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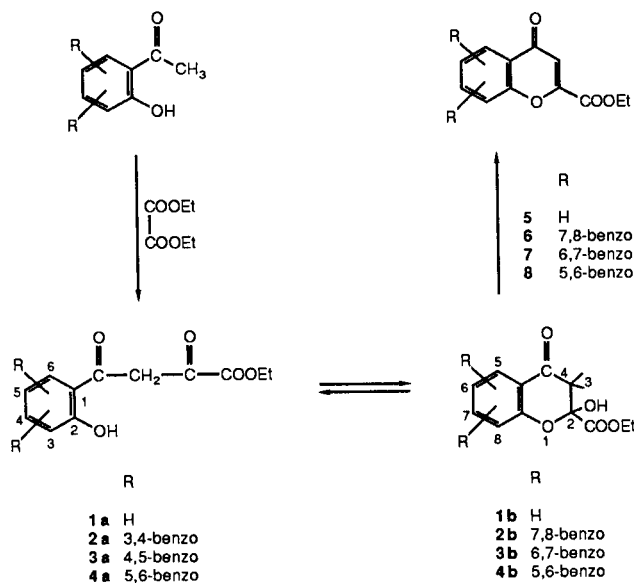
Ethyl chromone-2-carboxylate and all its benzoanalogs were prepared and caused to react with 1,2-diaminobenzene to give 2-(2-hydroxybenzoyl)methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline and its benzo analogs. The condensation products of diethyl oxalate and methyl hydroxyaryl ketones which were required for the preparation of the starting esters, were found to be subject to ring chain tautomerism.

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A number of publications deal with the reactions of chromone-2-carboxylates with two pronged nucleophiles such as hydrazine or diaminoethane which cause ring opening of the pyrone ring and formation of other heterocyclic systems [1,2,3]. However there seems to be no report dealing with reactions of such esters with 1,2-diaminobenzene. Results of such reactions are now presented.

The required starting esters were prepared essentially according to known methods by condensation of diethyl oxalate with the appropriate methyl hydroxyaryl ketone, followed by ring closure [4]. The ^1H nmr spectrum of the as yet unknown reaction product of 2-hydroxy-1-acetonaphthone and diethyl oxalate, which was expected to be ethyl 4-(2-hydroxy-1-naphthyl)-2,4-dioxobutanoate **4a**, indicated that the compound was its ring tautomer ethyl 1*H*-naphtho[2,1-*b*]-1-oxo-3-hydroxy-2,3-dihydropyran-3-carboxylate **4b**. Of course, dehydration of this compound readily gave the required ethyl 5,6-benzochromone-2-carboxylate **8** (Scheme I).

Scheme I



Because of this observation the other expected hydroxyaryl-2,4-dioxobutanoates **1a**, **2a**, **3a** were also investigated by ^1H nmr and found that in deuteriochloroform they were mixed with ring tautomers **1b**, **2b**, **3b**. The intensities of relevant signals indicated about 60% cyclization of ester **1a/b**, 40% of ester **2a/b** and 75% of ester **3a/b**. The observed spectral data are in Table I.

Incidentally, the ester **1a/b**, which had been reported as a solid of mp 107° [5] and later as an oil, which changed on standing to ethyl chromone-2-carboxylate, [6], was obtained as a solid of mp 79-80.5°, which did not change readily on standing.

It also should be mentioned that 3-hydroxy-2-acetonaph-

Scheme II

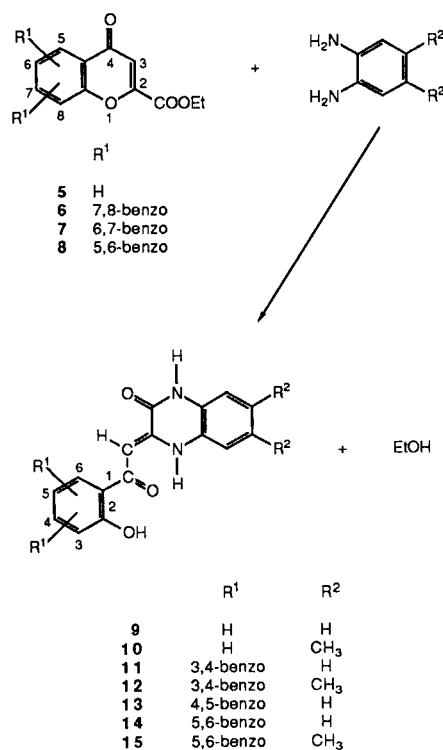


Table I

Compound No.	HO-Ar	HO-enol	-CH=	HO-ketal	-CH ₂ -	H-Ar	-CH ₂ CH ₃
1a/b	11.90	13.9 br	6.9	5.2 br	3.32, 2.92 AB	6.8-7.8 m	4.32, 4.26 dq, J = 7, 2H
	0.3H	0.2H	0.5H	0.6H	J = 16, 1.2H	4H	1.40, 1.30 dt, J = 7, 3H
2a/b	13.50	14.0 br	7.0	5.25 br	3.35, 3.03 AB	7.0-8.9 m	4.32 dq, J = 7, 2H
	0.6H	0.4H	0.8H	0.4H	J = 17, 0.8H	6H	1.39, 1.29 dt, J = 7, 3H
3a/b	11.10	[a]	7.3	4.60 br	3.39, 2.99 AB	7.2-7.9 m	4.38, 4.28 dq, J = 7, 2H
	0.2H		0.3H	0.6H	J = 17, 1.6H	5H, 8.4 s 1H	1.25, 1.35 dt, J = 7, 3H
4a/b	—	—	—	5.02 br	3.49, 3.06 AB	6.9-7.9 m	4.30 q, J = 7, 2H
				1.0H	J = 16, 2H	5H, 9.4 d	1.28 t, J = 7, 3H
						J = 8	

[a] Not observable.

Table II

Preparative and Analytical Information Regarding Reported Quinoxaline Compounds

Ester	Amine	Product	Yield %	° mp	Recrystallization solvent	Analyses					
						Calcd.		Found			
						C	H	N	C	H	N
5	[b]	10	84	299-302	Me cellosolve	70.12	5.23	9.09	70.32	5.08	9.37
6	[a]	11	53	304-305	Pyridine	72.72	4.27	8.48	72.45	3.98	8.69
6	[b]	12	61	297	Pyridine	73.73	5.06	7.82	73.47	4.88	7.39
7	[a]	13	60	> 320	Pyridine	72.72	4.27	8.48	72.93	4.58	8.73
8	[a]	14	73	286-287	Me cellosolve	72.72	4.27	8.48	72.38	4.13	8.12
8	[b]	15	67	289-290	Pyridine	73.73	5.06	7.82	73.53	4.85	7.58
16	[a]	18	81	261-263	Pyridine	73.24	4.68	8.13	73.40	4.91	8.40
17	[a]	19	95	266-267	Ethanol	73.24	4.68	8.13	73.55	4.94	7.86

[a] 1,2-Diaminobenzene. [b] 4,5-Dimethyl-1,2-diaminobenzene.

thone [7] which was required for the preparation of ester **3a/b** was prepared from 3-hydroxy-2-naphthoic acid by conversion to 3-methoxy-2-naphthoyl chloride, which was caused to react with diethyl ethoxymagnesiummalonate. Hydrolysis, decarboxylation and demethylation of the resulting diethyl 3-methoxy-2-naphthoymalonate gave the desired product [8].

The esters **1a/b**, **2a/b**, **3a/b** and **4b** could easily be converted to the corresponding ethyl chromone-2-carboxylates **5**, **6**, **7** and **8**.

The reaction of ester **5** with 1,2-diaminobenzene caused ring opening and amide formation with elimination of ethanol. The identity of the resulting yellow 2-(2-hydroxybenzoyl)methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline **9** was established by comparison with the compound obtained by condensation of 1,2-diaminobenzene with ester **1a/b** [9]. As expected esters **6**, **7** and **8** gave the same type of products **11**, **13** and **14** on reaction with 1,2-diaminobenzene. To test the general applicability of this kind of reaction the esters **5**, **6** and **8** were caused to react with 4,5-dimethyl-1,2-diaminobenzene. Analogous products **10**, **12** and **15** with methyl groups on the quinoxaline ring were obtained (Scheme II).

The ir spectra of all these compounds support their postulated structure. They contain several weak to medium bands near 3000 cm⁻¹ corresponding to O-H, N-H and C-H bonds and a strong band at 1670-1680 cm⁻¹ due to the C=O bond of the quinoxaline moiety [10]. There are additional strong bands between 1555 cm⁻¹ and 1620 cm⁻¹ characteristic of enamines [11]. However in bromoform suspension compound **9** had only a shoulder at 1615 cm⁻¹ not a band as reported for its spectrum taken in potassium bromide [9].

The uv spectra of the compounds contained significant maxima between 218 nm and 226 nm, and in the visible range between 405 nm and 475 nm most compounds had two distinct maxima which were about 23-28 nm apart. Observed data on ir and electronic spectra are presented in Table III.

The esters ethyl 4-(3-methoxy-2-naphthyl)-2,4-dioxobutanoate **16** and 4-(2-methoxy-1-naphthyl)-2,4-dioxobutanoate **17** were also prepared and condensed with 1,2-diaminobenzene (Scheme III). It was noticed that the ¹H nmr spectra of the esters exhibited extremely broad signals between 13.5 and 15.5 ppm for the enol OH. The spectra of

Table III

Spectral Data of Compounds **9-15, 18, 19**

Compound	IR [a]	UV [b]		Visible range [b]	
	Wave numbers cm^{-1}	λ max nm	log ϵ	λ max nm	log ϵ
9	1675, 1605, 1575, 1480, 1260	224	4.43	424 449	4.58 4.56
10	1675, 1610, 1580, 1375, 1205	226 276	4.37 3.94	434 462	4.58 4.56
11	1680, 1600, 1565, 1370, 1250	220	4.44	438 463	4.60 4.62
12	1670, 1600, 1590, 1565, 1235	218	4.48	447 478	4.58 4.59
13	1680, 1605, 1500, 1565, 1235	222 272	4.43 4.08	430 454	4.55 4.51
14	1680, 1620, 1600, 1570, 1375	224	4.67	437	4.44
15	1675, 1620, 1555, 1460, 1185	224	4.57	448	4.45
18	1680, 1595, 1525, 1370, 740	226 263	4.56 4.13	416	4.47
19	1660, 1605, 1560, 1365, 1250	224 266	4.52 3.96	405 425 sh	4.36 4.32

[a] The ir spectra were taken in bromoform suspension. The wave numbers of the 5 strongest bands are listed. [b] Electronic spectra in alcoholic solutions were taken.

Table IV

 ^1H NMR Data of Compounds **10-15, 18, 19** [a]

Compound	Aromatic H	Methinyl H [b]	O-H [b]	N-H [b]	CH_3 [b]
10	6.70-7.85 m 7H	[c]	13.00	12.08 13.26	2.18 6H
11	7.05-8.40 m 10H	6.86	15.08	12.18 13.26	
12	7.25-8.70 m 8H	6.80	15.04	12.02 13.12	2.12 3H [d] 2.18 3H [d]
13	8.50 s 2H 7.02 m 9H	[c]	12.39	12.22 13.35	
14	7.00-8.02 m 10H	6.42	10.47	12.04 13.44	
15	6.80-8.15 m 8H	6.40	10.45	11.90 13.60	2.22 6H [d]
18	7.00-8.16 m 10H	6.78		12.06 13.07	3.96 3H [e]
19	7.00-8.00 m 10H	6.28		12.10 13.50	3.88 3H [e]

[a] All spectra were taken in deuterated dimethyl sulfoxide with TMS as the internal standard. [b] All signals listed in these columns are singlets. [c] Signal combined with signal for Ar-H. [d] Methyl on quinoxaline ring. [e] Methyl of methoxy group.

EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus and are uncorrected. The ir spectra were taken on a Perkin-Elmer 1330 spectrometer, the uv and visible range spectra on a Beckman DB-GT, and the ^1H nmr spectra on a Hitachi Perkin-Elmer R 24-A instrument with TMS as internal standard. The analyses were performed by the Baron Consulting Co., Analytical Services, Orange CT, 06477, Dr. H. Agahigian, Director.

Ethyl 1*H*-Naphtho[2,1-*b*]-1-oxo-3-hydroxy-2,3-dihydropyran-3-carboxylate **4b**.

A mixture of 13.0 g of 2-hydroxy-1-acetonaphthone and 26 g of diethyl oxalate was added in portions to a solution of 3.5 g sodium in 100 ml of dry ethanol. The dark precipitate which formed after reflux for about 0.75 hour was collected, washed with dry ether and suspended in 200 ml of water. With stirring 15 ml of acetic acid was added and the product was taken up with ether. After washing with water and drying with sodium sulfate the ether was distilled and the residue, 13.4 g (67%) solidified, mp 125-126° (from ethanol); ir (bromoform): 1750, 1640, 1640, 1620, 1600, 1570, 1510, 1440, 1375, 1240, 1205 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{14}\text{O}_5$: C, 67.13; H, 4.93. Found: C, 67.40; H, 4.89. The following esters were prepared similarly.

Ethyl 4-(2-Hydroxyphenyl)-2,4-dioxobutanoate **1a/b**.

This compound was obtained in a yield of 65%, mp 79-80.5° (from heptane), lit 107° [5], oil [6].

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_5$: C, 61.02; H, 5.12. Found: C, 61.08; H, 5.05.

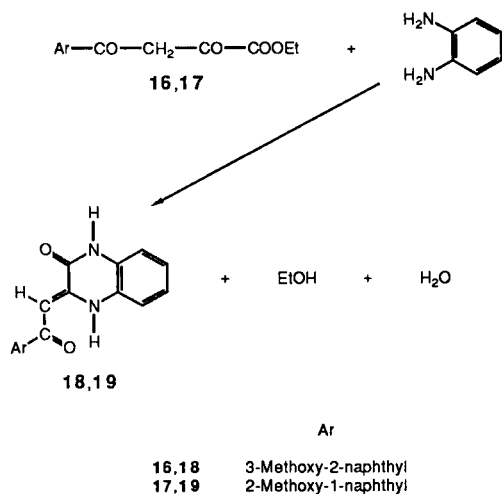
Ethyl 4-(1-Hydroxy-2-naphthyl)-2,4-dioxobutanoate **2a/b**.

This compound was obtained in a yield of 49%, mp 113-115° (from ethanol), lit 114-115° [4].

Ethyl 4-(3-Hydroxy-2-naphthyl)-2,4-dioxobutanoate **3a/b**.

This compound was obtained in a yield of 39%, mp 129° (from dilute ethanol), lit 129° [7].

Scheme III



the condensation products **18** and **19** helped in making the proper assignments of the N-H and O-H signals of compounds **10-15**. The N-H signals were found to be rather broad and in the range of 12-13.5 ppm, whereas the O-H signals were quite sharp and in a much wider range of 10.5-15.1 ppm (Table IV).

Ethyl 4-(2-Methoxy-1-naphthyl)-2,4-dioxobutanoate **17**.

To a solution of 1.3 g of sodium in 26 ml of dry ethanol was added 5.0 g of 2-methoxy-1-acetonaphthone and 10 ml of diethyl oxalate. After reflux for 4 hours the mixture was cooled and the hygroscopic solid which had formed was collected and dissolved in about 40 ml of water. The aqueous solution was acidified with 3 molar hydrochloric acid and the solid which formed, 3.4 g (45%) was collected, mp 64° (from heptane-petroleum ether); ir (in bromoform): 1730, 1625, 1590, 1510, 1275, 1250 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{16}\text{O}_5$: C, 67.99; H, 5.37. Found: C, 67.86; H, 5.14.

Ethyl 4-(3-Methoxy-2-naphthyl)-2,4-dioxobutanoate **16**.

To a solution of 0.8 g of sodium in 20 ml of dry ethanol were added 3.0 g of 3-methoxy-2-acetonaphthone and 6 ml of diethyl oxalate. The exothermic reaction was completed by refluxing for one hour. The dark solution which had formed was added to ice and water containing a small quantity of dilute hydrochloric acid. A solidifying oil, 3.5 g (78%) precipitated, mp 104° (from heptane); ir (bromoform): 1725, 1625, 1590, 1460, 1250, 1235 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{16}\text{O}_5$: C, 67.99; H, 5.37. Found: C, 67.91; H, 5.21.

Diethyl 3-Methoxy-2-naphthoylemalonate.

Freshly distilled diethyl malonate (17.6 g) was converted to its ethoxy-magnesium derivative [8] and a solution of 22.0 g of 3-methoxy-2-naphthoyl chloride [7] in 50 ml of ether was added. When the reaction appeared to be finished, stirring was continued for about 10 minutes, then 100 ml of an aqueous solution containing 12.5 ml sulfuric acid was added. The ether phase was separated, washed with water and dried with sodium sulfate. A crop of 32.7 g of crystallized residue was obtained after removal of the solvent. The mp was 94-95° (from heptane); ^1H nmr (in deuteriochloroform): 1.23 (t, 6H, J = 7), 3.90 (s, 3H), 4.24 (q, 4H, J = 7), 5.32 (s, 1H), 7.10-7.90 (m, 5H), 8.40 (s, 1H); ir (bromoform): 1755, 1735, 1630, 1305, 1250 cm^{-1} .

Anal. Calcd. for $\text{C}_{19}\text{H}_{20}\text{O}_5$: C, 66.27; H, 5.85. Found: C, 65.96; H, 6.00.

3-Methoxy-2-acetonaphthone.

A mixture of 25 g of crude diethyl 3-methoxy-2-naphthoylemalonate, 30 ml of acetic acid, 3.8 ml of sulfuric acid and 20 ml of water was refluxed for 6 hours. After cooling it was made alkaline with 20% sodium hydroxide and the organic material was extracted with ether. After washing with water and drying with sodium sulfate the ether was removed and the residue distilled at reduced pressure giving 10.1 g (69%) of an oil of bp 153-158° at 1.5-1.7 mm. This oil solidified and crystals of mp 42-43° (from petroleum ether) lit 47-48° [7] were obtained.

Ethyl 5,6-Benzochromone-2-carboxylate **8**.

A mixture of 15 g of crude 1*H*-naphtho[2,1-*b*]-1-oxo-3-hydroxy-2,3-dihydropyran-3-carboxylate **4b**, 100 ml of dry ethanol and 6 drops of concentrated sulfuric acid was refluxed for 6 hours. After cooling 13.5 g (96%) of solid of mp 146-147° (from benzene/heptane) was obtained; ^1H nmr (deuteriochloroform): 1.40 (t, 3H, J = 7), 4.42 (q, 2H, J = 7), 7.05 (s, 1H), 7.15-8.05 (m, 5H), 9.72-9.88 (m, 1H); ir (bromoform): 1735, 1645, 1620, 1440, 1255 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{O}_4$: C, 71.64; H, 4.51. Found: C, 71.72; H, 4.55.

Ethyl 6,7-Benzochromone-2-carboxylate **7**.

Crude ethyl 4-(3-hydroxy-2-naphthyl)-2,4-dioxobutanoate **3a/b** (0.9 g) was refluxed with 30 ml of two molar alcoholic hydrochloric acid for 3.5 hours. The crystals which formed on cooling to about -10° amounted to 0.4 g (47%), mp 152-154° (from ethanol); ^1H nmr (deuteriochloroform): 1.44 (t, 3H, J = 7), 4.45 (q, 2H, J = 7), 6.98 (s, 1H), 7.15-8.10 (m, 5H), 8.65 (s, 1H); ir (bromoform): 1735, 1650, 1625, 1260, 1235 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{O}_4$: C, 71.64; H, 4.51. Found: C, 71.53; H, 4.34.

2-(2-Hydroxybenzoyl)methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline **9**.

This compound was obtained by refluxing 2.0 g of ester **5** and 1.0 g of 1,2-diaminobenzene in 20 ml of acetic acid for 0.5 hour. The yield of the yellow product was 0.8 g (31%) and its mp 317-319° (from acetic acid), lit 309-310° [9].

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_3$: C, 68.57; H, 4.32; N, 9.99. Found: C, 68.74; H, 4.61; N, 10.07.

The same product was obtained by heating a mixture of 1.1 g of ester **5** and 0.55 g of 1,2-diaminobenzene in a xylene vapor bath to 135°. The initially formed dark melt resolidified after about 15 minutes. Heating was continued for about 2 hours and the ethanol which was formed was collected and identified by ir. The mixture was then cooled, washed with warm ethanol and ether, giving 0.78 g of **9**, mp 315-317°.

Using the same method the following compounds were obtained from the esters and amines indicated on Table II.

2-(2-Hydroxybenzoyl)methyl-3-oxo-6,7-dimethyl-1,2,3,4-tetrahydroquinoxaline **10**.

2-(1-Hydroxy-2-naphthoyl)methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline **11**.

2-(2-Hydroxy-2-naphthoyl)methyl-3-oxo-6,7-dimethyl-1,2,3,4-tetrahydroquinoxaline **12**.

2-(3-Hydroxy-2-naphthoyl)methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline **13**.

2-(2-Hydroxy-1-naphthoyl)methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline **14**.

2-(2-Hydroxy-1-naphthoyl)methyl-3-oxo-6,7-dimethyl-1,2,3,4-tetrahydroquinoxaline **15**.

The following two compounds were prepared by refluxing equimolecular amounts of ester and diamine in alcoholic solution [12]. The products were collected after cooling (Scheme III).

2-(3-Methoxy-2-naphthoyl)methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline **18**.

2-(2-Methoxy-1-naphthoyl)methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline **19**.

More preparative and spectral information on compounds **10-15** and **18, 19** is contained in Tables II-IV.

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