44-5; **11**, 34282-45-6; **12**, 34282-46-7; **13**, 34282-47-8; **14**, 34282-48-9; **15**, 34282-49-0; **16**, 34282-50-3; **17**, 34282-51-4; **18**, 34282-52-5.

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The Syntheses of 4-Acylamido-1,4-benzoxazine-2,3-diones and 4-(*p*-Toluenesulfonamido)-1,4-benzoxazine-2,3-dione

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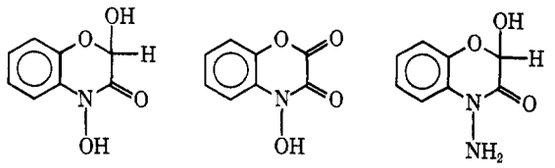
A general synthetic method for the synthesis of 4-acylamido-1,4-benzoxazine-2,3-diones (**8**) is described. Ortho-substituted hydrazines can be prepared by acid hydrolysis of the appropriate mesoionic sydnone. *o*-Benzyloxyphenylhydrazine hydrochloride (**4**) was prepared in this manner and acylated on the terminal nitrogen. The 1-(*o*-benzyloxyphenyl)-2-acylhydrazine (**5**) was treated with ethyl oxalyl chloride to give 1-(*o*-benzyloxyphenyl)-1-ethyloxalyl-2-acylhydrazine (**6**) which on hydrogenation afforded **8**. The synthesis of 4-(*p*-toluenesulfonamido)-1,4-benzoxazine-2,3-dione (**20**) was accomplished by the addition of sodium *p*-toluenesulfinite to the diazonium salt prepared from *o*-benzyloxyaniline. The resulting diimide **17** was reduced to the corresponding hydrazine **18**, which was treated with ethyl oxalyl chloride to afford 1-(*o*-benzyloxyphenyl)-1-ethyloxalyl-2-(*p*-toluenesulfonyl)hydrazine (**19**). This compound on hydrogenolysis of the benzyl protecting group cyclized to give **20**.

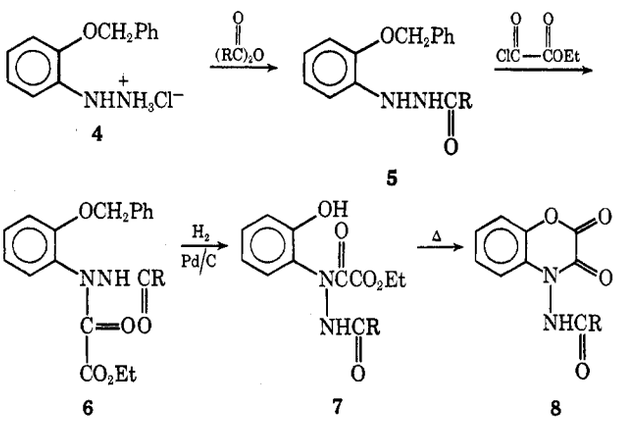
In view of the interesting chemistry and biological activity of the naturally occurring hydroxamic acids having the basic structure 2,4-dihydroxy-1,4-benzoxazin-3-one (**1**),[2-4] a study of the 4-amino analogs **3** and their derivatives was initiated.



1 **2** **3**

The preparative procedure utilized the acylation of *o*-benzyloxyphenylhydrazine (**4**) with either acetic anhydride or trifluoroacetic anhydride to afford the monoacylhydrazides **5a** and **5b**. The monoacylation of phenylhydrazines with anhydrides has been shown to occur at the terminal nitrogen.[5] The treatment of **5a** and **5b** with ethyl oxalyl chloride afforded the diacyl hydrazides **6a** and **6b**, respectively. Hydrogenolysis of **6a** produced a single product as determined by tlc analysis on silica gel. A crystalline compound, **8a**, was obtained when the oil produced by the hydrogenolysis of **6a** was heated in benzene. The nmr spectrum of the oil is consistent with structure **7**.

In the above sequence *o*-benzyloxyphenylhydrazine (**4**) was required as a starting material. *o*-Benzyloxyaniline hydrochloride (**9**) was prepared and converted to the corresponding diazonium salt, but the conventional method for the reduction of diazonium salts utilizing stannous chloride was found to be inapplicable in this case. Ek and Witkop[6] have also reported an unsuccessful attempt to reduce this diazonium salt



4 **5** **6** **7** **8**

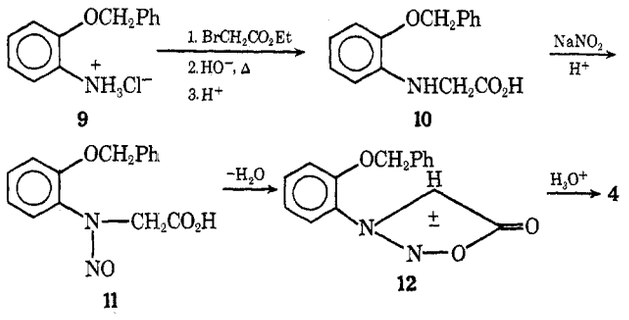
a, R = CH_3
b, R = CF_3

by the stannous chloride method, but Clerc-Bory[7] reported that this method gave a 72% yield of the desired product. Clerc-Bory also reported the melting point of this material to be 191°, which is 43° higher than the melting point of the product we obtained by an alternate route. Utilizing stannous chloride we also obtained a material melting at 191° but it would not undergo acylation with acetic anhydride.

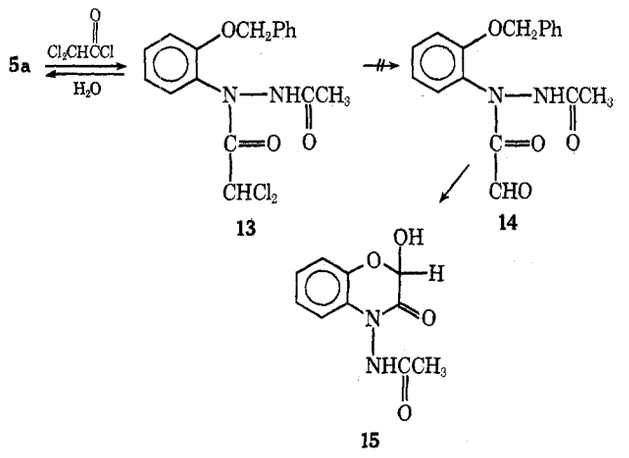
The acidic hydrolysis of mesoionic sydnones provided an alternate route for the preparation of ortho-substituted hydrazines.[8,9] 3-(*o*-Benzyloxyphenyl)sydnone (**12**) was prepared in good yield by cyclization of the nitroso intermediate **11**. This cyclization was found to proceed readily with the use of trifluoroacetic anhydride, while other dehydrating agents gave lower yields of **12**.[10] The hydrolysis of **12** with hot aqueous hydrochloric acid was accompanied by considerable tar formation, but, when dioxane–water was employed as the solvent, hydrolysis proceeded rapidly at room temperature with a minimum of decomposition.

The hydrazides **8** are the amino analogs of 4-hydroxy-1,4-benzoxazine-2,3-dione (**2**) which has properties

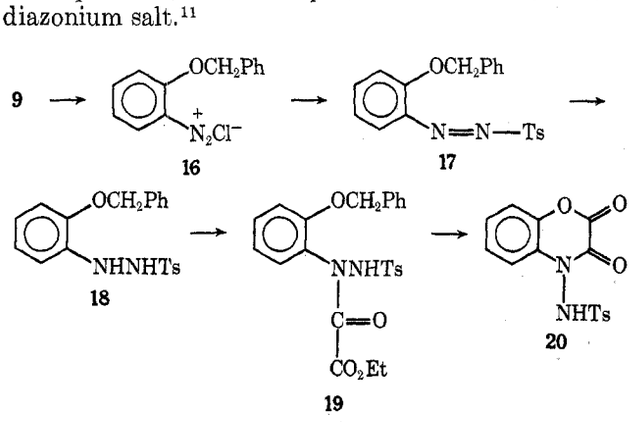
(1) Taken in part from the dissertation presented by M. D. Corbett, Nov 1970, to the Graduate School of the University of Kansas in partial fulfillment of the requirements for the Doctor of Philosophy Degree.
(2) A. I. Virtanen and P. K. Hietala, *Acta Chem. Scand.*, **14**, 499 (1960).
(3) J. A. Klun and T. A. Brindley, *J. Econ. Entomol.*, **59**, 711 (1966).
(4) G. L. Lammoureux, R. H. Shimabukuro, H. R. Swanson, and D. S. Frear, *J. Agr. Food Chem.*, **18**, 81 (1970).
(5) P. A. S. Smith, "Open Chain Nitrogen Compounds," Vol. 2, W. A. Benjamin, New York, N. Y., 1966.
(6) A. Ek and B. Witkop, *J. Amer. Chem. Soc.*, **76**, 5579 (1954).
(7) M. Clerc-Bory, *Bull. Soc. Chim. Fr.*, 337 (1954).
(8) L. B. Kier and E. B. Roche, *J. Pharm. Sci.*, **56**, 149 (1967).
(9) S. Aziz, A. F. Cockerill, and J. G. Tillett, *J. Chem. Soc. B*, 416 (1970).
(10) W. H. Nyberg and C. C. Cheng, *J. Med. Chem.*, **8**, 531 (1965).



similar to those of the hydroxamic acid **1**. An attempt to prepare the amino analog (**15**) of 2,4-dihydroxy-1,4-benzoxazin-3-one failed because it was not possible to convert the diacylhydrazide **13** to the aldehydic diacylhydrazide **14**. Under hydrolytic conditions, cleavage of the dichloroacetyl function in **13** occurs preferentially to regenerate **5a**. Currently, selective reduction of **8a** to yield **15** is being investigated.



An attempt to extend the above successful sequence (**4** → **8**) to the preparation of 4-(*p*-toluenesulfonamido)-1,4-benzoxazine-2,3-dione (**20**) met with little success, as the acylation of **4** with *p*-toluenesulfonyl chloride to give **18** proceeded in very low yield. An alternate synthesis of **18** was developed based on the known nucleophilic addition of *p*-toluenesulfinic acid to a diazonium salt.[11]



The diimide **17** formed readily at low temperatures when *p*-toluenesulfinic acid was added to a solution of the diazonium salt **16**. Reduction of **17** with zinc dust and acetic acid produced the desired tosyl hydrazine **18** in excellent yield. The hydrogenolysis of the benzyloxy group in **18** utilizing palladium-on-carbon catalyst failed due to apparent poisoning of the catalyst. The acylation of **18** with ethyl oxalyl chloride produced **19**, which underwent hydrogenolysis readily to give the desired 4-(*p*-toluenesulfonamido)-1,4-benzoxazine-2,3-dione (**20**).

(11) R. W. Hoffman, *Chem. Ber.*, **98**, 222 (1965).

Experimental Section[12]

***o*-Benzyloxyacetanilide.**—This procedure is similar to that of Ek and Witkop,[6] but these workers did not isolate the title compound.

o-Hydroxyacetanilide (60.4 g, 0.40 mol), benzyl bromide (68.4 g, 0.40 mol), and anhydrous K_2CO_3 (54.8 g, 0.40 mol) in 500 ml of Me_2CO were heated to reflux under N_2 for 12 hr. The solvent volume was reduced to about 300 ml and the residue was combined with 800 ml of C_6H_6 and washed with 100 ml of 5% NaOH, 300 ml of H_2O, and 100 ml of saturated NaCl solution. The C_6H_6 solution was dried (Na_2SO_4) and the solvent volume was reduced until solid material began to appear. Recrystallization (C_6H_6–Et_2O) gave 80.5 g (84%) of small white plates, mp 114.0–115.5°; spectral data are consistent with the assigned structure.

***o*-Benzyloxyaniline Hydrochloride** (**9**).—*o*-Benzyloxyacetanilide (80.5 g, 0.35 mol) in 400 ml of MeOH saturated with HCl was heated to reflux for 2 hr. The solvent was distilled at atmospheric pressure until a solid began to form. The mixture was allowed to cool and 500 ml of Et_2O was added. The mixture was cooled and the solid was collected by filtration and washed with 200 ml of Et_2O. The solid was stirred with 300 ml of Et_2O and collected and dried to give 60.7 g (78%) of fine white needles, mp 205–208°; spectral data are consistent with the assigned structure. This material must be stored below 10° to prevent decomposition. This procedure is more convenient than that previously reported.[6,13]

Ethyl *N*-(*o*-Benzyloxyphenyl)glycinate.—*o*-Benzyloxyaniline hydrochloride (**9**, 35.4 g, 0.15 mol) and anhydrous NaOAc (24.6 g, 0.30 mol) were mixed in 60 ml of absolute EtOH. To this stirred suspension was added ethyl bromoacetate (25.2 g, 0.15 mol). This mixture was stirred under an N_2 atmosphere and heated to reflux for 5 hr. The reaction mixture was combined with 150 ml of C_6H_6 and washed with 150 ml of H_2O and 50 ml of saturated NaCl solution. The organic solution was dried (Na_2SO_4) and the solvent was removed *in vacuo* to give a light brown oil, which was used immediately in the next reaction due to its instability. Spectral data are consistent with the assigned structure.

***N*-(*o*-Benzyloxyphenyl)glycine** (**10**).—Crude ethyl *N*-(*o*-benzyloxyphenyl)glycinate (theory 0.15 mol) was stirred in 90 ml of 10% EtOH containing NaOH (9.0 g, 0.225 mol) under an N_2 atmosphere. The mixture was heated to reflux for 30 min and the resultant orange solution was neutralized with 6 *N* HCl to give an oil. The suspension of the oil in H_2O was stirred and cooled until it solidified. The solid was collected by filtration and dissolved in 100 ml of EtOH. Crystallization was achieved by the addition of 30 ml of H_2O, followed by cooling for several hours. The solid was collected by filtration and recrystallized from Et_2O–petroleum ether (bp 60–68) to yield 26.4 g (69%) of **10** as fine white needles, mp 119–121°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.88; H, 6.03; N, 5.70.

***N*-(*o*-Benzyloxyphenyl)-*N*-nitrosoglycine** (**11**).—*N*-(*o*-Benzyloxyphenyl)glycine (**10**, 12.8 g, 0.05 mol) was stirred in 100 ml of MeOH and treated with 10 ml of 5 *N* HCl to effect dissolution. The solution was cooled to 0° with an ice bath and treated with $NaNO_2$ (3.45 g, 0.05 mol) dissolved in 40 ml of H_2O in the course of 15 min. The solution was stirred and cooled for an additional 30 min, after which the green solution was combined with 200 ml of C_6H_6. The C_6H_6 solution was washed twice with 100 ml of H_2O and dried (Na_2SO_4). The solvent was evaporated to 50 ml of total volume for use in the next reaction. The nitroso compound **11** can be isolated by further evaporation of the sol-

(12) Melting points were obtained on a calibrated Thomas-Hoover Unimelt and are corrected. Ir data were recorded on a Beckman IR-10 spectrophotometer and nmr data on Varian Associates A-60, A-60A, and HA-100 spectrometers (TMS). Microanalyses were performed by Midwest Microlabs, Inc., Indianapolis, Ind., and on an F & M 185 C, H, N analyzer, University of Kansas.

(13) A. Sieglitz and H. Koch, *Ber.*, **58B**, 78 (1925).

vent *in vacuo* to a total of 30 ml. Crystals formed when the solution was cooled and the solid was collected by filtration. Recrystallization twice from C_6H_6 gave yellow needles, mp 93.5–95.0°; positive Lieberman nitroso reaction; the spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.78. Found: C, 63.28; H, 5.13; N, 9.95.

***N*-(*o*-Benzyloxyphenyl)sydnone (12).**—A crude concentrated C_6H_6 solution of *N*-(*o*-benzyloxyphenyl)-*N*-nitrosoglycine, **11** (theory 0.05 mol) was combined with 100 ml of anhydrous Et_2O, cooled to 10°, and treated with 25 g of trifluoroacetic anhydride in portions of several grams each. The solution was allowed to warm to 25° and the solvent volume was reduced to about 70 ml with a stream of N_2. Crystals formed and the mixture was cooled. The solid was collected by filtration and recrystallized (C_6H_6–Et_2O) to yield 7.6 g (57% from **10**) of **11** as white plates, mp 93.0–94.5°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.06; H, 4.61; N, 10.68.

***o*-Benzyloxyphenylhydrazine Hydrochloride (4).**—*N*-(*o*-Benzyloxyphenyl)sydnone (**12**, 10.0 g, 0.037 mol) was stirred at 25° under an N_2 atmosphere in 200 ml of 67% dioxane in H_2O containing 0.52 equiv of HCl for 4 hr. The solvent was removed *in vacuo*, and the residue was dried under high vacuum. The solid residue was dissolved in a minimal amount of hot absolute EtOH. Crystallization was effected by adding ten volumes of Et_2O to the solution and cooling. The solid was collected and recrystallized (EtOH–Et_2O) to give 7.0 g (73%) of **4** as a gray solid, mp 144–145° dec; spectral data are consistent with the assigned structure. Compound **4** is unstable and can only be stored for several days with cooling.

1-(*o*-Benzyloxyphenyl)-2-acetylhydrazine (5a).—*o*-Benzyloxyphenylhydrazine hydrochloride (**4**, 1.25 g, 0.005 mol), acetic anhydride (0.6 g, 0.005 mol), and anhydrous NaOAc (1.1 g, 0.011 mol) in 25 ml of anhydrous Et_2O were stirred for 10 hr at 25°. The mixture was combined with 100 ml of C_6H_6 and washed with 50 ml of H_2O, 50 ml of 0.1 *N* HCl, 50 ml of H_2O, and 30 ml of saturated NaCl solution. The organic solution was dried (Na_2SO_4) and the solvent was removed to give an oil which crystallized from Et_2O to give 1.0 g (77%) of **5a** as white plates, mp 130.0–131.5°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 69.96; H, 6.27; N, 11.19.

1-(*o*-Benzyloxyphenyl)-1-dichloroacetyl-2-acetylhydrazine (13).—1-(*o*-Benzyloxyphenyl)-2-acetylhydrazine (**5a**, 2.04 g, 0.008 mol), anhydrous $NaHCO_3$ (0.84 g, 0.01 mol), and dichloroacetyl chloride (1.2 g, 0.008 mol) were stirred in 60 ml of anhydrous C_6H_6 for 2 hr at 25°. The reaction mixture was combined with 200 ml of C_6H_6 and washed with 100 ml of H_2O and 50 ml of saturated NaCl solution. The C_6H_6 solution was dried (Na_2SO_4) and the solvent was removed *in vacuo* to produce a solid material, which was recrystallized (C_6H_6) to give 2.5 g (86%) of **9** as a white powder, mp 147–149°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{17}H_{16}N_2O_3Cl_2$: C, 55.60; H, 4.39; N, 7.63. Found: C, 55.35; H, 4.48; N, 7.73.

1-(*o*-Benzyloxyphenyl)-1-ethyloxalyl-2-acetylhydrazine (6a).—1-(*o*-Benzyloxyphenyl)-2-acetylhydrazine (**5a**, 2.3 g, 0.009 mol), anhydrous $NaHCO_3$ (0.9 g, 0.01 mol), and ethyl oxalyl chloride (1.36 g, 0.01 mol) in 60 ml of C_6H_6 were stirred for 1 hr at 25°. The reaction mixture was combined with 100 ml of Et_2O and washed twice with 30 ml of H_2O and once with 30 ml of saturated NaCl solution. The organic solution was dried (Na_2SO_4) and the solvent was removed *in vacuo* to give a thick oil (2.1 g, 70%); spectral data are consistent with the assigned structure.

4-Acetamido-1,4-benzoxazine-2,3-dione (8a).—Crude 1-(*o*-benzyloxyphenyl)-1-ethyloxalyl-2-acetylhydrazine (**6a**, 2.1 g, 0.006 mol) was hydrogenated at 25° under 1-atm pressure with 200 mg of 5% Pd/C as the catalyst and 50 ml of EtOAc as the solvent. When the uptake of H_2 stopped, the catalyst was removed by filtration and the solvent was removed *in vacuo* to give an oil. The oil was dissolved and heated in C_6H_6 until a solid had formed. The C_6H_6 solution was cooled and the solid was collected by filtration. Several more crops were collected by heating the mother liquor until more solid formed. The solid fractions were combined and recrystallized (Me_2CO–C_6H_6) to give 0.9 g (45%) of **8a** as small white crystals, mp 240–242°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{10}H_8N_2O_4$: C, 54.55; H, 3.66; N, 12.72. Found: C, 54.85; H, 3.70; N, 12.89.

1-(*o*-Benzyloxyphenyl)-2-trifluoroacetylhydrazine (5b).—*o*-Benzyloxyphenylhydrazine hydrochloride (**4**, 5.0 g, 0.02 mol), anhydrous $NaHCO_3$ (3.4 g, 0.04 mol), and trifluoroacetic anhydride (5.0 g, 0.024 mol) were stirred at 25° for 6 hr in 50 ml of anhydrous Et_2O. The reaction mixture was combined with 70 ml of C_6H_6 and washed twice with 70 ml of H_2O. The organic solution was dried (Na_2SO_4) and the solvent was removed to give an oil, which crystallized from Et_2O–petroleum ether to give 5.5 g (89%) of **5b**. Recrystallization from C_6H_6–petroleum ether gave fine white crystals, mp 108–110°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{15}H_{13}N_2O_2F_3$: C, 58.07; H, 4.22; N, 9.03. Found: C, 57.80; H, 4.21; N, 9.26.

1-(*o*-Benzyloxyphenyl)-1-ethyloxalyl-2-trifluoroacetylhydrazine (6b).—1-(*o*-Benzyloxyphenyl)-2-trifluoroacetylhydrazine (**5b**, 3.1 g, 0.01 mol), anhydrous $NaHCO_3$ (1.0 g, 0.012 mol), and ethyl oxalyl chloride (1.5 g, 0.012 mol) were stirred at 25° for 12 hr in 50 ml of anhydrous C_6H_6. The mixture was combined with 100 ml of Et_2O and washed twice with 50 ml of H_2O. The organic solution was dried (Na_2SO_4) and the solvent was removed *in vacuo* to give an oil (3.0 g, 97%); spectral data are consistent with the assigned structure.

4-Trifluoroacetamido-1,4-benzoxazine-2,3-dione (8b).—Crude 1-(*o*-benzyloxyphenyl)-1-ethyloxalyl-2-trifluoroacetylhydrazine (**6b**, 3.0 g, 0.01 mol) was hydrogenated at 25° under 1-atm pressure with 200 mg of 5% Pd/C as the catalyst and 50 ml of EtOAc as the solvent. The reaction was allowed to proceed until 225 ml (0.01 mol) of H_2 had been taken up. The catalyst was removed by filtration and the solvent was removed *in vacuo* to give an oil which crystallized from Et_2O–petroleum ether to give 0.9 g (33% overall) of **8b** as fluffy white crystals. An additional 0.6 g (22%) of **8b** was obtained by the addition of more petroleum ether to the mother liquor of the first crop. Recrystallization from C_6H_6–petroleum ether gave a total of 1.3 g (50%) of **8b** as a white solid, mp 217–220°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{10}H_5N_2O_4F_3$: C, 43.81; H, 1.84; N, 10.22. Found: C, 43.54; H, 1.66; N, 10.26.

1-(*o*-Benzyloxyphenyl)-2-(*p*-toluenesulfonyl)diimide (17).—*o*-Benzyloxyaniline hydrochloride (11.8 g, 0.05 mol) dissolved in 100 ml of MeOH and 100 ml of 3 *N* HCl was stirred and cooled to 0°. To this solution was added $NaNO_2$ (3.45 g, 0.05 mol) dissolved in 25 ml of H_2O in the course of 15 min. The solution was stirred and cooled for 15 min, after which it was cooled to −5°. The solution was adjusted to pH 5 with NaOAc (30 g in 150 ml of H_2O). A precooled (−5°) solution of sodium *p*-toluenesulfinite (8.9 g, 0.05 mol) in 150 ml of H_2O was added rapidly to this solution, resulting in the formation of solid lumps. The mixture was stirred and the lumps were disintegrated to a powder after stirring for 1 hr at −5°. The solid was collected by filtration and dissolved in 300 ml of C_6H_6. The C_6H_6 solution was washed with 100 ml of H_2O, 100 ml of 5% $NaHCO_3$ solution, and 100 ml of H_2O. The organic solution was dried (Na_2SO_4) and the solvent was removed *in vacuo* to give a solid which was recrystallized by dissolving in hot C_6H_6 and adding Et_2O to give 16.9 g (92%) of **17** as pale orange needles, mp 113–116°; the spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{20}H_{18}N_2O_3S$: C, 65.56; H, 4.95; N, 7.64. Found: C, 65.45; H, 4.68; N, 7.60.

1-(*o*-Benzyloxyphenyl)-2-(*p*-toluenesulfonyl)hydrazine (18).—1-(*o*-Benzyloxyphenyl)-2-(*p*-toluenesulfonyl)diimide (**17**, 14.6 g, 0.04 mol) was suspended and stirred in 250 ml of 95% EtOH at 0°. To this suspension was added 40 ml of HOAc, followed by Zn dust (13.4 g, 0.20 g-atom). The mixture was stirred and cooled for 1 hr, after which the ice bath was removed and stirring was continued for 1 hr. The thick suspension was filtered and the filtrate was saved. The filter cake was dispersed in 60 ml of EtOH and 20 ml of HOAc and heated on a steam bath for 15 min, then filtered. The filtrate was saved and the filter cake was treated twice more with hot HOAc in EtOH to give two more filtrates. The combined filtrates were treated with two volumes of H_2O and cooled to 5° for several hours. The solid was collected by filtration and recrystallized (90% EtOH) to give 9.7 g (66%) of **18** as pale yellow needles, mp 134–136°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{20}H_{20}N_2O_3S$: C, 65.20; H, 5.47; N, 7.60. Found: C, 65.48; H, 5.51; N, 7.64.

1-(*o*-Benzyloxyphenyl)-1-ethyloxalyl-2-(*p*-toluenesulfonyl)hydrazine (19).—1-(*o*-Benzyloxyphenyl)-2-(*p*-toluenesulfonyl)hydrazine (**18**, 3.6 g, 0.015 mol) and ethyl oxalyl chloride (1.5 g, 0.011 mol) were stirred and heated to 50° in anhydrous C_6H_6 containing $NaHCO_3$ (0.84 g, 0.01 mol) for 2 hr. The reaction mixture was combined with 50 ml of C_6H_6 and washed four times with 70 ml of H_2O and once with 50 ml of saturated NaCl solution. The C_6H_6 solution was dried (Na_2SO_4) and the solvent was removed to give a dark oil, which crystallized slowly from 10 ml of Et_2O. Recrystallization (Me_2CO–Et_2O) gave 2.0 g (44%) of **19** as white crystals, mp 113–114.5°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{24}H_{24}N_2SO_6$: C, 61.52; H, 5.16; N, 5.98. Found: C, 61.17; H, 5.30; N, 5.61.

4-(*p*-Toluenesulfonamido)-1,4-benzoxazine-2,3-dione (20).—1-(*o*-Benzyloxyphenyl)-1-ethyloxalyl-2-(*p*-toluenesulfonyl)hydrazine (**19**, 0.46 g, 0.001 mol) was hydrogenated at 25° under 1-atm pressure with 100 mg of 5% Pd/C as the catalyst and 40 ml of EtOAc as the solvent. The uptake of H_2 slowed appreciably after 0.001 mol had been consumed. The catalyst was removed by filtration and the solvent was removed *in vacuo* to give a solid which was recrystallized (C_6H_6) to give 0.20 g (63%) of an amorphous white solid, Recrystallization (Me_2CO–Et_2O) gave the same white solid, mp 200–202°; spectral data are consistent with the assigned structure.

Anal. Calcd for $C_{15}H_{12}N_2O_5S$: C, 54.21; H, 3.64; N, 8.43. Found: C, 54.11; H, 3.49; N, 8.75.

Registry No.—**4**, 34288-06-7; **5a**, 34288-07-8; **5b**, 34288-08-9; **8a**, 34288-09-0; **8b**, 34288-10-3; **10**, 34288-11-4; **11**, 34288-12-5; **12**, 34288-13-6; **13**, 34288-14-7; **17**, 34288-15-8; **18**, 34288-16-9; **19**, 34288-17-0; **20**, 34288-18-1; *o*-benzyloxyacetanilide, 34288-19-2.

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Heteroaromatic Fused-Ring Mesoionic Compounds. Sydno[3,4-*a*]quinoxalines[1]

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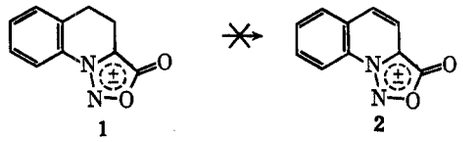
A number of derivatives of sydno[3,4-*a*]quinoxalines have been synthesized from 3-(*o*-nitrophenyl)sydnone. Incorporation of the five-membered mesoionic sydnone ring into a conjugated fused-ring heteroaromatic system produces compounds of enhanced stability toward thermal and aqueous acid-catalyzed decomposition. Susceptibility toward base-catalyzed reaction is increased. SCF molecular orbital treatments were found to be useful in predicting electronic absorption spectra, relative stability of tautomers, and the probable site of O alkylation.

Sydnones have been the most extensively studied member of mesoionic heterocyclic systems.[2] Classified as nonbenzenoid aromatic compounds, sydnones possess an unusual electronic structure characterized by an interplay of charge separation and electron delocalization. A large number of sydnone derivatives have been reported to date, many of which have been found to possess one or more of a wide variety of biological activities.[3] Despite this activity in sydnone chemistry, no conjugated heteroaromatic fused-ring sydnones have been reported.[4] Hammick and Voaden[5] have reported unsuccessful attempts to prepare sydno[3,4-*a*]quinoline (**2**) from 4,5-dihydrosydno[3,4-*a*]quinoline (**1**).



1 **2**

We wish to report the syntheses of a number of quinoxaline ring-fused sydnones. The effect upon the molecular properties of sydnones produced by this ring fusion were examined by quantum chemical and spectroscopic methods.

Results and Discussion

Despite the failures to prepare **2** and the absence of reported examples of heteroaromatic fused-ring sydnone derivatives, there is no apparent rationale to suggest a destabilizing influence effected by such a ring fusion. Stabilization achieved by such extended conjugation might be of practical significance, since many of the simple sydnones with potentially useful biological activities lack thermal stability and frequently darken upon exposure to light and air.[6]

The initial objective of this investigation was sydno[3,4-*a*]quinoxalin-4-one (**3**), chosen in part because of the electron-withdrawing effect upon the sydnone 4 position as depicted in the valence-bond representation **3b**. Electron-withdrawing substituents at C-4 in sydnones have been observed to enhance their stability, especially toward acid-catalyzed ring-opening hydrolysis.[7]

In order to estimate the perturbation of the sydnone π-electron system effected by this ring fusion, we have compared the results of semiempirical Pople–Parr–Pariser SCF–MO treatments of the π systems of *N*-phenylsydnone and **3**. For sydnones, the results of this type of treatment compare favorably with those obtained from CNDO/2 calculations.[8] The results of

(1) Taken in part from the M.S. Thesis of J. P. O'Donnell, SUNY/B, Sept 1971. Presented at the 3rd Northeast Regional Meeting of the American Chemical Society, Buffalo, N. Y., Oct 13, 1971.

(2) W. Baker and W. D. Ollis, *Quart. Rev., Chem. Soc.*, **11**, 15 (1959); F. H. C. Stewart, *Chem. Rev.*, **64**, 129 (1964).

(3) L. B. Kier and E. B. Roche, *J. Pharm. Sci.*, **56**, 149 (1967); E. Ackermann, *Pharmazie*, **22**, 537 (1967).

(4) M. Ohta and H. Kato in "Nonbenzenoid Aromatics," Vol. I, J. P. Snyder, Ed., Academic Press, New York, N. Y., 1969.

(5) D. L. Hammick and D. J. Voaden, *J. Chem. Soc.*, 3303 (1961).

(6) *N*-Methylsydnone darkens upon distillation at reduced pressure even in a short-path Kugelrohr distillation apparatus.

(7) F. H. C. Stewart, unpublished results cited in ref 2.

(8) F. P. Billingsley and J. E. Bloor, *Theor. Chim. Acta*, **11**, 325 (1968).