Substituted γ-Lactones. XXX (1).
Reactions of α-Keto-β-Substituted-γ-butyrolactones with Diamines

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The condensation reaction between α-keto-β-aroyl (or acyl)-γ-butyrolactones, **4a-4e** and *o*-phenylenediamine or 2,3-diaminonaphthalene leads under retrograde aldol condensation involving loss of formaldehyde to formation of 3-substituted-3,4-dihydro-2(1*H*)quinoxalinones or benzo[*g*]quinoxalinones, **7a-7g**, respectively as a new convenient synthesis of this type of heterocyclic systems. The reaction of type **4** compound with 4,5-diaminopyrimidine, **8**, was found to proceed differently. 2-[(4-Amino-5-pyrimidinyl)amine]-4-oxo-3-(hydroxymethyl)-4-phenyl-2-butenoic acid **9** was the only product formed when the reaction between **4a** and **8** was run in ethanol. The same reaction in glacial acetic acid proceeds with loss of formaldehyde, to afford 7-phenacylidene-7,8-dihydro-6(1*H*)-pteridinone **10**. The reaction between type **4** compounds and ethylenediamine or 1,4-phenylenediamine leads to the formation of the bis-condensation products **13-15**, respectively.

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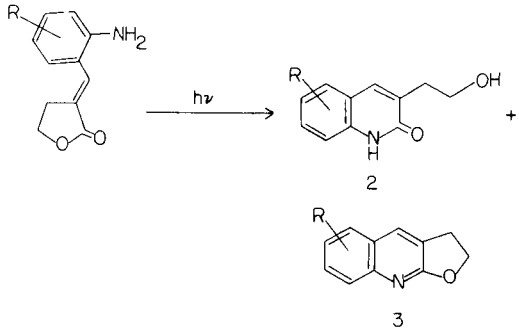
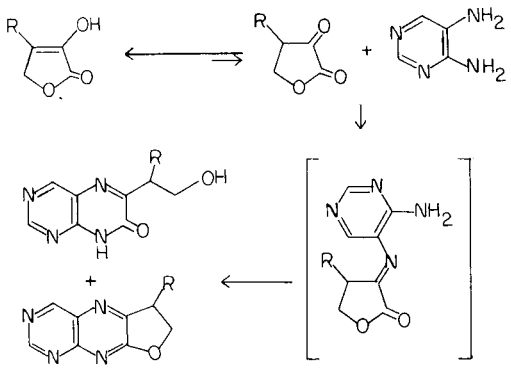
Some time ago we showed that *E*-α-(2-aminoarylidene)-γ-butyrolactones, **1** (4), upon photolysis yielded a mixture of two products, 3-(2-hydroxyethyl)carbostyriles, 2, and 2,3-dihydro[2,3-*b*]furoquinolines, **3**. This method was also applied for a simple 4-step synthesis of maculine, a dictamine alkaloid, of the furoquinoline group (4b).



These results seem to indicate that appropriately substituted γ-butyrolactones might represent feasible starting materials for a convenient route toward construction of the furopteridine ring, especially the linearly condensed furo[2,3-*g*]pteridine system, of which a number of important natural products are derived (Scheme I). Therefore,

Scheme I



an investigation of the reaction between α-keto-β-butyrolactones (systematic name is 3-hydroxy-2(5*H*)-furanone) and *ortho*-arylenediamines was begun (3). For several reasons we choose to attempt these condensations with β-aroyl(acyl)-α-keto-γ-butyrolactones as the carbonyl species.

A. Synthesis and Structure of α-Keto-β-Substituted-γ-Butyrolactones.

The chemical and pharmaceutical versatility (3,5b,6) of α-keto-β-substituted-γ-butyrolactones of type **4** and their synthetic applicability are of considerable current interest. The multifunctional character of these small molecules confers an intriguing synthetic potential some aspects of which were developed by us.

Scheme II

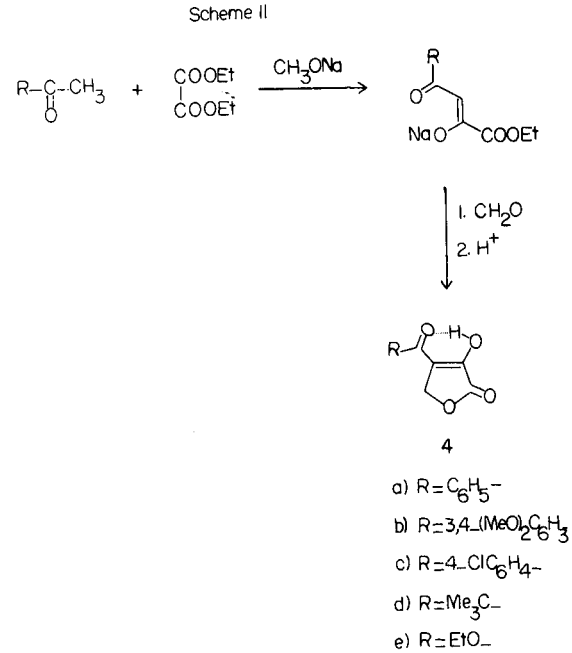


Table I

^{13}C-NMR Chemical Shifts of Compounds **4a-4e** (a)

Compound No.	Solvent	Temperature C°	C-2	C-3	C-4	C-5	C-1′
4a	$CDCl_3$	50	166.251	154.849	119.974	67.583	190.456
4a	DMSO-d_6	50	169.380	144.283	121.606	67.750	189.222
4b	DMSO-d_6	19	169.643	143.093	122.318	68.040	187.500
4c	$CDCl_3$	29	167.109	152.681	120.209	67.785	188.888
4d	$CDCl_3$	40,50	166.756	153.150	119.546	67.692	205.259
4d	DMSO-d_6	40	169.793	141.798	120.810	68.164	201.005
4e	$CDCl_3$	19	166.95	150.453	116.139	66.310	163.895

(a) Chemical shifts in δ ppm against TMS as internal standard.

The preparation of α-keto-β-substituted-γ-butyrolactones **4a-4e** were based on the method employed by Nield (5a) and modified by Manning (6) (Scheme II). Compounds **4a-4e** conceivably could occur as three tautomers **4A, 4B** and **4C**, but all previous studies done on these type of compounds have shown that they exist practically exclusively in the enolic form **4A** (5-7). There was no indication of the tautomeric forms **4B** and **4C** either by their ir-spectra in the crystalline state, by their ^{1}H-nmr spectra in dimethyl sulfoxide-d_6 or deuterochloroform solutions or by their mass spectra in the gas phase. Additional and conclusive evidence for these compounds to exist in the tautomeric form **4A** was provided by ^{13}C-nmr spectroscopy.

In Table I the observed chemical shifts are reported and assigned. Unambiguous evidence for the structure of type **4** compound is obtained from interpretation of the ^{13}C-^{1}H coupling constants (Table II). Only tautomer **4A** is in agreement with the observed pattern for the C-3, namely an allylic coupling with the protons at C-5 with a coupling constant ^3J = 2.9 (t) (compound **4a**) and ^3J = 3.19 (t) (compound **4d**). Compounds **4b**,**4c** and **4e** only show a poorly or unresolved triplet, but with agreeing chemical shift positions. Attempts of resolve these peaks into the expected triplets utilizing Eu(fod)$_3$ were unsuccessful. Compounds **4a** and **4d** show a significant change in their ^{13}C chemical shifts in dependency of solvents. It is noteworthy that in deuterochloroform solution **4a** as well as **4d** show a downfield shift for the C-1′ resonance indicating involvement of this carbonyl group in H-bonding in this solvent (Table I).

Table II

^{13}C-^{1}H Coupling Constants for **4a-4e**

Compound No.	C-3	C-4	C-5	C-1′
4a	^3J = 2.9 (t)	^2J = 5.01 (t)	^1J = 155.52 (t)	^3J = 3.6 (t)
4b	(a)	^2J = 4.16 (t)	^1J = 155.65 (t)	(b)
4c	(a)	^2J = 3.84 (t)	^1J = 155.49 (t)	^3J = 3.33 (t)
4d	^3J = 3.19 (t)	^2J = 5.19 (t)	^1J = 155.96 (t)	^3J = 4.59 (t)
4e	^3J = 3.18 (t) (a)	^2J = 5.14 (t)	^1J = 156.47 (t)	—

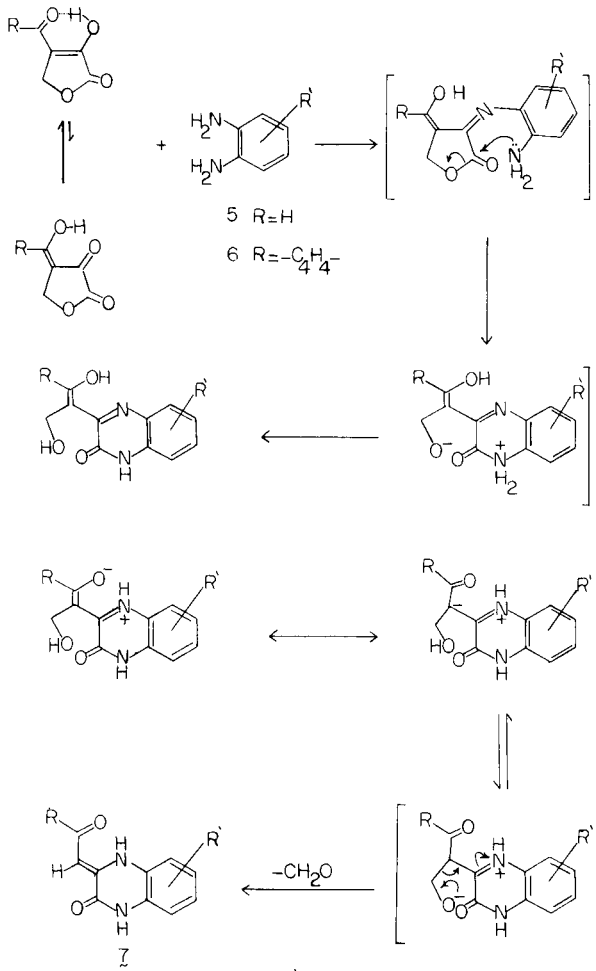
(a) These peaks appeared only at poorly resolved triplets. (b) Though the protons at the 2- and 6-positions of the phenyl group are not equivalent, the peak for the undecoupled C=O group appeared to be a triplet at δ 187.558, 187.522 and 187.479.

B. Reaction of Type **4** Compounds with Diamines.

The condensation reactions of **4a-4e** with *o*-phenylenediamine, **5**, and 2,3-diaminonaphthalene, **6**, afforded the 3-Substituted-3,4-dihydro-2(1*H*)-quinoxalinones and benzo[*g*]quinoxalinones, **7a-7g**, respectively. The structural assignments are based on the mode of reaction and elemental analysis. In additions, the melting points and spectroscopic data of these compounds agreed, when available, with published ones of the same compounds prepared by several other routes (8-22).

Formation of **7a-7g** is thought to proceed *via* a sequence as outlined in Scheme III. The reaction is initiated by a nucleophilic attack of the amino group on the α-keto moiety of type **4** compounds forming a Schiff base which was not isolated. Through attack of the second amino group on the lactone carbonyl group opening occurs. The final step of the reaction sequence is a retro aldol condensation in which formaldehyde is split off to give the end products **7a-7g**. The generated formaldehyde was trapped by an alcoholic dimedone solution and isolated as methylenedimedone.

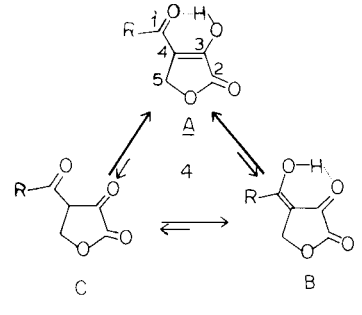
Scheme III



5 R=H
6 R=-C_4H_4-

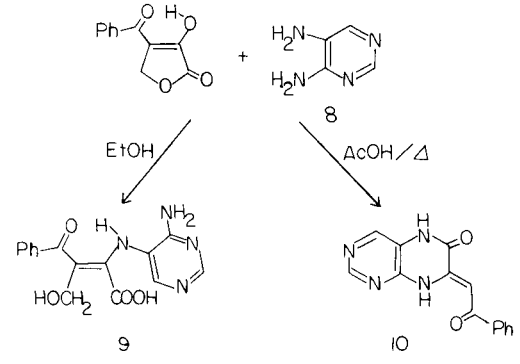
7

a) R = C_6H_5- R' = H
b) R = 3,4-$(MeO)_2C_6H_3$- R' = H
c) R = 4-ClC_6H_4- R' = H
d) R = Me_3C- R' = H
e) R = EtO- R' = H
f) R = C_6H_5- R' = benzo[g]
g) R = 3,4-$(MeO)_2C_6H_3$- R' = benzo[g]



The reaction of type **4** compound with 4,5-diaminopyrimidine, **8**, however proceeded differently. Depending on the reaction condition, different products were obtained in these condensations (Scheme IV). Compound **9** was

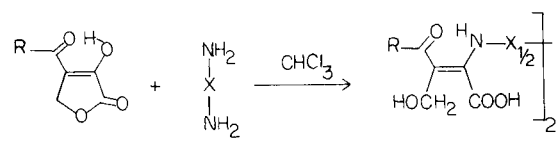
Scheme IV



the only product formed when the reaction between **4a** and **8** was run in ethanol as a solvent. Its structure was assigned based on the consideration that in a neutral medium the more nucleophilic amino group of the 5-position of **7** would be involved in Schiff base formation with **4a**. According to its ir- and ^{1}H-nmr spectrum, **9** occurs as a Zwitterionic species involving protonation of one (or both) of the two amino groups. Condensation of **4a** with **8** in glacial acetic acid in which the 5-amino group is protonated, afforded 7-phenacylidene-7,8-dihydro-6(1*H*)-pteridinone, **10**. The condensation in this case starts with Schiff base formation involving the amino group in the 4-position which in this medium remains unprotonated.

The condensations of **4a** and **4d**, respectively with other diamines proceeds essentially in the same fashion. Formation of a Schiff base and opening of the lactone ring was observed. Diamines which were used included 1,2-ethylenediamine, **11**, and 1,4-phenylenediamine, **12**. They yielded compounds **13-15**. The structures of the compounds derived of **11** again were not the expected ones because neither of the products (with or without a retro aldol condensation) were isolated. Instead, the bis-condensation products **13** and **14** were the products of these reac-

Scheme V



11 X= -CH_2CH_2-
12 X= 
13 R=Ph- X= -CH_2CH_2-
14 R=Me_3C- X= -CH_2CH_2-
15 R=Ph- X= 

tions (Scheme V). These structures are analogous to the structure of the product formed by condensation of **4a** and **12**. Again their structures were assigned on the basis of elemental analysis and spectroscopical data.

The bis-condensation compound **13-15** according to ir as well as ^{1}H- and ^{13}C-nmr evidence occur in the Zwitterionic form rather than in the free amino acid form. Thus, the ^{1}H- resonance of the -COOH group appears in the aromatic region (δ 7-8.5) and not between δ 10-13. Also the value for the ^{13}C resonance of the carboxylic acid C-atom of δ 175.3 of **14** is compatible with the resonance of a carboxylate group attached to a double bond (Figure 1).

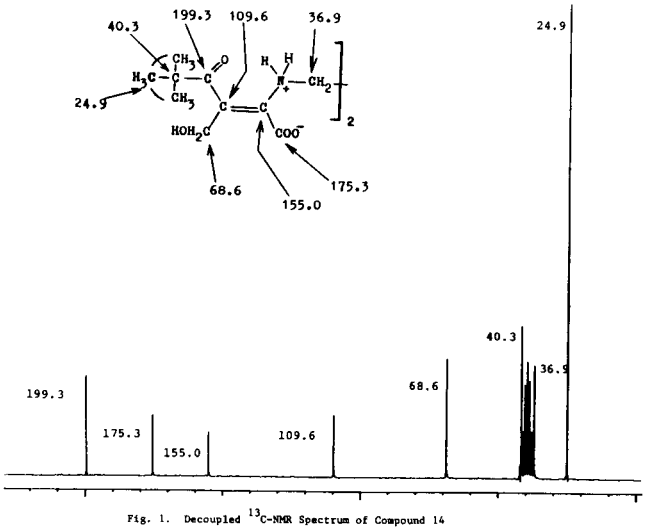


Fig. 1. Decoupled ^{13}C-NMR Spectrum of Compound 14

Attempts to close the lactone ring of these compounds failed. Thus, by treating compound, **9**, with thionyl chloride, PPA, sulfuric acid or acetic acid did not cause lactonization. Instead, only fragmentation into the starting materials was observed. When treating **13** with acetic acid anhydride acetylation took place and 3-acetoxy-4-benzoyl-2(5*H*)-furanone was isolated almost quantitively.

EXPERIMENTAL

General.

Melting points were determined with a Fisher-Johns and/or Melt-Temp melting point apparatus and are uncorrected. Infrared spectra were recorded using a Perkin-Elmer Model 599 spectrometer calibrated against 1601 cm^{-1} band of polystyrene. The ^{1}H-nmr spectra were recorded on a Varian T-60 spectrometer. The ^{13}C-nmr spectra were recorded on a Nicolet NT300 narrow-bore spectrometer (75.5 MHz) with an 1180 E data system. Chemical shifts are expressed in δ relative to tetramethylsilane as internal standard and coupling constants (J values) in hertz. MS data were obtained on a Perkin-Elmer RMU-7 mass spectrometer and/or Kratos MS80 instrument with a DS-55 data system. Elemental analyses were preformed at M-H-W Laboratories, Phoenix, Arizona.

α-Keto-β-substituted-γ-butyrolactones **4**.

General Procedure.

A dry 2 ℓ three-necked round bottom-flask equipped with a heavy-duty stirrer, thermometer, and 250 ml pressure-equalized addition funnel, was charged with 40 g (0.67 mole) of 95% sodium methylate and 570 ml dry ether. The suspension was cooled to 0-5° using a dry ice-acetone bath to which was added dropwise a mixture of 95.3 ml (0.67 mole) diethyl oxalate and 0.67 mole of the appropriately substituted acetophenone (or a pinacolone) over a period of 30 min while maintaining the temperature at 5-10°. After addition was completed the temperature of the mixture was maintained at 20° for 3 hours. The flask was then cooled to 5-10° and the reaction mixture hydrolyzed within 1 hour with 500 ml ice water while maintaining the temperature at 5-10°. Now 67 ml (0.67 mole) of 37% aqueous formaldehyde was added all at once. Vigorous stirring for 10-20 minutes caused all solid materials to dissolve and two layer formed which had to be separated immediately. The organic layer was washed with 75 ml ice-water combined with the aqueous layer, cooled to 10° and acidified with 100 ml concentrated hydrochloric acid. The product usually was collected after stirring for 15 minutes. It was filtered off, washed with ice water and dried.

4-Benzoyl-3-hydroxy-2(5*H*)-furanone (**4a**).

This compound was obtained in a yield of 75%, mp = 157° (ethanol) (lit (5a) mp = 157° (ethanol)); ir (potassium bromide): 3300, 3000-2200, 1760, 1720, 1690, 1630 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 5.3 (s, 2H,-CH_2O), 7.67 (m, 5H, Ar*H*), 8.5 (s, 1H was deuterium oxide exchangeable); ms: M$^+$ = 204 (RI = 5.7%), 160 (40.8), 159 (2.3), 132 (65.9), 131 (23.6), 105 (100), 77 (59.2).

4-(3,4-Dimethoxybenzoyl)-3-hydroxy-2(5*H*)-furanone (**4b**).

This compound was obtained a yield of 76%, mp = 180° (methanol); ir (potassium bromide): 3550-2200, 1790, 1640 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.9 (s, 6H, 2 OCH_3), 5.1 (s, 2H, CH_2O), 7.5 (m, 3H, Ar*H*), 11•1 (s, 1H was deuterium oxide exchangeable); ms: M$^+$ = 264 (RI = 25.1), 192 (34.8), 177 (7.5), 165 (100.00), 161 (11.4), 137 (7.2), 122 (7.4), 121 (7.6), 92 (10.5), 79 (21.1), 77 (26.7), 55 (8.1), 51 (10.3).

Anal. Calcd. for $C_{13}H_{12}O_6$: C, 59.09; H, 4.58. Found: C, 58.9; H, 4.53.

4-(4-Chlorobenzoyl)-3-hydroxy-2(5*H*)-furanone (**4c**).

This compound 13%, mp = 112° (benzene) (lit (5b), mp = 114°); ir (potassium bromide): 3540-2500, 1790, 1640 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 5.3 (s, 2H, CH_2O), 7.6 (m, 4H, Ar*H*), 9.6 (s, 1H was deuterium oxide exchangeable); ms: M$^+$ = 234 (RI = 12.5%), 194 (19.1), 168 (26.4), 166 (83.5), 141 (35.6), 139 (100.0), 131 (39.7), 113 (17.7), 111 (54.7), 103 (23.1), 78 (8.7), 77 (8.6).

4-(2,2-Dimethylpropanoyl)-3-hydroxy-2(5*H*)-furanone (**4d**).

This compound was obtained in a yield of 50%, mp = 150° (benzene); ir (potassium bromide): 3200, 3000, 1790, 1670 cm^{-1}; ^{1}H-nmr (deuterochloroform); δ 1.3 (s, 9H, C(CH_3)$_3$), 5.2 (s, 2H, CH_2O), 10.2 (s, 1H was deuterium oxide exchangeable); ms: M$^+$ = 184 (RI = 38.8%), 140 (10.3), 129 (18.8), 100 (86.2), 72 (20.3), 57 (53.6), 55 (12.7), 41 (35.7).

Anal. Calcd. for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.67; H, 6.60.

4-Carboethoxy-3-hydroxy-2(5*H*)-furanone (**4e**).

To 250 g (1.17 moles) of ethyl sodium oxalacetate suspended in 500 ml of water at 5-10° was added in two portions 350 ml (1.17 moles) of 37% aqueous formaldehyde solution. The reaction mixture was left for 35 minutes at 10-15°. After cooling by a dry ice-methanol bath 114 ml of concentrated hydrochloric acid was added while stirring was continued for about 15 minutes. Colorless plate-like crystals were obtained which were washed with carbon tetrachloride and dried; yield = 82%; mp = 105° (Chloroform/carbon tetrachloride (lit (23), mp = 108°); ir (potassium bromide): 3360, 1800, 1700, 1670 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1•4 (t, 3H, CH_2-CH_3), 4.7 (q, 2H, CH_2-CH_3), 4.9 (s, 2H, CH_2O), 7.5 (s, 1H was deuterium oxide exchangeable); ms: M$^+$ = 172 (RI = 54.5%), 144 (7.2), 128 (96.0), 127 (94.7), 115 (17.9), 101 (10.2), 100 (94.9), 99 (88.9), 97 (29.4), 88 (49.8), 87 (21.1), 86 (16.9), 82 (23.0), 73 (59.8), 72 (94.2), 71 (64.3), 69 (82.1), 68 (93.0), 56 (33.3), 55 (93.8), 54 (100.0).

Anal. Calcd. for $C_7H_8O_5$: C, 48.84; H, 4.68. Found: C, 49.15; H, 4.97.

3-Substituted-3,4-dihydro-2(1*H*-quinoxalinones **7**.

General Procedures.

A) To a solution of **4** in chloroform was added an equivalent amount of diamine **5** or **6** in chloroform and warmed briefly to complete solution. After a few minutes a yellow precipitate slowly formed. It was filtered off after a few days standing at room temperature. The respective product was purified by crystallization from suitable solvents.

B) Methanolic solutions of equivalent amounts of **4** and diamine **5** or **6** were refluxed for several hours. Upon cooling the respective product precipitated and was removed by filtration and recrystallized for purification from suitable solvents.

3-Phenacylidene-3,4-dihydro-2(1*H*)-quinoxalinone (**7a**).

This compound was obtained in a yield of 85% (method A), mp = 278-280° (ethanol) (lit (13) 268-269 (acetone), lit (17) 263-264 (*N,N*-dimethylformamide)); ir (potassium bromide): 3120, 1690, 1625 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 6.7 (s, 1H, =C*H*), 7.4 (m, 9H, Ar*H*), 11.8, 13.5 (2s, 2H were deuterium oxide exchangeable); ms: M$^+$ = 264 (RI = 100%), 263 (73), 247 (9.5), 235 (96.6), 219 (5.20), 207 (7.8), 187 (73), 159 (24.5), 131 (16.2), 105 (27.25).

Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.71; H, 4.51; N, 10.60. Found: C, 72.61; H, 4.39; N, 10.56.

3-(3,4-Dimethoxyphenacylidene)-3,4-dihydro-2(1*H*)-quinoxalinone (**7b**).

This compound was obtained in a yield of 85.2% (method B), mp = 282° (ethanol); ir (potassium bromide): 3500-1950 (diffuse band) (24), 1680 (w), 1620 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.8 (s, 6H, 2 OC*H*$_3$), 6.7 (s, 1H, = C*H*), 7.3 (m, 7H, Ar*H*), 11.8, 13.5 (2s, 2H were deuterium oxide exchangeable); ms: M$^+$ = 324 (RI = 52.4%), 306 (15.7), 186 (11.9), 165 (100), 138 (93.7), 131 (9.6), 123 (9.3), 119 (9.9) 92 (11.61), 79 (12.3), 77 (23.2).

Anal. Calcd. for $C_{18}H_{16}N_2O_4$: C, 66.65; H, 4.97; N, 8.64. Found: C, 66.65; H, 4.99; N, 8.41.

3-(4-Chlorophenacylidene)-3,4-dihydro-2(1*H*)quinoxalinone (**7c**).

This compound was obtained in a yield of 48.8% (method B), mp = 285-286° (ethanol); ir (potassium bromide): 3100, 1675 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 6.7 (s, 1H, = C*H*), 7.0-7.97 (m, 8H, Ar*H*), 12.0, 13.6 (2s, 2H were deuterium oxide exchangeable); ms: M$^+$ = 298, 300 (RI = 100.0, 32.6%), 270, 272 (12.0, 4.6), 269, 271 (45.8, 15.8), 206 (10.5), 187 (35.3), 159 (46.4), 139, 141 (96.2, 38.2), 111, 113 (42.6, 15.3).

Anal. Calcd. for $C_{16}H_{11}ClN_2O_2$: C, 64.34; H, 3.69. Found: C, 63.87; H, 3.99.

3-(3,3-Dimethyl-2-oxo-1-butylidene)-3,4-dihydro-2(1*H*)-quinoxalinone (**7d**).

This compound was obtained in a yield of 68% (method B), mp = 238° (methanol); ir (potassium bromide): 3150, 1680, 1620 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 1.1 (s, 9H, C(C*H*$_3$)$_3$, 6.2 (s, 1H, = C*H*), 7.0-7.2 (m, 4H, Ar*H*), 11.7, 13.3 (2s, 2H were deuterium oxide exhangeable); ms: M$^+$ = 244 (RI = 24.7%), 187 (100.0), 160 (10.2), 131 (18.4), 104 (2.3), 85 (2.5).

Anal. Calcd. for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.14. Found: C, 68.96; H, 6.46; N, 11.37.

2-Ethoxycarbonylmethylene-3-oxo-1,2,3,4-tetrahydroquinoxaline (**7e**).

This compound was obtained in a yield of 41.2% (method B reflux for 66 hours), mp = 221° (methanol) (lit (9) mp = 210° (butyl cellosolve)); ir (potassium bromide): 3200, 3000, 1690, 1650, 1620 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): (20°) δ 1.19, 1.25 (2t, 2 OCH$_2$C*H*$_3$), 3.82 (s, -C(=N)-C*H*$_2$-(C=O)-), 4.11, 4.16 (2q, 2 OC*H*$_2$CH$_3$), 5.51 (s, -HN-C=C*H*-(C=O)-), 6.98-7.76 (4m, Ar*H*), 11.07, 11.747 (2s were deuterium oxide exchangeable) (ketimine/enamine tautomers 62:38); ms, M$^+$ = 232 (RI = 29.6%), 186 (100.0), 160 (15.3), 159 (23.7), 158 (34.8), 130 (28.6), 103 (40.5), 102 (11.1), 90 (41.8).

Anal. Calcd. for $C_{12}H_{12}N_2O_3$: C, 62.02; H, 5.21; N, 12.06. Found: C, 62.10; H, 5.24; N, 12.07.

3-Phenacylidene-3,4-dihydro-2(1*H*)-benzo[*g*]quinoxalinone (**7f**).

This compound was obtained in a yield of 55% (method B), mp = 334° (*N,N*-dimethylformamide) (lit (13) mp = 343° (dimethyl sulfoxide)); ir (potassium bromide): 3480, 3180, 1692, 1620 cm^{-1}; ms: M$^+$ = 314 (RI = 100.0%), 313 (15.4), 297 (2.5), 296 (3.2), 286 (15.2), 285 (55.5), 271 (3.7), 269 (3.2), 268 (2.2), 237 (24.8), 209 (28.9), 184 (8.1), 143 (15.8), 140 (13.2), 127 (9.8), 105 (72.2).

Anal. Calcd. for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.61; H, 4.74; N, 8.79.

3-(3,4-Dimethoxyphenacylidene)-3,4-dihydro-2(1*H*)-benzo[*g*]quinoxalinone (**7g**).

This compound was obtained in a yield of 57% (method B), mp = 300° (*N,N*-dimethylformamide); ir (potassium bromide): 3460, 3180, 1745, 1690, 1620 cm^{-1}; ms: M$^+$ = 374 (RI = 76.3%), 373 (6.4), 345 (7.0), 237 (16.12), 236 (43.5), 209 (17.1), 208 (16.5), 187 (9.13), 173 (21.9), 165 (100.0), 140 (15.9), 138 (51.8).

Anal. Calcd. for $C_{22}H_{18}N_2O_4$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.43; H, 5.16; N, 7.66.

2[(4-Amino-5-pyrimidinyl)amine]-4-oxo-3-(hydroxymethyl)-4-phenyl-2-butenoic Acid (**9**).

To a stirred solution of 1.10 g (0.01 mole) of 4,5-diaminopyrimidine in 100 ml ethanol was added a solution of 2.04 g (0.01 mole) of **4a** in 50 ml ethanol. The reaction mixture was stirred for 1 hour and was left to stand overnight. The product which separated out was filtered off, yield = 2.5 g (95%), mp = 155° (ethanol); ir (potassium bromide): 3440, 3360, 3300, 3190, 1745, 1675, 1645 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 4.87 (s, 2H, C*H*$_2$OH), 7.17-7.53, 7.67-7.96 (2m, 12H, 7H, Ar*H*, 5H were deuterium oxide exchangeable).

Anal. Calcd. for $C_{15}H_{14}N_4O_4$: C, 57.31; H, 4.49; N, 17.83. Found: C, 57.22; H, 4.85; N, 17.45.

7-Phenacylidene-7,8-dihydro-6(1*H*)-pteridinone (**10**).

A solution of 0.80 g (0.007 mole) of 4,5-diaminopyrimidine and 1.46 g (0.004 mole) of **4a** in 20 ml glacial acetic acid was refluxed for 10 minutes and poured into ice water. The precipitate was filtered off, washed with sodium bicarbonate solution and water, Yield = 0.433 g (35%); mp = 307° (ethanol); ir (potassium bromide): 3300-2500, 1685, 1634, 1620 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6); δ 6.8 (s, 1H, = C*H*), 7.27-7.9 (m, 5H, Ar*H*), 8.1 (s, 1H, N=C*H*), 8.4 (s, 1H, -N-C*H*=N-), 11.9, 12.8 (2s, 2H were deuterium oxide exchangeable); ms: M$^+$ = 266 (RI = 100%), 265 (79.7), 237 (27.5), 189 (44.7), 161 (15.3), 120 (18.4).

Anal. Calcd. for $C_{14}H_{10}N_4O_2$: C, 63.15; H, 3.79; N, 21.04. Found: C, 63.12; H, 4.01; N, 20.83.

2,2-(1,2-Ethylenediamino)-bis-[4-oxo-3-(hydroxymethyl)-4-phenyl-2-butenoic Acid] (**13**).

To a solution of 2 g (0.01 mole) of **4a** in 50 ml of chloroform was added 1 ml of ethylenediamine and allowed to stand overnight when a colorless solid precipitated, yield = 3.7 g (79%), mp = 144° (methanol); ir (potassium bromide): 3660-3300, 3290-2300, 1770, 1750, 1648 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 3.0 (s, 4H, -(C*H*$_2$)$_2$-), 4.9 (s, 4H, 2 C*H*$_2$OH), 7.33-7.90 (2m, 16H, 10H, Ar*H*, 6H were deuterium oxide exchangeable.)

Anal. Calcd. for $C_{24}H_{24}N_2O_8$: C, 61.53; H, 5.16; N, 5.98. Found: C, 61.23; H, 5.33; N, 5.92.

2,2-(1,2-Ethylenediamino)-bis-[5,5-dimethyl-4-oxo-3-(hydroxymethyl)--2-hexenoic] Acid (**14**).

Preparation was essentially the same as **13** 0.5 g (0.0025 mole) of **4d** and 0.26 ml of ethylenediamine gave a yield of 0.375 g (35.7%); colorless needles, mp = 173° (methanol); ir (potassium bromide): 3660-3340, 3330-1900, 1770, 1740, 1625 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 1.2 (s, 18H, C(C*H*$_3$)$_3$), 3.1 (s, 4H, -(C*H*$_2$)$_2$-), 4.67 (s, 4H 2C*H*$_2$OH), 8.77 (s (br), 6H were deuterium oxide exchangeable).

Anal. Calcd. for $C_{20}H_{32}N_2O_8$: C, 56.06; H, 7.53; N, 6.54. Found: C, 56.15; H, 7.19; N, 6.45.

2,2-(1,4-Phenylenediamino)-bis-[4-oxo-3-(hydroxymethyl)-4-phenyl-2-butenoic Acid] (**15**).

It was prepared similarly from **4a** and 1,4-phenylenediamine, yield = 35.5% colorless crystals, mp = 147°; ir (potassium bromide): 3500-1900, 1749, 1632 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 4.9 (s, 4H, 2 CH_2OH), 6.8 (s, 4H, phenylene protons), 7.43-7.9 (m, 10H, Ar*H*), 8.5 (s, 6H were deuterium oxide exchangeable).

Anal. Calcd. for $C_{28}H_{24}N_2O_8$: C, 65.11; H, 4.68; N, 5.42. Found: C, 64.92; H, 4.80; N, 5.33.

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