

Keto-Enol Tautomerism of β -Keto Ester Derivatives.Reaction of β -Dicarbonyl Compounds with Diamines

George Bobowski* and John Shavel, Jr. (1)

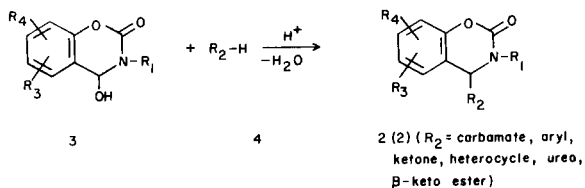
Warner-Lambert/Parke-Davis, Pharmaceutical Research Division, 2800 Plymouth Road,
Ann Arbor, Michigan 48105

Received November 12, 1979

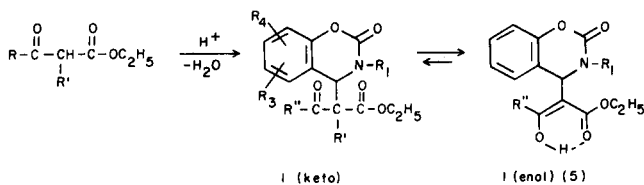
A series of α -[3-alkyl-3,4-dihydro-2-oxo-2H-1,3-benzoxazin-4-yl]- β -keto ester derivatives **1** (Table I) were synthesized by the condensation of 3-alkyl-3,4-dihydro-4-hydroxy-2H-1,3-benzoxazine-2-ones **3** (2) with β -keto esters **4** in the presence of traces of mineral acids under azeotropic conditions. Condensation of **1** with hydrazines **5** gave pyrazolone derivatives **2** (Table II). Condensation of β -diketone derivatives **6** with hydrazines **5** and with 1,2-benzenediamine (**8**) resulted in the formation of pyrazoles (**7a-c**) and diazepine derivatives **12** (Table III) and **13**, respectively.

J. Heterocyclic Chem., **17**, 519 (1980).

In the previous paper (2) of this series we had described the condensation of 3-alkyl-3,4-dihydro-4-hydroxy-2H-1,3-benzoxazin-2-ones **3** with compounds having active hydrogen, giving 4-substituted derivatives of type **2**.



This paper describes the utilization of straight-chained or cyclic β -keto esters **4** as the nucleophile. The condensations were generally accomplished by the method used previously (2), *i.e.*, in benzene or toluene under azeotropic conditions in the presence of traces of mineral acids as catalysts. The β -keto esters **4** condensed practically exclusively at their more reactive α -position with **3** to give derivatives **1** (Table I) whose enolic content was invariably much greater than that of the starting esters.

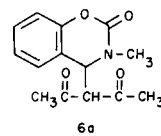


The infrared spectra showed qualitatively the extent of enolization by displaying a strong band of conjugative chelated ester at about 1640 cm^{-1} , the benzoxazinone band at *ca.* 1725 cm^{-1} usually remaining unchanged. The proton magnetic resonance (pmr) spectroscopy, however, proved to be an excellent tool in measuring the enol content quantitatively up to about 95% accuracy (as far as the sensitivity of the instrument permitted it). Separate resonance signals were nearly always observed for the protons of the various groups in the keto and enol tautomers.

Identification of these peaks was possible from chemical shifts and spin-spin splittings. The relative intensities of keto and enol resonances were then obtained by integration.

The strong enolization of the β -keto esters **1** of Table I (except those lacking α -hydrogen) contrasts sharply with the weak enolization of the diketones **6** (2). This difference obviously stems from the effect of the α -benzoxazinyl group on the normal enolization of β -diketones and β -keto esters.

In the case of β -diketones, it is known (6) that neat 2,4-pentanedione is 85% enolic, while 3-methyl-2,4-pentanedione (7) is 30% enolic. The 2,4-pentanedione derivative **6a** (2), with the still bulkier α -benzoxazinyl substituent, turns out to be essentially non-enolic.



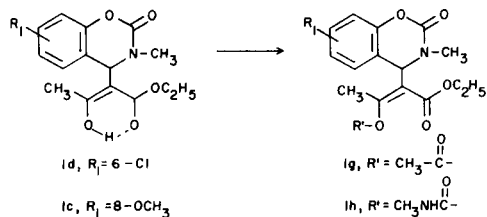
In the case of β -keto esters, the situation is quite different. Burdette and Rogers (8) have shown that smaller electron-withdrawing groups such as fluoro, chloro, or cyano in the α -position of β -keto esters enhance enolization, while bulkier ones such as bromo, decrease enolization. We now find that the bulky, electron-withdrawing, α -benzoxazinyl group, strongly enhances enolization in compounds **1**, rather than suppressing it as predicted from Burdette and Rogers (8) and from β -diketones **6**. All β -keto ester derivatives in Table I which possess free α -hydrogen are enolized from 40 to about 100%. Some of the isolated products represent a mixture of both forms; others are obtained as enol tautomers only. In one instance it was possible to separate both tautomers (compounds **1b** and **1c**) into pure forms by fractional crystallization. They differ considerably in their melting points, infrared and pmr spectra, and retain their uniqueness as separate entities

both in solid form and in solution.

In analogy to the unsubstituted starting β -keto esters, compounds **1** exhibit similar patterns in the chemical shifts of the methyl protons. Thus, the methyl protons nearest to a carbonyl group in the keto form resonate by 0 to 13 Hz downfield as compared to that in the enol form. Another characteristic common to most β -keto esters in Table I (excepting the naphthyl homologues **1f**) is the up-field shift of the *N*-methyl resonances in the enol tautomers by 4 to 10 Hz and the downfield shift in their benzylic singlets in the range of 10 to 20 Hz. For example, when pure tautomers **1b** and **1c** are mixed in a 1:1 ratio, there are two distinctive *N*-methyl singlet resonances at 2.96 (enol) and 3.12 (keto); their respective benzylic protons resonate at 5.22 (d, $J = 6.5$ Hz, keto) and 5.44 Hz (s, enol) ppm.

Another feature of enol tautomers is their relative stability. For example, when pure **11** in benzene solution containing traces of 4-methylbenzenesulfonic acid (similar conditions as during its preparation) was refluxed for 10 hours, the starting enol (**11**) was recovered unchanged in 85% yield, the mother liquor still containing some **11** and a small amount of non-isolable material. No corresponding keto tautomer was obtained.

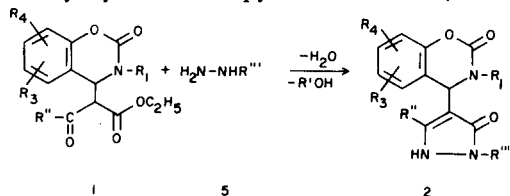
The enolized β -keto ester derivatives are easily transformed into enol esters or enol carbamates as exemplified by the formation of an acetate **1g** and carbamate **1k**, respectively.



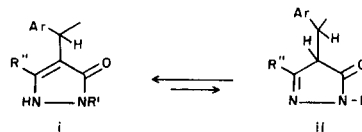
All pmr spectra were determined in deuteriochloroform, a solvent which does not modify the percentage of enol (**9**).

The last two columns in Table I show percentage of enol tautomers and the resonance positions of enolic protons. More detailed assignments are made in the experimental examples.

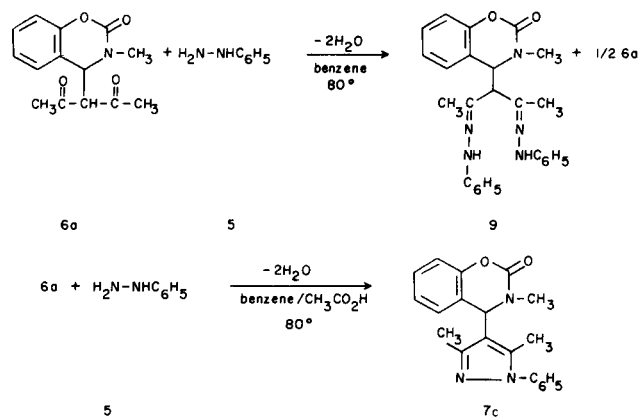
We were interested in synthesizing pyrazolone derivatives of benzoxazines in the hope of improving their anti-inflammatory activity. The β -keto ester derivatives **1** reacted with hydrazines **5** at room temperature, or on brief heating, in the presence of glacial acetic acid, giving satisfactory yields of pyrazolones **2** (Table II).



Mixture of keto and enol tautomers gave always the same product **2**. Although two tautomers (**i** and **ii**) are possible, in all cases only the vinylogous amide type tautomer (**i**) was present as evidenced by a sharp benzylic proton singlet at about 5.5 ppm and an exchangeable N-H proton at about 11.0 ppm.



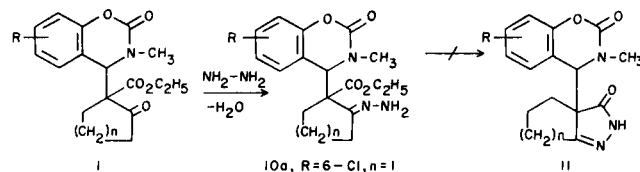
The β -diketone derivative **6a** (**2**) on heating with one molar equivalent of phenylhydrazine under azeotropic conditions gave only bishydrazone **9**, one half of **6a** remaining intact. However, in the presence of excess glacial acetic acid (other conditions being equal), the expected pyrazole derivative **7c** was obtained in 66% yield.



The 8-methoxy analogue of **6a** (**6b**) (**2**) and hydrazine hydrate in the presence of glacial acetic acid gave the pyrazole derivative **7a**.

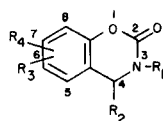
The benzoylacetone derivative **6c** (**2**) condensed with anhydrous hydrazine in ethanol at room temperature giving the corresponding pyrazole **7b**.

Attempts to condense cyclic β -keto ester analogues with hydrazine to obtain bicyclic pyrazolone derivatives **11** were unsuccessful. The reaction stopped at the hydrazone stage as exemplified by the formation of **10**.



The condensation of 2,4-pentanedione derivative **6a** with 1,2-benzenediamine (**8**) under azeotropic conditions required prolonged reaction time to give the desired diazepine **12** in 49% yield. A second product resulting from that reaction in 12% yield was a fully conjugated, yellow phenolic diazepine derivatives **13**. The formation of

Table I

 α -(3-Alkyl-3,4-dihydro-2-oxo-2H-1,3-benzoxazin-4-yl)- β -keto Ester Derivatives I

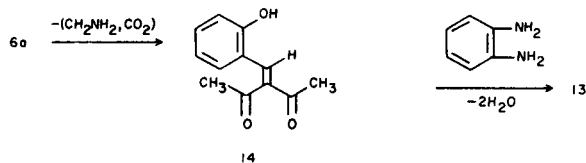
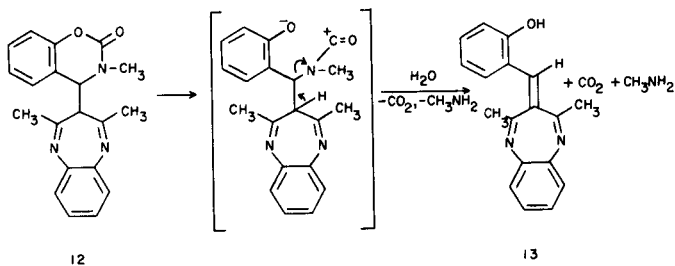
Compound	R ₁	R ₂	R ₃	R ₄	M.p. °C	% Yield	Empirical Formula	Analysis							
								Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N	% Enol (b)	δ (ppm) OH _e (c)
1a (a)	CH ₃		H	H	140-141	88	C ₁₁ H ₁₁ NO ₃	61.85	5.88	4.81	61.85	6.02	5.00	75	13.03
1b	"		H	8-OCH ₃	100-101	33.5 (d)	C ₁₆ H ₁₃ NO ₃	59.80	5.96	4.36	59.79	6.04	4.48	2 (e)	(k)
1c	"		H	8-OCH ₃	147-148	16.5 (d)	C ₁₆ H ₁₃ NO ₃	59.80	5.96	4.36	59.73	5.91	4.19	98 (f)	13.00
1d	"	"	6-Cl	H	149.5-151	72	C ₁₈ H ₁₁ NO ₃	55.31	4.95	4.30	55.42	5.11	4.34	98 (f)	13.02
1e		"	6-Cl	H	161-162	26 (g)	C ₂₀ H ₂₁ ClNO ₃	60.99	6.14	3.57	61.27	6.14	3.51	98 (f)	13.33
1f	CH ₃				147-148(h)	51	C ₁₃ H ₁₁ NO ₃	66.85	5.61	4.10	67.07	5.76	4.13	50 (i)	14.55
1g	"		6-Cl	H	160-161	73	C ₁₇ H ₁₄ ClNO ₃	55.52	4.93	3.81	55.79	4.96	3.71	—	—
1h	CH ₃		H	8-OCH ₃	160-161	74	C ₁₃ H ₁₃ N ₂ O ₃	57.13	5.86	7.40	57.43	5.99	7.21	—	—
1i	"		(j)	H	142-143	41	C ₁₆ H ₁₁ NO ₃	65.27	6.39	4.24	65.10	6.22	4.30	—	—
1j	"	"	(j)	6-Cl	186-187(h)	39	C ₁₈ H ₁₀ ClNO ₃	59.10	5.51	3.83	58.88	5.31	4.10	—	—
1k	"		(j)	6-Cl	144-145	60	C ₁₇ H ₁₁ ClNO ₃	58.04	5.16	3.98	57.99	5.11	3.92	—	—
1l	"		H	8-OCH ₃	148-149	29 (l)	C ₁₁ H ₁₁ NO ₃	58.63	5.58	4.56	58.33	5.61	4.45	98	13.04

(a) This compound was previously reported (2). Contains an approximate content of enol as indicated. (b) All measurements are at 25° ± 2°. (c) The values of enolic protons are considered as those due to intramolecular association (chelation). (d) The total yield of the keto and enol tautomers (compounds 1b and 1c) could be considerably higher than indicated here (50%) if all

contents would be isolated from the mother liquor which contains both tautomers. (e) Contains minimum 98% keto tautomer. (f) As could be determined, it is 98% enol. (g) Due to great solubility, no more product could be isolated by direct crystallization. (h) Melts with decomposition. (i) Contains about 50/50 mixture of both tautomers. (j) There is no evidence of any enolization, neither by chemical (ferric chloride) nor physical (pmr) methods. (k) Enol tautomer not detected by pmr; its presence in very small amounts is assumed only by very slow positive reaction with ferric chloride. (l) The low yield of isolated enol tautomer is due to its great solubility in most organic solvents. However, the mother liquor contained about equal mixture of both tautomers as determined by pmr spectroscopy.

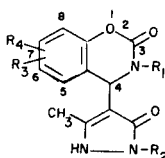
13 could have resulted from the cleavage of cyclic carbamate, followed by a β -elimination of carbon dioxide and methanamine. Conversely, the elimination might have

occurred first and the intermediate **14** could then have condensed with **8** to give **13**.



An attempt to condense **1a** with **8** to obtain diazepinone derivative **15** was unsuccessful. The condensation took place only at the ketone carbonyl (or its enolized form),

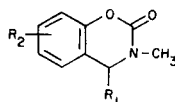
Table II

4(2,5-Dihydro-1,3-substituted-5-oxo-1*H*-pyrazol-4-yl)-3,4-dihydro-3-alkyl-2*H*-1,3-benzoxazin-2-ones (2)

Compound	R ₁	R ₂	R ₃	R ₄	M.p. °C	% Yield	Empirical Formula	C	Calcd.			Analysis		
									H	N	C	H	N	δ (ppm) N-H (a)
2a	CH ₃		H	H	209-210 (b)	52	C ₁₉ H ₁₇ N ₃ O ₃	68.05	5.11	12.53	68.25	5.34	12.74	11.27
2b	"	"	H	8-OCH ₃	228-229 (b)	63	C ₂₀ H ₁₉ N ₃ O ₄	65.74	5.24	11.50	65.94	5.32	11.36	11.35
2c	"	"	6-Cl	H	255-256 (b)	81	C ₁₉ H ₁₆ ClN ₃ O ₃	61.71	4.36	11.36	61.77	4.49	11.17	11.45
2d	"	"	R ₃ , R ₄ =		237-238 (b)	52	C ₂₂ H ₂₁ N ₃ O ₃	71.67	4.97	10.90	71.60	5.09	10.89	11.09
2e	"	-CH ₂ CH ₂ -	H	H	104-105	56	C ₂₁ H ₂₁ N ₃ O ₃	69.40	5.83	11.56	69.43	5.99	11.31	10.68
2f	"	CH ₃	H	8-OCH ₃	212-213 (b)	67	C ₁₉ H ₁₇ N ₃ O ₄	59.40	5.65	13.85	59.56	5.71	14.02	10.75
2g			6-Cl	H	167-168 (b)	60	C ₂₄ H ₂₀ ClN ₃ O ₃	65.83	5.52	9.60	65.92	5.40	9.87	11.15
2h	CH ₃	H	H	8-OCH ₃	255-256 (b)	86	C ₁₄ H ₁₃ N ₃ O ₄	58.12	5.23	14.53	57.94	5.36	14.33	10.12(c)

(a) Determined in DMSO-*d*₆. (b) Melts with decomposition. (c) Both NH protons resonate at the same field.

Table III

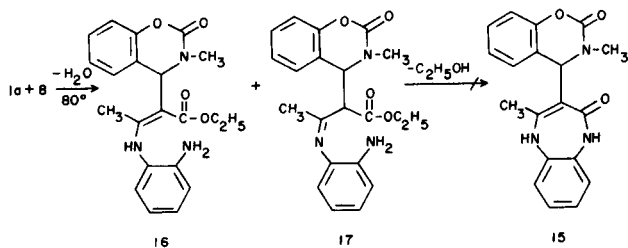
Condensation Products of 4(β-Diketo)-3,4-dihydro-3-methyl-2*H*-1,3-benzoxazin-2-ones (6) with Hydrazines and 1,2-Benzenediamine

Compound	R ₁	R ₂	M.p. °C	% Yield	Empirical Formula	C	Calcd.			Found	
							H	N	C	H	N
7a		8-OCH ₃	214-215 (a)	55	C ₁₅ H ₁₇ N ₃ O ₃	62.70	5.96	14.63	62.63	5.94	14.63
7b		H	147-148	58	C ₁₉ H ₁₇ N ₃ O ₂	71.46	5.37	13.16	71.17	5.31	12.93
7c		H	144-145 (a)	66	C ₂₀ H ₁₉ N ₃ O ₂	72.05	5.74	12.61	72.34	5.84	12.76
9		H	216-217 (a)	85 (b)	C ₂₆ H ₂₇ N ₅ O ₂	70.72	6.16	15.86	70.92	6.38	15.96
12		H	196-197 (a)	49	C ₂₀ H ₁₉ N ₃ O ₂	72.05	5.74	12.61	72.28	5.77	12.31

(c)

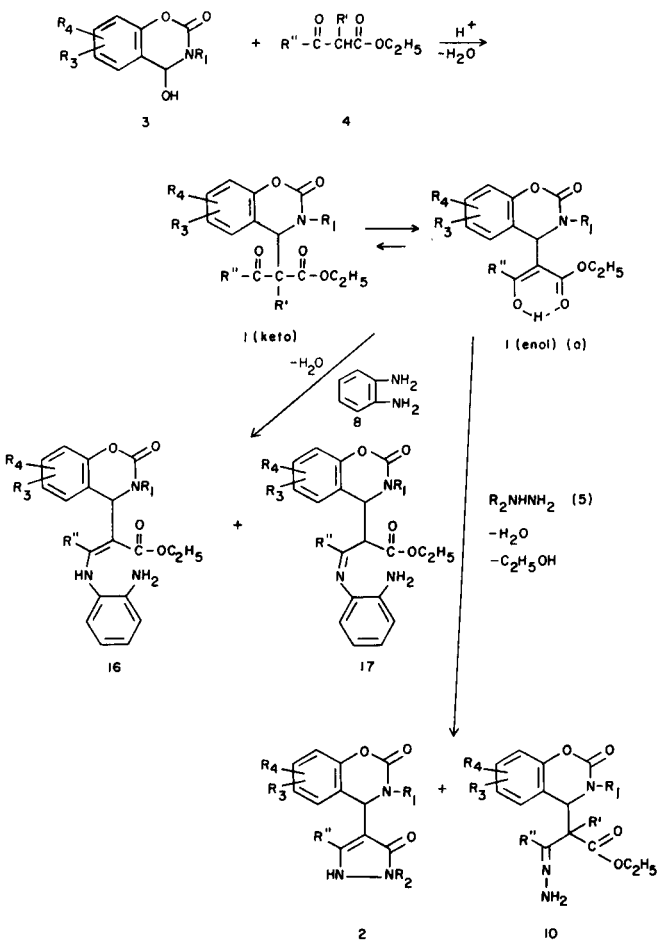
(a) Melts with decomposition. (b) The yield is based on the amount of phenyl hydrazine consumed; one half of starting **6a** remained unused in the process. (c) For the other phenolic diazepine derivative **13**, see Experimental.

but no condensation of the second amino group with an ester function (in analogy to the formation of pyrazolone derivatives) could be effected. Two isomers, resulting from the mono-condensation, were isolated whose melting points and spectra differ considerably. The conjugated enamino ester derivative **16** (30% yield) represents the major product and the amino derivative **17** constitutes only about 5%.



Since other conditions of reaction were about similar or even more stringent than during the preparation of pyrazolone derivatives **2**, those results show clearly great difference in the ease of formation of the five versus the

Scheme I

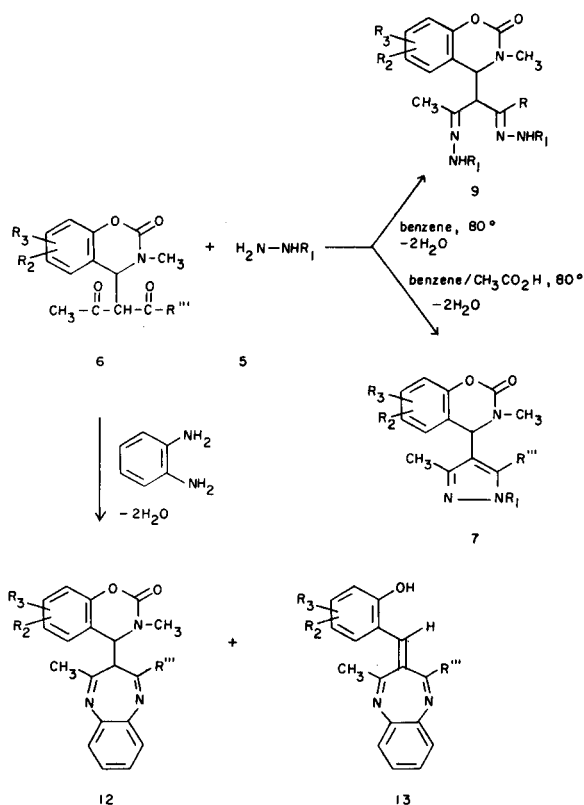


(a) Enolization possible only when $R' = H$.

seven-membered ring, the former being many-fold more favorable.

In this brief study we have described the somewhat unique properties of α -(benzoxazinyl)- β -keto esters, their keto-enol equilibria, and their reactions with diamino derivatives. The sequence of reactions is presented in Schemes I and II.

Scheme II



EXPERIMENTAL

Physical constants, yields, and analytical values for the compounds below are reported in Tables I-III. 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 spectrophotograph. Unless otherwise stated, the former was determined as solution in 95% ethanol and the latter as Nujol mulls. The pmr 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 benzene, acetone, heptane in varying proportions, as the eluent. The chromatograms were developed in an iodine chamber.

The formation of β -keto ester derivatives **1** (Table I) were essentially quantitative and generally free from side reactions. Whenever the isolations of products by direct crystallization gave poor yields, no attempts were made to use more involved operational techniques like column chromatography, since the starting materials are rather inexpensive. It is conceivable that the mother liquors might still contain additional quantities of the major (isolated) tautomer or the other one which was not isolated at all (or as a minor component of the isolated mixture), due to its greater solubility in the particular media. Consequently, the deter-

mination of the enol content was performed only on the analytically pure compounds. When a mixture of both tautomers was isolated, only one name corresponding to the keto tautomer is used. However, when the enol content exceeded 70%, the compound is presented as enol tautomer in the structural formula with the percentage indicated in Table I as well as in the individual experimental procedures.

The pmr resonances for the aromatic protons were usually not included. Occasionally, the peaks of lone protons were not specified if they were buried under an envelope of other aliphatic protons.

Ethyl α -Acetyl-3,4-dihydro-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1b**).

A solution of 16.7 g. (0.08 mole) of 3,4-dihydro-4-hydroxy-8-methoxy-3-methyl-2H-1,3-benzoxazin-2-one (**3a**) (2), 11.5 g. (0.089 mole) of ethyl acetoacetate and 0.01 g. of 4-methylbenzenesulfonic acid monohydrate in 300 ml. of dry benzene was refluxed for 90 minutes, while 1.4 ml. of water separated in a Dean-Stark trap. After the solvent was evaporated, the semi-solid colorless residue was taken up with 100 ml. of diethyl ether, refluxed for 30 minutes, and allowed to stand overnight at room temperature. The resulting white crystals (13.5 g., m.p. 98-103°) contained about 93% of the keto tautomer. Recrystallization from acetonitrile gave 9.1 g. (35.5% yield) of pure ethyl α -acetyl-3,4-dihydro-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1b**) as white crystals, m.p. 100-101°; uv (ethanol): λ max nm (ϵ) 225 (11,500), 251 (7500), 281 (3200); ir (nujol): 1724 (C=O, benzoxazinone, keto, and ester functions); (chloroform): 1735 (ester C=O), 1723 (benzoxazinone and keto functions) cm^{-1} ; pmr (deuteriochloroform): δ 1.13 (3H, t, J = 7.0 Hz, CH_2CH_3), 2.30 (3H, CH_3CO), 3.12 (3H, NCH₃), 3.88 (3H, CH_3O), 4.04 [3H, m, J = 7.0 Hz, CH_2CH_3], and 1H (-CO-CH-CO-), 5.22 (1H, d, J = 6.5 Hz, ArCH) ppm.

Anal. Calcd. for $\text{C}_{16}\text{H}_{19}\text{NO}_6$: C, 59.80; H, 5.96; N, 4.36. Found: C, 59.79; H, 6.04; N, 4.48.

Ethyl 3,4-Dihydro- α -(1-hydroxyethylidene)-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1c**).

The original filtrate and the mother liquor of analytical ethyl α -acetyl-3,4-dihydro-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1b**), containing predominantly the enol tautomer, were combined, evaporated to dryness and triturated with hot ethyl acetate. After staying overnight at 5°, 6.2 g. (24% yield) of enol tautomer was obtained, m.p. 143-145°. Recrystallization from ethyl acetate gave 4.4 g. (16.5% yield) of analytically and tautomericly pure ethyl 3,4-dihydro- α -(1-hydroxyethylidene)-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1c**) as white crystals, m.p. 147-148°; uv (ethanol): λ max nm (ϵ) 225 sh (11,500), 252 (7350), 280 sh (3500); ir (nujol): 1716 (C=O, benzoxazinone), 1626 (C=C-CO₂C₂H₅); (chloroform): 1721, 1711 (C=O, benzoxazinone), 1638-1611 (C=C-CO₂C₂H₅) cm^{-1} ; pmr (deuteriochloroform): δ 1.12 (3H, t, J = 7.5 Hz, CH_2CH_3), 2.26 (3H, $\text{CH}_3\text{-C=C}$), 2.96 (3H, N-CH₃), 3.86 (3H, OCH₃), 4.00 (2H, q, J = 7.5 Hz, CH_2CH_3); 5.44 (1H, ArCH), 13.00 (1H, enolic) ppm.

Anal. Calcd. for $\text{C}_{16}\text{H}_{19}\text{NO}_6$: C, 59.80; H, 5.96; N, 4.36. Found: C, 59.73; H, 5.91; N, 4.19.

Ethyl 6-Chloro-3,4-dihydro- α -(1-hydroxyethylidene)-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1d**).

A solution of 6-chloro-3,4-dihydro-4-hydroxy-3-methyl-2H-1,3-benzoxazin-2-one [**3b**, 16.4 g., 0.077 mole, (2)], 11.0 g. (0.087 mole) of ethyl acetoacetate and 0.01 g. of 4-methylbenzenesulfonic acid monohydrate in 300 ml. of benzene was refluxed for one hour, while 1.4 ml. of water separated in a Dean-Stark trap. The thin layer chromatography showed one spot ($R_f = 0.5$) of faster mobility than that of the starting material ($R_f = 0.3$). After the solvent was removed *in vacuo*, the residue was crystallized from 2-propanol giving 18.1 g. (72% yield) of pure enol ester derivative **1d**, m.p. 149.5-151°; uv (ethanol): λ max nm (ϵ) 225 sh (10,300), 246 (8150), 286 sh (1000); ir (nujol): 1724 (C=O, benzoxazinone), 1629, 1611 (C=C-CO₂C₂H₅); (chloroform): 1718-1708 (benzoxazinone), 1633, 1608 (C=C-CO₂C₂H₅) cm^{-1} ; ppm (deuteriochloroform): δ 1.14 (3H, t, J = 7.5 Hz, CH_2CH_3), 2.28 (3H, $\text{CH}_3\text{-C=C}$), 2.97 (3H, N-CH₃), 4.02 (2H, q, J = 7.5 Hz, CH_2CH_3), 5.46 (1H, ArCH),

13.02 (1H, enolic) ppm.

Anal. Calcd. for $\text{C}_{15}\text{H}_{17}\text{NO}_6$: C, 55.31; H, 4.95; N, 4.30; Cl, 10.88. Found: C, 55.42; H, 5.11; N, 4.34; Cl, 10.99.

Ethyl 6-Chloro-3-cyclohexyl-3,4-dihydro- α -(1-hydroxyethylidene)-2-oxo-2H-1,3-benzoxazine-4-acetate (**1e**).

A solution of 14.1 g. (0.05 mole) of 6-chloro-3-cyclohexyl-3,4-dihydro-4-hydroxy-2H-1,3-benzoxazin-2-one (**3c**) (2), 1.8 g. (0.06 mole) of ethyl acetoacetate and 0.02 g. of 4-methylbenzenesulfonic acid monohydrate in 250 ml. of benzene was refluxed for 4 hours, while 0.9 ml. of water separated in a Dean-Stark trap. After the solvent was evaporated, the honey-like residue was crystallized from 2-propanol giving 5.1 g. (26% yield) of pure ethyl 6-chloro-3-cyclohexyl-3,4-dihydro- α -(1-hydroxyethylidene)-2-oxo-2H-1,3-benzoxazine-4-acetate (**1e**) as white crystals, m.p. 161-162°; uv (ethanol): λ max nm (ϵ) 228 infl. (11,000), 252 sh (7500), 290 (2350); ir (nujol): 1720, 1711 (C=O, benzoxazinone), 1640, 1610 (C=C-CO₂C₂H₅) cm^{-1} ; pmr (deuteriochloroform): δ 1.17 (3H, t, J = 7.0 Hz, CH_2CH_3), 1.20 to 2.10 (10H, cyclohexane moiety), 2.33 (3H, $\text{CH}_3\text{C=C}$), 3.28 (1H, broad, m, N ν H), 4.15 (2H, q, J = 7.0, CH_2CH_3), 5.44 (1H, s, ArCH), 13.33 (1H, enolic) ppm.

Anal. Calcd. for $\text{C}_{22}\text{H}_{23}\text{ClNO}_6$: C, 60.99; H, 6.14; N, 3.57. Found: C, 61.27; H, 6.14; N, 3.51.

Ethyl α -Acetyl-2,3-dihydro-2-methyl-3-oxo-1H-naphth[1,2-e][1,3]oxazine-1-acetate (**1f**).

A solution of 18.3 g. (0.08 mole) of 1-hydroxy-2-methyl-1H-naphth[1,2-e][1,3]oxazin-3(2H)one (**3d**) (2), 11.5 g. (0.0885 mole) of ethyl acetoacetate and 0.005 g. of 4-methylbenzenesulfonic acid monohydrate was refluxed for 2 hours, while 1.2 ml. of water separated in a Dean-Stark trap. After the solvent was removed, the semi-solid residue was crystallized from ether giving 19.0 g. of white crystals, m.p. 144-145° dec. Recrystallization from 2-propanol gave 14.0 g. (51% yield) of analytically pure product **1f** containing approximately 1:1 mixture of keto and enol tautomers, m.p. 147-148° dec; uv (ethanol): λ max nm (ϵ) 229 (61,000), 248-261 plateau (8500), 264 (8600), 274 sh (7700), 289 (5000), 310 (1600), 324 (1700); ir (nujol): 1718 (C=O, cyclic carbamate and ester functions),

1630 (C=C-CO₂C₂H₅), 1598 (C=C) cm^{-1} ; pmr (deuteriochloroform): δ 1.17 (3H, m, J = 7.0 Hz, CH_2CH_2 of keto and enol tautomers overlapping), 2.23 (ca. 1.5 H, CH_3CO , enol fraction), 2.41 (ca. 1.5 H, keto fraction), 3.75 (ca. 0.5 H, d, J = 3.0 Hz, COCHCOOC₂H₅), 4.14 (2H, m, J = 7.0 Hz, CH_2CH_3 of both forms overlapping), 5.81 (0.5 H, s, ArCH, enol), 5.98 (0.5 H, d, J = 3.0 Hz, ArCH, keto tautomer), 14.55 (0.5 H, enolic proton) ppm.

Anal. Calcd. for $\text{C}_{19}\text{H}_{19}\text{NO}_6$: C, 66.85; H, 5.61; N, 4.10. Found: C, 67.07; H, 5.76; N, 4.13.

Ethyl α -[1-(Acetyloxy)ethylidene]-6-chloro-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1g**).

A solution of 7.0 g. (0.0215 mole) of ethyl 6-chloro-3,4-dihydro- α -(1-hydroxyethylidene)-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1d**), 10 ml. of acetic anhydride and 10 drops of triethylamine in 50 ml. of ethyl acetate was allowed to stand at 25° for 2 days. The solution was stirred with cold water, made neutral with aqueous sodium bicarbonate and separated. The organic phase was washed with water, dried over sodium sulfate and evaporated to dryness *in vacuo*. Crystallization of the residue from methanol gave 4.8 g. of analytically pure enol acetate (**1g**), m.p. 160-161°. Concentration of the mother liquor to a low volume gave 1.3 g. of additional product (total yield 73%), m.p. 159-160°; uv (ethanol): λ max nm (ϵ) 224 (20,050), 277 (1250), 286 (1200); ir (nujol): 1755 (C=O, C=C(CH₃)-O₂CCH₃), 1730, 1719 (benzoxazinone and -CO₂C₂H₅), 1658 (C=C) cm^{-1} ; (chloroform): 1768 (C=O, C=C-O₂CCH₃), 1720, 1711 (benzoxazinone and -CO₂C₂H₅), 1640 (C=C-O₂C-CH₃) cm^{-1} ; pmr (deuteriochloroform): δ 1.19 (3H, t, J = 7.0 Hz, CH_2CH_3), 2.28 (3H, $\text{CH}_3\text{-C=C}$), 2.39 (3H, CH_3CO_2), 2.96 (3H, N-CH₃), 4.15 (2H, q, J = 7.0 Hz, CH_2CH_3), 5.56 (1H, s, ArCH) ppm.

Anal. Calcd. for $\text{C}_{17}\text{H}_{18}\text{ClNO}_6$: C, 55.52; H, 4.93; N, 3.81. Found: C, 55.79; H, 4.96; N, 3.71.

Ethyl α -[1-[[Methylaminocarbonyl]oxy]ethylidene]-3,4-dihydro-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1h**).

A solution of 9.6 g. (0.03 mole) of ethyl 3,4-dihydro- α -(1-hydroxyethylidene)-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1c**), 11.4 g. (0.2 mole) of methyl isocyanate and 0.5 ml. of triethylamine in 300 ml. of benzene was refluxed for 7 hours. The tlc (benzene:acetone:heptane, 2:2:1) showed complete reaction, the new product having slower mobility ($R_f = 0.3$) than the starting **1c** ($R_f = 0.4$). The solvent and excess isocyanate were removed *in vacuo* and the residue was crystallized from ethyl ether-isopropyl ether, giving 8.4 g. (74% yield) of enol carbamate (**1h**) as white crystals, m.p. 160-161°; uv (ethanol): λ max nm (ϵ) 246 sh (5800), 285 (1950); ir (chloroform): 3450 (NH), 1754 (C=C-O₂C-NHCH₃), 1740, 1728 (benzoxazinone and -CO₂C₂H₅), 1670 (C=C-CO₂C₂H₅); (nujol): 3400 (NH), 1747 (C=C-O₂CNHCH₃), 1730 (benzoxazinone), 1712 (CO₂C₂H₅), 1669 (C=C-CO₂C₂H₅) cm⁻¹; ppm (deuteriochloroform): δ 1.17 (3H, t, J = 7.0 Hz, CH₂CH₃), 2.35 (3H, CH₃C=C), 2.82 (3H, N-CH₃), 2.91 (d, J = 6.0 Hz, NHCH₃), 3.81 (3H, OCH₃), 4.10, (2H, q, J = 7.0, CH₂CH₃), 5.26 (1H, ArCH), 5.35 (1H, d, J = 6.0 Hz, NHCH₃) ppm.
Anal. Calcd. for C₁₇H₂₂N₂O₇: C, 57.13; H, 5.86; N, 7.40. Found: C, 57.43; H, 5.99; N, 7.21.

Ethyl 1-(3,4-Dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-2-oxocyclohexanecarboxylate (**1i**).

A solution of 9.0 g. (0.05 mole) of 3,4-dihydro-4-hydroxy-3-methyl-2H-1,3-benzoxazin-2-one (**3e**) (2), 11.0 g. (0.064 mole) of ethyl 2-oxocyclohexanecarboxylate and 0.01 g. of 4-methylbenzenesulfonic acid monohydrate in 250 ml. of benzene was refluxed for 3 hours, while 0.9 ml. of water separated in a Dean-Stark trap. The solution was evaporated to dryness *in vacuo*, and the residue was crystallized from 2-propanol, giving 6.7 g. (41% yield) of product **1i** as white crystals, m.p. 142-143°, uv (ethanol): λ max nm (ϵ) 265 (1000), 272 (1000); ir (nujol): 1738, 1721 (C=O, benzoxazinone and saturated COOC₂H₅); (chloroform): 1726-1710 (C=O, benzoxazinone and saturated ester) cm⁻¹; pmr (deuteriochloroform): δ 1.10 to 1.90 [9H, t, J = 7.0 Hz (CH₂CH₃) and 6H of cyclohexane moiety overlapping], 2.42 (2H, t, 4.0 Hz, CH₂C=O) 3.04 (3H, N-CH₃), 4.36 (2H, q, CH₂CH₃), 5.44 (1H, s, ArCH) ppm.
Anal. Calcd. for C₁₈H₂₁NO₅: C, 65.24; H, 6.39; N, 4.24. Found: C, 65.10; H, 6.22; N, 4.30.

Ethyl 1-(6-Chloro-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-2-oxocyclohexanecarboxylate (**1j**).

A solution of 10.7 g. (0.05 mole) of 6-chloro-3,4-dihydro-4-hydroxy-3-methyl-2H-1,3-benzoxazin-2-one (**3b**) (2), 8.6 g. (0.06 mole) of ethyl 2-oxocyclohexanecarboxylate and 0.01 g. of 4-methylbenzenesulfonic acid monohydrate in 300 ml. of benzene was refluxed for 3 hours until the theoretical volume of water had separated. The solvent was removed *in vacuo*, and the gummy residue was crystallized from ether giving 7.1 g. (39% yield) of **1j** as white crystals, m.p. 185-186° dec. An analytical sample was obtained by recrystallization from acetonitrile, m.p. 186-187° dec; uv (ethanol): λ max nm (ϵ) 264 (1000), 272 (950); ir (nujol): 1735, 1701 (C=O, benzoxazinone, ester, ketone) cm⁻¹; pmr (deuteriochloroform): δ 1.00 to 2.00 [envelope of 6 protons of cyclohexane moiety and 1.24 (3H, t, J = 7.0 Hz, CH₂CH₃), 2.33 (2H, m, CH₂C=O), 2.93 (3H, NCH₃), 4.18 (2H, q, J = 7.0 Hz, CH₂CH₃), 5.25 (1H, ArCH) ppm.
Anal. Calcd. for C₁₈H₂₀ClNO₅: C, 59.10; H, 5.51; N, 3.83. Found: C, 58.88; H, 5.31; N, 4.10.

Ethyl 1-(6-Chloro-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-2-oxocyclopentanecarboxylate (**1k**).

A solution of 7.1 g. (0.03 mole) of 6-chloro-3,4-dihydro-4-hydroxy-3-methyl-2H-1,3-benzoxazin-2-one (**3b**), 5.2 g. (0.033 mole) of ethyl 2-oxocyclopentanecarboxylate and 0.01 g. of 4-methylbenzenesulfonic acid monohydrate in 200 ml. of benzene was refluxed for 3 hours, while 0.54 ml. of water had separated. After the solvent was removed *in vacuo*, the residue was crystallized from isopropyl ether giving 6.4 g. (60% yield) of product **1k**, m.p. 144-145°. An analytical sample, m.p. 145-146°, was obtained by recrystallization from acetonitrile; uv (ethanol): λ max nm

(ϵ) 223 (6900), 276 (1100), 283 (1050); ir (nujol): 1740 (ester C=O), 1735 (ketone, benzoxazinone C=O) cm⁻¹; pmr (deuteriochloroform): δ 1.32 (3H, t, J = 7.0 Hz, CH₂CH₃), 3.06 (3H, N-CH₃), 4.27 (2H, q, J = 7.0 Hz, CH₂CH₃), 5.33 (1H, s, ArCH) ppm.

Anal. Calcd. for C₁₇H₁₈ClNO₅: C, 58.04; H, 5.16; N, 3.98. Found: C, 57.99; H, 5.11; N, 3.92.

Methyl 3,4-Dihydro- α -(1-hydroxyethylidene)-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1l**).

A solution of 4.2 g. (0.02 mole) of **3a** (2), 3.5 g. (0.03 mole) of methyl acetoacetate and 0.01 g. of 4-methylbenzenesulfonic acid monohydrate in 150 ml. of benzene was refluxed for 2 hours, while 0.36 ml. of water separated in a Dean-Stark trap. After the solution was evaporated *in vacuo*, the colorless semi-solid was crystallized from ether-cyclohexane to give 2.1 g. of white, crystalline solid, m.p. 144-146°. This product, having about 95% of enol content, was recrystallized from cyclohexane-ethyl acetate giving 1.7 g. (29% yield) of pure enol tautomer **1l**, m.p. 148-149°; uv (ethanol): λ max nm (ϵ) 225 sh (11,900), 251 (7350), 280 sh (3500); ir (chloroform): 1721, 1711 (C=O, benzoxazinone), 1638-1610 (C=C-CO₂CH₃) cm⁻¹; pmr (deuteriochloroform): δ 2.22 (3H, CH₃-C=C), 2.90 (3H, N-CH₃), 3.38 (3H, CH₃O-C-), 3.82 (3H, CH₃O-Ar), 5.36 (1H, ArCH), 13.04 (1H, enolic) ppm.
Anal. Calcd. for C₁₅H₁₇NO₆: C, 58.63; H, 5.58; N, 4.56. Found: C, 58.33; H, 5.61; N, 4.45.

The original mother liquor, containing about equal amounts of keto and enol tautomers (by pmr) did not yield any more product by attempted direct crystallization.

Attempted Tautomerization of Methyl 3,4-Dihydro- α -(1-hydroxyethylidene)-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1l**).

A solution of 1.0 g. of pure enol **1l** and 25 mg. of 4-methylbenzenesulfonic acid monohydrate (similar conditions as during the preparation of **1l**) was refluxed for 10 hours. After the solvent was removed, the nearly colorless residue was crystallized from ethyl acetate-ethyl ether giving 0.85 g. of **1l**, m.p. 148-149°. A mixture m.p. with an analytical product was not depressed and the spectra were identical. The mother liquor still contained a small amount of **1l** and some apparent decomposition products but no more solid could be isolated.

Condensation of β -Keto Esters **1** with Hydrazines **5**.

4-(2,5-Dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)-3,4-dihydro-3-methyl-2H-1,3-benzoxazin-2-one (**2a**) (Table II).

A solution of 12.0 g. (0.0414 mole) of ethyl α -acetyl-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1a**) (2), 5.5 g. (0.051 mole) of phenylhydrazine and 10 drops of glacial acetic acid in 100 ml. of absolute ethanol was allowed to stand 2 days at 25°. The resulting nearly white, analytically pure crystals (5.3 g.) were collected, m.p. 210-211° dec. Concentration of the mother liquor to a low volume gave 1.9 g. (total yield 52%) of additional crop of **2a**, m.p. 209-210° dec; uv (ethanol): λ max nm (ϵ) 247 (14,000), 260-268 plateau (11,200); ir (nujol): 3050 (NH), 1717 (C=O, benzoxazinone), 1621, 1588 (C=C-CO-); (acetonitrile): 3520 (NH), 1718 (benzoxazinone), 1653, 1590 (C=C-CO-) cm⁻¹; pmr (DMSO-d₆): δ 1.88 (3H, CH₃C=C), 3.00 (3H, N-CH₃), 5.65 (1H, s, ArCH), 11.27 (1H, deuterium oxide-exchangeable, NH) ppm.

Anal. Calcd. for C₁₉H₁₇N₃O₅: C, 68.05; H, 5.11; N, 12.53. Found: C, 68.25; H, 5.34; N, 12.74.

4-(2,5-Dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)-3,4-dihydro-8-methoxy-3-methyl-2H-1,3-benzoxazin-2-one (**2b**).

A solution of 10.0 g. (0.0312 mole) of ethyl 3,4-dihydro- α -(1-hydroxyethylidene)-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1c**), 4.2 g. (0.044 mole) of phenylhydrazine and 5 drops of glacial acetic acid in 150 ml. of absolute ethanol was allowed to stand at room temperature for 4 days and subsequently heated at 50° for 3 hours. The solution was concentrated to a low volume and gave, after cooling, 7.1 g. (63% yield) of **2b**, m.p. 228-229° dec. An analytical sample, m.p. 229-230° dec, was obtained by recrystallization from ethyl acetate; uv (ethanol): λ max nm

(ϵ) 246 (14,000), 271 (11,900); ir (nujol): 3100 (NH), 1720 (C=O, benzoxazinone), 1640-1594 (C=C-CO) cm^{-1} ; pmr (DMSO- d_6): δ 2.12 (3H, $\text{CH}_3\text{-C}=\text{C}$), 2.88 (3H, N- CH_3), 3.85 (OCH $_3$), 5.66 (1H, Ar- CH), 11.35 (NH) ppm.

Anal. Calcd. for $\text{C}_{20}\text{H}_{19}\text{N}_3\text{O}_4$: C, 65.74; H, 5.24; N, 11.50. Found: C, 65.94; H, 5.32; N, 11.36.

6-Chloro-4-(2,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)-3,4-dihydro-3-methyl-2H-1,3-benzoxazin-2-one (**2c**).

A solution of ethyl 6-chloro-3,4-dihydro- α -(1-hydroxyethylidene)-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1d**, 8.0 g., 0.0246 mole), 3.6 g. (0.033 mole) of phenylhydrazine and 0.2 ml. of glacial acetic acid in 110 ml. of absolute ethanol was allowed to stand at room temperature for 12 days. The resulting product **2c** as off-white crystals was collected by filtration (7.4 g., 81% yield), m.p. 254-255° dec. An analytical sample, m.p. 255-256° dec, was obtained by recrystallization from ethanol; uv (ethanol): λ max nm (ϵ) 226 (18,450), 272 (10,550); ir (nujol): 3400, 3130 (NH), 1712 (C=O, benzoxazinone), 1622, 1593 (C=C-CO-) (CH_3CN): 3540 (NH), 1724 (benzoxazinone), 1625 (C=C-CO) cm^{-1} ; pmr (DMSO- d_6): δ 2.16 (3H, $\text{CH}_3\text{C}=\text{C}$), 2.83 (3H, N- CH_3), 5.63 (1H, s, Ar CH), 11.45 (1H, exchangeable with deuterium oxide, NH) ppm.

Anal. Calcd. for $\text{C}_{19}\text{H}_{18}\text{ClN}_3\text{O}_5$: C, 61.71; H, 4.36; N, 11.36; Cl, 9.59. Found: C, 61.77; H, 4.49; N, 11.17; Cl, 9.47.

1-(2,5-Dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)-1,2-dihydro-2-methyl-3H-naphth[1,2- e][1,3]oxazin-3-one (**2d**).

A solution of 10.24 g. (0.03 mole) of ethyl α -acetyl-2,3-dihydro-2-methyl-3-oxo-1H-naphth[1,2- e][1,3]oxazine-1-acetate (**1f**, about 50:50 mixture of keto and enol tautomers), 4.2 g. (0.039 mole) of phenylhydrazine and 10 drops of glacial acetic acid in 120 ml. of absolute ethanol was allowed to stay at room temperature for 3 days. There separated 4.9 g. of off-white crystals of analytical purity, m.p. 237-238° dec. Concentration of the filtrate to a low volume gave 1.2 g. (total yield 52%) of additional product **2d**, m.p. 236-237° dec; uv (ethanol): λ max nm (ϵ) 228 (68,200), 272-278 plateau (14,000), 323 (2000); ir (nujol): 3140 (NH), 1709 (C=O, benzoxazinone), 1618, 1578 (C=C-CO) cm^{-1} ; pmr (DMSO- d_6): δ 2.04 (3H, $\text{CH}_3\text{-C}=\text{C}$), 3.07 (3H, N- CH_3), 6.18 (1H, s, Ar- CH) ppm.

Anal. Calcd. for $\text{C}_{22}\text{H}_{21}\text{N}_3\text{O}_5$: C, 71.67; H, 4.97; N, 10.90. Found: C, 71.60; H, 5.09; N, 10.89.

4-[2,5-Dihydro-3-methyl-5-oxo-1-(2-phenylethyl)-1H-pyrazol-4-yl]-3,4-dihydro-3-methyl-2H-1,3-benzoxazin-2-one (**2e**).

A solution of 8.0 g. (0.0275 mole) of ethyl α -acetyl-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1a**) (2), 3.75 g. (0.0275 mole) of *N*-(2-phenylethyl)hydrazine and 1 ml. of glacial acetic acid in 100 ml. of absolute ethanol was refluxed for 2 hours until the reaction was complete. After the solvent was evaporated *in vacuo*, the residue was crystallized from acetonitrile giving 7.5 g. of product **2e**, m.p. 101-102°. Recrystallization from acetonitrile gave 5.7 g. (56% yield) of pure **2e** as white crystals, m.p. 104-105°; uv (ethanol): λ max nm (ϵ) 253 (7350); ir (nujol): 3370 (NH), 1718 (C=O, benzoxazinone), 1593 (C=C-CO-); (chloroform): 3620, 3300 (NH), 1705 (benzoxazinone), 1594 (C=C-CO) cm^{-1} .

Anal. Calcd. for $\text{C}_{21}\text{H}_{21}\text{N}_3\text{O}_5$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.43; H, 5.99; N, 11.31.

4-(2,5-Dihydro-1,3-dimethyl-5-oxo-1H-pyrazol-4-yl)-3,4-dihydro-8-methoxy-3-methyl-2H-1,3-benzoxazin-2-one (**2f**).

A solution of 6.0 g. (0.0187 mole) of ethyl 3,4-dihydro- α -(1-hydroxyethylidene)-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1c**), 4.0 g. (0.037 mole) of methyl hydrazine and 5 drops of glacial acetic acid in 100 ml. of ethanol was allowed to stand for 2 days at 25° and then refluxed for 5 hours. The solvent and excess methylhydrazine were removed *in vacuo* and the residue was crystallized from acetonitrile giving 3.8 g. (67% yield) of pure product **2f** as white crystals, m.p. 212-213° dec; uv (ethanol): λ max nm (ϵ) 225 sh (12,800), 254 (6800), 280 sh (2000); ir (DMSO) 3230 (NH), 1707 (C=O, benzoxazinone), 1618 (C=C-CO-) cm^{-1} ; pmr (DMSO- d_6): δ 1.85 (3H, $\text{CH}_3\text{-C}=\text{C}$), 2.87 (3H, N- CH_3 , benzoxa-

zinone), 3.34 (3H, N CH_3 , pyrazolone), 3.84 (3H, OCH $_3$), 5.52 (1H, Ar CH), 10.75 (1H, NH) ppm.

Anal. Calcd. for $\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_4$: C, 59.40; H, 5.65; N, 13.85. Found: C, 59.56; H, 5.71; N, 14.02.

6-Chloro-3-cyclohexyl-4-(2,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)-3,4-dihydro-2H-1,3-benzoxazin-2-one (**2g**).

A solution of 4.6 g. (0.0117 mole) of ethyl 6-chloro-3-cyclohexyl-3,4-dihydro- α -(1-hydroxyethylidene)-2-oxo-2H-1,3-benzoxazine-4-acetate (**1e**), 1.5 g. (0.014 mole) of phenylhydrazine and 0.5 ml. of glacial acetic acid in 50 ml. of absolute methanol was allowed to stand for 20 hours at 25°. The resulting product (**2g**) as off white crystals of analytical purity, was collected (2.6 g.), m.p. 167-168° dec. Concentration of the filtrate to a low volume gave 0.5 g. of additional material (total yield 60%), m.p. 166-167° dec; uv (ethanol): λ max nm (ϵ) 224 (19,650), 245 sh (13,700), 263-276 plateau (10,500); ir (nujol), 3400, 3050 (NH), 1721 (C=O, benzoxazinone), 1627, 1591 (C=C-CO-) cm^{-1} ; pmr (DMSO- d_6): δ 1.10 to 2.00 (10H, cyclohexane moiety), 3.50 (1H, m, N CH), 5.76 (1H, s, Ar CH), 11.15 (1H, NH) ppm.

Anal. Calcd. for $\text{C}_{22}\text{H}_{24}\text{ClN}_3\text{O}_5$: C, 65.83; H, 5.52; N, 9.60. Found: C, 65.92; H, 5.40; N, 9.87.

4-(2,3-Dihydro-5-methyl-3-oxo-1H-pyrazol-4-yl)-3,4-dihydro-8-methoxy-3-methyl-2H-benzoxazin-2-one (**2h**).

A solution of 3.13 g. (0.01 mole) of ethyl α -acetyl-3,4-dihydro-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (**1b**), 1.0 g. of hydrazine hydrate (85% solution) and 2.0 ml. of glacial acetic acid in 25 ml. of absolute ethanol was allowed to stand at room temperature for 20 hours. The resulting white, shiny crystals (1.9 g.) of **2h** of analytical purity were obtained by filtration, m.p. 255-256° dec. The filtrate was evaporated to dryness under reduced pressure, the residue was taken up with cold water and the resulting crude crystals collected on filter, m.p. 249-251 dec. Recrystallization from ethyl acetate gave 0.6 g. (total yield 86%) of white **2h**, m.p. 255-256° dec; uv (ethanol): λ max nm (ϵ) 226 sh (12,750), 260 sh (2300), 281 (2000), 290 (1950); ir (nujol): 3230 (NH), 1690 (C=O, benzoxazinone), 1630 (C=C-CO-) cm^{-1} ; pmr (DMSO- d_6): δ 2.02 (3H, C=C- CH_3), 2.80 (3H, N- CH_3), 3.80 (3H, OCH $_3$), 5.49 (1H, s, Ar CH), 10.54 [2H, exchangeable with deuterium oxide, (NH) $_2$] ppm.

Anal. Calcd. for $\text{C}_{14}\text{H}_{15}\text{N}_3\text{O}_4$: C, 58.12; H, 5.23; N, 14.53. Found: C, 57.94; H, 5.36; N, 14.33.

4-(3,5-Dimethyl-1H-pyrazol-4-yl)-3,4-dihydro-8-methoxy-3-methyl-2H-1,3-benzoxazin-2-one (**7a**) (Table III).

A solution of 2.8 g. (0.01 mole) of 3-(3,4-dihydro-8-methoxy-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-2,4-pentanedione (**6b**) (2), 1.0 g. of hydrazine hydrate (85%) and 2.0 ml. of glacial acetic acid in 25 ml. of absolute ethanol was allowed to stand at 25° for 20 hours. The resulting sugar-like, white crystals (0.9 g.) were collected, m.p. 208-209° dec. After the filtrate was evaporated to dryness *in vacuo*, the residue was taken up with cold water and the white precipitate was collected by filtration (1.1 g.), m.p. 203-205° dec. The combined crops were recrystallized from ethyl acetate to give 1.6 g. (55% yield) of an analytically pure product **7a**, m.p. 214-215° dec; uv (ethanol): λ max nm (ϵ) 273 (1850), 280 (1860); ir (nujol): 3420 (NH), 1723 (C=O, benzoxazinone) cm^{-1} ; pmr (deuteriochloroform): δ 2.20 [6H, s, C- CH_3] $_2$, 2.89 (3H, N- CH_3), 3.86 (3H, OCH $_3$), 5.49 (1H, s, Ar CH), 10.23 (1H, exchangeable with deuterium oxide, NH) ppm.

Anal. Calcd. for $\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_5$: C, 62.70; H, 5.96; N, 14.63. Found: C, 62.63; H, 5.94; N, 14.63.

3,4-Dihydro-3-methyl-4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)-2H-1,3-benzoxazin-2-one (**7b**).

A solution of 8.5 g. (0.0345 mole) of 2-(3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-1-phenyl-1,3-butanedione (**6c**) (2) and 2.0 g. of anhydrous hydrazine in 75 ml. of absolute ethanol was allowed to stand for 2 days at 25°. The solution was evaporated *in vacuo* and the residue was crystallized from acetonitrile giving 5.2 g. of pure **7b** as white crystals, m.p. 148-149°. Concentration of the filtrate to a low volume

gave 1.2 g. (total yield 58%) of additional product, m.p. 147-148°; uv (ethanol): λ max nm (ϵ) 240 sh (9000), 276 (1600); ir (nujol): 3200 (NH), 1692 (C=O, benzoxazinone); (chloroform): 3470, 3200 (NH), 1720, 1709 (C=O, benzoxazinone) cm^{-1} ; pmr (deuteriochloroform): δ 1.95 (3H, $\text{CH}_3\text{-C}=\text{C}$), 2.80 (3H, N- CH_3), 5.63 (1H, s, ArCH), 6.80 to 7.30 (4H, m, aromatic protons), 7.45 (5H, s, phenyl), 10.05 (1H, very broad, exchangeable with deuterium oxide NH) ppm.

Anal. Calcd. for $\text{C}_{19}\text{H}_{17}\text{N}_3\text{O}_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.17; H, 5.31; N, 12.93.

4-(3,5-Dimethyl-1-phenyl-1H-pyrazol-4-yl)-3,4-dihydro-3-methyl-2H-1,3-benzoxazin-2-one (7c).

A solution of 7.0 g. (0.027 mole) of 3-(3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-2,4-pentanedione (6a) (2), 2.9 g. (0.027 mole) of phenylhydrazine and 8 ml. of glacial acetic acid in 120 ml. of benzene was refluxed for 4 hours, while the theoretical volume of water separated in a Dean Stark trap. The solution was cooled to 0°, made neutral with ammonium hydroxide and separated. The benzene layer was washed with water, dried over sodium sulfate and evaporated to dryness *in vacuo*. The amber-like semi-solid was crystallized from diethyl ether-isopropyl ether giving 6.0 g. (66% yield) of product 7c as off-white crystals, m.p. 143-144° dec. An analytical sample, m.p. 144-145° dec, was obtained by recrystallization from cyclohexane and then from ether; uv (ethanol): λ max nm (ϵ) 245 (13,750); ir (nujol): 1715 (C=O, benzoxazinone) cm^{-1} ; pmr (deuteriochloroform): δ 2.16, 2.21 [6H, ($\text{CH}_3\text{-C}=\text{C}$)₂], 2.99 (3H, N- CH_3), 5.65 (1H, s, ArCH) ppm.

Anal. Calcd. for $\text{C}_{20}\text{H}_{19}\text{N}_3\text{O}_2$: C, 72.05; H, 5.74; N, 12.61. Found: C, 72.34; H, 5.84; N, 12.76.

3,4-Dihydro-3-methyl-4-[2-(phenylhydrazono)-1-[1-(phenylhydrazono)ethyl]-propyl]-2H-1,3-benzoxazin-2-one (9) (Table III).

A solution of 5.2 g. (0.02 mole) of 3-(3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-2,4-pentanedione (6a) (2) and 2.2 g. (0.02 mole) of phenylhydrazine in 125 ml. of benzene was refluxed for 3 hours, while 0.3 ml. of water separated in a Dean-Stark trap. The tlc (acetone:benzene:heptane, 2:2:1) showed the new product to migrate slightly faster ($R_f = 0.46$) than the starting diketone ($R_f = 0.4$), which was still present. Concentration of the solution to about 50 ml. and cooling gave 2.3 g. (85% yield, based on phenylhydrazine used for the reaction) of analytically pure bis-hydrazone 9 as white crystals, m.p. 216-217° dec; uv (ethanol): λ max nm (ϵ) 283 (36,500), 300 sh (26,000); ir (nujol): 3300 (NH), 1718 (C=O, benzoxazinone), 1598 (C=N); (chloroform): 3630, 3370 (NH), 1719 (benzoxazinone), 1599 (C=N) cm^{-1} ; pmr (DMSO- d_6): δ 1.48 (3H, $\text{CH}_3\text{-C}=\text{N}$), 1.96 (3H, $\text{CH}_3\text{-C}=\text{N}$), 3.03 (3H, N- CH_3), 3.56 (1H, d, J = 6.5 Hz, -CH-), 5.40 (1H, d, J = 6.5, ArCH), 8.82 (NH) ppm.

Anal. Calcd. for $\text{C}_{26}\text{H}_{27}\text{N}_5\text{O}_2$: C, 70.72; H, 6.16; N, 15.86. Found: C, 70.92; H, 6.38; N, 15.96.

4-(2,4-Dimethyl-3H-1,5-benzodiazepin-3-yl)-3,4-dihydro-3-methyl-2H-1,3-benzoxazin-2-one (12) (Table III).

A solution of 18.3 g. (0.07 mole) of 3-(3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-2,4-pentanedione (6a), 7.6 g. (0.07 mole) of 1,2-benzenediamine and 5 ml. of glacial acetic acid was refluxed under nitrogen for 5 hours while the theoretical volume of water had separated. The tlc (benzene:acetone:heptane, 2:2:1) showed absence of starting diketone derivative ($R_f = 0.4$) and presence of two spots at $R_f = 0.30$ (ca. 65%) and $R_f = 0.35$ (ca. 25%), respectively. The solution was evaporated to dryness *in vacuo*. Trituration of the residue with hot 2-propanol and cooling gave 11.3 g. (49% yield) of diazepine derivative 12 as yellow crystals, m.p. 195-196° dec ($R_f = 0.3$). An analytical sample, m.p. 196-197° dec, was obtained by recrystallization from 2-propanol-isopropanol ether; uv (ethanol): λ max nm (ϵ) 213 (26,600), 236 sh (15,000), 273 (6600), 310 sh (3000); ir (nujol): 1740, 1720 (C=O, benzoxazinone), 1638 (C=N); (chloroform): 1725 (benzoxazinone), 1638 (C=N) cm^{-1} ; pmr (deuteriochloroform): δ 1.83 (3H, $\text{CH}_3\text{C}=\text{N}$), 2.46 (3H, $\text{CH}_3\text{C}=\text{N}$), 2.86 (3H, N- CH_3), 3.94 (2H, AB-quartet, J = 11.0 Hz, ArCH-CH) ppm.

Anal. Calcd. for $\text{C}_{20}\text{H}_{19}\text{N}_3\text{O}_2$: C, 72.05; H, 5.74; N, 12.61. Found: C, 72.28; H, 5.77; N, 12.31.

2-[(2,4-Dimethyl-3H-1,5-benzodiazepin-3-ylidene)methyl]phenol (13).

The mother liquor of the original crop (11.3 g.) was evaporated, taken up with ether and passed over 40 g. of Florisil, ether being used as an eluent. Fractions 1-4 (50 ml. each) contained the faster moving product, $R_f = 0.35$. After the solvent was removed, the combined residue was crystallized from isopropyl ether giving 2.9 g. (12% yield) of the elimination product, 2-[(2,4-dimethyl-3H-1,5-benzodiazepin-3-ylidene)methyl]phenol 13, as bright yellow crystals, m.p. 204-205° dec. ($R_f = 0.35$). An analytical product was obtained by recrystallization from ethyl acetate-isopropyl ether; uv (ethanol): λ max nm (ϵ) 212 sh (36,500), 234 sh (24,000), 273 (9400), 326 (4650); ir (nujol): 3390 (OH), 1638, 1615 (N=C-C=C); (chloroform): 3400 (OH), 1639, 1620 (N=C-C=C); cm^{-1} ; pmr (deuteriochloroform): δ 1.58 (3H, $\text{CH}_3\text{C}=\text{N}$), 2.56 (3H, $\text{CH}_3\text{C}=\text{N}$), 4.21 (1H, OH), 6.43 (1H, CH=C) ppm.

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}$: C, 78.23; H, 5.84; N, 10.14. Found: C, 78.36; H, 5.92; N, 9.95.

Ethyl 1-(6-Chloro-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-2-hydrazonecyclopentanecarboxylate (10).

A solution of 5.0 g. (0.0164 mole) of ethyl 1-(6-chloro-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazin-4-yl)-2-oxocyclopentanecarboxylate (1k) and 3.0 g. of anhydrous hydrazine in 75 ml. of absolute ethanol was refluxed for 3 hours. The tlc (acetone:benzene:heptane, 2:2:1) showed absence of the starting 1k and presence of two new spots at $R_f = 0.3$ (ca. 65%) and $R_f = 0.18$ (ca. 30%), respectively. The solution was evaporated to dryness *in vacuo*, and the residue was crystallized from acetonitrile giving 2.7 g. of ester hydrazone 10, m.p. 177-179°. Recrystallization from acetonitrile gave 2.3 g. (44% yield) of analytically pure 10 as white crystals ($R_f = 0.3$), m.p. 180-181°. The product having slower migration ($R_f = 0.18$) could not be isolated by crystallization; uv (ethanol): λ max nm (ϵ) 232 sh (6200), 285 (2000), 294 (1800); ir (nujol): 3380 (NH), 1732 (C=O, benzoxazinone and unconjugated ester), 1639 (C=N) cm^{-1} ; pmr (deuteriochloroform): δ 1.32 (3H, t, J = 7.5 Hz CH_2CH_3), 1.50 to 2.10 (6H, cyclopentane moiety), 2.94 (3H, N CH_3), 4.12 (2H, NH₂), 4.24 (2H, q, J = 7.5 Hz, CH_2CH_3), 4.50 (1H, s, ArCH) ppm.

Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{ClN}_2\text{O}_3$: C, 55.82; H, 5.51; N, 11.49; Cl, 9.69. Found: C, 56.01; H, 5.50; N, 11.26; Cl, 9.67.

Ethyl α -[1-[(2-Aminophenyl)amino]ethylidene]-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (16).

A solution of 8.0 g. (0.0275 mole) of a 1:1 mixture of tautomers 1a and 1b and 3.0 g. (0.0275 mole) of 1,2-benzenediamine in 200 ml. of benzene was refluxed for 5 hours, while 0.4 ml. of water separated in a Dean-Stark trap. The solution was evaporated to dryness. The tlc (acetone:benzene:heptane, 3:2:1, in ammonia atmosphere) showed two new spots, $R_f = 0.4$ (ca. 60%) and $R_f = 0.3$ (ca. 20%). The solvent was removed, and the residue was triturated with ether-ethyl acetate giving 3.1 g. (30% yield) of ethyl α -[1-[(2-aminophenyl)amino]ethylidene]-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (16), m.p. 156-157°. An analytical sample, m.p. 158-159°, was obtained by recrystallization from ethanol; uv (ethanol): λ max nm (ϵ) 222 sh (24,800), 290 (13,300); ir (nujol): 3410, 3330, 3170 (NH), 1694 (C=O, benzoxazinone), 1645, 1622, 1575 (C=C-CO₂C₂H₅); (chloroform): 3460, 3370 (NH), 1709 (benzoxazinone), 1641, 1620, 1578 (C=C-CO₂C₂H₅) cm^{-1} ; pmr (deuteriochloroform): δ 1.07 (3H, t, J = 7.5 Hz, CH_2CH_3), 2.13 (3H, $\text{CH}_3\text{C}=\text{C}$), 3.00 (3H, N- CH_3), 3.92 (2H, NH₂), 4.02 (2H, q, J = 7.5 Hz, CH_2CH_3), 5.54 (1H, ArCH), 10.45 (1H, HN-C=C), ppm.

Anal. Calcd. for $\text{C}_{21}\text{H}_{23}\text{N}_3\text{O}_4$: C, 66.13; H, 6.08; N, 11.02. Found: C, 66.02; H, 6.23; N, 11.14.

Ethyl α -[1-[(2-Aminophenyl)imino]ethyl]-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (17).

The original mother liquor from 16 was passed over 30 g. of Florisil, ether-ethyl acetate being used as eluents. The first 5 fractions (50 ml.

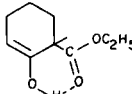
each), containing predominantly the slower moving isomer ($R_f = 0.3$), were crystallized from ethyl acetate giving 0.4 g. of the imino derivative, ethyl α -[1-(2-aminophenyl)imino]ethyl]-3,4-dihydro-3-methyl-2-oxo-2H-1,3-benzoxazine-4-acetate (17), m.p. 195-196°; uv (ethanol): λ max nm (ϵ) 220 sh (24,500), 289 (13,500); ir (nujol): 3500, 3400, 3200 (NH), 1707 (C=O, benzoxazinone), 1635, 1637, 1611 (N=C-CH-CO₂C₂H₅); (chloroform): 3460, 3370, 2220 (NH), 1702, 1610, 1675, 1660, 1650, 1640, (benzoxazinone and amino-imino ester) cm⁻¹; pmr (deuteriochloroform): δ 1.20 (3H, t, J = 7.5 Hz, CH₂CH₃), 2.04 (3H, N-CH₃), 2.84 (3H, N-CH₃), 4.10 (3H, m, CH₂CH₃, and N=C-CH), 5.63 (1H, d, J = 6.0 Hz, ArCH) ppm.

Anal. Calcd. for C₂₁H₂₃N₃O₄: C, 66.13; H, 6.08; N, 11.02. Found: C, 66.17; H, 6.00; N, 10.94.

Acknowledgement.

We wish to thank Professor E. L. Eliel for most helpful discussions. The authors are grateful to 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.

REFERENCES AND NOTES

- (1) Present address: Yardley Place, Mendham, New Jersey.
- (2) G. Bobowski and J. Shavel, Jr., *J. Org. Chem.*, **32**, 953 (1967).
- (3) G. Bobowski and J. Shavel, Jr., *J. Heterocyclic Chem.*, **15**, 1193 (1978).
- (4) G. Bobowski and J. Shavel, Jr., manuscript in press.
- (5) Enolization is possible only when there is a free α -hydrogen. Although, theoretically at least, enolization could involve the *gamma* hydrogen (to form ) , no such case was observed.
- (6) H. S. Jarrett, M. S. Sadler and J. N. Shoolery, *J. Chem. Phys.*, **21**, 2092 (1953).
- (7) L. W. Reeves, *Can. J. Chem.*, **35**, 1351 (1957).
- (8) J. L. Burdett and Max T. Rogers, *J. Am. Chem. Soc.*, **86**, 2105 (1964).
- (9) C. Giessner-Prettre, *Compt. Rend.*, **250**, 2547 (1960).