Regional Research Laboratory

Syntheses and Interconversions of Some *s*-Triazolo[3,4-a]isoquinolines

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s-Triazolo[3,4-a]isoquinoline (II) and its 3-methyl analogue (III) have been synthesized from 1-isoquinolylhydrazine (I) by cyclisation with formic and acetic acid. The 3-hydroxy derivative (IV) has been shown to exist in the lactam form. Methylation with methyl iodide gave the *N*-methyl derivative (V). Dimethyl sulphate and diazomethane also led exclusively to the same product. The *O*-methyl derivative (IX) could be obtained only through the 3-chloro compound (VIII). The chlorine atom in VIII undergoes nucleophilic replacement easily. The 3,6-dichloro derivative (X) has also been prepared. Several interconversions in the series are described. Aryl hydrazones (XVIII) prepared from (I) have been oxidatively cyclised to give 3-aryl-*s*-triazolo[3,4-a]isoquinolines (XIX). U.V., I.R. and P.M.R. spectra have been recorded and used for assignment of structures in some cases.

The synthesis of fused *s*-triazoles from 2-hydrazinopyridine and 2-hydrazinoquinoline has been the subject of earlier investigations by one of the present authors (2,3). Attention was now directed to the synthesis of *s*-triazolo[3,4-a]isoquinoline (II) and its derivatives carrying substituents at positions 2 and 3. The reaction sequences for the syntheses and interconversions are outlined in Scheme A.

s-Triazolino[3,4-a]isoquinoline-3-one (IV) is expected to exhibit lactam-lactim tautomerism. Its I.R. spectrum (KBr., nujol) shows a strong carbonyl absorption at 1705 cm^{-1}. U.V. spectral data obtained in ethanol are given in Table I. Addition of a drop of acid does not change either the intensity or the position of the absorption maxima; alkali produces the expected bathochromic shift, indicative of the existence of the enolic form in alkaline medium.

IV reacts with methyl sulphate/alkali, methyl iodide/silver oxide and diazomethane to give the *N*-methyl derivative (V) as indicated by the persistence of the carbonyl absorption at 1700 cm^{-1} and by the similarity of its U.V. absorption spectrum to that of the parent compound (IV) in neutral solution. TLC of the crude methylation product in three different solvent systems failed to reveal the presence of the *O*-methyl derivative, 3-methoxy-*s*-triazolo-[3,4-a]isoquinoline (IX). IX could be obtained only through 3-chloro-*s*-triazolo[3,4-a]isoquinoline (VIII) which is prepared by refluxing IV with phosphorus oxychloride and dimethylaniline or by prolonged heating with phosphorus oxychloride in an autoclave. IV and VIII with acetic anhydride gave the same acetyl derivative which is presumably the *O*-acetylated product (VI) on the basis of its I.R. spectrum. (CO, 1715 cm^{-1}; C-O-C, 1250 cm^{-1}).

Refluxing IV with phosphorus pentasulphide in xylene gives 3-mercapto-*s*-triazolo[3,4-a]isoquinoline (VII), also obtainable from I and carbon disulphide. VII resists dethiation even on prolonged heating with Raney nickel. However, desulphurisation can be effected by heating with dilute nitric acid and subsequent treatment with aqueous sodium hydroxide solution. VII can be methylated to give 3-*S*-methyl-*s*-triazolo[3,4-a]isoquinoline (XVII) (Scheme B).

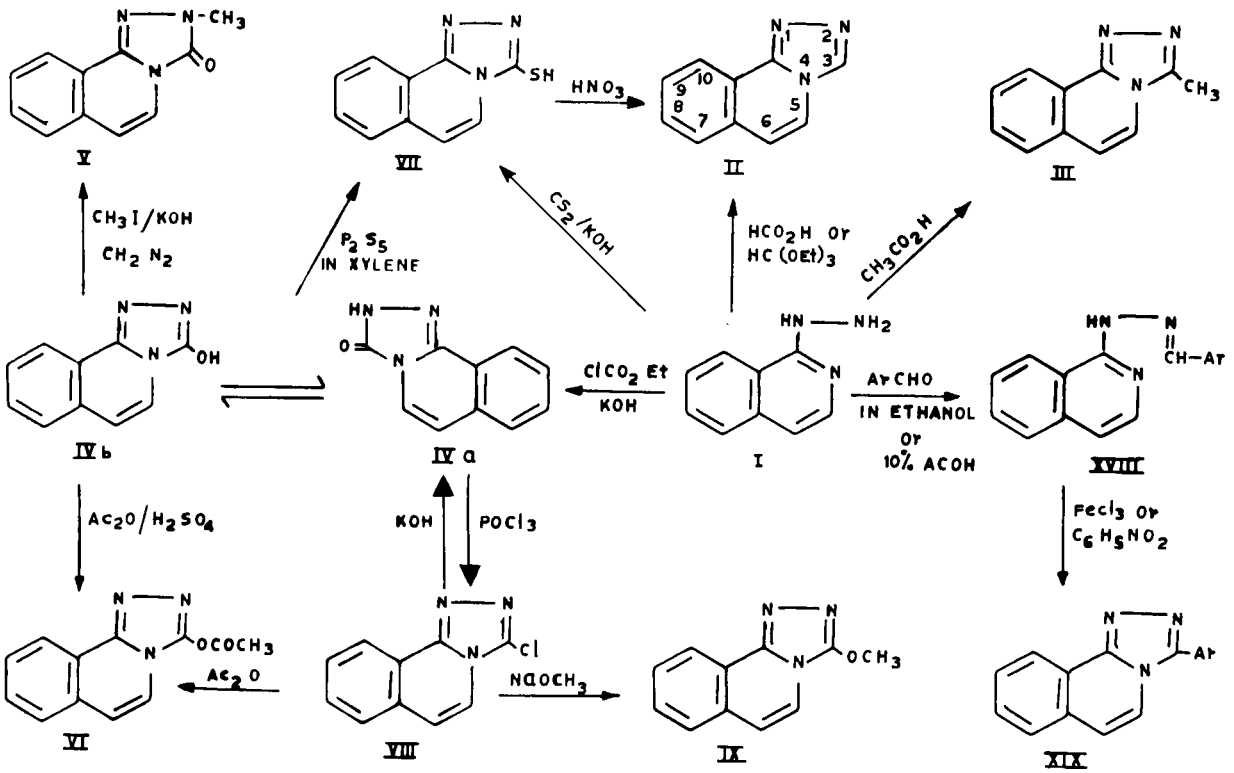
Mercapto-*s*-triazoles on oxidative chlorination are known to yield sulphonyl chlorides and the method finds general use for the synthesis of corresponding sulphonamides (4, 5). However, VII on reaction with chlorine in methanolic hydrogen chloride or chloroform-water mixture, gives VIII (*cf.* 6). This simple method appears to be of general application for the preparation of chloro-*s*-triazoles which are otherwise obtainable only from hydroxy-*s*-triazoles by drastic methods. The yield in the present instance was 85% and other examples of its use will be published elsewhere.

The chlorine atom in VIII is reactive and can be used to introduce suitable functional groups at the 3-position of *s*-triazolo[3,4-a]isoquinoline (Scheme B).

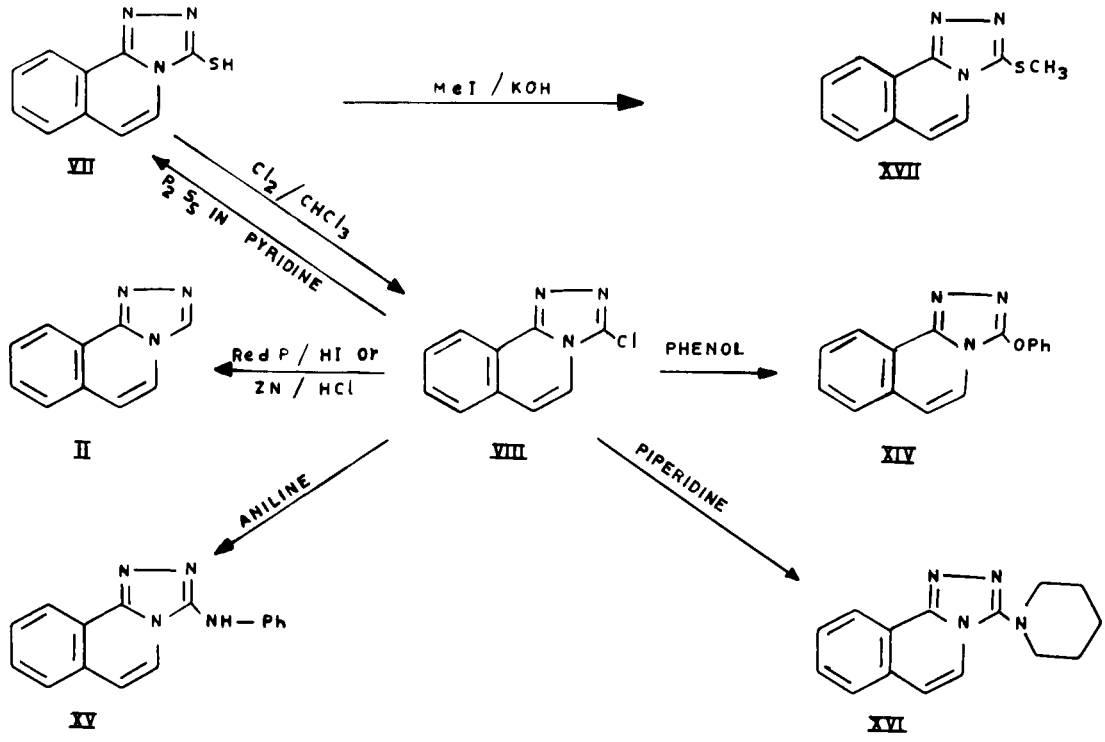
Heating IV with a mixture of phosphorus pentachloride and phosphorus oxychloride in a sealed tube followed by chromatography gives a white crystalline dichloro derivative. It is 3,6-dichloro-*s*-triazolo-[3,4-a]isoquinoline (X) as its P.M.R. spectrum shows the absence of the C_3 and C_6 protons. This is confirmed by reducing it with red phosphorus/hydroiodic acid to a monochloro derivative which is shown to be 6-chloro-*s*-triazolo[3,4-a]isoquinoline (XI) both by its P.M.R. spectrum and synthesis from 4-chloro-1-isoquinolylhydrazine (XII). Reduction of X with excess of zinc/hydrochloric acid leads to II and hydrolysis with aqueous sodium hydroxide solution to 6-chloro-*s*-triazolino[3,4-a]-isoquinoline-3-one (XIII) which can also be synthesised from XII (Scheme C).

It has been shown earlier (2,3) that azaheterocyclic hydrazones are converted in good yields to fused *s*-triazoles by oxidative cyclisation using ferric chloride or nitrobenzene. Using these reagents fourteen *s*-triazolo[3,4-a]isoquinolines (XIX; Table 4)

SCHEME - A



SCHEME - B



SCHEME–C

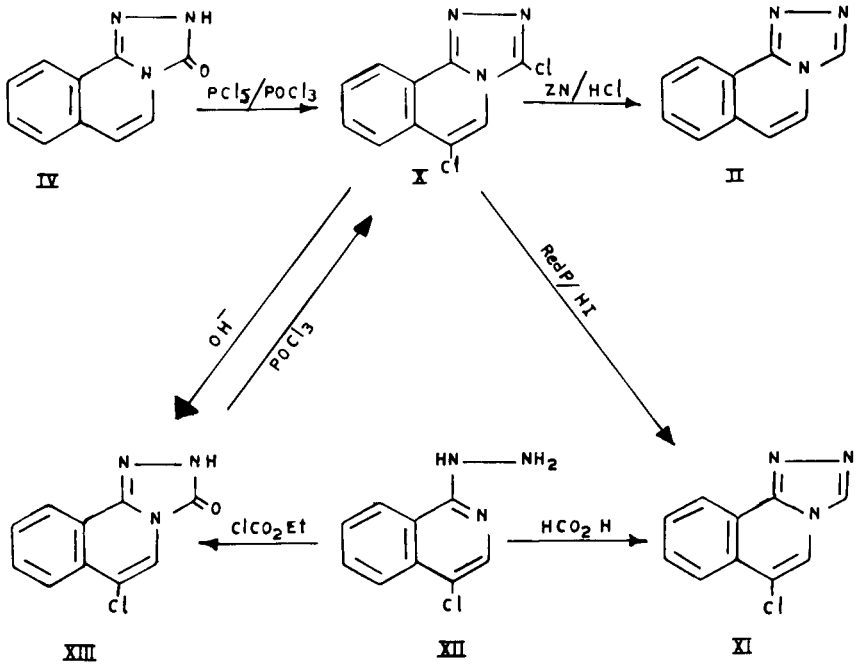


TABLE I

	200	220	240	260	280	300	320	340 mμ	360
II	210		240			305			
III	201		248			Sh 308	Sh 322		
IV & IV+ACID	210		250				320		
IV + ŌH	222		265				330		
V	215		255				320		
VI	209		262				322		
VII	224							352	
VIII	204		250			Sh	Sh		
IX	208		254		Sh				
XVII	215		256			Sh			
XIX	204		247				Sh	Sh	

(SPECTRA RECORDED IN ETHANOL)
Sh = SHOULDER
THE HEIGHT IN EACH CASE IS PROPORTIONAL TO Log E..
XIX: Ar = 4-Cl-C_6H_5

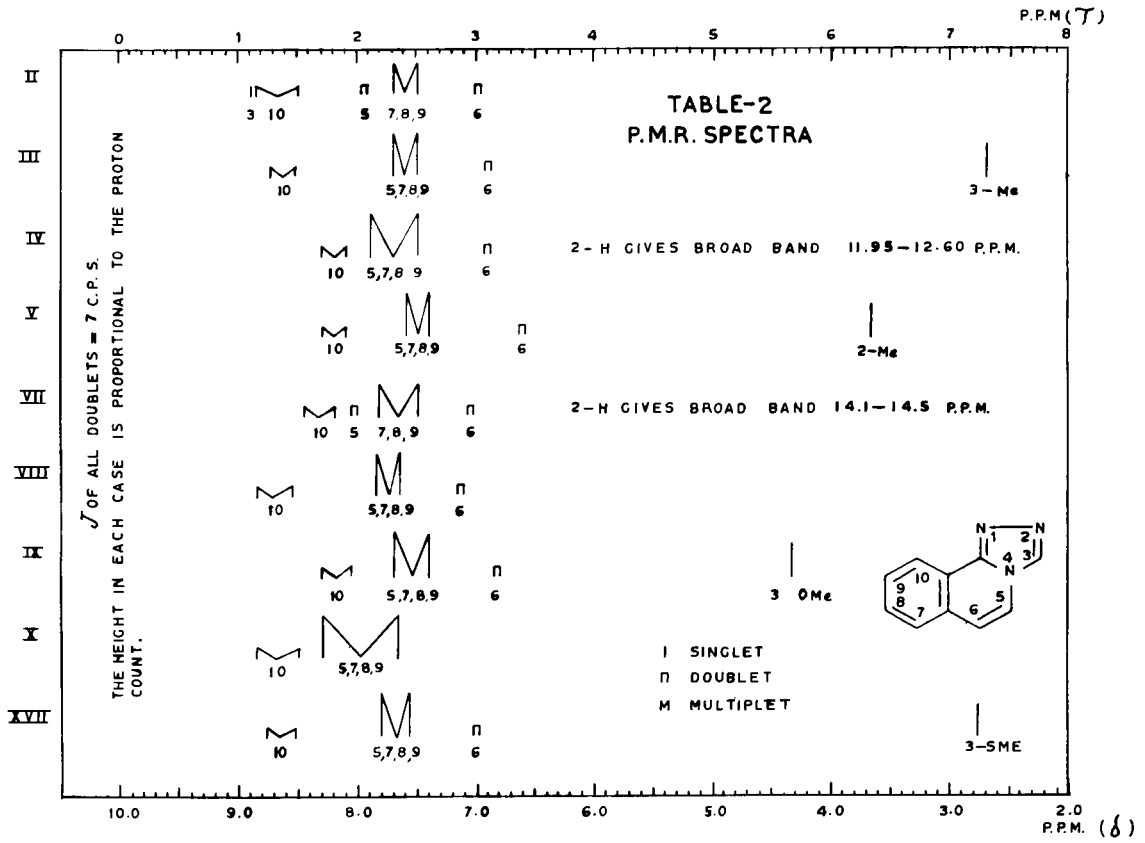
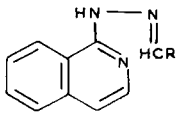


TABLE 3

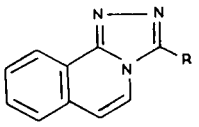
1-Isoquinolylarylhydrazones



Compound No.	R	Formula	Analyses Carbon % Calcd.	Carbon % Found	Hydrogen % Calcd.	Hydrogen % Found	Nitrogen % Calcd.	Nitrogen % Found	m.p., °C	Yield %
1	4-H_3-C-C_6H_4	$C_{17}H_{15}N_3$	78.16	78.10	5.75	5.84	16.09	15.90	168-170	85
2	2-HOOC-C_6H_4	$C_{17}H_{13}N_3O_2$	70.10	69.92	4.46	4.60	14.43	14.33	210-212	95
3	2-HO-C_6H_4	$C_{16}H_{13}N_3O$	73.00	72.85	4.94	5.12	15.97	15.74	305	88
4	4-H_3CO-C_6H_4	$C_{17}H_{15}N_3O$	73.64	73.35	5.41	5.18	15.16	15.30	158-160	90
5	2-H_3CO-C_6H_4	$C_{17}H_{15}N_3O$	73.64	73.92	5.41	5.61	15.16	15.08	232-234	88
6	3-H_3CO-C_6H_4	$C_{17}H_{15}N_3O$	73.64	73.70	5.41	5.63	15.16	14.96	158	85
7	4-Cl-C_6H_4	$C_{16}H_{12}ClN_3$	68.20	68.50	4.26	4.40	14.92	14.72	165	80
8	2-Cl-C_6H_4	$C_{16}H_{12}ClN_3$	68.20	68.04	4.26	4.50	14.92	14.58	143-145	87
9	2,4-Cl_2-C_6H_3	$C_{16}H_{11}Cl_2N_3$	60.76	60.82	3.48	3.21	13.29	13.42	198-200	90
10	4-O_2N-C_6H_4	$C_{16}H_{12}N_4O_2$	65.75	65.95	4.11	3.82	19.17	18.86	215	88
11	2-O_2N-C_6H_4	$C_{16}H_{12}N_4O_2$	65.75	65.40	4.11	4.30	19.15	18.94	140	98
12	3-O_2N-C_6H_4	$C_{16}H_{12}N_4O_2$	65.75	65.38	4.11	4.32	19.17	18.87	180	85
13	2-C_4H_3S	$C_{14}H_{11}N_3S$	66.40	66.18	4.35	4.50	16.64	16.32	133-135	78
14	3-C_4H_3S	$C_{14}H_{11}N_3S$	66.40	66.61	4.35	4.18	16.64	16.40	172	75

TABLE 4

3-Substituted-*s*-Triazolo[3,4-a]isoquinolines



Compound No.	R	Formula	Analyses Carbon % Calcd.	Found	Hydrogen % Calcd.	Found	Nitrogen % Calcd.	Found	m.p., °C	Yield %
1	4-H_3C-C_6H_4	$C_{17}H_{13}N_3$	78.74	78.81	5.05	5.05	16.21	16.15	196-198	85
2	2-HOOC-C_6H_4	$C_{17}H_{11}N_3O_2$	70.58	70.27	3.83	4.08	14.53	14.29	288-290	88
3	2-HO-C_6H_4	$C_{16}H_{11}N_3O$	73.55	73.20	4.25	4.40	16.08	15.80	310-312	75
4	4-H_3CO-C_6H_4	$C_{17}H_{13}N_3O$	74.16	74.03	4.76	4.69	15.26	15.37	190-192	87
5	2-H_3CO-C_6H_4	$C_{17}H_{13}N_3O$	74.16	73.90	4.76	4.50	15.26	15.18	189-190	85
6	3-H_3CO-C_6H_4	$C_{17}H_{13}N_3O$	74.16	74.20	4.76	4.90	15.26	15.00	193-195	95
7	4-Cl-C_6H_4	$C_{16}H_{10}ClN_3$	68.70	68.90	3.58	3.40	15.27	15.30	250-251	82
8	2-Cl-C_6H_4	$C_{16}H_{10}ClN_3$	68.70	68.50	3.58	3.70	15.27	15.10	170-171	85
9	2,4-Cl_2-C_6H_3	$C_{16}H_9Cl_2N_3$	61.14	60.76	2.86	2.83	13.37	13.41	165	88
10	4-O_2N-C_6H_4	$C_{16}H_{10}N_4O_2$	66.20	66.06	3.47	3.60	19.30	19.18	315	85
11	2-O_2N-C_6H_4	$C_{16}H_{10}N_4O_2$	66.20	66.18	3.47	3.50	19.30	19.25	222-224	88
12	3-O_2N-C_6H_4	$C_{16}H_{10}N_4O_2$	66.20	65.90	3.47	3.70	19.30	18.95	266-268	87
13	2-C_4H_3S	$C_{14}H_9N_3S$	66.94	66.50	3.58	3.70	16.70	16.60	270	72
14	3-C_4H_3S	$C_{14}H_9N_3S$	66.94	66.60	3.58	3.72	16.70	16.40	242-245	70

Oxidative cyclisation was carried out with nitrobenzene except in Sl. Nos. 2, 13 and 14 where ferric chloride was used.

have now been synthesised from hydrazones (XVIII; Table 3) obtained from I. Oxidative cyclisation using bromine in acetic acid, as advocated by Gibson (7) was also tried with benzaldehyde-1-isoquinolylhydrazone, but yielded a resinous mass from which the expected 3-phenyl-*s*-triazolo[3,4-a]isoquinoline could not be isolated.

Table 2 gives the P.M.R. spectral data and assignments of some of the title compounds. In the parent *s*-triazolo[3,4-a]isoquinoline (II), the isolated proton at C_3 between two nitrogen atoms gives a sharp singlet at δ = 8.9 p.p.m. The protons at C_5 and C_6 show a typical AB pattern with the C_6 proton doublet centred at δ = 7 p.p.m. and the C_5 proton doublet at δ = 7.95 p.p.m. (J = 7 c.p.s.).

The three aromatic protons at C_7, C_8 and C_9 show up as a multiplet between 7.5-7.7 p.p.m. but the proton at C_{10} absorbs considerably downfield as a multiplet at 8.5-8.8 p.p.m., probably due to deshielding by nitrogen.

In the 3-methyl derivative (III) the signal due to the C_3 proton of II is absent, the methyl signal appearing at δ = 2.7 p.p.m. The C_{10} proton multiplet (8.5-8.8 p.p.m.) and the C_6 proton doublet (δ = 6.9 p.p.m.; J = 7 c.p.s.) are in the same region as in II but, the doublet of the C_5 proton is merged in the aromatic multiplet of C_7, C_8 and C_9 protons (7.5-7.75 p.p.m.). This paramagnetic shift of the C_5 proton can also be seen in IV, V, VIII, IX, X and XVII.

The *N*-methyl (V), *O*-methyl (IX) and the *S*-methyl (XVII) derivatives give spectra very similar to the *C*-methyl derivative (III), excepting the difference in chemical shifts of the methyl groups.

The N*H* proton in IV shows up as a broad band very far downfield at between 11.95-12.60 p.p.m. and similarly the N*H* proton of VII occurs between 14.1 and 14.5 p.p.m.

The P.M.R. spectrum of VIII differs from II only in the absence of the C_3 proton signal, thus locating the chlorine at C_3. In X not only signals due to C_3 and C_6 protons are missing, but the character of the aromatic multiplet also changes due perhaps to the deshielding effect of the C_6-Cl on the protons at C_5 and C_7, the 4-proton multiplet now spreading between 7.67-8.30 p.p.m.

1-Isoquinolylhydrazine (I) (8) and 4-chloro-1-isoquinolylhydrazine (XII) required for this work were prepared by methods known *per se* through the action of hydrazine hydrate on 1-chloroisoquinoline (9) and 1,4-dichloroisoquinoline (10).

EXPERIMENTAL

Melting points were determined in capillary tubes and are uncorrected. I.R. spectra were determined in potassium bromide pellets or Nujol mulls, with a Perkin Elmer Model 221 spectrometer. U.V. spectra were recorded on a Unicam SP 700 model spectrometer. The P.M.R. spectra were run on a Varian A-60 instrument, in deuteriochloroform with tetramethylsilane as the internal reference (11). Compounds prepared by more than one method were checked by mixed melting points and I.R. spectra. All yields are of recrystallized materials.

s-Triazolo[3,4-a]isoquinoline (II).

(a) 1-Isoquinolylhydrazine (I) (1.59 g.) was heated with 10 ml. of formic acid at 80-85° for 4.5 hours. After removal of the formic acid under reduced pressure, the residue was dissolved in water and extracted with ether to remove unreacted I. Evaporation of the aqueous layer left II, yield 1.4 g. (82%), needles m.p. 113-115° from benzene.

Anal. Calcd. for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84. Found: C, 70.80; H, 4.30; N, 24.77.

(b) Compound I (1.59 g.) and 3 ml. of ethyl orthoformate in 30 ml. of xylene were refluxed for 3.5 hours. Removal of the xylene under reduced pressure gave II, 1.5 g. (88%), from benzene.

(c) Compound VII (2.0 g.) was gently heated with 20 ml. of dilute nitric acid (1:5) for 5 hours, the nitric acid evaporated and 0.5 ml. of 10% sodium hydroxide solution added. Extraction into hot benzene gave II, 0.7 g. (45%).

3-Methyl-*s*-triazolo[3,4-a]isoquinoline (III).

It was prepared from I and glacial acetic acid following the procedure under IIa, yield 86%, m.p. 166-167° from water.

Anal. Calcd. for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 71.90; H, 5.20; N, 22.60.

s-Triazolino[3,4-a]isoquinoline-3-one (IV).

(a) Compound I (15.9 g.) in 250 ml. ethanol, 13 g. of ethyl chloroformate and 8.4 g. of potassium hydroxide in 20 ml. of water were refluxed for 2.5 hours, ethanol was distilled off, 20 ml. of 5% potassium hydroxide solution added and undissolved material filtered. Acidification of the filtrate with hydrochloric acid gave IV, yield 16 g. (87%), m.p. 271-272° from ethanol or dimethylformamide.

Anal. Calcd. for $C_{10}H_7N_3O$: C, 64.86; H, 3.81; N, 22.69. Found: C, 64.60; H, 3.89; N, 22.51.

(b) Compound I (1.59 g.) and 0.72 g. of urea were heated at 150-160° for 8 hours, cooled, dissolved in 25 ml. of 5% sodium hydroxide solution and filtered. Acidification of the filtrate as above gave IV 1.4 g. (75%), 271-272°.

2-Methyl-*s*-triazolino[3,4-a]isoquinoline-3-one (V).

Compound IV (1.85 g.), 50 ml. of acetone, 1.3 g. of dimethyl sulphate and 2.0 g. of anhydrous potassium carbonate were refluxed for 10 hours and the mixture was worked up as usual to give V, yield 1.9 g. (90%) m.p. 153-155° from ethanol.

Anal. Calcd. for $C_{11}H_9N_3O$: C, 66.32; H, 4.55; N, 21.10. Found: C, 66.10; H, 4.70; N, 20.90.

Furthermore V was obtained on methylation with diazomethane and methyl iodide/silver oxide. The crude methyl ethers did not reveal the presence of the *O*-methyl isomer (IX) by thin layer chromatography on silica gel using three different solvent systems, *viz.*, benzene-methanol (4:1), petroleum ether (40°-60°) - methanol (3:2) or ethyl acetate. V and IX separate well in these solvent systems.

3-Acetoxy-*s*-triazolo[3,4-a]isoquinoline (VI).

Compound IV (0.92 g.) and 3 ml. of acetic anhydride were warmed with 0.1 ml. of concentrated sulphuric acid for 30 minutes, poured onto crushed ice, filtered and the solid was washed with 2% sodium hydroxide, followed by water. Yield 0.8 g., (72%), m.p. 229° from chloroform.

Anal. Calcd. for $C_{12}H_9N_3O_2$: C, 63.43; H, 3.90; N, 18.49. Found: C, 63.05; H, 4.10; N, 18.20.

VIII and acetic anhydride also gave VI in 75% yield.

3-Mercapto-*s*-triazolo[3,4-a]isoquinoline (VII).

Compound I (1.59 g.) in 30 ml. of ethanol, 1.52 g. of carbon disulphide and 0.56 g. of potassium hydroxide in 5 ml. of water were refluxed for 3 hours, the excess ethanol was distilled off, 20 ml. of potassium hydroxide solution (5%) was added and filtered. The filtrate on acidification with hydrochloric acid gave VII, 1.6 g. (90%) m.p. 262° from ethanol.

Anal. Calcd. for $C_{10}H_7N_3S$: C, 59.67; H, 3.50; N, 20.87. Found: C, 59.70; H, 3.30; N, 20.50.

(b) Compound IV (1.85 g.) and 2.23 g. of phosphorus pentasulphide in 50 ml. of dry xylene were refluxed for 3 hours. Xylene was removed under reduced pressure, the residue poured onto crushed ice, 25 ml. of 5% sodium hydroxide solution added and filtered. VII was liberated by acidification with hydrochloric acid, yield 1.2 g. (60%) from ethanol, m.p. 262°.

3-Chloro-*s*-triazolo[3,4-a]isoquinoline (VIII).

(a) Compound IV (1.85 g.), 5 ml. of phosphorus oxychloride and 10 ml. of dimethylaniline were heated in an oil bath at 140-150° for 9 hours. Excess phosphorus oxychloride was distilled off under reduced pressure, the residue was then decomposed with water and steam distilled to remove dimethylaniline, yield, 1.5 g. (73%), m.p. 166-167° from hot water.

Anal. Calcd. for $C_{10}H_6ClN_3$: C, 58.97; H, 2.97; N, 20.63; Cl, 17.43. Found: C, 59.20; H, 3.10; N, 20.40; Cl, 17.33.

(b) Compound IV (9.2 g.) and 100 ml. of phosphorus oxychloride were heated at 150-160° in a glass autoclave for 30 hours and worked up as above except that ammonium hydroxide was added after removal of the phosphorus oxychloride, yield 9.0 g. (90%), m.p. 166-167°.

(c) Two g. of VII was suspended in a mixture of 25 ml. of chloroform and 15 ml. of water. A slow stream of chlorine was bubbled into the mixture for 3 hours below 10°. The chloroform layer was separated, and the aqueous layer extracted with chloroform. The combined dried chloroform extracts on evaporation yielded VII, 1.7 g. (85%), m.p. 166-167°.

3-Methoxy-*s*-triazolo[3,4-a]isoquinoline (IX).

Two g. of VIII, and 0.65 g. of sodium methoxide in 50 ml. of dry methanol were refluxed for 10 hours. Filtration and evaporation of the methanol gave IX, 1.82 g. (90%), m.p. 92° from ethanol:water (3:2).

Anal. Calcd. for $C_{11}H_9N_3O$: C, 66.32; H, 4.55; N, 21.10. Found: C, 66.05; H, 4.27; N, 21.14.

3,6-Dichloro-*s*-triazolo[3,4-a]isoquinoline (X).

(a) A mixture of 9.25 g. of IV, 15.2 g. of phosphorus pentachloride and 23 g. of phosphorus oxychloride was heated in a glass autoclave at 150-160° for 7 hours. After distilling off the excess phosphorus oxychloride under reduced pressure, the residue was decomposed with ice-water and excess ammonia was added. The gummy solid which separated out was crystallized from benzene. This on passing repeatedly over neutral alumina column with benzene as eluent gave X (3.0 g., 29%), m.p. 167-169°.

Anal. Calcd. for $C_{10}H_5Cl_2N_3$: C, 50.42; H, 2.10; N, 17.67; Cl, 29.40. Found: C, 50.48; H, 2.25; N, 17.56; Cl, 29.09.

(b) Compound XIII (1.09 g.) and 7 ml. of phosphorus oxychloride were heated in a sealed tube at 140-150° for 20 hours. Removal of the phosphorus oxychloride under reduced pressure and basification with excess ammonia afforded X, (0.6 g., 68%), m.p. 167-169°.

Hydrolysis of VIII and X.

Heating with 10% sodium hydroxide solution or 2% sulphuric acid yielded IV and XIII respectively.

1-Hydrazino-4-chloroisoquinoline (XII).

1,4-Dichloroisoquinoline (7.92 g.) and 2.4 g. of hydrazine hydrate were refluxed in 60 ml. of dioxan for 3 hours. After removal of dioxan under reduced pressure the contents were poured into cold water and the separated crude product was crystallized from ethanol to yield XII, 4.4 g. (57%), m.p. 139°.

Anal. Calcd. for $C_9H_8ClN_3$: C, 55.81; H, 4.13; N, 21.76; Cl, 18.34. Found: C, 55.52; H, 3.05; N, 21.45; Cl, 17.94.

6-Chloro-*s*-triazolo[3,4-a]isoquinoline (XI).

(a) Compound X (1.19 g.), 0.5 g. of red phosphorus and 3 ml. of hydroiodic acid were refluxed in 7 ml. of acetic acid for 7 hours, the mixture basified with sodium hydroxide and the liberated crude product crystallized from ethanol to yield XI, 0.75 g. (75%), m.p. 240°.

Anal. Calcd. for $C_{10}H_6ClN_3$: C, 58.97; H, 2.97; N, 20.63; Cl, 17.43. Found: C, 59.40; H, 2.90; N, 20.32; Cl, 16.70.

Similar reduction of VIII led to II, which was isolated by extraction in chloroform. Reduction with zinc/hydrochloric acid gave II both from VIII and X.

(b) XI was also prepared from 1.94 g. of XII and 10 ml. of formic acid as described for II (a), yield, 1.8 g. (78%), m.p. 240°.

6-Chloro-*s*-triazolino[3,4-a]isoquinoline-3-one (XIII).

This was prepared from 1.93 g. of XII, 1.30 g. of ethyl chloroformate and 0.56 g. of potassium hydroxide in alcohol as described for IV (a), yield, 0.5 g. (23%), m.p. 275-277° from dioxan.

Anal. Calcd. for $C_{10}H_6ClN_3O$: C, 54.66; H, 2.73; N, 19.14. Found: C, 54.15; H, 2.44; N, 18.86.

3-Phenoxy-*s*-triazolo[3,4-a]isoquinoline (XIV).

Two g. of VIII, 20 ml. of phenol and 2.0 g. of anhydrous potassium carbonate were gently refluxed in an oil bath for 7 hours and the reaction mixture poured into aqueous sodium hydroxide solution. XIV separated after trituration, yield 2.1 g. (77%), m.p. 155° from ethanol.

Anal. Calcd. for $C_{16}H_{11}N_3O$: C, 73.55; H, 4.24; N, 16.08. Found: C, 73.40; H, 4.08; N, 15.90.

3-Anilino-*s*-triazolo[3,4-a]isoquinoline (XV).

One g. of VIII and 6 ml. of aniline were gently refluxed for 2 hours. Trituration with dilute hydrochloric acid removed unreacted aniline leaving XV as a solid, yield 1.3 g. (92%), m.p. 270° from ethanol.

Anal. Calcd. for $C_{16}H_{12}N_4$: C, 73.83; H, 4.65; N, 21.53. Found: C, 73.52; H, 4.80; N, 21.30.

3-Piperidino-*s*-triazolo[3,4-a]isoquinoline (XVI).

This compound was prepared as described above from 0.5 g. of VIII and 4 ml. of piperidine, yield 0.6 g. (80%), m.p. 201° from ethanol.

Anal. Calcd. for $C_{15}H_{14}N_4$: C, 71.40; H, 6.39; N, 22.21. Found: C, 71.29; H, 6.40; N, 22.32.

3-Methylthio-*s*-triazolo[3,4-a]isoquinoline (XVII).

To 2 g. of VII dissolved in 40 ml. of 1 *N* potassium hydroxide solution was added 1.7 g. of methyl iodide and the mixture was stirred at room temperature for 30 minutes. The crude product which separated was collected and crystallized from ethanol, yield 1.6 g. (75%), m.p. 142°.

Anal. Calcd. for $C_{11}H_9N_3S$: C, 61.36; H, 4.21; N, 19.51. Found: C, 61.16; H, 4.12; N, 19.35.

1-Isoquinolylarylhydrazones (XVIII).

Equimolar proportions of 1-isoquinolylhydrazine and the corresponding aldehyde in ethanol or 10% acetic acid were condensed by heating on a water bath for 45-60 minutes. The reaction mass was poured into water and the precipitated crude hydrazones filtered off and used as such for further cyclisation. Analytical samples were obtained by recrystallization from ethanol or benzene. Yields, melting points and analytical data are presented in Table 3.

3-Aryl-*s*-triazolo[3,4-a]isoquinolines (XIX).

These were obtained by oxidative cyclisation of the hydrazones (XVIII) with nitrobenzene or ferric chloride as described earlier (3). Table 4 lists the compounds synthesised and their analytical data.

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