

Reaction of Biguanides and Related Compounds. XII.¹⁾ Condensations of Arylbiguanides and Amidinoisoureas with Isatins

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The reactions of arylbiguanides with isatin and with 1-methylisatin gave 2-oxo-3-arylbiguanidylidene-indoles and 4-amino-6-arylamino-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-*s*-triazines, respectively. Analogously, N-amidino-O-alkylisoureas reacted with isatin and 1-methylisatin to afford 2-oxo-3-alkoxyamidinoamidinylidene-indoles and 4-amino-6-alkoxy-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-*s*-triazines, respectively. The structures of these compounds were discussed.

A number of condensations of biguanides with carboxylic acids, aldehydes, and ketones have hitherto been known to give *s*-triazines.³⁾ In continuation of our works on the condensations with cyclization of systems containing carbonyl groups to biguanides and its analogues, we examined the behaviors of isatin and the N-methyl derivative to arylbiguanides and N-amidino-O-alkylisoureas.

Reactions of Arylbiguanides and N-Amidino-O-alkylisoureas with 1-Methylisatin

It has been reported that arylbiguanides react with sterically unhindered simple ketones to give 4-amino-6-arylamino-2,2-disubstituted 1,2-dihydro-*s*-triazines or 4,6-diamino-1-aryl-2,2-disubstituted 1,2-dihydro-*s*-triazines, respectively.⁴⁾ Biguanides are also known to react with carboxamides to afford 4,6-diamino-2-substituted *s*-triazines.⁵⁾ In the reaction of arylbiguanides with 1-methylisatin, therefore, two different behaviors may be expected, because 1-methylisatin possesses both of keto carbonyl and amide carbonyl groups.

When equimolar quantities of arylbiguanides (I) and 1-methylisatin (II) were heated in ethanol in the absence of any catalyst for 1–5 hr under refluxing conditions, a colorless product was obtained in a fairly good yield. Compound (II) possesses two active center, amide carbonyl and keto carbonyl groups, toward I. If the initial nucleophilic attack of the terminal amino group of I occurs on the amide carbonyl group, 4-amino-6-arylamino-2-(*o*-methylaminobenzoyl)-*s*-triazines (III) would be formed through the imidazolidone ring cleavage followed by cyclization. On the other hand, the initial attack on the keto carbonyl group would give two isomeric compounds, 4-amino-6-arylamino-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-*s*-triazines (IV) and 4,6-diamino-1-aryl-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-*s*-triazines (V), by analogy with the reaction between I and simple aliphatic ketones.

The mass spectrum of the product obtained exhibited the strong molecular ion peak corresponding to that of the condensation product of molecular equivalents of I and II with elimination of one molecule of water. The infrared (IR) absorption spectrum indicated the characteristic absorption assignable to the carbonyl group at 1700 cm⁻¹. These spectral data and the elemental analyses of the product could not distinguish the possible compounds

1) Part XI: M. Furukawa, T. Yoshida, and S. Hayashi, *Bull. Chem. Soc. Japan*, **47**, 2893 (1974).

2) Location: *Oe-hon Machi, Kumamoto, 862, Japan*.

3) a) E.J. Modest, in "Heterocyclic Compounds," Vol. 7, R.C. Elderfield, ed., Wiley, New York and London, 1961, p. 627, 663; b) E.M. Smolin and L. Rapoport, "*s*-Triazines and Derivatives," Interscience, New York, 1959, p. 225, 239, 242, 258, 283.

4) E.J. Modest and P. Levine, *J. Org. Chem.*, **21**, 14 (1956).

5) a) C.G. Overberger and S.L. Shapiro, *J. Am. Chem. Soc.*, **76**, 93 (1954); b) D.E. Nagy, U.S. Patent 2309661 (1943), [*Chem. Abstr.*, **37**, 3768 (1943)].

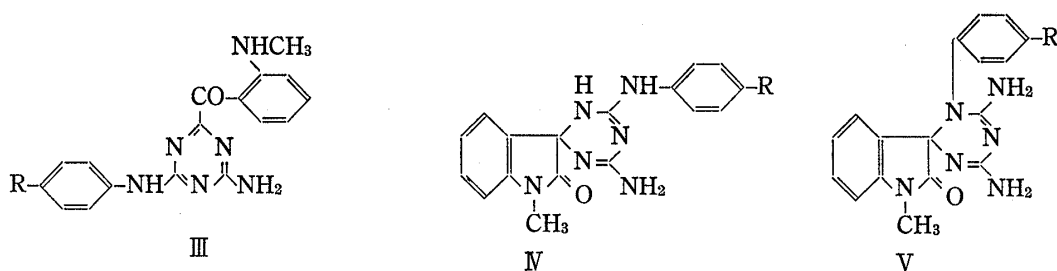


Chart 1

(III, IV, and V). In order to elucidate the structure of the product, it was first examined by the hydrazone-forming test using 2,4-dinitrophenylhydrazine whether the product possesses the keto carbonyl group in the molecule or not. In the result, no formation of the hydrazone was observed at any rate, while the similar compound, 4-amino-6-arylamino-2-benzoyl-*s*-triazines (VI), which was prepared by the condensation of I with ethyl benzoylformate, formed readily the corresponding hydrazones (VII) with 2,4-dinitrophenylhydrazine. The reaction of I with 1-methyl-2-oxo-3-phenylhydrazinylideneindole, in which the keto carbonyl group of II was protected by the phenylhydrazinylidene group, was attempted. However, no trace of any product was obtained and the materials were quantitatively recovered unchanged. On the basis of these results, it is reasonable to conclude that the amide carbonyl group does not undergo the nucleophilic attack with ring cleavage.

Although a distinction between the possible structure IV and V on the basis of elemental analyses and spectral data alone is impossible, evidence in favour of structure IV was provided by the synthetic confirmation of V and by the facile conversion to IV. Generally, it is known that, in the presence of basic⁶⁾ or weak acid catalysis^{6b,7)} or in the absence of any catalyst,⁴⁾ the compound (I) condenses with carbonyl reagents to form anilino-dihydro-*s*-triazines and under strong acid catalysis formation of aryl-dihydro-*s*-triazines occurs. Moreover, the aryl-dihydro-*s*-triazines undergo the irreversible intramolecular rearrangement to the isomeric anilino-dihydro-*s*-triazines by the treatment with an excess of alkali at elevated temperature.⁸⁾ The preparation of V hydrochloride was successfully carried out by heating equimolar quantities of I hydrochloride and II in ethanol in the presence of a catalytic amount of hydrochloric acid under refluxing condition in a low yield. The conversion of V hydrochloride to the free base was readily achieved by the treatment with an equivalent amount of sodium ethoxide in ethanol at room temperature. On the other hand, when V hydrochloride was heated with an excess of sodium hydroxide in dilute ethanol for a few hours under reflux, the facile rearrangement to IV occurred. These results might provide the unequivocal evidence for the structures of IV and V.

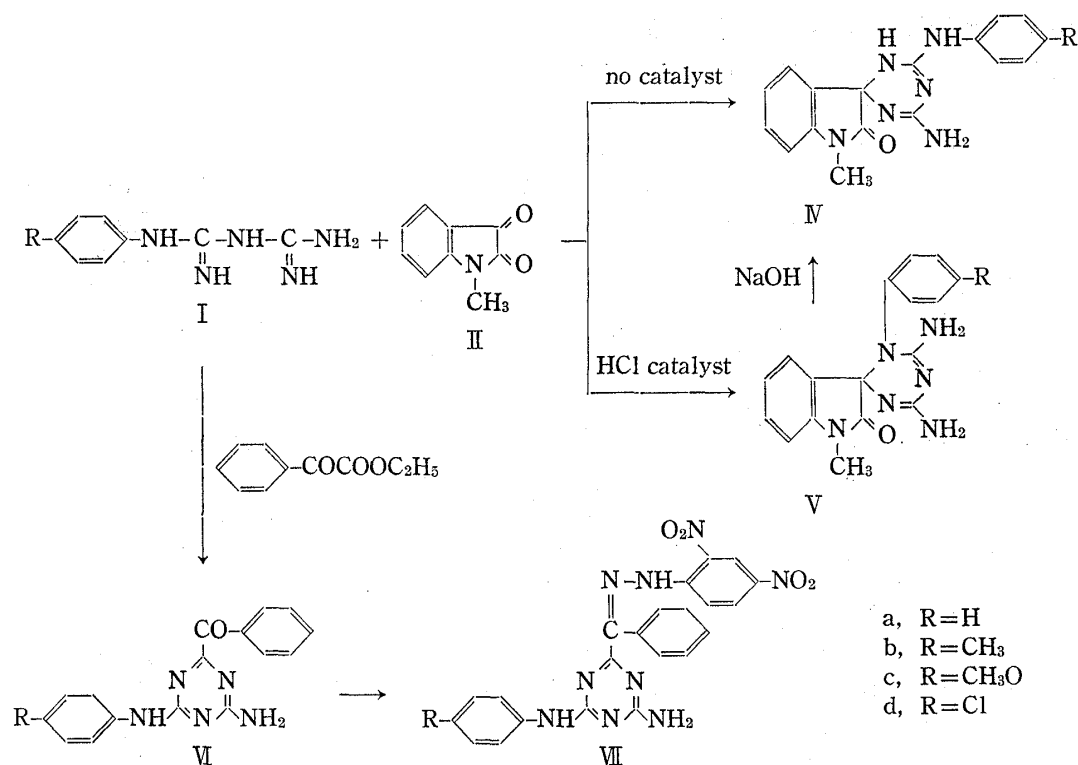
N-Amidino-O-alkylisoureas (VIII) are also expected to show the similar behaviors to I toward II, because the similar functional moiety is involved in the molecule. We have reported the similar but sometimes different reactivities of VIII on carbonyl compounds.⁹⁾ When equimolar quantities of VIII and II were heated in ethanol for 5 hr under reflux, a colorless

6) a) S. Birtwell, F.H.S. Curd, J.A. Hendry, and F.L. Rose, *J. Chem. Soc.*, **1948**, 1645; b) B.H. Chase, J.P. Thurston, and J. Walker, *J. Chem. Soc.*, **1951**, 3439.

7) a) N.N. Crouse, *J. Org. Chem.*, **16**, 492 (1951); b) S. Birtwell, *J. Chem. Soc.*, **1952**, 1279.

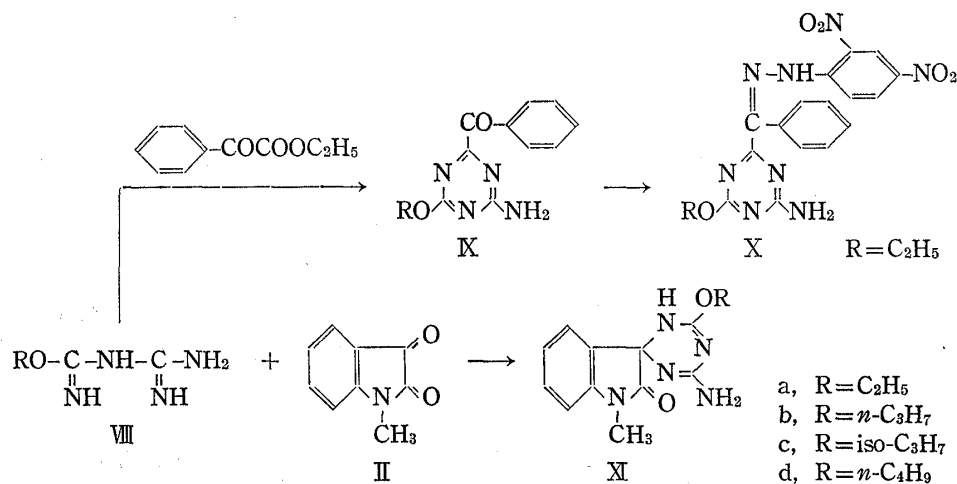
8) E.J. Modest, *J. Org. Chem.*, **21**, 1 (1956).

9) a) M. Furukawa, T. Yoshida, Y. Kojima, and S. Hayashi, *Chem. Pharm. Bull. (Tokyo)*, **21**, 478 (1973); b) M. Furukawa, T. Yoshida, M. Goto, and S. Hayashi, *Chem. Pharm. Bull. (Tokyo)*, **21**, 2594 (1973); c) M. Furukawa, Y. Fujino, S. Yoshimatsu, Y. Kojima, and S. Hayashi, *Chem. Pharm. Bull. (Tokyo)*, **20**, 611 (1972); d) S. Hayashi, M. Furukawa, J. Yamamoto, and Y. Nishijima, *Chem. Pharm. Bull. (Tokyo)*, **16**, 474 (1968); e) S. Hayashi, M. Furukawa, Y. Fujino, and H. Morishita, *Chem. Pharm. Bull. (Tokyo)*, **19**, 1789 (1971); f) M. Furukawa, K. Matsuoka, T. Yoshida, Y. Kojima, and S. Hayashi, *Chem. Pharm. Bull. (Tokyo)*, **22**, 1 (1974).



product was obtained in a low yield. The IR absorption spectrum of the product exhibited the characteristic absorption assignable to the carbonyl group at 1700 cm^{-1} . The product indicated the negative hydrazone-forming test, while the similar compound, 4-amino-6-alkoxy-2-benzoyl-*s*-triazines (IX), which were readily prepared by condensation of VIII with ethyl benzoylformate, gave easily the corresponding phenylhydrazones (X) by the usual method. Therefore, the type III structure, in which the keto carbonyl group is involved, might be negligible for the product. The type V structure should be also negligible, because it is structurally impossible to form. Accordingly, the product may be assumed to be the type IV compound, 4-amino-6-alkoxy-2-(1'-methyl-2'-oxo-3'-indolidene)-*s*-triazines (XI).

Supports for the assigned structure XI were provided by the elemental analyses and spectral data. In the mass spectrum, the molecular ion peak corresponding to XI was observed as an abundant peak. The ultraviolet (UV) absorption spectrum exhibited a quite similar absorption pattern to that of the compound (IV).



Reactions of Arylbiguanides and N-Amidino-O-alkylisoureas with Isatin

In spite of the expectation that it might be analogous to the reaction with II, both of I and VIII showed quite different behaviors toward isatin (XII). When equimolar quantities of I and XII were heated in ethanol in the absence of any catalyst for 5 hr under reflux, a yellow product was obtained in a comparatively good yield. The mass spectrum of the product indicated the molecular ion peak corresponding to that of the condensation product of molecular equivalents of I and XII with loss of one molecule of water. The elemental analysis agreed with the calculated value of the condensation product. However, the absorption patterns in the UV and IR spectra were quite different from those of IV. The UV spectrum of the condensation product of Ia with XII indicated two maximum absorption bands at 237 ($\log \epsilon = 4.40$) and 263 nm ($\log \epsilon = 4.39$), while that of IVa showed a maximum absorption band at 263 nm ($\log \epsilon = 4.29$). In the IR spectrum, the unequivocal absorption assignable to a carbonyl group was not observed. Although it is generally known that the cyclization to *s*-triazines by the reaction with ketones is possible only in aromatic arylbiguanides but not aliphatic alkylbiguanides, an alkylbiguanide of 3-oxopentamethylenebiguanide reacted readily with XII under the similar conditions to give the similar product. This suggests that the product is not cyclization product (type IV and V). Different from the reaction with II, the hydrochloride of I did not react with XII in the presence of hydrochloric acid catalyst, the materials being quantitatively recovered unchanged. The structure similar to III for the product was also evidently denied by no formation of any hydrazones. On the other hand, XII is known to react with amines, hydrazines, hydroxylamine, and semicarbazide to give the corresponding 2-oxo-3-indolide derivatives.¹⁰ On the basis of these facts and results, it is suggested that the product would be 2-oxo-3-arylbiguanidylidene-indoles (XIII).

Support for the structure XIII was provided by the UV absorption spectrum, which showed a quite analogous absorption pattern to that of a similar compound of 2-oxo-3-phenylhydrazinylidene-indole. The result that the hydrolysis of the product with aqueous hydrochloric acid solution gave XII provides another support. The structure XIII would be

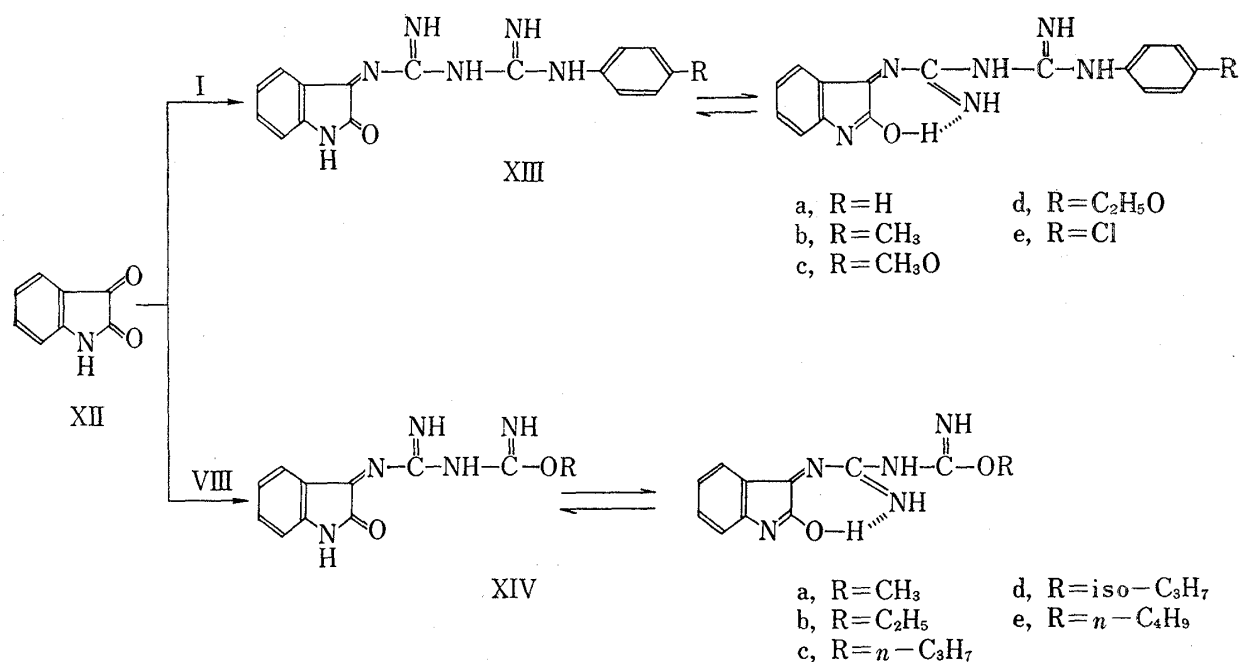


Chart 4

10) a) P.L. Julian, E.W. Meyer, and H.C. Printy, in "Heterocyclic Compounds," Vol. 3, R.C. Elderfield, ed., Wiley, New York and London, 1960, p. 216; b) R.M. Piccirilli and F.D. Popp, *Heterocyclic Chem.*, **10**, 671, 877 (1973).

stabilized by the formation of hydrogen bond in the tautomeric lactim structure. Isatin XII is well known to behave both as a lactam and a lactim. The fact that the unequivocal absorption of the carbonyl group was not observed in the IR spectrum of XIII can, therefore, be explained reasonably.

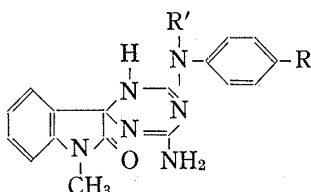
The compound (VIII) also showed the quite similar behaviors toward XII, as expected. When VIII was allowed to react with an equimolar quantity of XII under the similar reaction conditions, the yellow crystals of 2-oxo-3-alkoxyamidinoamidinylidene-indoles (XIV) were obtained in low yields. The structure of XIV was established by the elemental analyses and spectral data. The UV spectrum showed a quite similar absorption pattern to that of XIII and the mass spectrum exhibited the strong molecular ion peak. The unequivocal absorption assignable to the carbonyl group in the IR spectrum was not observed, probably due to the tautomeric lactim structure.

Experimental

All the melting points are uncorrected. IR spectra were measured on a JASCO IRA-1 Grating Infrared Spectrometer. UV spectra were obtained with a Hitachi 124 Spectrophotometer. Mass spectra were determined at 75 eV on a JEOL JMS-01SG Mass Spectrometer.

4-Amino-6-arylamino-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-s-triazine (IV)—General Procedure: Powdered arylbiguanide hydrochloride (4 mmole) was added with stirring to a hot solution of NaOEt prepared by dissolving Na (4 mg-atom) in dry EtOH (20 ml). Deposited NaCl was filtered off and 1-methylisatin (4 mmole) was added to the filtrate. The mixture was heated for 1–5 hr under reflux and the precipitates deposited gradually during heating were collected by filtration. Detailed data were summarized in Table I.

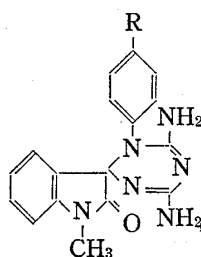
TABLE I. 4-Amino-6-arylamino-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-s-triazine (IV)



No.	R	R'	Yield (%)	mp (°C)	Formula	Analysis %			IR ν_{\max}^{KBr} cm^{-1}
						Calcd. (Found)			
						C	H	N	CO
IVa	H	H	84	261–262	$\text{C}_{17}\text{H}_{16}\text{ON}_6$	63.73 (63.73)	5.04 (4.81)	26.24 (26.27)	1700
IVb	CH_3	H	73	253–254	$\text{C}_{18}\text{H}_{18}\text{ON}_6$	64.65 (64.31)	5.43 (5.51)	25.14 (25.16)	1705
IVc	CH_3O	H	84	246–247	$\text{C}_{18}\text{H}_{18}\text{O}_2\text{N}_6$	61.70 (61.38)	5.18 (5.20)	23.99 (23.70)	1700
IVd	Cl	H	88	261–262	$\text{C}_{17}\text{H}_{15}\text{ON}_6\text{Cl}$	57.52 (57.72)	4.26 (4.22)	23.63 (23.58)	1700
IVe	H	CH_3	50	268–269	$\text{C}_{18}\text{H}_{18}\text{ON}_6$	64.65 (64.57)	5.43 (5.38)	25.14 (24.95)	1700

4,6-Diamino-1-aryl-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-s-triazine (V)—General Procedure: A mixture of arylbiguanide hydrochloride (5 mmole), 1-methylisatin (5 mmole), EtOH (30 ml), and two drops of concentrated hydrochloric acid was heated for 36 hr under reflux and then concentrated. The precipitates deposited on cooling were collected by filtration, washed with EtOH and recrystallized from EtOH to give 4,6-diamino-1-aryl-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-s-triazine hydrochloride. The powdered hydrochloride was added with stirring to a hot solution of an equivalent amount of NaOEt prepared by dissolving Na in EtOH. Deposited NaCl was filtered off and the filtrate was concentrated by

TABLE II. 4,6-Diamino-1-aryl-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-s-triazine (V)



No.	R	Yield (%)	mp (°C)	Formula	Analysis %			IR ν_{\max}^{KBr} cm^{-1}	
					Calcd.	Found			
					C	H	N		
Vb	CH ₃	35	199—200	C ₁₈ H ₁₈ ON ₆	64.65 (64.14)	5.43 (5.27)	25.14 (25.06)	1715	
Vc	CH ₃ O	25	194—195	C ₁₈ H ₁₈ O ₂ N ₆	61.70 (61.85)	5.18 (5.45)	23.99 (23.63)	1725	
Ve	C ₂ H ₅ O	18	200—201	C ₁₉ H ₂₀ O ₂ N ₆	62.62 (62.72)	5.53 (5.33)	23.06 (23.08)	1720	

evaporation under reduced pressure. The precipitates deposited upon cooling were collected by filtration and recrystallized from EtOH to give colorless prisms. Detailed data were summarized in Table II.

Conversion of 4,6-Diamino-1-aryl-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-s-triazine (V) into 4-Amino-6-arylamino-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-s-triazine (IV)—A solution of 4,6-diamino-1-aryl-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-s-triazine hydrochloride (1 mmole) in dilute EtOH containing NaOH (2 mmole) was heated for 3 hr under reflux. Deposited NaCl was removed by filtration and the filtrate was concentrated by distillation. The precipitates deposited on cooling were recrystallized from EtOH-dimethyl formamide. The compounds obtained were identified with the authentic samples prepared by the method described above by mixed melting point determination and comparison of the IR spectra.

TABLE III. 4-Amino-6-arylamino-2-benzoyl-s-triazine (VI)

No.	Yield (%) ⁱ	mp (°C)	Formula	Analysis (%)					
				Calcd.			Found		
				C	H	N	C	H	N
VIa	40	163	C ₁₆ H ₁₃ ON ₅	65.97	4.50	24.04	65.64	5.01	23.96
VIIb	67	187	C ₁₇ H ₁₅ ON ₅	66.87	4.95	22.94	66.35	5.19	22.83
VId	59	184	C ₁₆ H ₁₂ ON ₅ Cl	58.99	3.69	21.51	59.37	3.60	21.30

4-Amino-6-arylamino-2-benzoyl-s-triazine (VI)—General Procedure: A solution of arylbiguanide (10 mmole) and ethyl benzoylformate (10 mmole) in dry EtOH (10 ml) was heated for 5 hr under reflux. The precipitates deposited on cooling were collected by filtration and recrystallized from EtOH. Detailed data were summarized in Table III. Conversion to the 2,4-dinitrophenylhydrazone was readily achieved by the treatment with 2,4-dinitrophenylhydrazine by the usual method.

4-Amino-2-benzoyl-6-ethoxy-s-triazine (IX)—To a solution of N-amidino-O-ethoxyisourea hydrochloride (0.82 g, 5 mmole) in dry EtOH (50 ml) was added with stirring an ethanolic solution of NaOEt prepared by dissolving Na (0.115 g, 5 mg-atom) in dry EtOH (20 ml). Deposited NaCl was filtered off and ethyl benzoylformate (0.69 g, 5 mmole) was added to the filtrate. After the mixture was heated for 5 hr under reflux, the mixture was concentrated by partial evaporation under reduced pressure and then poured into ice-water. The separated product was extracted with ether and the ethereal layer was dried over Na₂SO₄ and evaporated by distillation. The residue was recrystallized from EtOH to give colorless prisms (0.70 g, 58%), mp 145°. *Anal.* Calcd. for C₁₂H₁₂O₂N₂: C, 59.01; H, 4.95; N, 22.94. Found: C, 59.23; H, 5.16; N, 22.71. Mass Spectrum *m/e*: 244 (M⁺).

TABLE IV. 4-Amino-6-alkoxy-2-(1'-methyl-2'-oxo-3'-indolidene) 1,2-dihydro-s-triazine (XI)

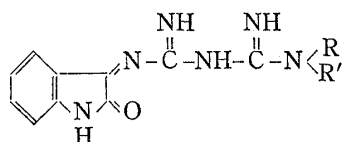
No.	Yield (%)	mp (°C)	Formula	Analysis % Calcd. (Found)			IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} CO
				C	H	N	
XIa	11	139—141	$\text{C}_{13}\text{H}_{15}\text{O}_2\text{N}_5$	57.13 (57.36)	5.53 (5.35)	25.63 (25.90)	1695
XIb	21	249—250	$\text{C}_{14}\text{H}_{17}\text{O}_2\text{N}_5$	58.52 (58.55)	5.96 (5.60)	24.38 (24.69)	1700
XIc	20	243—244	$\text{C}_{14}\text{H}_{17}\text{O}_2\text{N}_5$	58.52 (58.28)	5.96 (5.83)	24.38 (24.64)	1705
XId	23	236—237	$\text{C}_{15}\text{H}_{19}\text{O}_2\text{N}_5$	59.78 (59.54)	6.36 (6.12)	23.24 (23.21)	1700

2,4-Dinitrophenylhydrazone of 4-Amino-2-benzoyl-6-ethoxy-s-triazine (X)—A solution of 2,4-dinitrophenylhydrazine (0.20 g, 1 mmole) in EtOH (10 ml) containing a few drops of hydrochloric acid was added to a solution of 4-amino-2-benzoyl-6-ethoxy-s-triazine (0.24 g, 1 mmole) in EtOH (20 ml). After removal of EtOH by partial evaporation, the precipitates deposited on cooling were collected by filtration and recrystallized from EtOH to give yellow prisms (0.30 g, 71%), mp 233°. *Anal.* Calcd. for $\text{C}_{18}\text{H}_{16}\text{O}_5\text{N}_8$: C, 50.95; H, 3.80; N, 26.41. Found: C, 51.40; H, 3.67; N, 26.05.

4-Amino-6-alkoxy-2-(1'-methyl-2'-oxo-3'-indolidene)-1,2-dihydro-s-triazine (XI)—General Procedure: A solution of NaOEt prepared by dissolving Na (0.23 g, 10 mg-atom) in dry EtOH (20 ml) was added with stirring N-amidino-O-alkylisourea (10 mmole) in dry EtOH (50 ml) and deposited NaCl was filtered off. To the filtrate was added 1-methylisatin (10 mmole) and the mixture was heated for 5 hr under reflux. After removal of EtOH by evaporation under reduced pressure, the residue was poured into ice-water. The precipitates deposited were filtered off and the filtrate was evaporated under reduced pressure. The residue was recrystallized from EtOH to give colorless crystals. Detailed data were summarized in Table IV.

2-Oxo-3-arylbiguanidylidene-indole (XIII)—General Procedure: Powdered arylbiguanide hydrochloride (10 mmole) was added with stirring to a hot solution of NaOEt prepared by dissolving Na (0.23 g, 10 mg-atom) in dry EtOH (20 ml). Deposited NaCl was filtered off and a solution of isatin (10 mmole)

TABLE V. 2-Oxo-3-arylbiguanidylidene-indole (XIII)



No.	R	R'	Yield (%)	mp (°C)	Formula	Analysis % Calcd. (Found)		
						C	H	N
XIIIa	C_6H_5	H	65	208—209	$\text{C}_{16}\text{H}_{14}\text{ON}_6$	62.73 (63.16)	4.61 (4.68)	27.44 (27.25)
XIIIb	<i>p</i> - CH_3 - C_6H_4	H	50	200—201	$\text{C}_{17}\text{H}_{16}\text{ON}_6$	63.73 (63.65)	5.04 (4.90)	26.24 (26.32)
XIIIc	<i>p</i> - CH_3O - C_6H_4	H	71	218—219	$\text{C}_{17}\text{H}_{16}\text{O}_2\text{N}_6$	60.70 (60.23)	4.80 (5.23)	24.99 (24.55)
XIIId	<i>p</i> - $\text{C}_2\text{H}_5\text{O}$ - C_6H_4	H	57	189—190	$\text{C}_{18}\text{H}_{18}\text{O}_2\text{N}_6$	61.70 (61.64)	5.18 (5.42)	23.99 (23.63)
XIIIe	<i>p</i> -Cl- C_6H_4	H	50	221—222	$\text{C}_{16}\text{H}_{13}\text{ON}_6\text{Cl}$	56.39 (56.83)	3.84 (3.78)	24.66 (24.12)
XIIIf	C_6H_5	CH_3	75	186—187	$\text{C}_{17}\text{H}_{16}\text{ON}_6$	63.73 (63.90)	5.04 (5.05)	26.24 (26.38)
XIIIg	$\text{O} \begin{cases} \text{CH}_2-\text{CH}_2 \\ \text{CH}_2-\text{CH}_2 \end{cases}$		33	224—225	$\text{C}_{14}\text{H}_{16}\text{O}_2\text{N}_6$	55.99 (55.73)	5.37 (5.37)	27.99 (27.88)

in EtOH (50 ml) was added to the filtrate. The mixture was heated for 3 hr under reflux and then concentrated by partial evaporation. The precipitates deposited on cooling were collected by filtration and recrystallized from EtOH to give pale yellow crystals. Detailed data were summarized in Table V.

2-Oxo-3-alkoxyamidinoamidinylidene-indole (XIV)—General Procedure: A solution of NaOEt prepared by dissolving Na (0.23 g, 10 mg-atom) in dry EtOH (20 ml) was added with stirring to N-amidino-O-alkylisourea hydrochloride (10 mmole) in dry EtOH (50 ml) and deposited NaCl was removed by filtration. Isatin (10 mmole) was added to the filtrate and the mixture was heated for 5 hr under reflux. After allowing to stand overnight, the precipitates deposited were filtered off. The filtrate was poured into ice-water and extracted with ether. The ethereal layer was dried over Na₂SO₄ and then evaporated to dryness. The residue was recrystallized from EtOH to give pale yellow crystals. Detailed data were summarized in Table VI.

TABLE VI. 2-Oxo-3-alkoxyamidinoamidinylidene-indole (XIV)

No.	Yield (%)	mp (°C)	Formula	Analysis (%)					
				Calcd.			Found		
				C	H	N	C	H	N
XIVa	16	188	C ₁₁ H ₁₁ O ₂ N ₅	53.87	4.52	28.56	54.07	4.25	28.28
XIVb	46	150	C ₁₂ H ₁₃ O ₂ N ₅	55.59	5.05	27.02	55.95	4.93	27.08
XIVc	44	129	C ₁₃ H ₁₅ O ₂ N ₅	57.13	5.53	25.65	56.90	5.49	25.96
XIVd	40	112	C ₁₃ H ₁₅ O ₂ N ₅	57.13	5.53	25.65	56.71	5.83	25.52
XIVe	45	80	C ₁₄ H ₁₇ O ₂ N ₅	58.52	5.96	24.38	58.68	6.03	24.42