Some Reactions with 2:3-Indolone Derivatives

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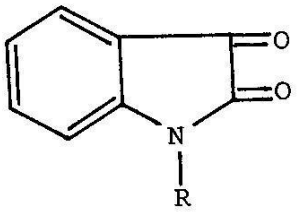
Summary: 1,2,4-Triazol (4,3-a)-indol-3-one, N^1-(5-thioxo-1,2-dihydro-1,2,4-triazol-3-yl) indol-2,3-dione, indole-(3,2-b) quinoxaline, 4,5-tetrahydro-1,3-diazin (2,1-a) indol-3-hydrazone, 5,6-substituted 1,2,4-triazin-3-one, 1-(3-imino indol-2-one)pyrimidin-2,4-dione, 3-[2-(5-benzylidene-4-thiazolidinone)diazo] indol-2-ones and 2-thioxo-1,3-diazin-5-one derivatives have been synthesized through the interaction between indole-2,3-dione and various bifunctional compounds.

All the compounds have been characterized by their IR and elemental analysis. A representative number of compounds have been characterized by ^{1}H-NMR spectral studies.

Indole-2,3-dione (I_a) has become of increasing importance in recent years owing to its pharmacological properties [1-4], in addition to its use as 1,2-dicarbonyl compound for the syanthesis of several heterocyclic compounds [1]. These observations prompted us to undertake the synthesis of related compounds containing the indole nucleus. The results were explained on the basis of reactions mechanism theories.

It has been observed in the present work that isatin I_a reacts with ethyl chloroformate in the presence of pyridine [5] yielding the ethyl ester derivative I_b, which on treatment with arylamine, hydrazine hydrate and thiosemicarbazide in dry benzene gave the corresponding anilide (I_c), hydrazide (I_d) and thiosemicarbazide (I_e) respectively. Monoacetylhydrazido-derivative (I_f) was obtained by warming I_d with glacial acetic acid for few minutes.

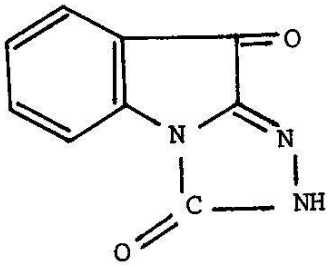


(I)

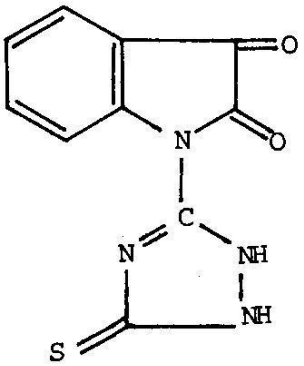
	R
(I_a)	H
b	$COOC_2H_5$
c	$CONHC_6H_4Br$-p
d	$CONH\ NH_2$
e	$CONHNHCSNH_2$
f	$CONHNHCOCH_3$

Compound I_d underwent ring closure when heated with glacial acetic acid-sod. acetate to give 1,2,4-triazolo(4,3-a) indol-3-one (II), while cyclization of I_e under the same

condition gave N^1-(5-thioxy-1,2-dihydro-1,2,4-triazol-3-yl) indol-2,3-dione (III).



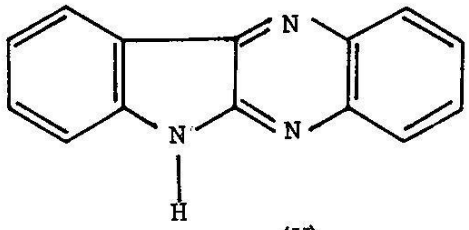
(II)



(III)

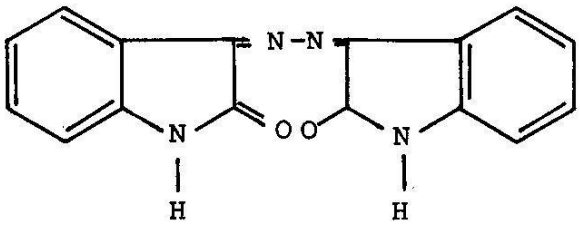
3-Alkyl or (aryl) imino and 3-mono hydrazone-indol-2-one (IV_{a-e}) have been obtained by normal condensation of I_a with various aliphatic (or aromatic) amines and hydrazine hydrate [6]. Reductive cyclization of IV_c gave indole-(2,3-b)-quinoxaline [7] V.

	R
a	CH_2CH_2OH
b	4-pyridyl
c	$C_6H_4NO_2$-o
d	C_6H_4Br-p
e	NH_2

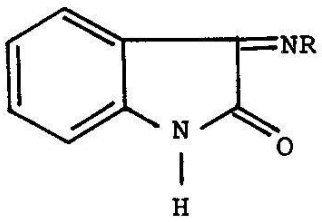


(V)

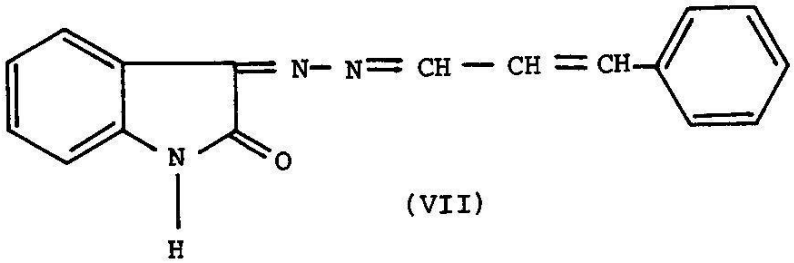
Condensation reaction of IV_e with I_a gave the bis compound VI, while IV_e when condensed with unsaturated aldehyde under the same condition yielded the conjugated system VII.



(VI)



(IV)



(VII)

The reactivity of the exocyclic conjugation system-C=N-N=C- with the olefinic group =CH-R in VII promoted us to investigate its behaviour towards the action of thiophenol derivatives. Thus, when VII is fused with excess 2-methyl or 4-chloro thiophenol, the sulphides $VIII_{a,b}$ were obtained according to the 1,4-addition.

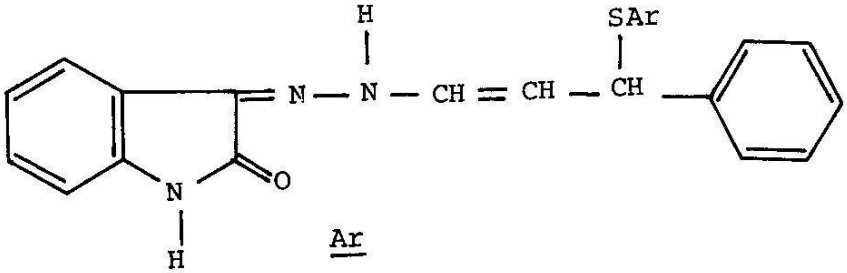
Condensation of IV_e with ethanol amine afforded the imino derivative IX, which was cyclized using Ac_2O-pyridine to give compound X.

Sulphonyl hydrazone derivatives $XI_{a,b}$ have been obtained through the condensation of I_a with p-sulphone hydrazide acetanilide and the reaction of IV_e with 4-toluene sulphonyl chloride in pyridine media [8].

The reaction of I_a with 1-cyano-guanidine led to the formation of cyanoguanidone derivative XII.

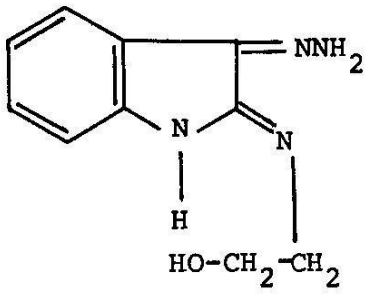
Acid hydrazides of isatin $XIII_{a-c}$ were obtained [9] by condensation of I_a with some acid hydrazide derivatives in absolute ethanol-glacial acetic acid. Acidic hydrolysis of $XIII_a$ using hydrochloric acid, gave the β-keto-carboxylic acid derivative $XIII_d$.

When IV_d was allowed to react with aryl acid hydrazide, compound $XIII_c$ was obtained. On the other hand $XIII_c$ was directly obtained from the reaction of I_a and aryl acid hydrazide. Identification of $XIII_c$ obtained by both the methods was established by comparison of their ir, its bands

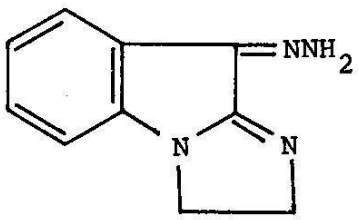


(VIII)

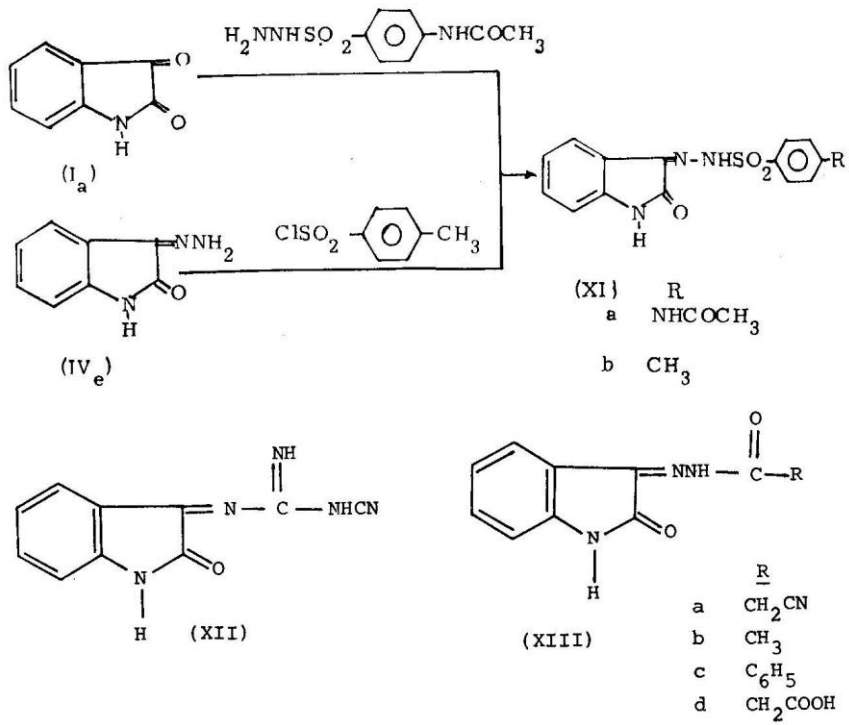
	Ar
a	$C_6H_4CH_3$-o
b	C_6H_4Cl-p



(IX)



(X)



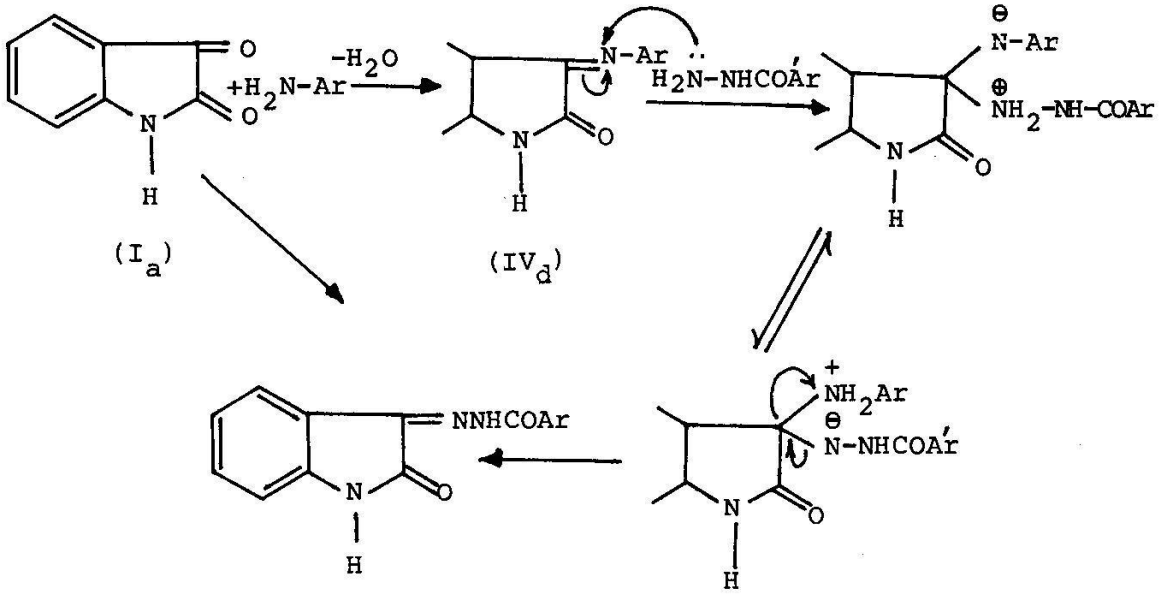
as well as by mp., mmp. In this reaction the displacement of 3-aryl-imino group by the phenyl acid hydrazido function occured due to the difference between the nucleophilic power of acid hydrazido group and the imino groups [10] as shown in the scheme I.

Condensation of I_a with oxalyl hydrazide (2:1) gave rise to the bis compound XIV, which when reacted with semicarbazide hydrochloride in dry THF [11], gave 5,6-disubstituted-1,2,4-triazin-3-one XV.

Isatin-3-semicarbazone XVI_a [12] underwent ring closure on heating with absolute ethanol to give N^1-(iminoindol-2-one-3-yl)-4-methyl-6-phenyl-pyrimidin-2-one XVII.

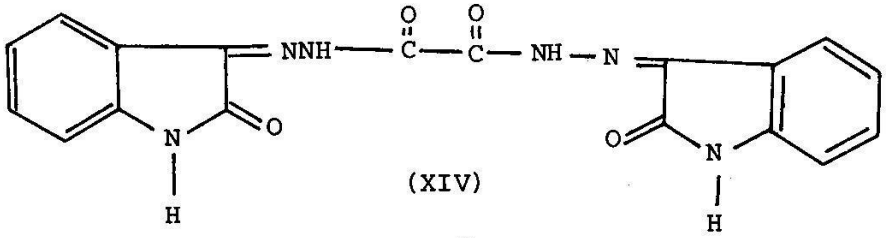
The reaction of ethylbenzoylacetate [14], with isatin-semicarbozone XVI_a in alcoholic medium, gave N^1 (iminoindol-2-one-3-yl)-6-phenyl-pyrimidin-2,4-dione XVIII, the reaction take place as shown in Scheme-II).

3-[2-(5-Arylidene-4-thiazolidinone)diazo] indol-2-ones $XIX_{a,b}$ have been synthesized [1], by treating isatine thiosemicarbazone XVI_b [13],

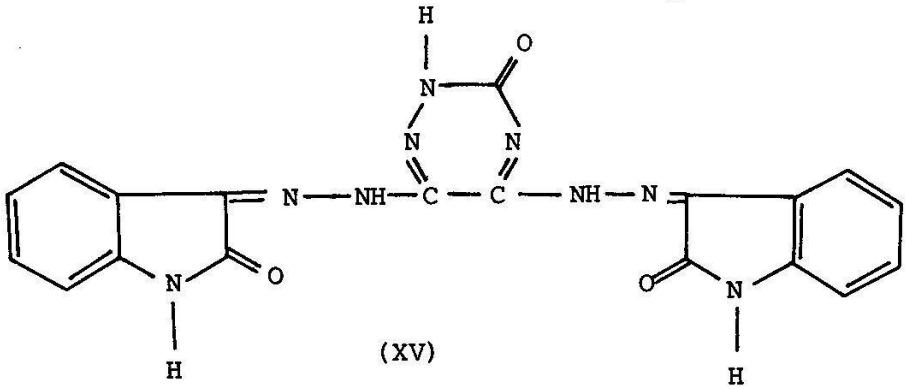


($XIII_c$) (Ar = C_6H_4Br-p, Ar′ = C_6H_5)

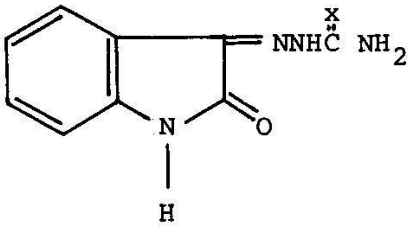
Scheme I



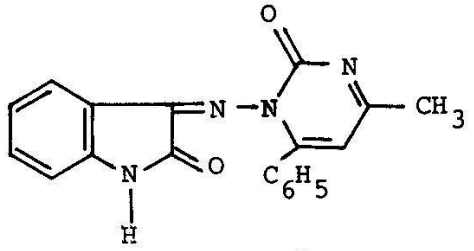
(XIV)



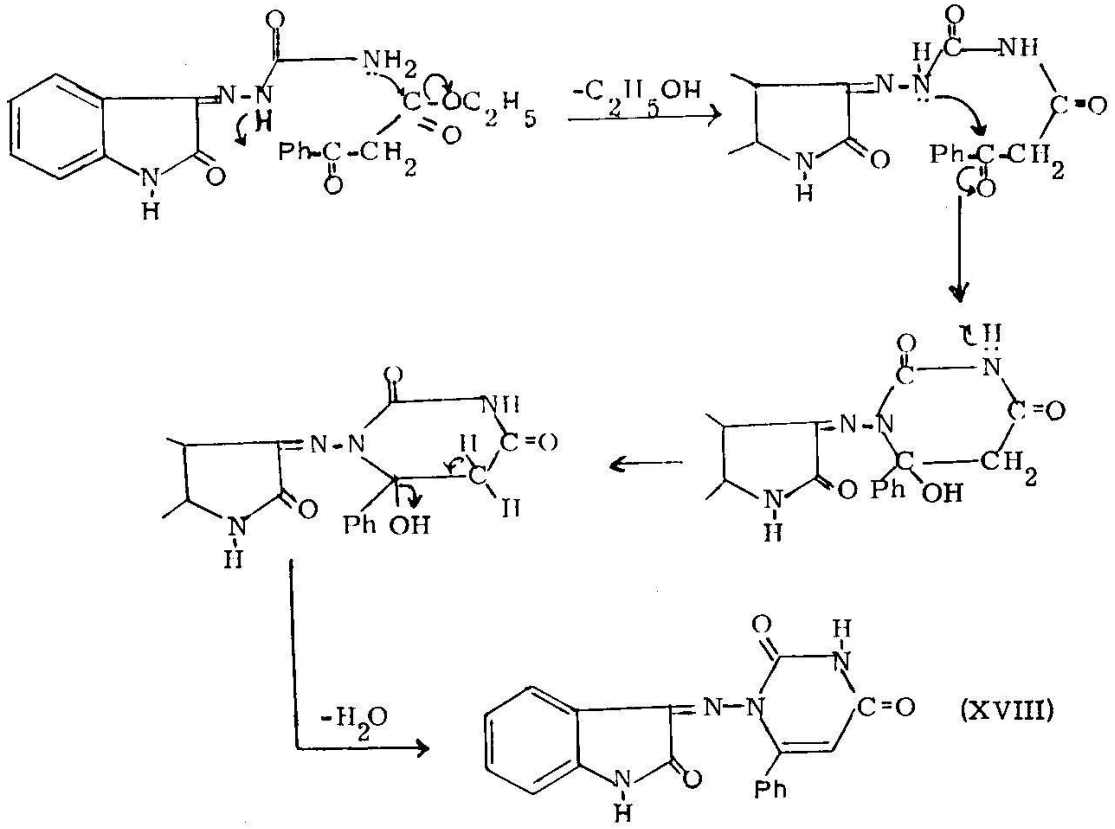
(XV)



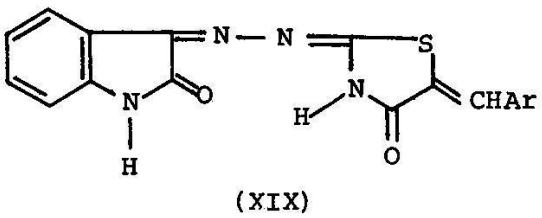
(XVI) a, x = O
b, x = S



(XVII)



Scheme II



(XIX)

	Ar
a	$C_6H_3(Cl)_2$-O
b	$C_6H_3(Cl)_2$-O,p

and different aryl aldehydes in glacial acetic acid.

Cyclocondensation reaction of XVI_b with p-hydroxyphenyl-pyruvic acid in absolute ethanol, followed by potassium carbonate soln. gave 2-thioxo-1,3-diazin-5-one derivative XX [15].

Finally, condensation of I_a with 2-hydrazinobenzimidazole gave XXI, which was cyclized to give the condensed heterocyclic compound XXII [7].

Experimental

Melting points of all synthesized compounds are uncorrected. Infrared spectra were recorded on Perkin-Elmer (model-337) in KBr Pellets. PMR spectra were recorded in (TFA) on Perkin-Elmer (model-RB-12; 60 MHz). TMS was taken as an internal standard.

Indol-2:3-dione I_a was synthesized according to the method of W.C. Swmpter [16].

Formation of I_b:

To a soluti on of I_a (0.01 M) in dry pyridine (50 ml) was added ethyl-chloroformate (0.02 M) and the reaction mixture was refluxed for ½ hr, cooled and acidify with dilute hydrochloric acid. The solid obtained on dilution was filtered and recrystallized to give I_b (cf. Table-1).

Reaction of amine, hydrazine and thiosemicarbazide with I_b-formation of $I_{c,d,e}$:

A mixture of I_b (0.01 M), p-bromoaniline, hydrazinehydrate and thiosemicarbazide (0.01 M) in dry benzene (100 ml) was refluxed for 2 hr. The reaction mixture was cooled and the solid obtained was filtered and recrystallized from the proper solvent to give $I_{c,d,e}$ respectively (cf. Table-1).

Acylation of I_d : Formation of I_f:

A mixture of I_d (0.01 M) and Ac_2O-AcOH (1:1-50 ml) was refluxed for ¼ hr. and cooled. The solid obtained was recrystallized to give I_f (cf. Table-1).

Cyclization of I_d : Formation of II:

A mixture of I_d (0.01 M) and Ac_2O-Pyridine (1:1-50 ml) was refluxed for 4 hour, cooled. The reaction mixture was poured on ice then acidified with hydrochloric acid. The solid obtained was recrystallized to give II. (cf., Table-1).

Cyclization of I_e : Formation of III:

A mixture of I_e (o.01 M), glacial acetic acid (50 ml) and sodium acetate (slight excess.) was heated for 4 hours, cooled then poured on ice. The solid obtained was recrystallized to give III (cf., Table-1).

Condensation of I_a with amines : Formation of IV_{a-d}:

A mixture of I_a (0.01 M) and the appropriate amine namely (ethanol-amine, 4-aminopyridine, 2-nitroaniline and 4-bromoaniline) (0.01 M) in absolute ethanol, was refluxed for 2 hr. The reaction mixture, on cooling gave a solid precipitate which was filtered and recrystallized to give the products (cf., Table-1). PMR of Compound IV_a as shown in Table-II.

Table-I: Physical Data of Compounds (Ib - VIIIb)

Compd. No.	Solvent	M.p. C°	Yield %	Molecular formula	Analysis Found/calcd.		I.R. Spectra of the New Compounds (cm^{-1})							
					Sulphur		OH	NH_2	NH	CH	endo-cyclic -C=O	exo-cyclic O -C-	C=N	C=S
I_b	C_6H_6	185	90	$C_{11}H_9NO_4$	-	-	-	-	-	2950	1730	1630	1600	-
I_c	C_2H_5OH	268	80	$C_{15}H_9N_2Br^+O_3$	-	-	-	-	3320	-	1740	1640	1600	-
I_d	C_2H_5OH	240	70	$C_9H_7N_3O_3$	-	-	-	3350	3190	-	1680	1650	1590	-
I_e	CH_3OH	195	70	$C_{10}H_8N_4SO_3$	12.00	12.00	-	3390	3250	-	1670	1650	-	1200
									3180			1620		
I_f	CH_3CO_2H	215	50	$C_{11}H_9N_3O_4$	-	-	-	-	3300	2950	1680	1650	1580	-
									3190					
II	CH_3CO_2H	235	60	$C_9H_5N_3O_2$	-	-	-	-	3120	-	1730	1640	1620	-
													1590	
III	CH_3CO_2H	255	60	$C_{10}H_6N_4SO_2$	13.50	13.00	-	-	3250	-	1690	1620	1595	1200
									3150					
IV_a	C_2H_5OH	150	90	$C_{10}H_{10}N_2O_2$	-	-	3500	-	3320	3150	1740	-	1610	-
										2980			1590	
IV_b	CH_3OH	207	70	$C_{13}H_9N_3O$	-	-	-	-	3200	-	1740	-	1620	-
													1580	
IV_c	C_2H_5OH	275	50	$C_{14}H_9N_3O_3$	-	-	-	-	3420	-	1720	-	1610	-
													1600	
IV_d*	CH_3CO_2H	260	70	$C_{14}H_9N_2BrO$	-	-	-	-	3390	-	1700		1610	-
													1600	

Table-I (cont'd.)

Compd. No.	Solvent	M.p. C°	Yield %	Molecular formula	Analysis Found/calcd.		I.R. Spectra of the New Compounds (cm^{-1})							
					Sulphur		OH	NH_2	NH	CH	endo-cyclic -C=O	exo-cyclic O -C-	C=N	C=S
IV_e	C_2H_5OH	250	90	$C_8H_7N_3O$	-	-	-	3400	3200	-	1680	-	1610 1580	-
V	CH_3OH	280	70	$C_{14}H_9N_3$	-	-	-	-	3400	-	-	-	1610 1590 1570	-
VI	C_2H_5OH	222	90	$C_{16}H_{10}N_4O_2$	-	-	-	-	3400	3100 2920	1720	-	1620 1610	-
VII	CH_3OH	190	95	$C_{17}H_{13}N_3O$	-	-	-	-	3350	-	1720	-	1610 1590	-
$VIII_a$	C_6H_6	195	60	$C_{24}H_{21}N_3SO$	8.5	8.02	-	-	3380 3150	-	1720	-	1610 1590	-
$VIII_b$	C_6H_6	185	60	$C_{23}H_{18}N_3SCl^{+++}O$	7.7	7.58	-	-	3350 3200	3050 2950	1720	-	1620 1600	-

+ Br, Fd.: 23.00, Calcd.: 23.75; Br^{++}, Fd: 26.8, calcd: 26.58; Cl^{+++}, Fd: 8.10, Calcd: 8.43.

* (IVb) shows absorption band at 1550 and 1350 cm^{-1} due to NO_2 group.

Satisfactory C, H and N analysis have been obtained for all the compounds.

Table-II

Compound No.	Chemical Shift δ	Multiplicity	Preliminary assignment
IV_a	4.0	Singlet	(1H)——OH
	3.47	Triplet	$-CH_2CH_2OH$
	7.8	Singlet	>NH

Reductive Cyclization of IV_c : Formation of V:

A mixture of IV_c (0.01 M) and zinc dust (3 gm) in 100 ml ethanol-acetic acid (50ml.-50ml) was refluxed for 4 hours. The reaction mixture was filtered hot. The solid obtained after cooling was recrystallized to give V (cf., Table-I).

Reaction of I_a with hydrazine hydrate: Formation of IV_c:

A mixture of I_a (0.01 M) and hydrazine hydrate (0.01 M) was kept at room temperature for 10 mint., 100 ml absolute ethanol was added and was heated under reflux for 20 mint. The reaction mixture was left to be cooled, for 10 mint. then added absolute ethanol (100 ml). The solid obtained was recrystallized give IV_e (cf., Table-I).

Condensation of IV_e with aldehyde and ketone : Formation of VII and VI:

i) A mixture of IV_e (0.01 M) and crotonaldehyde or isatin (0.01 M) in absolute ethanol (100 ml) was heated for 1hr., cooled and diluted with cold water. The solid obtained was recrystallized to give VII and VI (cf., Table-I).

PMR of compound VII shown:

a) a quartet at δ 6.0 (C=C olefinic Ha)
b) multiplet at δ 7.2 (aromatic proton).
c) and singlet at δ 7.9 (NH).

ii) Formation of VI:

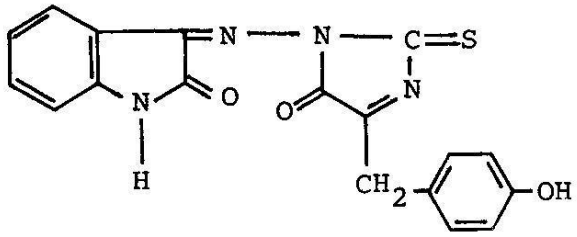
A mixture of I_a (0.01 M) and IV_e (0.01 M) was refluxed in absolute ethanol for 2 hours. The reaction mixture was diluted with cold water and filtered off. The solid obtained was recrystallized to give VI (cf., Table-I).

Formation of $VIII_{a,b}$:

A mixture of (VII (0.01 M) and 4-methylthiophenol or 2-chlorothiophenol (0.01), was heated at 180° (oil-bath) for 6 hours. The solid obtained was triturated with petroleum ether (60-80) to give the addition products $VIII_{a,b}$ respectively (cf., Table-I).

Condensation of IV_e with ethanol amine : Formation of IX:

A mixture of IV_e (0.01 M) and ethanolamine (0.01 M) refluxed for 4 hrs. in absolute ethanol (100 ml). The reaction mixture was cooled and



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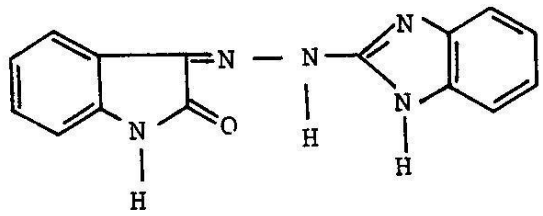
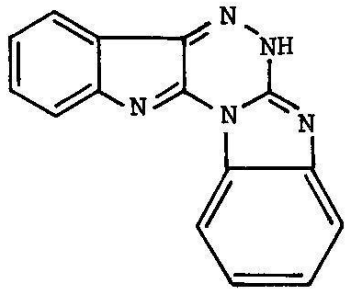


(XXI)



(XXII)

the solid obtained was recrystallized to give IX (cf., Table-III).

Cyclization of IX : Formation of X:

A mixture of IX and Ac_2O-pyridine (1:4-100 ml.) was refluxed for 6 hrs., then acidified with dil. HCl and diluted with water. The solid obtained was recrystallized to give X (cf., Table-III).

Condensation of I_a with sulphonyl hydrazide derivative : Formation of XI_a:

A mixture of I_a (0.01 M) and p-sulphonyl hydrazide acetanilide (0.01M) in absolute ethanol was refluxed for 1 hour. The solid obtained was recrystallized to give XI_a (cf., Table-III).

Reaction of IV_e with p-toluene-sulphonyl chloride : Formation of XI_b:

A mixture of IV_e (0.01 M) and p-toluene-sulphonyl chloride (0.01 M) in dry pyridine (50 ml) was heated for 1 hour, then diluted with water, and acidified using hydrochloric acid. The solid obtained was filtered and recrystallized to give XI_b (cf. Table-III).

Condensation of I_a with 1-cyanoguanidine : Formation of XII:

A mixture of I_a (0.01 M) and 1-cyanoguanidine (0.01 M) in absolute ethanol (100 ml) was refluxed for 1 hour. The reaction mixture was cooled, the separated solid was filtered and recrystallized to give XII (cf., Table-III).

3-Substituted hydrazone-2-indolinons $XIII_{a-c}$:

A mixture of I_a (0.01 M) and acid hydrazide (0.01 M) in 50 ml of ethanol containing one drop of glacial acetic acid was refluxed on a water bath for 2 hrs. The reaction mixture was cooled, the separated solid was filtered and recrystallized from the proper solvent to give XIII (cf., Table-III). PMR of compounds $XIII_{a-c}$ as shown in Table-IV.

Acid hydrolysis of $XIII_a$: Formation of $XIII_d$:

$XIII_a$ (0.01 M) was suspended in 100 ml of hydrochloric acid (20%). The suspension was warmed on hot

Table-III: Physical Data of Compounds (IX - XXII)

Compd. No.	Solvent	M.P. C°	Yield %	Molecular formula	Analysis Found/calcd. sulpher		I.R. Spectra of the New Compounds (cm^{-1}) OH	NH_2	NH	CH	C=N endo-cyclic	-C=O exo-cyclic	O=C-	C=N	C=S
IX	C_2H_5OH	235	50	$C_{10}H_{12}N_4O$	-	-	3500	3420 3220	3350	3010	-	-	- 1580	1620	-
X	C_2H_5OH	ab,300	60	$C_{10}H_{10}N_4$	-	-	-	3420	- 2970	2990	-	-	- 1590	1620	-
XI_a	CH_3CO_2H	185	90	$C_{16}H_{14}N_4SO_4$	9.1	8.8	-	- 3180	3400	3010	-	1720	1640 1600	1620	-
XI_b	CH_3CO_2H	218	80	$C_{15}H_{13}N_3SO_3$	10.4	10.15	-	- 3200	3400 2980	3050	-	1720	- 1600	1620	-
XII*	C_2H_5OH	175	80	$C_{10}H_7N_5O$	-	-	-	- 3310	3400	-	2210	1730	- 1610	1630	-
$XIII_a$	CH_3OH	220	90	$C_{11}H_8N_4O_2$	-	-	-	- 3150	3380	2980	2250	1730	1660 1590	1620	-
$XIII_b$	C_2H_5OH	285	80	$C_{10}H_9N_3O_2$	-	-	-	- 3200	3400	3020	-	1680	1620 1580	1600	-
$XIII_c$	C_2H_5OH	205	80	$C_{15}H_{11}N_3O_2$	-	-	-	- 3200	3400	-	-	1720	1650 1590	1610	-
$XIII_d$	CH_3OH	245	60	$C_{11}H_9N_3O_4$	-	-	3520	- 3150	3350	3000	-	1720 1650	1680	1600	-

Table-III: (cont'd.)

Compd. No.	Solvent	M.P. C°	Yield %	Molecular formula	Analysis	I.R. Spectra of the New Compounds (cm^{-1})								
					Found/calcd. sulpher	OH	NH_2	NH	CH	C=N endo-cyclic	-C=O exo-cyclic	O -C-	C=N	C=S
XIV	CH_3CO_2H	ab,300	90	$C_{18}H_{12}N_6O_4$	-	-	-	-	3300	-	-	1730	1670	1610	-
								3200				1650	1590		
XV	CH_3CO_2H	ab,300	60	$C_{19}H_{13}N_9O_3$	-	-	-	-	3400	-	-	1740	-	1600	-
								3320			1710		1590		
XVII	C_2H_5OH	260	60	$C_{19}H_{13}N_4O_2$	-	-	-	-	3410	2990	-	1720	1680	1600	-
													1570		
XVIII	C_2H_5OH	265	50	$C_{18}H_{11}N_4O_3$	-	-	-	-	3400	-	-	1670	1620	1590	-
								3250							
XIX_a	CH_3CO_2H	285	40	$C_{18}H_{10}N_4S\overset{+}{C}l_2O_2$	8.0	7.94	-	-	3400	3020	-	1720	-	1620	1180
								3180			1690		1590		
XIX_b	CH_3CO_2H	265	60	$C_{18}H_{10}N_4S\overset{++}{C}l_2O_2$	7.9	7.94	-	-	3400	2980	-	1730	-	1610	1170
								3190			1700		1590		
XX	C_2H_5OH	285	70	$C_{18}H_{12}N_4SO_3$	9.0	8.91	3500	-	3400	2920	-	1700	-	1620	-
									2880		1670		1590		
XXI	Dil.C_2H_5OH	190	90	$C_{15}H_{11}N_5O$	-	-	-	-	3400	-	-	1700	-	1600	-
								3300					1580		
XXII	D.M.F.	235	60	$C_{15}H_9N_5$	-	-	-	-	3200	-	-	-	-	1610	-
													1600		

+ Cl, Fd: 16.95, Calcd: 17.61, ++Cl, Fd: 17.5, Calcd: 17.8.

* XII shown absorption band at 1060 - 1080 cm^{-1} [N-C(=N)-N] of guanidine.

Satisfactory C, H and N analysis have been obtained for all the compounds.

Table-IV

Compound No.	Chemical shift δ	Multiplicity	Preliminary assignment
$XIII_a$	5.8	Singlet	$-N(H)COCH_2CN$
	7.8	Singlet	> N-H (heterocyclic)
$XIII_b$	2.12	singlet	$(3H)-COCH_3$
	5.7	Singlet	$-NH-CO-CH_3$ (amide)
	7.9	Singlet	> NH (heterocyclic)
$XIII_c$	5.55	Singlet	$-N(H)-CO-C_6H_5$ (amide)
	7.1	multiplet	(5-H) C_6H_5
	7.9	Singlet	> NH (heterocyclic)

plate for ½ hr. The crystalline solid that separated was filtered, washed with cooled water and finally recrystallized to give $XIII_d$ (cf., Table-III).

Reaction of IV_d with benzoic acid hydrazide : Formation of $XIII_c$:

A mixture of IV_a (0.01 M) and benzoic acid hydrazide (0.01 M) in 100 ml. ethanol containing few drops of piperidine, was refluxed for 4 hours. The reaction mixture was cooled, the separated solid was filtered, washed well with ethanol and petroleum ether. The solid obtained was recrystallized and identified as compound $XIII_c$ (mp., mmp., ir spectrum). The mother liquor was concentrated and then titurated with few drops of methanol. The solid obtained was recrystallized and identified as p-bromoaniline (mp., mmp, ir specterum).

Condensation of I_a with oxalyl hydrazide : Formation of XIV:

A mixture of I_a (0.02 M) and oxalyl hydrazide (0.01 M) in absolute ethanol (100 ml) was refluxed for 1 hour. The reaction mixture was cooled, the separated solid was filtered and recrystallized to give XIV (cf., Table-III).

Cyclization of XIV : Formation of XV:

A mixture of XIV (0.01 M) and semicarbazide hydrochloride (0.01 M in 20 ml. H_2O) in glacial acetic acid was heated for 2 hrs. The reaction mixture was cooled and diluted with water. The solid obtained was filtered and recrystallized to give XV (cf., Table-III).

Condensation of isatin-3-semicarbazone with 1,3-diketons : Formation of XVII, XVIII:

A mixture of isatin-3-semicarbazone (0.01 M) and benzoyl acetone or benzoyl ethyl acetate (0.01 M) in absolute ethanol (100 ml) was refluxed for 1 hour. The reaction mixture was cooled, the obtained solid was filtered and recrystallized to give XVII and XVIII respectively (cf. Table-III).

Cyclocondensation of isatin-3-thiosemicarbazone XVI_b:

a) Formation of XIX:

A mixture of XVI_b (0.01 M), chloroacetic acid (0.05 M) and sodium acetate (0.01 M) was refluxed in glacial acetic acid (40 ml) for 30 minutes. An appropriate aryl aldehydes (0.01 M) was then added and the mixture was further refluxed for 6 hours. The reaction mixture was cooled, the solid obtained was filtered and recrystallized to give $XIX_{a,b}$ (cf. Table-III).

b) Formation of XX:

A mixture of XVI_b (0.01 M) and p-hydroxy phenyl pyruvic acid in absolute ethanol (100 ml) was refluxed for 1 hour. A solution of K_2CO_3 (10 %) was added and the mixture further refluxed on water bath for 3 hours. The reaction mixture was cooled and acidify with dilute hydrochloric acid. The solid obtained was filtered and recrystallized to give XX (cf., Table-III).

Condensation of I_a with 2-hydrazinobenzimidazole : Formation of XXI:

A mixture of I_a (0.01 M) and 2-hydrazinobenzimidazole (0.01 M) in absolute ethanol (100 ml) was refluxed for 1 hour. The reaction mixture was diluted with cold water and the solid obtained was recrystallized to give XXI (cf., Table-III).

Cyclization of XXI : Formation of XXII:

A mixture of XXI (0.01 M) and sodium acetate (0.02 M) in 100 ml glacial acetic acid was refluxed for 6 hours. The reaction mixture was cooled and diluted with cold water. The solid obtained was filtered and recrystallized to give XXII (cf., Table-III).

References

1. K.C. Joshi, V.N. Pathak and S.K. Jain, *J. Indian Chem. Soc.*, ***LVII***, *1176 (1980).*
2. D. Gabor, L. Karoly, P. Laszlo and S. Klara, *(Egyesult Gyogysyer as Taps Zergyar) Hung. C.A. 74, 88068q (1971).*
3. R.S. Varma and W.L. Nobles, *J. Med. Chem.*, ***10***, *972 (1967).*
4. D.J. Bauer and P.W. Sadler, *Brit. J. Pharmacol.*, ***15***, *101 (1960).*
5. H. Jahine, H.A. Zaher, Y. Akhnookh and Z.El-Gendy, *Indian J. of Chem.*, ***16B***, *689 (1978).*
6. I.A. Khan, Ph.D. Thesis, Lucknow University, (1977).
7. N.P. Buu-Hoi and P. Jacquignon, *J. Chem. Soc., 3095 (1959).*
8. H.A. Zaher, H. Jahine, O. Sherif and R. Mohammady, *Indian J. of Chem.*, ***18B***, *316 (1979).*
9. R.S. Varma and I.A. Khan, *J. Indian Chem. Soc.*, ***LVIII***, *813 (1981).*
10. R.S. Varma, *J. Indian Chem. Soc.*, ***55***, *1052 (1978).*
11. K. Dennis, P. William, *(Dep. Chem. Univ. Alabama, Univ., Ala.) Synthesis (5), 351 (1974) Eng. C.A. 81, 5281 (1974).*
12. J. Daunis, R. Jacquier, M. Rigall and P. Viallefont, *Bull. Soc. Chim. Fr., 2289 (1970).*
13. D.J. Bauer and P.W. Sadler, *Brit. J. Pharmacol.*, ***15***, *101 (1960).*
14. H.K. Gakhar, S. Bharadwaj, A. Jain and P. Baneja, *J. Indian Chem. Soc.*, ***LVIII***, *1017 (1981).*
15. S. Jan, N. Karel, (Prirodo Ved. Fak., Univ. Falackeho, Olomouc, (Zech.). *C.A. 75, 20361v (1971).*
16. W. C. Sumpter, *Chem. Rev., 34, 407 (1944).*