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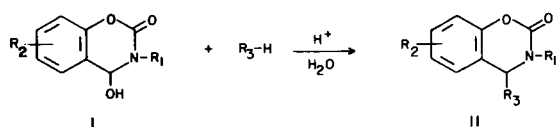
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Received March 27, 1978

A series of 3,4-Dihydro-2-oxo-(3-substituted-2*H*-1,3-benzoxazin-4-yl)ureas (II, Table I) and 3,4-dihydro-2-oxo-(3-substituted-2*H*-1,3-benzoxazin-4-yl)thioureas (Table II) was prepared by treating 3,4-dihydro-4-hydroxy-3-substituted-2*H*-1,3-benzoxazin-2-ones with ureas and thioureas, respectively. In the presence of alcoholic alkali these compounds underwent transacylation to dihydro-6-(2-hydroxyaryl)-1,3,5-triazine-2,4-(1*H*,2*H*)diones (Table III) and their 4-thio analogues (Table IV).

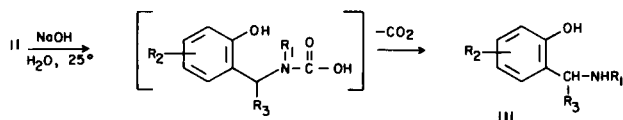
J. Heterocyclic Chem., 15, 1193 (1978)

In the previous paper (2) we had described a facile, acid-catalyzed condensation of 3-alkyl-3,4-dihydro-4-hydroxy-2*H*-1,3-benzoxazin-2-ones (I) with compounds having active hydrogens to give 4-substituted derivatives (II).



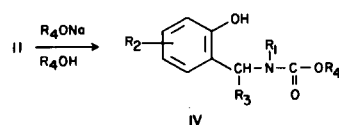
This paper describes the utilization of ureas as the nucleophile. Substituted ureas were generally condensed with 4-hydroxybenzoxazinones in benzene or chloroform under the azeotropic conditions in the presence of traces of mineral acids. For the unsubstituted ureas, because of their low solubilities in nonpolar solvents, anhydrous ethanol or *N,N*-dimethylformamide were used as the reaction media. When two equivalents of 4-hydroxybenzoxazinone derivatives were used, the bis benzoxazines were obtained. The naphthyl analogues such as 2-alkyl-1-hydroxy-1*H*-naphth[1,2-*e*][1,3]oxazin-3(2*H*)ones condensed with the ureas in an analogous way (Table I). The thioureas condensed as easily under similar conditions with 4-hydroxybenzoxazinones giving the thio analogues in comparable yields (Table II).

While being relatively stable towards acidic reagents, compounds of type II were shown (2) to be very sensitive to alkali, and undergo cleavage of the cyclic carbamate giving the 2-(aminomethyl)phenol derivatives of type III.



This in effect, constitutes a new and facile method of obtaining substituted 2-hydroxybenzylamines which are otherwise inaccessible.

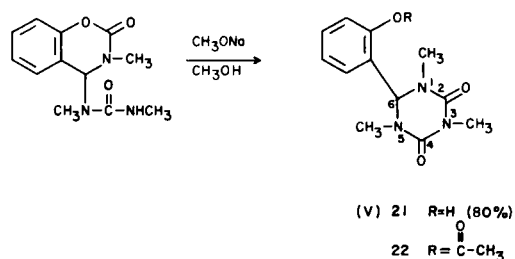
When the reaction was carried out in anhydrous alcohol,



the open-chained phenolic carbamates IV were obtained.

The above sequences were always followed when the 4-substituent (R₃) did not contain any functional group capable of participating in the reaction. However, when

R₃ was an urea derivative -NR-C(=O)-NHR'', the transacylation to the urea nitrogen occurred to form the symmetrical triazinedione 21.

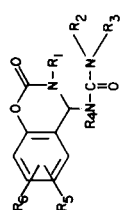


The infrared absorption spectrum (Nujol mull) of 21 exhibits the OH absorption at 3200 cm⁻¹ and two strong carbonyl bands at 1697 and 1640 cm⁻¹, respectively. The nmr (deuteriochloroform) spectrum shows a sharp peak for 1,5-methyls at 2.85, 3-methyl at 3.25, H-6 at 5.61, and broad band for the phenolic proton at 8.15 ppm. The nmr and infrared spectra of an acetate ester of 21 (22) (formed by treating 21 with cold acetic anhydride) showed practically no change, except for the disappearance of the free OH and presence of an acetyl function [ν_{c=O} 1765 cm⁻¹; δ 2.32 (CH₃CO) ppm, Table III].

The thiourea derivatives follow the same pattern giving 1-alkyl-tetrahydro-6-(2-hydroxyaryl)-4-thioxo-1,3,5-triazin-2(1*H*)ones (Table IV).

Table I

(3-Alkyl-3,4-dihydro-2-oxo-2H-1,3-benzoxazin-4-yl)ureas

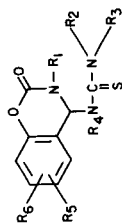


Compound	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Empirical Formula	M.p. °C	% Yield	Calcd.		Found			
										C	H	N	C	H	N
1	CH ₂ CH=CH ₂	H	CH ₃	CH ₃	H	H	C ₁₄ H ₁₇ N ₃ O ₃	148-149	81 (b)	61.08	6.22	15.26	61.18	6.27	15.20
2	CH ₂ C(O)C ₂ H ₅	H	CH ₃	CH ₃	H	H	C ₁₅ H ₁₉ N ₃ O ₃	139-140	90 (b)	56.06	5.96	13.08	55.76	6.10	13.16
3	CH ₃	H	H	H	H	H	C ₁₀ H ₁₁ N ₃ O ₃	203-204	88 (c)	54.29	5.01	19.00	54.18	5.28	19.25
4	CH ₃	H	H	H	H	8-OCH ₃	C ₁₁ H ₁₃ N ₃ O ₄	216-218 (a)	85 (c)	52.58	5.22	16.73	52.30	5.51	16.47
5	CH ₂ CH=CH ₂	H	CH	CH	6-Cl	H	C ₁₄ H ₁₆ ClN ₃ O ₃	140-141	78 (b)	54.29	5.21	13.57	54.58	5.30	13.64
6	CH ₂ CH=CH ₂	H	CH ₃	CH ₃	H	8-OCH ₃	C ₁₅ H ₁₉ N ₃ O ₄	150-151	58 (b)	59.00	6.27	13.76	59.27	6.39	13.54
7	CH ₃	H		H	H	H	C ₁₉ H ₁₈ N ₄ O ₅	269-270 (a)	69 (c)	59.68	4.75	14.65	59.65	4.88	14.92
8	CH ₃	H	C ₆ H ₅	C ₆ H ₅	7-OCH ₃	H	C ₂₃ H ₂₁ N ₃ O ₄	210-211 (a)	69 (b)	68.47	5.25	10.42	68.27	5.31	10.40
9	CH ₃	H	C ₆ H ₅	H	H	H	C ₁₆ H ₁₅ N ₃ O ₃	194-195 (a)	72 (b)	64.63	5.09	14.14	64.66	5.30	14.43
10	CH ₃	H	CH ₃	CH ₃		R ₅ , R ₆ = 5,6-	C ₁₆ H ₁₇ N ₃ O ₃	197-198 (a)	83 (b)	64.20	5.72	14.04	64.48	5.58	13.91

(a) Melts with decomposition. (b) Prepared *via* Method A. (c) Prepared *via* Method B.

Table II

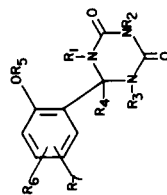
(3-Alkyl-3,4-dihydro-2-oxo-2H-1,3-benzoxazin-4-yl)thioureas



Compound	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Empirical Formula	M.p. °C	% Yield	Calcd.			Found		
										C	H	N	C	H	N
11	CH ₃	H	H	H	H	H	C ₁₀ H ₁₁ N ₃ S ₂	206-207 (a)	79 (c)	50.62	4.67	17.71	50.87	4.84	17.42
12	CH ₃	H		H	H	H	C ₁₉ H ₁₈ N ₄ S ₄	219-220 (a)	51 (d)	57.28	4.55	14.06	57.57	4.86	14.01
13	CH ₃	H	H	H	H	H	C ₁₀ H ₁₀ BrN ₃ S ₂	213-214 (a)	72 (d)	37.90	3.19	13.23	38.19	3.20	13.45
14	CH ₃	H	H	H	H	H	C ₁₀ H ₁₀ ClN ₃ S ₂	213-214 (a)	94 (d)	44.20	3.71	15.46	44.33	3.79	15.60
15	CH ₃	H	CH ₃	H	H	H	C ₁₁ H ₁₃ N ₃ S ₂	198-199 (a)	77 (b)	52.57	5.21	16.72	52.87	5.41	16.77
16	CH ₃	H	C ₆ H ₅	H	H	H	C ₁₆ H ₁₅ N ₃ S ₂	203-204 (a)	92 (b)	61.32	4.82	13.11	61.39	4.97	13.25
17		H	CH ₃	H	H	H	C ₁₆ H ₂₀ ClN ₃ S ₂	194-195 (a)	76 (b)	54.31	5.70	11.87	54.58	5.59	12.01
18	CH ₃	H	CH ₃	H		H	C ₁₅ H ₁₅ N ₃ S ₂	203-204 (a)	82 (b)	59.78	5.02	13.94	59.70	5.10	14.01
19		H	CH ₃	H	H	H	C ₁₅ H ₂₂ N ₄ O ₂ S	178-179 (a)	69 (b)	55.88	6.88	17.38	55.75	6.99	17.64

(a) Melts with decomposition. (b) Prepared *via* Method A. (c) Prepared *via* Method B. (d) Prepared *via* Method C.

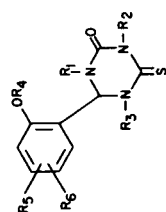
Table III


1-Alkylidihydro-6-(2-hydroxyaryyl)-1,3,5-triazine-2,4-(1*H*,3*H*)diones

Compound	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	Empirical Formula	M.p. °C	% Yield	Calcd.			Found		
											C	H	N	C	H	N
21	CH ₃	CH ₃	CH ₃	H	H	H	H	C ₁₂ H ₁₅ N ₃ O ₃	206-207	80	57.82	6.07	16.86	58.08	6.17	16.89
22	CH ₃	CH ₃	CH ₃	H	COCH ₃	H	H	C ₁₉ H ₁₇ N ₃ O ₄	132-133	85	57.72	5.88	14.43	57.87	6.13	14.21
23	CH ₃	H	H	H	H	H	H	C ₁₀ H ₁₁ N ₃ O ₃	244-245 (a)	87	54.29	5.01	19.00	54.21	5.17	19.29
24	CH ₃	H	H	H	H	3-OCH ₃	H	C ₁₁ H ₁₃ N ₃ O ₄	208-209 (a)	85	52.58	5.22	16.73	52.47	5.33	16.66
25	CH ₂ -C(=O)-OH	CH ₃	CH ₃	H	H	H	H	C ₁₃ H ₁₅ N ₃ O ₅	194-195 (a)	48	53.24	5.16	14.33	53.37	5.47	14.25
26	CH ₃		H	H	H	H	H	C ₁₆ H ₁₅ N ₃ O ₃	196-197 (a)	57	64.63	5.09	14.14	64.74	4.88	14.42
27	CH ₃	CH ₃	CH ₃	H	H	R ₆ , R ₇ =		C ₁₆ H ₁₇ N ₃ O ₃	227-229 (a)	91	64.20	5.72	14.04	64.15	5.81	13.84
28	CH ₃		H		H	4-OCH ₃	H	C ₂₃ H ₂₁ N ₃ O ₄	208-209 (a)	87	68.47	5.25	10.42	68.40	5.30	10.16
29	CH ₃	CH ₃	CH ₃	H	CONHC ₂ H ₅	H	H	C ₁₅ H ₂₀ N ₄ O ₄	122-123	87	56.24	6.29	17.49	56.08	6.24	17.67
30	CH ₃	CH ₃	CH ₃	H		H	H	C ₂₆ H ₂₅ N ₃ O ₄	95-96	81	70.41	5.68	9.48	70.29	5.62	9.41
31	CH ₂ CH=CH ₂	CH ₃	CH ₃	H	H	3-OCH ₃	H	C ₁₅ H ₁₉ N ₃ O ₄	118-119	79	59.00	6.27	13.76	58.70	6.39	13.95
32	CH ₂ CH=CH ₂	CH ₃	CH ₃	H	H	H	H	C ₁₄ H ₁₇ N ₃ O ₃	157-158	75	61.08	6.22	15.26	61.22	6.39	15.17
33	CH ₂ CH=CH ₂	CH ₃	CH ₃	H	H	5-Cl	H	C ₁₄ H ₁₆ ClN ₃ O ₃	174-175	76	54.29	5.21	13.57	54.39	5.32	13.33

(a) Melts with decomposition.

Table IV
1-Alkyltetrahydro-6-(2-hydroxyary)-4-thioxo-1,3,5-triazin-2(1H)ones



Compound	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Empirical Formula	M.p. °C	% Yield	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
34	CH ₃	H	H	H	H	H	C ₁₀ H ₁₁ N ₃ O ₂ S	259-260 (a)	70	50.62	4.67	17.71	50.92	4.96	17.60
35	CH ₃	H	H	COCH ₃	H	H	C ₁₂ H ₁₃ N ₃ O ₃ S	196-197 (a)	85	51.60	4.69	15.04	51.75	4.62	15.17
36	CH ₃	H	H	H	5-Br	H	C ₁₀ H ₁₀ BrN ₃ O ₂ S	260-261 (a)	78	37.99	3.19	13.29	38.17	3.39	13.31
37	CH ₃	H	H	H	5-Cl	H	C ₁₀ H ₁₀ ClN ₃ O ₂ S	253-254 (a)	67	44.20	3.71	15.46	44.36	3.79	15.43
38	CH ₃	CH ₃	H	H	H	H	C ₁₁ H ₁₃ N ₃ O ₂ S	186-187 (a)	66	52.57	5.21	16.72	52.77	5.38	16.60
39	CH ₃		H	H	H	H	C ₁₆ H ₁₅ N ₃ O ₂ S	219-220 (a)	67	61.32	4.82	13.41	61.33	4.95	13.31

(a) Melts with decomposition.

EXPERIMENTAL

Physical constants, yields, and analytical values for the compounds below are reported in Tables I-IV. Melting points were determined using a Thomas-Hoover capillary melting point apparatus which was calibrated against known standards. The ultraviolet and infrared spectra were obtained, respectively, with a Beckman DK-1 spectrophotometer and a Baird Model 455 double-beam spectrograph. Unless otherwise stated, the former were determined as solution in 95% ethanol and the latter as Nujol mulls. The nmr spectra were recorded on a Varian A-60 spectrometer with tetramethylsilane as an internal reference. Thin layer chromatography was carried out on silica gel G (Stahl) using acetone, benzene, and heptane in varying proportions, as the eluent. The chromatograms were developed by spraying with iodine solution in ethanol.

3,4-Dihydro-3-alkyl-4-ureido-2H-1,3-benzoxazin-2-ones (Table I) and 4-Thioureido Analogues (Table II).

The examples below illustrate three general methods used for their syntheses.

(1,2-Dihydro-2-methyl-3-oxo-3H-naphtho[1,2-e][1,3]oxazin-1-yl)-N,N'-dimethylurea (10), Method A.

A solution of 10.0 g. (0.0437 mole) of 1-hydroxy-2-methyl-1H-naphth[1,2-e][1,3]oxazin-3(2H)one, 4.6 g. (0.052 mole) of N,N'-dimethylurea and 0.01 g. of *p*-toluenesulfonic acid monohydrate in 300 ml. of anhydrous chloroform was refluxed for 1 hour while 0.7 ml. of water separated in a Dean-Stark trap. The solvent was evaporated and the residue was crystallized from ethyl acetate to give 8.7 g. of analytically pure white crystals, m.p. 197-198° dec. Concentration of the mother liquor to a low volume gave 2.1 g. (total yield, 83%) of an additional product, m.p. 196-198° dec.; ν max (ethanol): nm (ϵ) 227 (61,200), 266 sh (4,700), 272-277 plateau (5,400), 283 (4,600), 287 (4,300), 307 (1,100), 321 (1,100), 321 (1,400); ir (nujol): 3010 (NH), 1739 sh, 1725 (C=O), 1635 (C=O), 1520 (NHCO) cm^{-1} .

Anal. Calcd. for C₁₆H₁₇N₃O₃: C, 64.20; H, 5.72; N, 14.04. Found: C, 64.48; H, 5.58; N, 13.91.

(3,4-Dihydro-3-methyl-2-oxo-2H-benzoxazin-4-yl)urea (3), Method B.

To a hot solution of 5.0 g. (0.028 mole) of 3,4-dihydro-4-hydroxy-3-methyl-2H-1,3-benzoxazin-2-one and 2.5 g. (0.042 mole) of urea in 80 ml. of absolute ethanol was added 5 drops of ethanolic hydrogen chloride, whereupon white crystals began to separate. After 4 hours at 25°, 5.4 g. (88% yield) of the urea derivative was obtained, m.p. 202-203° dec. An analytical sample, m.p. 203-204° dec., was obtained by recrystallization from ethanol; ν max (ethanol): nm 226 (11,200), 266 sh (4,650), 274 (5,400), 288 (4,300); ir (nujol): 3400, 3320 (NH), 1723, 1635 (C=O), 1509 (NHCO) cm^{-1} .

Anal. Calcd. for C₁₀H₁₁N₃O₃: C, 54.29; H, 5.01; N, 19.00. Found: C, 54.18; H, 5.28; N, 19.25.

(6-Bromo-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-thiourea (13), Method C.

A mixture of 6.5 g. (0.025 mole) of 6-bromo-3,4-dihydro-4-hydroxy-3-methyl-2H-1,3-benzoxazin-2-one, 2.0 g. (0.0263 mole) of thiourea, and 0.05 g. of *p*-toluenesulfonic acid monohydrate was dissolved in 30 ml. of dry N,N-dimethylformamide at 40° and allowed to stand at room temperature for 30 hours. The solvent was removed *in vacuo* at 40°. The residue was taken up with 80 ml. of acetonitrile and refluxed for 30 minutes to give 5.9 g. of white crystals, m.p. 206-207° dec. Concentration of

the filtrate to a low volume gave 0.8 g. of an additional product, m.p. 207-208° dec. An analytical sample, m.p. 210-211° dec., was obtained by recrystallization from acetonitrile-tetrahydrofuran (1:1); ν λ max (ethanol): nm (ϵ) 225 (10,300), 266.5 (16,920), 292 (4,800); ir (nujol): 3420 (w), 3250 (m), 3170 (s), 1709 (C=O, vs), 1617 (s) cm^{-1} .

Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{BrN}_3\text{O}_2\text{S}$: C, 37.90; H, 3.19; N, 13.29; S, 10.14. Found: C, 38.19; H, 3.20; N, 13.45; S, 10.22. *N,N'*-Bis(3,4-dihydro-3-methyl-2-oxo-2*H*-1,3-benzoxazin-4-yl)thiourea (**12**).

To a solution of 8.14 g. (0.0455 mole) of 3,4-dihydro-4-hydroxy-3-methyl-2*H*-1,3-benzoxazin-2-one and 1.5 g. (0.0198 mole) of thiourea in 75 ml. of dry *N,N*-dimethylformamide was introduced dry hydrogen chloride to pH 2.0 causing the temperature rise to 50°. After the solution was allowed to stand for 20 hours at room temperature, the solvent was removed *in vacuo*. The oily residue was taken up with 100 ml. of ethyl acetate and refluxed for 1 hour to give 7.6 g. of white crystals, m.p. 220-221° dec. Recrystallization from acetonitrile gave analytically pure product, m.p. 220-221° dec.; ν λ max (ethanol): nm (ϵ) 223 sh (25,400), 256 (13,320), 275 sh (7,200), 287 sh (2,700); ir (nujol): 3240 (N-H), 1738 (C=O) cm^{-1} .

Anal. Calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}_4\text{S}$: C, 57.28; H, 4.55; N, 14.06; S, 8.05. Found: C, 57.33; H, 4.64; N, 14.13; S, 8.04.

1-Alkyldihydro-6-(2-hydroxyaryl)-1,3,5-triazine-2,4(1*H*,3*H*)diones, (Table III).

Dihydro-6-(2-hydroxyphenyl)-1,3,5-trimethyl-1,3,5-triazine-2,4(1*H*,3*H*)dione (**21**).

A mixture of 8.0 g. of *N*-(3,4-dihydro-3-methyl-2-oxo-2*H*-1,3-benzoxazin-4-yl)-*N,N'*-dimethylurea and 3.0 g. of sodium hydroxide pellets in 100 ml. of anhydrous methanol was stirred for 20 minutes and the resulting yellowish colored solution was allowed to stand at room temperature for 3 hours.

Thin layer chromatography (silica gel G; acetone:benzene:heptane, 3:2:1) showed complete conversion, the new product having a slightly faster mobility ($R_f = 0.18$) than the starting material ($R_f = 0.15$). The solution was adjusted to pH 5.0 with acetic acid at 20° and the solvent was removed *in vacuo* at 30°. The residue was taken up with 20 ml. of water and extracted twice with 150 ml. of ethyl acetate. The combined extracts were washed with water and dried over sodium sulfate. Concentration of the solution to ca. 50 ml. and cooling gave 6.4 g. (80%) of analytically pure, white crystals, m.p. 206-207° dec.; ν λ max (ethanol): nm (ϵ) 218 sh (9,000), 278 (3,400), 284 sh (3,200); ir (nujol): 3200 (OH), 1697 (C=O, s) cm^{-1} ; pmr (deuteriochloroform): δ 2.85 (6H, 1,5 CH_3), 3.25 (3H, 3- CH_3), 5.61 (H-6), 8.15 (OH) ppm.

Anal. Calcd. for $\text{C}_{12}\text{H}_{15}\text{N}_3\text{O}_3$: C, 57.82; H, 6.07; N, 16.86. Found: C, 58.08; H, 6.17; N, 16.89.

6-[2-(Acetyloxy)phenyl]dihydro-1,3,5-trimethyl-1,3,5-triazine-2,4(1*H*,3*H*)dione (**22**).

A solution of 1.0 g. of dihydro-6-(2-hydroxyphenyl)-1,3,5-trimethyl-1,3,5-triazine-2,4(1*H*,3*H*)dione, 1.0 ml. of acetic anhydride and 5 drops triethylamine in 20 ml. of dry ethyl acetate was allowed to stand at room temperature for 15 hours. Water (5 ml.) was added to decompose excess acetic anhydride, the organic phase was dried over sodium sulfate and the solvent was evaporated *in vacuo*. Recrystallization of the residue from isopropyl ether-ethyl acetate (2:1) gave 1.0 g. (85%) of analytically pure, shiny needles, m.p. 132-133°; ν λ max (ethanol): nm (ϵ) 264 (460), 270 (400); ir (nujol): 1765 (ester C=O), 1700, 1665 (N-C=O), 1184 (Ar-OC=O, s) cm^{-1} ; pmr (deuteriochloroform): δ

232 (CH₃CO), 2.82 (6H, s, 1,5- CH_3), 3.28 (3- CH_3), 5.46 (H-6) ppm.

Anal. Calcd. for $\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}_4$: C, 57.72; H, 5.88; N, 14.43. Found: C, 57.87; H, 6.13; N, 14.21.

Dihydro-6-(2-hydroxyphenyl)-1-methyl-1,3,5-triazine-2,4(1*H*,3*H*)dione (**23**).

To a stirred solution of 1.6 g. of (3,4-dihydro-3-methyl-2-oxo-2*H*-1,3-benzoxazin-4-yl)urea in 150 ml. of absolute ethanol was added 0.8 g. of potassium hydroxide pellets and allowed to stir for 4 hours at room temperature. The white crystalline precipitate of the resulting potassium salt (1.7 g., m.p. 252-254° dec.) was filtered off and redissolved in 10 ml. of ice-cold water. The aqueous solution was adjusted to pH 5.5 with acetic acid while 1.4 g. (87%) of white crystals separated, m.p. 243-245° dec. Recrystallization from ethanol gave analytically pure product, m.p. 244-245° dec.; ν λ max (ethanol): nm (ϵ) 217 sh (8,800), 278 (3,140); ir (nujol): 3320 (N-H), 3200 (OH), 1703, 1670 (C=O) cm^{-1} ; pmr (deuteriochloroform): δ 2.72 (1- CH_3), 5.77 (H-6, d, J = 3.0 Hz), 7.92 (OH), 9.37, 9.80 (NH)₂ ppm.

Anal. Calcd. for $\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}_3$: C, 54.29; H, 5.01; N, 19.00. Found: C, 54.21; H, 5.17; N, 19.29.

Dihydro-6-(2-hydroxy-3-methoxyphenyl)-1-methyl-1,3,5-triazine-2,4(1*H*,3*H*)dione (**24**).

A mixture of 6.0 g. of (3,4-dihydro-8-methoxy-3-methyl-2-oxo-2*H*-1,3-benzoxazin-4-yl)urea and 2.0 g. of potassium hydroxide pellets in 400 ml. of absolute ethanol was stirred for 7 hours at room temperature and allowed to stand in the refrigerator overnight. The resulting white crystals of the potassium salt (6.6 g., m.p. 237-238°) were dissolved in 40 ml. of ice-cold water and the solution was adjusted to pH 5.5 with acetic acid to give 5.1 g. (85%) of white crystals, m.p. 208-209° dec. Recrystallization from tetrahydrofuran-ethyl acetate (1:1) and then from ethanol gave the analytically pure product, m.p. 208-209° dec.; ν λ max (ethanol): nm (ϵ) (8,800), 282 (3,260); ir (nujol): 3550 (free OH), 3350 (N-H), 3200 (assoc. OH), 1710, 1692, 1680 (C=O) cm^{-1} ; pmr (DMSO-*d*₆): δ 2.63 (1- CH_3), 3.69 (ArOCH₃), 5.58 (H-6, d, J = 2.5 Hz) ppm.

Anal. Calcd. for $\text{C}_{11}\text{H}_{18}\text{N}_3\text{O}_4$: C, 52.58; H, 5.22; N, 16.73. Found: C, 52.47; H, 5.33; N, 16.66.

Hexahydro-6-(2-hydroxyphenyl)-3,5-dimethyl-2,4-dioxo-1,3,5-triazine-1-acetic Acid (**25**).

A mixture of 4.0 g. of ethyl 4-[[dimethylamino]carbonyl]-amino]-3,4-dihydro-2-oxo-2*H*-1,3-benzoxazine-3-acetate, 1.5 g. of potassium hydroxide pellets in 49 ml. absolute ethanol was stirred for 15 minutes at room temperature and allowed to stand for 90 minutes. The ice cold water was added and adjusted to pH 5.0 with dilute hydrochloric acid. After the solvent was removed *in vacuo* at 25°, the aqueous residue was extracted twice with 75 ml. of ethyl acetate. The combined extracts were washed with water, dried over sodium sulfate and the solvent concentrated to a low volume to give 1.6 g. of white crystals m.p. 193.5-195° dec. Recrystallization from ethyl acetate gave analytically pure product, m.p. 194-195° dec.; ν λ max (ethanol): nm (ϵ) 216 sh (9,000), 278 (3,200), 283 sh (3,100); ir (nujol): 3010 (OH), 1743 (HO-C=O), 1664 (N-C=O) cm^{-1} ; pmr (DMSO-*d*₆): 2.78 (5- CH_3), 3.12 (3- CH_3), 3.59, 4.31 (2H, dd, J = 17.0 Hz, non-equivalent CH₂), 5.81 (H-6) ppm.

Anal. Calcd. for $\text{C}_{13}\text{H}_{15}\text{N}_3\text{O}_5$: C, 53.24; H, 5.16; N, 14.33. Found: C, 53.37; H, 5.47; N, 14.25.

Dihydro-6-(2-hydroxyphenyl)-1-methyl-3-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)dione (**26**).

A suspension of 6.0 g. (0.02 mole) of *N*-(3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-*N'*-phenylurea and 2.0 g. of potassium hydroxide pellets in 60 ml. of absolute methanol was stirred for 1 hour. Acetic acid was added to pH 5.0, and the solution was evaporated to dryness *in vacuo*. The residue was taken up with water and extracted twice with 100 ml. of ethyl acetate. The residue was refluxed with 100 ml. of isopropyl ether for 1 hour and gave, on cooling, 3.7 g. of white crystals, m.p. 192-194° dec. Recrystallization from acetonitrile gave 3.4 g. (57% yield) of analytically pure product, m.p. 196-197° dec.; uv λ max (ethanol): nm (ϵ) 116 infl. (14,000), 275.5 (3,050), 282 sh (2,950); ir (chloroform): 3615 (OH), 3470 (NH), 1725, 1680 (C=O) cm^{-1} ; pmr (DMSO- d_6): δ 2.72 (CH₃), 5.70 (H-6, d, J = 3.5 Hz), 8.35 (H-5, d, J = 3.5 Hz), 9.98 (OH) ppm.

Anal. Calcd. for C₁₆H₁₅N₃O₃: C, 64.63; H, 5.09; N, 14.14. Found: C, 64.74; H, 4.88; N, 14.42.

Dihydro-6-(2-hydroxy-1-naphthalenyl)-1,3,5-trimethyl-1,3,5-triazine-2,4(1H,3H)dione (27).

A mixture of 8.0 g. of *N*-(1,2-dihydro-2-methyl-3-oxo-3H-naphtho[1,2-*e*][1,3]oxazin-1-yl)-*N,N'*-dimethylurea and 3.5 g. of potassium hydroxide pellets in 100 ml. of absolute ethanol was stirred for 20 minutes and the resulting clear, yellowish solution was acidified with ice-cold acetic acid to pH 5.5, and the excess ethanol was removed *in vacuo* at 30°. The residue was taken up with 25 ml. of water and extracted twice with 200 ml. of ethyl acetate. The combined organic extracts were washed with 50 ml. of water, dried over sodium sulfate and concentrated to ca. 120 ml. to give 6.2 g. of analytically pure white crystals, m.p. 227.5-229° dec. Concentration of the mother liquor to ca. 50 ml. and cooling gave 1.1 g. of white crystals (total yield: 91%), m.p. 227-229°; uv λ max (ethanol): nm (ϵ) 237 (76,400), 258 sh (3,200), 266 (4,600), 279 (5,840), 290 (5,000), 322 (2,900), 334 (3,500); ir (nujol): 3100 (OH), 1695 (C=O, s), 1635 (C=O, s) cm^{-1} ; pmr (deuteriochloroform): δ 2.72 (6H, s, 1,5-CH₃), 6.55 (H-6), 8.75 (OH) ppm.

Anal. Calcd. for C₁₆H₁₇N₃O₃: C, 64.20; H, 5.72; N, 14.04. Found: C, 64.15; H, 5.81; N, 13.84.

Dihydro-6-(2-hydroxy-4-methoxyphenyl)-1-methyl-3,6-diphenyl-1,3,5-triazine-2,4(1H,3H)dione (28).

To a stirred suspension of 10.0 g. (0.025 mole) of (3,4-dihydro-7-methoxy-3-methyl-2-oxo-4-phenyl-2H-1,3-benzoxazin-4-yl)-*N'*-phenylurea in 150 ml. of methanol was added 3.0 g. of sodium hydroxide pellets and the resulting clear yellowish solution was allowed to stand at 25° for 2 hours. Glacial acetic acid was added at 0° to pH 5.0, and the solvent was removed *in vacuo*. The residue was taken up with 200 ml. of ethyl acetate and 100 ml. of tetrahydrofuran, washed, dried over sodium sulfate, and concentrated to ca. 80 ml. giving 7.1 g. of white crystalline product of analytical purity, m.p. 208-209° dec. Further concentration of the mother liquor gave 1.6 g. (total yield: 87%) of additional material, m.p. 208-209° dec.; uv λ max (ethanol): nm (ϵ) 230 infl. (4,600), 277 (1,340), 284 (1,220); ir (nujol): 3380 (NH), 3220-3050 (OH), 1711, 1668 (C=O) cm^{-1} .

Anal. Calcd. for C₂₃H₂₁N₃O₄: C, 68.47; H, 5.25; N, 10.42. Found: C, 68.40; H, 5.30; N, 10.16.

Dihydro-6-(2-hydroxy-3-methoxyphenyl)-3,5-dimethyl-1-(2-propenyl)-1,3,5-triazine-2,4(1H,3H)dione (31).

A solution of crude *N*-(3,4-dihydro-8-methoxy-2-oxo-3-(2-propenyl)-2H-1,3-benzoxazin-4-yl)-*N,N'*-dimethylurea (15.5 g., 0.051 mole) and 6.0 g. of potassium hydroxide pellets in 50 ml. of anhydrous methanol was allowed to stand at room temperature for 2 hours. The solution was adjusted to pH 5.5 with cold dilute

acetic acid and the excess methanol was removed *in vacuo* at 30°. The aqueous residue was extracted with ethyl acetate, the extract was dried over sodium sulfate, and the solvent was removed *in vacuo*. Crystallization from isopropyl ether gave 11.0 g. of white crystals, m.p. 118-119°. Upon concentration of the mother liquor to a low volume, an additional crop of 1.3 g. of off-white crystalline product was obtained (total yield, 79%), m.p. 116-118°. Recrystallization from isopropyl ether-ethyl acetate (2:1) gave analytically pure product, m.p. 118-119°; uv λ max (ethanol): nm (ϵ) 225 sh (10,100), 283 (3,420); ir (nujol): 3270 (OH), 1690, 1658 (C=O), 1266 (Ar-O-CH₃) cm^{-1} .

Anal. Calcd. for C₁₅H₁₉N₃O₄: C, 59.00; H, 6.27; N, 13.76. Found: C, 58.70; H, 6.39; N, 13.95.

Dihydro-6-(2-hydroxyphenyl)-3,5-dimethyl-1-(2-propenyl)-1,3,5-triazine-2,4(1H,3H)dione (32).

A mixture of 10.0 g. of *N*-(1,3,4-dihydro-2-oxo-3-(2-propenyl)-2H-1,3-benzoxazin-4-yl)-*N,N'*-dimethylurea and 4.3 g. of potassium hydroxide pellets in 100 ml. of absolute ethanol was stirred for 4 hours at room temperature. Ice cold water and acetic acid were added to pH 5.5, and the solvent was removed *in vacuo* at 25°. The residue was taken up with ethyl acetate, washed with water, dried over sodium sulfate, and the solvent evaporated. Recrystallization of the residue from isopropyl ether gave 5.7 g. of analytically pure white crystals, m.p. 157.5-159°. Upon concentration of the mother liquor to a low volume, an additional crop of 2.6 g. of product (total yield: 75%), m.p. 157-158° was obtained; uv λ max (ethanol): 220 sh (9,000), 280 (3,400); ir (nujol): 3190 (OH), 1690, 1654 (C=O, s) cm^{-1} .

Anal. Calcd. for C₁₄H₁₇N₃O₃: C, 61.08; H, 6.22; N, 15.26. Found: C, 61.22; H, 6.39; N, 15.17.

6-(5-Chloro-2-hydroxyphenyl)dihydro-3,5-dimethyl-1-(2-propenyl)-1,3,5-triazine-2,4(1H,3H)dione (33).

A mixture of 11.0 g. (0.0358 mole) of *N*-[6-chloro-3,4-dihydro-2-oxo-3-(2-propenyl)-2H-1,3-benzoxazin-4-yl]-*N,N'*-dimethylurea, and 4.5 g. of potassium hydroxide pellets in 150 ml. of absolute methanol was stirred for 10 minutes, and the resulting clear, yellowish solution was allowed to stand at room temperature for 3 hours. The solution was adjusted to pH 5.5 with ice-cold dilute acetic acid, and the excess methanol was removed *in vacuo* at 30°. The aqueous residue was extracted with 350 ml. of ethyl acetate, the extracts were washed with 10 ml. of a saturated sodium chloride aqueous solution and dried over sodium sulfate. Concentration of the solution to ca. 80 ml. and cooling gave 5.5 g. of analytically pure white crystals, m.p. 174-175°. Further concentration of the mother liquor to a low volume gave an additional crop of 1.7 g. of product, m.p. 174-175°. Upon evaporation of the mother liquor to dryness and treatment with 20 ml. of refluxing isopropyl ether, 1.2 g. (total yield: 76%) of nearly white crystals, m.p. 173-174°, was obtained; uv λ max (ethanol): nm (ϵ) 229 (9,550), 290 (3,380); ir (nujol): 3180 (OH), 1700, 1642 (C=O) cm^{-1} .

Anal. Calcd. for C₁₄H₁₆ClN₃O₃: C, 54.29; H, 5.21; N, 13.57; Cl, 11.45. Found: C, 54.39; H, 5.32; N, 13.33; Cl, 11.26.

1-Alkyl-dihydro-6-(2-hydroxyaryl)-4-thio-1,3,5-triazine-2,4(1H,3H)diones (Table IV).

Tetrahydro-6-(2-hydroxyphenyl)-1-methyl-4-thioxo-1,3,5-triazin-2(1H)one (34). To a solution of 5.4 g. (0.023 mole) of (3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)thiorurea in 50 ml. of dry methanol was added 3.0 g. of potassium hydroxide pellets and allowed to stand at 5° overnight. The solution was treated with glacial acetic acid to pH 5.0, and the solvent was removed *in vacuo*. The residue was stirred with cold water and

the resulting white crystals (4.3 g., m.p. 255-256° dec.) were collected by filtration. Recrystallization from ethyl acetate-tetrahydrofuran gave 3.8 g. (70% yield) of analytically pure product, m.p. 259-260° dec.; uv λ max (ethanol): nm (ϵ) 268 (20,650); ir (nujol): 3280 (NH, OH), 1700 (C=O), 1550 (CONH) cm^{-1} ; pmr (DMSO- d_6): δ 2.70 (CH₃), 5.74 (H-6, d, J = 2.7 Hz) ppm.

Anal. Calcd. for C₁₀H₁₁N₃O₂S: C, 50.62; H, 4.67; N, 17.71; S, 13.51. Found: C, 50.92; H, 4.96; N, 17.60; S, 13.54.

6-[2(Acetyloxy)phenyl]dihydro-1-methyl-4-thio-1,3,5-triazine-2,4(1H,3H)dione (35).

A solution of 4.5 g. (0.0198 mole) of tetrahydro-6-(2-hydroxyphenyl)-1-methyl-4-thio-1,3,5-triazin-2(1H)one, 8.0 g. of acetic anhydride and 2 ml. of triethylamine in 25 ml. of dry *N,N*-dimethylformamide was allowed to stand 24 hours at 25°. The solution was evaporated *in vacuo*, and the residue was crystallized from ethyl acetate giving 4.5 g. (85% yield) of pure acetate, m.p. 196-197° dec.; uv λ max (ethanol): nm (ϵ) (20,800); ir (nujol): 3190, 3100 (NH), 1770 (C=O ester), 1713, 1681 (NHCO) cm^{-1} ; pmr (DMSO- d_6): δ 2.30 (COCH₃), 2.63 (N-CH₃), 5.78 (H-6, d, J = 3.5 Hz), 9.98 (H-5, d, J = 3.5 Hz), 10.12 (H-3) ppm.

Anal. Calcd. for C₁₂H₁₃N₃O₃S: C, 51.60; H, 4.69; N, 15.04; S, 11.48. Found: C, 51.75; H, 4.62; N, 15.17; S, 11.25.

6(6-Bromo-2-hydroxymethyl)tetrahydro-1-methyl-4-thio-1,3,5-triazin-2(1H)one (36).

A mixture of 4.9 g. (0.0155 mole) of (5-bromo-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-yl)thiourea and 1.9 g. of sodium methoxide (0.031 mole) in 40 ml. of absolute methanol was stirred for 1 hour. The resulting clear solution was treated with acetic acid to pH 5.5 and evaporated to dryness *in vacuo*. The residue was extracted twice with 50 ml. of tetrahydrofuran-ethyl acetate, dried over sodium sulfate and evaporated to dryness. Crystallization of the residue from ethanol gave 3.8 g. (78% yield) of pure product as white crystals, m.p. 260-261° dec.; uv λ max (ethanol): nm (ϵ) 226 infl. (11,300), 269.5 (20,000), 295 infl. (3,300); ir (nujol): 3190 (NH, OH), 1690 (C=O), 1572 (NHCO) cm^{-1} ; pmr (DMSO- d_6): δ 2.70 (CH₃), 5.78 (H-6, d, J = 4.0 Hz), 10.37 (OH), 10.61 (H-3) ppm.

Anal. Calcd. for C₁₀H₁₀BrN₃O₂S: C, 37.99; H, 3.19; N, 13.29; S, 10.14. Found: C, 38.17; H, 3.39; N, 13.31; S, 10.42.

6-(5-Chloro-2-hydroxyphenyl)tetrahydro-1-methyl-4-thio-1,3,5-triazin-2(1H)one (37).

A mixture of 10.0 g. (0.0368 mole) of 6-chloro-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-yl)thiourea and 4.0 g. (0.0736 mole) of sodium methoxide in 120 ml. of absolute methanol was stirred 1 hour. To the clear, yellowish solution was added acetic acid dropwise to pH 5.5 and the resulting white precipitate (10.0 g.) was collected by filtration, m.p. 248-249° dec. Recrystallization from ethyl acetate gave 6.7 g. (67% yield) of pure product, m.p. 253-254° dec.; uv λ max (ethanol): nm (ϵ) 225-228.5 (20,400), 295 infl. (3,500); ir (nujol): 3190 (OH, NH), 1690

(C=O), 1570 (NHCO) cm^{-1} .

Anal. Calcd. for C₁₀H₁₀ClN₃O₂S: C, 44.20; H, 3.71; N, 15.46; Cl, 13.05. Found: C, 44.36; H, 3.79; N, 15.43; Cl, 12.86.

Tetrahydro-6-(2-hydroxyphenyl)-1,3-dimethyl-4-thio-1,3,5-triazin-2(1H)one (38).

A mixture of 12.6 g. (0.05 mole) of *N*-(3,4-dihydro-2-methyl-2-oxo-1,3-benzoxazin-4-yl)-*N'*-methylthiourea and 5.4 g. (0.1 mole) of sodium methoxide was stirred one hour at 25°. Acetic acid was added to pH 5.5 and the solution was evaporated *in vacuo*. The residue was taken up with water, stirred 1 hour and collected (11.8 g., m.p. 183-184° dec.) by filtration. Crystallization from tetrahydrofuran-ethyl acetate gave 8.4 g. (66% yield) of analytically pure product as white crystals, m.p. 186-187° dec.; uv λ max (ethanol): nm (ϵ) 270 (19,700); ir (nujol): 3320 (OH, NH), 1705 sh, 1692 (C=O), 1520 (NHCO) cm^{-1} ; pmr (DMSO- d_6): δ 2.80 (1-CH₃), 3.38 (3-CH₃), 5.78 (H-6, broad), 10.02 (2H, OH, NH) ppm.

Anal. Calcd. for C₁₁H₁₃N₃O₂S: C, 52.57; H, 5.21; N, 16.72. Found: C, 52.77; H, 5.38; N, 16.60.

Tetrahydro-6-(2-hydroxyphenyl)-1-methyl-3-phenyl-4-thio-1,3,5-triazin-2(1H)one (39).

A mixture of 15.0 g. (0.084 mole) of *N*-(3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-yl)-*N'*-phenylthiourea and 5.0 g. (0.093 mole) of sodium methoxide in 200 ml. of absolute methanol was stirred for 1 hour at 25°. The resulting yellow solution was treated with acetic acid to pH 6.0 at 0°, and the solution was evaporated to dryness *in vacuo*. The residue was taken up with water and the white crystals (13.7 g., m.p. 215-217° dec.) were collected by filtration. Recrystallization from acetonitrile-tetrahydrofuran gave 9.2 g. (67% yield) of analytically pure white crystals, m.p. 219-220° dec.; uv λ max (ethanol): nm (ϵ) 269.5 (16,850); ir (nujol): 3280, 3190 (NH, OH), 1691 (C=O), 1563 (NHCO) cm^{-1} .

Anal. Calcd. for C₁₆H₁₅N₃O₂S: C, 61.32; H, 4.82; N, 13.41; S, 10.23. Found: C, 61.33; H, 4.95; N, 13.31; S, 10.13.

Acknowledgements.

We wish to thank Professor E. L. Eliel for most helpful discussions. The authors are indebted to the Analytical and Physical Chemistry Department under the supervision of Mr. A. D. Lewis. In particular we wish to thank Mrs. U. Zeek for microanalyses, Dr. R. C. Greenough, Mr. R. Puchalski, Mr. R. DeSimone and Mr. R. E. Saville for the determination of spectra.

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