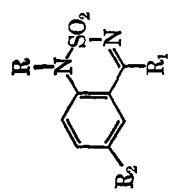
The 2,1,3-benzothiadiazine 2,2-dioxides (II and III) that were prepared are listed in Table I.

Catalytic hydrogenation of 4-phenyl-1H-2,1,3-benzothiadiazine 2,2-dioxide (II, R_1 = C_6H_5 R_2 = H) in acetic acid solution using Adams catalyst proceeded with the absorption of 1 mole of hydrogen to give the 3,4-dihydro derivative. The resulting compound showed a doublet centered at τ 4.2 attributable to the tertiary hydrogen at the 4-position, which collapsed to a singlet in acidic solution.[4]

Treatment of *o*-hydroxy ketones with sulfamide in a similar manner led to 1,2,3-benzoxathiazine 2,2-

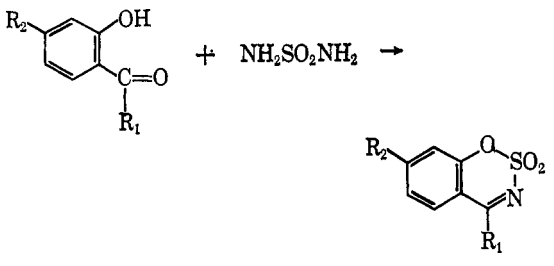
(4) The n.m.r. spectrum was obtained with a Varian DP-60 n.m.r. spectrometer using dimethylformamide-d_7 solvent and tetramethylsilane as the internal reference standard.

TABLE I. 2,1,3-BENZOTHIADIAZINE 2,2-DIOXIDES



R	R_1	R_2	Procedure	Yield, %	M.p., °C.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Calcd., % S	Found, % C	Found, % H	Found, % N	Found, % S	λ_{max}^{EtOH} (ε), mμ
H	CH_3	H	A	68	209–211[a]	$C_8H_8N_2O_2S$	48.97	4.11	14.28	16.34	49.49	4.34	14.51	16.00	223 (24,000), 264 (6800), 347 (25,400)
H	C_6H_5	H	A	97	216–217[a]	$C_{13}H_{10}N_2O_2S$	60.45	3.90	10.85	12.41	60.56	4.00	11.03	12.45	223 (20,400), 269 (12,100), 359 (3200)
H	C_6H_5	Cl	A	53	206–208[b]	$C_{13}H_9ClN_2O_2S$[c]	53.34	3.10	9.57	10.95	53.52	3.07	9.53	10.95	231 (27,400), 268 (10,300), 295 (sh) (5300), 372 (3100)
CH_3	C_6H_5	H	B[d]	96[e]	206.5–208[b]	$C_{14}H_{12}N_2O_2S$	61.75	4.44	10.29	11.77	61.84	4.44	10.17	12.01	228 (21,700), 276 (12,650), 365 (3950)
$C_6H_5CH_2$	C_6H_5	H	B	57[e]	153–154[f]	$C_{20}H_{16}N_2O_2S$	68.44	4.63	8.04	9.20	68.80	4.69	8.27	9.30	226 (21,750), 274 (13,650), 293 (slight sh) (10,450), 360 (4650)

[a] Recrystallized from isopropyl alcohol. [b] Recrystallized from ethyl acetate. [c] *Anal.* Calcd.: Cl, 12.11. Found: Cl, 12.12. [d] This compound was prepared also by the reaction between N-methyl-*o*-aminobenzophenone and sulfamide (*cf.* Experimental Section). [e] This yield is based upon the amount of 4-phenyl-1H-2,1,3-benzothiadiazine 2,2-dioxide actually consumed in the reaction, taking into account recovered starting material. [f] Recrystallized from anhydrous ethanol.



VIIa, $R_1 = CH_3$; $R_2 = H$
b, $R_1 = C_6H_5$; $R_2 = CH_3O$-

dioxides (VII), a previously unreported heterocyclic system.

Experimental Section[5,6]

Procedure A. Preparation of 4-Methyl-1H-2,1,3-benzothiadiazine 2,2-Dioxide.—A mixture of 20.25 g. (0.15 mole) of 2-aminoacetophenone and 74 g. (0.75 mole) of sulfamide was heated at 140° with stirring for 2 hr. An additional 74 g. of sulfamide was added and stirring and heating were continued at 180–190° for 6 hr. After cooling, the mixture, consisting of a hard cake, was stirred thoroughly with 250 ml. of a 3% sodium hydroxide solution. The mixture was filtered and the filtrate was acidified with acetic acid. The precipitate was removed by filtration and purified by recrystallization.

Procedure B. Preparation of 1-Methyl-4-phenyl-2,1,3-benzothiadiazine 2,2-Dioxide (IIIa).—To 5.19 g. (0.02 mole) of 4-phenyl-1H-2,1,3-benzothiadiazine 2,2-dioxide was added 10 ml. of a 10% sodium hydroxide solution and 20 ml. of ethanol. The solution was cooled to 10°, 4 ml. of methyl iodide was added, and the mixture was stirred at room temperature for 24 hr., using an efficient reflux condenser on the reaction flask. Water (25 ml.) was added and the reaction mixture was filtered. There was obtained 3.65 g. of yellow platelets melting at 205–208°. Acidification of the filtrate with acetic acid gave 1.59 g. of recovered starting material.

1-Methyl-4-phenyl-2,1,3-benzothiadiazine 2,2-Dioxide (IIIa).—A mixture of 5.0 g. (0.024 mole) of N-methyl-o-aminobenzophenone[7] and 6.99 (0.72 mole) of sulfamide was heated at 170–180° for 24 hr. An additional 6.9 g. of sulfamide was added and the mixture was again heated at 170–180° for an additional 24 hr. The mixture was stirred with 25 ml. of water, then with 25 ml. of ether and filtered. There was obtained 5.04 g. (77%) of a tan solid melting at 204–206°. This material was identical with the material prepared by procedure B, as shown by a mixture melting point and comparison of infrared spectra.

4-Phenyl-3,4-dihydro-1H-2,1,3-benzothiadiazine 2,2-Dioxide (IV).—A solution of 12.9 g. (0.05 mole) of 4-phenyl-1H-2,1,3-benzothiadiazine 2,2-dioxide in 250 ml. of acetic acid was hydrogenated at an initial pressure of 3 atm. using 200 mg. of platinum oxide as catalyst. One mole of hydrogen was absorbed after 3 hr. The mixture was warmed to dissolve all of the organic material and the catalyst was removed by filtration. On cooling the solution, 2.76 g. of starting material precipitated. The acetic acid was removed from the filtrate by concentration *in vacuo* and the residue was recrystallized from ethanol. Filtration gave an additional 1.96 g. of starting material. The filtrate was again concentrated to dryness and the residue was recrystallized from benzene. There was obtained 3.0 g. (36%, based on recovered starting material) of yellow prisms melting at 133–136°. Additional recrystallization raised the melting point to 133.5–135°: λ_{max}^{EtOH} 228 mμ (sh) (ε 9100), 278 (3200), and 355 (710).

Anal. Calcd. for $C_{13}H_{12}N_2O_2S$: C, 59.98; H, 4.65; N, 10.76; S, 12.32. Found: C, 60.51; H, 4.38; N, 11.03; S, 12.13.

4-Methyl-1,2,3-benzoxathiazine 2,2-Dioxide (VIIa).—A mixture of 13.165 g. (0.1 mole) of 2′-hydroxyacetophenone and 24 g. (0.25 mole) of sulfamide was stirred and heated in an oil bath at 130° for 1 hr. An additional 24 g. of sulfamide was added, heating was continued at 130° for 0.5 hr., and then the temperature was raised slowly to 180°. After heating the reaction mixture at this temperature for 3 hr. with stirring, the mixture was allowed to cool and was stirred with a mixture of 150 ml. of water and 150 ml. of methylene chloride. The organic layer was separated and the solvent was removed. There was obtained 8.25 g. (42%) of material melting at 114–118°. Recrystallization from ethanol gave tan prisms melting at 119–121°: λ_{max}^{EtOH} 264 mμ (ε 9950) and 308 mμ (ε 1700).

Anal. Calcd. for $C_8H_7NO_3S$: C, 48.73; H, 3.58; N, 7.10; S, 16.26. Found: C, 48.88; H, 3.62; N, 7.13; S, 15.94.

4-Phenyl-7-methoxy-1,2,3-benzoxathiazine 2,2-Dioxide (VIIb).—Utilizing the procedure described above for 4-methyl-1,2,3-benzoxathiazine 2,2-dioxide with an equivalent amount (22.8 g.) of 2-hydroxy-4-methoxybenzophenone there was obtained, after recrystallization of the crude product from isopropyl alcohol, 8.61 g. (30%) of light yellow prisms melting at 148.5–150°: λ_{max}^{EtOH} 241 mμ (sh) (ε 7800), 246 (7850), 302 (15,100), and 320 (14,700).

Anal. Calcd. for $C_{14}H_{11}NO_4S$: C, 58.12; H, 3.84; N, 4.84; S, 11.08. Found: C, 58.51; H, 3.66; N, 4.82; S, 11.37.

(5) All melting points are corrected.

(6) Microanalyses were performed by Mr. Norman Knight and associates and n.m.r. data were obtained by Dr. George Slomp and Mr. Forrest MacKellar of our Physical and Analytical Chemistry Department. The author is indebted also to Miss Lorraine Pschigoda for infrared spectral data, to Miss Betty Zimmer for the ultraviolet spectra data, and to Mr. Albert Lallinger for excellent technical assistance.

(7) L. H. Sternbach, *et al.*, *J. Org. Chem.*, **27**, 3787 (1962).

The Preparation of Mercaptomethyl Hydroquinones, Catechols, and Related Compounds

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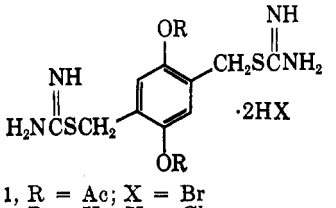
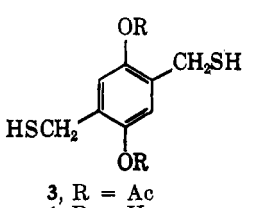
We have recently described[1] a synthesis of acetylated bromomethylphenols which makes mono- and poly(bromomethyl)hydroquinone and catechol diacetates readily available. We wish to report here results of our investigations dealing with the conversions of several of these intermediates into the corresponding mercaptomethyl derivatives.

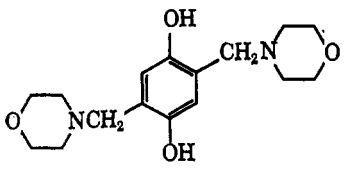
A general thiol synthesis which would appear to be applicable to our starting materials is the base cleavage of S-alkylthiuronium salts.[2] Bisisothiuronium salt **1** was therefore prepared and, in turn, allowed to react with morpholine under conditions known to be ef-



1, R = Ac; X = Br
2, R = H; X = Cl



3, R = Ac
4, R = H



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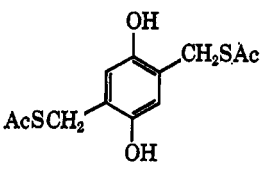

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(1) D. L. Fields, J. B. Miller, and D. D. Reynolds, *J. Org. Chem.*, **29**, 2640 (1964).

(2) Benzyl bromide, for example, has been converted to benzyl mercaptan in 70–75% yield by this procedure: R. L. Frank and P. V. Smith, *J. Am. Chem. Soc.*, **68**, 2103 (1946).