TRANSFORMATIONS OF SUBSTITUTED 5-AMINOPYRIMIDINES UNDER CONDITIONS OF THE DIAZOTIZATION

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Received January 14th, 1985

Reaction of nitrous acid with 4-substituted and 4,6-disubstituted 5-aminopyrimidines *Ia—In* produces 4-substituted and 4,5-disubstituted 1,2,3-triazoles *IIa—IIv*, resp. Under similar conditions, 2,5-diaminopyrimidines *XIIa—XIId* give $N_{(7)}$-oxides of 2-amino-4-aralkylthiopyrimido-[5,4-*d*]-1,2,3-triazines *XIIIa—XIIId*, and 5-amino-4-chloropyrimidines *In* and *X* give 2-diazocyanoacetamides *XIa* and *XIb*, resp. Also described are syntheses of 5-formylaminopyrimidines *XVa—XVg* from glycine ethyl ester *via* sodium salt *XVI*.

Whereas diazotization of primary amines derived from carbocyclic aromatics produces relatively stable diazonium salts, action of nitrous acid on heterocyclic aromatic amines often results in ring opening and conversions into other heterocyclic systems[1]. Within the 5-aminopyrimidine group, diazotization of 5-aminouracil and cognate compounds was studied in detail[2-5]. Angeli[2] found that diazotization of 5-aminouracil gave 5-diazouracil; the same product was also obtained later[6] by diazotization of 5-amino-2,4-dichloropyrimidine. However, structure of diazouracil and its hydrolytic splitting into 1,2,3-triazole-4-carboxamide were elucidated only recently[7-9]. In 1976 Thurber and coworkers[9,10] described preparation of 0^5-6(S)-cyclo-5-diazouridine and its hydrolysis in aqueous acetonitrile at 100°C giving 1,2,3-triazole derivatives and studied mechanism of this reaction.

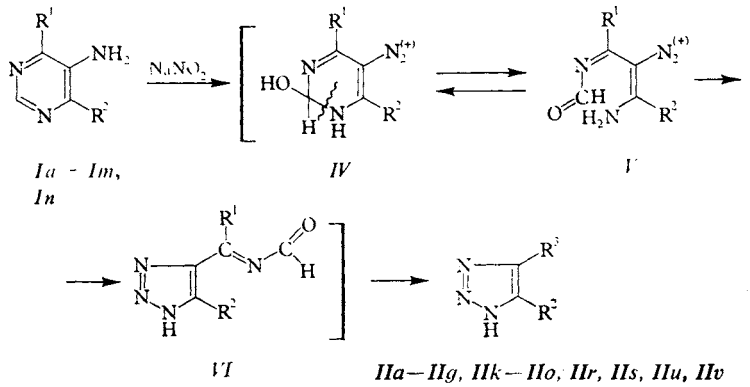
Within the context of investigation of pyrimidines having potential antineoplastic effects we dealt with structure of the compounds formed under conditions of the diazotization of 4-substituted and 4,6-disubstituted 5-aminopyrimidines, and we found that the reaction produces either substituted 1,2,3-triazoles or bicyclic systems or derivatives of diazocyanoacetamide, which depends on character of substituents and on the reaction conditions.

It is known[11,12] that reaction of nitrous acid with 4,5-diaminopyrimidines produces pyrimido[4,5-*d*]triazole derivatives, and similarly from 4-mercapto- and 4-hydroxy--5-aminopyrimidines resulting products are derivatives of pyrimido[4,5-*d*]-1,2,3--thiadiazole and pyrimido[4,5-*d*]-1,2,3-oxadiazole. We were interested in diazotization of 5-aminopyrimidines *Ia—In* whose 4- and 6-substituents contain no mobile

hydrogen atoms. We have found that in these cases the reaction is accompanied by the pyrimidine ring contraction with formation of 4,5-disubstituted derivatives of 1,2,3-triazole *IIa–IIv*, the structure of the triazoles formed being dependent on both character of the 4- and 6-substituents in the starting 5-aminopyrimidines and the diazotization conditions.

The first group of 5-aminopyrimidine derivatives studied by us comprised 6-alkyl-(aralkyl)thio-5-amino-4-methoxypyrimidines *Ia–Ie*. Reaction of sodium nitrite with compounds *Ia–Id* in hydrochloric acid produces high yields of methyl esters of 4-alkyl(aralkyl)thio-1,2,3-triazole-5-carboxylic acids *IIa–IId*, the nature of the alkyl(aralkyl)thio group having no effect on the reaction course. Composition and structure of the products *IIa–IId* formed followed from elemental analyses and spectra, and it was confirmed by resynthesis in the case of triazole *IIa*. The IR spectra of the compounds obtained exhibit, besides the bands in the region 1 720 cm^{-1} due to absorption of the ester group, also bands in the region from 800 to 1 200 cm^{-1} which are characteristic for 1,2,3-triazole ring. The mass spectra contained peaks of the molecular ions corresponding to the structures suggested (in the values of their molecular masses). The ^1H NMR spectra lack the proton signals of the pyrimidine 2-proton atom which are present in the analogous spectra of the starting sulphides *Ia–Id*. Structure of the triazole *IIa* obtained at the above-mentioned conditions from pyrimidine *Ia* was confirmed synthetically by transformation of *IIa* with diazomethane into the N-methyl derivative *IIIa* and comparison of its properties with those of the analogous product obtained by action of diazomethane on the known 4-carboxy-5-mercapto-1*H*-1,2,3-triazole[13] (*III*). The compounds *IIIa* obtained by these two ways have identical physico-chemical constants and spectral characteristics; the position of methyl group at nitrogen atom of the 1,2,3-triazole ring was not determined.

The formation of triazoles *IIa–IId* from pyrimidines *Ia–Id* can be expressed by Scheme 1. It is presumed that the reaction of nitrous acid with 5-aminopyrimidines



Ia – Im, In *IV* *V*

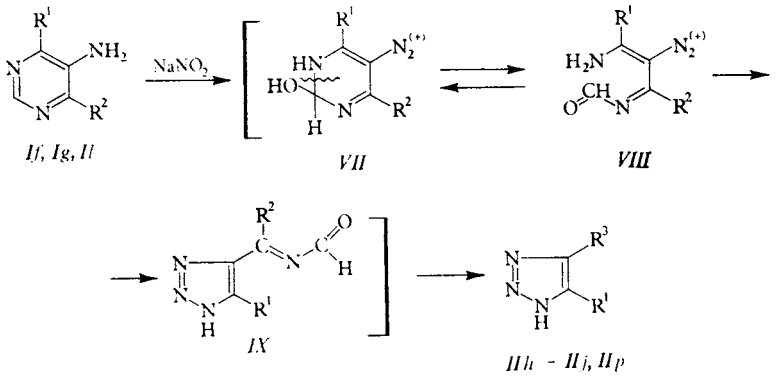
VI *IIa–IIg, IIk–IIo, IIr, IIs, IIu, IIv*

SCHEME 1

Ia–Id in hydrochloric acid involves a nucleophilic addition of water to $N_{(1)}=C_{(2)}$ bond with formation of the hydrated form *IV* which stands in equilibrium with the open tautomeric form *V*, subsequent intramolecular reaction of diazo group with amino group of compound *V* with formation of the 1,2,3-triazole system *VI*, and final hydrolytic splitting off of N-formyl group with formation of esters *IIa–IId*. The scheme suggested is considered more probable (because it involves ring closure of energetically favourable 1,2,3-triazole ring with smaller number of intermediates) than the alternative pathway involving hydratation of the $N_{(3)}=C_{(4)}$ bond and subsequent splitting of this bond which is characteristic[7] for conversion of diazouracil in alkaline medium.

Structure of the 1,2,3-triazoles formed is affected substantially by the medium in which the diazotization of 5-aminopyrimidines is carried out. The reaction of sodium nitrite with pyrimidines *Ie–Ig* in acetic acid produces the respective 4-N--formylcarbamoyl-1,2,3-triazoles *IIe–IIg*. The hydration and pyrimidine ring opening take place according to Scheme 1, but the intermediate triazole *VI* is hydrolyzed by an alternative way to give the N-formylcarbamoyl derivatives *IIe–IIg*. Composition and structure of compounds *IIe–IIg* was confirmed by elemental analyses, mass spectra (the presence of intensive peaks due to the molecular ion corresponding to the molecular mass of compounds *IIe–IIg* and of the fragments proving unambiguously the presence of CONHCHO grouping in these compounds), and IR spectra (the presence of two absorption bands in the regions 1 720–1 730 and 1 680 cm^{-1} due to two C=O groups).

If the diazotization of *If* is carried out in hydrochloric acid, hydrochloride of S-methyl 5-chloro-1,2,3-triazole-4-thiocarboximidate (*IIh*) is obtained which is easily hydrolyzed to S-methyl 4-chloro-1,2,3-triazole-5-thiocarboxylate (*IIi*). The diazotization of the analogous *Ig* at the same conditions only gave the final transformation product S-benzyl 4-chloro-1,2,3-triazole-5-thiocarboxylate (*IIj*) along



SCHEME 2

with considerable amount of unreacted starting compound *Ig*. These conversions of the pyrimidines *If* and *Ig* can be explained by opening of the hydrated pyrimidine ring at the $C_{(2)}$—$N_{(3)}$ bond (Scheme 2).

Furthermore, we followed the diazotization course of the 4,6-disubstituted pyrimidines *Ih*–*Im*. The reaction course depends on character of the 4- and 6-substituents which affect the position of opening of the hydrated pyrimidine ring (*IV* or *VII*) at $N_{(1)}$—$C_{(2)}$ or $C_{(2)}$—$N_{(3)}$ bond and also affect the nature of the 4- and 5-substituents of the 1,2,3-triazoles formed.

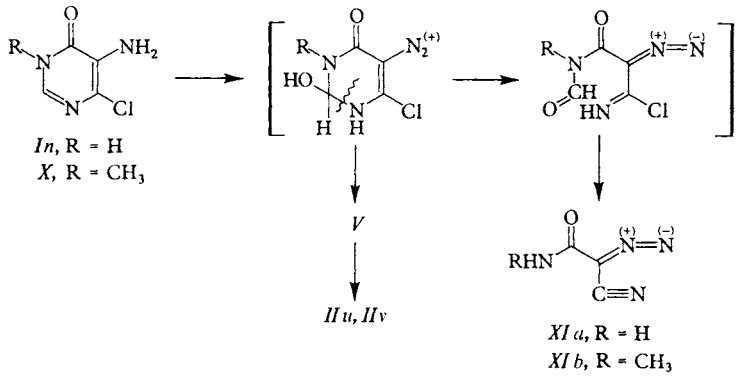
The diazotization of 5-amino-6-benzylthio-4-dimethylaminopyrimidine (*Ih*) in hydrochloric acid leads to the pyrimidine ring opening at $N_{(1)}$—$C_{(2)}$ position (according to Scheme 1), but the intermediate 1,2,3-triazole *VI* is stabilized by formation of 4-benzylthio-5-(N,N-dimethylguanyl)-1,2,3-triazole (*IIk*) which was isolated from the reaction mixture in the form of hydrochloride.

The diazotization of 5-aminopyrimidines containing identical substituents at both the positions 4 and 6 makes it impossible (due to the symmetrical substitution) to decide whether the conversion follows Scheme 1 (hydration of $N_{(1)}$—$C_{(2)}$ bond) or Scheme 2 (hydration of $C_{(2)}$—$N_{(3)}$ bond), because both the ways of hydration and splitting of the 5-aminopyrimidines lead finally to the same 1,2,3-triazoles. So the reaction of nitrous acid with 5-amino-4,6-dimethoxypyrimidine (*Ii*) in aqueous hydrochloric acid gave O-methyl 4-methoxy-1,2,3-triazole-5-carboximidate (*III*). Analogous course was taken by the diazotization of 5-amino-4,6-bis(dimethylamino)-pyrimidine (*Ij*) which gave 4-dimethylamino-5-(N,N-dimethyl-N′-formylguanyl)--1,2,3-triazole (*IIm*); the compound *IIm* is isomeric with the hydrated form of 5-diazo-4,6-bis(dimethylamino)pyrimidine of general formula *IV*, and its structure (as a 1,2,3-triazole derivative) was proved by the presence of the characteristical absorption band in its IR spectrum at 3 150 cm^{-1}.

With the unsymmetrically 4,6-disubstituted 5-aminopyrimidines the character of the products isolated enables the determination of the conversion mechanism, *i.e.* whether it goes by Scheme 1 or 2. So, *e.g.* the diazotization of 5-amino-6-dimethylamino-4-methoxypyrimidine (*Ik*) gave hydrochloride of 4-methoxy-5-(N,N--dimethylguanyl)-1,2,3-triazole (*IIn*) whose structure was proved by analogy of its IR spectrum with those of compounds *IIa*–*IId*; hence the conversion proceeds according to Scheme 1. In the diazotization of 5-amino-4-chloro-6-(1-piperidyl)-pyrimidine (*Il*) we could isolate 5-cyano-4-(1-piperidyl)-1,2,3-triazole (*IIo*) in the yield 23% and 4-chloro-5-(N-(1-piperidyl)guanyl)-1,2,3-triazole (*IIp*) in the yield 47%. The triazole *IIo* is formed according to Scheme 1 (the hydrated pyrimidine ring *IV* is opened at $N_{(1)}$—$C_{(2)}$ position), whereas the triazole *IIp* is formed according to Scheme 2 (the pyrimidine ring opening at the $C_{(2)}$—$N_{(3)}$ bond); so far this is the only case where simultaneous formation of the two 1,2,3-triazole derivatives was observed as the consequence of the two types of hydration of the starting pyrimidine taking place side by side.

As it was stated above the diazotization of 5-aminouracil gives diazouracil[2]. The available literature, however, presents no data on the diazotization of 5-amino-4--hydroxypyrimidine (*Im*). We have found that the diazotization of *Im* in hydrochloric acid gives two derivatives of 1,2,3-triazole: 1,2,3-triazole-5-carboxamide (*IIr*) and its N-formyl derivative *IIs*, the latter compound being easily hydrolyzed to *IIr* on boiling in water. Structure of *IIr* was determined by comparison of its physico--chemical and spectral data with literature data[9,14,15], and it was confirmed by its alkaline hydrolysis giving the known 1,2,3-triazole-4-carboxylic acid (*IIt*)[9,15,16]. From the structure of *IIr* it is obvious that the conversion proceeded according to Scheme 1.

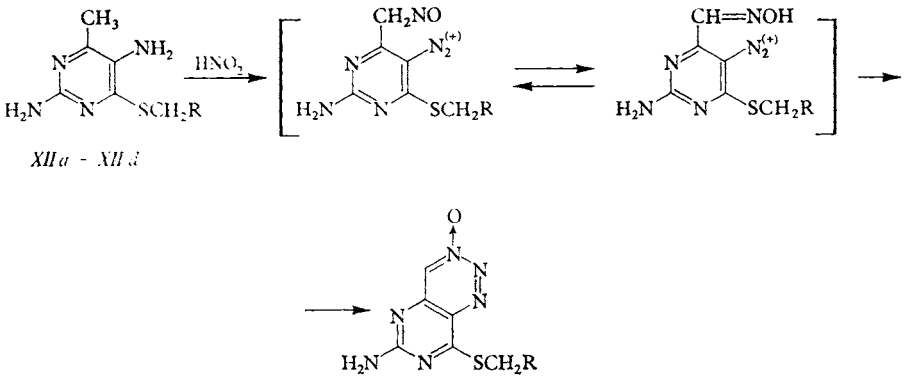
A distinct effect of the 6-substituent on the diazotization course was observed with 5-amino-6-chloro-4-hydroxypyrimidine (*In*) and its 3-methyl derivative *X*. Reactions of *In* and *X* with nitrous acid gave 2-diazocyanoacetamide (*XIa*) and its N-methyl derivative *XIb*, resp., as the main products; according to mass spectra (the presence of the respective peaks of molecular ions), however, the raw reaction mixtures also contained 5-chloro-1,2,3-triazole-4-carboxamide (*IIu*) and 5-chloro-4--(N-methylcarbamoyl)-1,2,3-triazole (*IIv*), respectively. We presume the conversions of the pyrimidines *In* and *X* to proceed according to Scheme 3, the hydrated intermediate *IV* being split at the $N_{(1)}$—$C_{(2)}$ bond, whereupon the open tautomer *V* undergoes cyclization to *IIu* and *IIv*, resp., besides the main competitive dehydrohalogenation to diazocyanoacetamides *XIa* and *XIb*, respectively (Scheme 3).



SCHEME 3

In contrast to the above-mentioned conversions of 5-aminopyrimidines *Ia*–*Im*, the reactions of 6-aralkylthio-2,5-diamino-4-methylpyrimidines *XIIa*–*XIId* with nitrous acid take a different course. Literature[17] describes the diazotization of 2,5-diamino-4-methylthiopyrimidine (*XIIe*) which gives the normal diazo compound. In our case it was found that action of excess nitrous acid leads to formation of $N_{(7)}$-oxides of 2-amino-4-aralkylthiopyrimido[5,4-*d*]-1,2,3-triazines *XIIIa*–*XIIId*.

The reaction does not depend on the medium, having the same course in both hydrochloric and acetic acids, and the compounds *XIIIa–XIIId* were even isolated (although in far lower yields) when one equivalent of nitrous acid only was used. In the cases mentioned the hydrolytic ring opening of the intermediate 5-diazopyrimidine (giving the 1,2,3-triazole derivatives) does not take place, but there takes place a reaction between diazo group and the nitrosomethylene grouping formed by action of excess nitrous acid, which results in formation of the $N_{(7)}$-oxides *XIIIa–XIIId*.

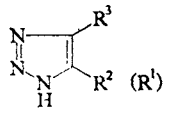


XIIa – XIId

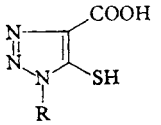
XIIIa–XIIId, for substituents see Table III

SCHEME 4

The reaction course is given in Scheme 4. Structure of the compounds *XIIIa–XIIId* was confirmed by their spectra: the IR spectra exhibit characteristic absorption bands of the original 2-NH_2 group and lack the band of diazo group; the ^{1}H NMR spectra contain, besides the proton signals due to the thiobenzyl grouping, a signal in the region of 8·3 ppm characteristic of the proton of triazine ring.



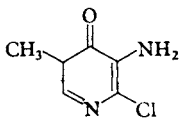
IIa–IIr, for substituents see Table II
IIs, R^2 = H, R^3 = CONHCHO
IIt, R^2 = H, R^3 = COOH
IIu, R^2 = Cl, R^3 = $CONH_2$
IIv, R^2 = Cl, R^3 = $CONHCH_3$



III, R = H
IIIa, R = CH_3 (position is not determined)

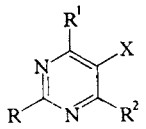
The starting 5-amino-4-methoxy-6-methylthiopyrimidine[18] (*Ia*), 5-amino-6-benzylthio-4-methoxypyrimidine[18] (*Ib*), 5-amino-4-chloro-6-methylthiopyrimidine[19] (*If*), 5-amino-6-benzylthio-4-chloropyrimidine[19] (*Ig*), 5-amino-4-chloro-6-(1-piperidyl)-

pyrimidine[20] (*Il*), 5-amino-4-chloro-6-oxo-1,6-dihydropyrimidine[18] (*In*), 5-amino--4-methoxy-6-thioxo-1,6-dihydropyrimidine[21] (*Io*), 5-amino-4-dimethylamino-6-thioxo-1,6-dihydropyrimidine[22,23] (*Ip*), and 5-amino-4-chloro-1-methyl-6-oxo-1,6-dihydropyrimidine[18] (*X*) were prepared by known procedures. The pyrimidines



X

Ic–*Ie* and *Ih* were synthetized from *Io* or *Ip* by the procedure analogous to that of *Ib*. 5-Amino-4,6-bis(dimethylamino)pyrimidine (*Ij*) was prepared by reduction of 4,6-bis(dimethylamino)-5-nitropyrimidine (*XIVa*) with sodium dithionite; compound *XIVa* was obtained by reaction of the known 4-(dimethylamino)-6-chloro-5-nitropyrimidine[24] (*XIVb*) with aqueous dimethylamine. Similarly 6-aminopyrimidine *Ii* was prepared by reduction of 4,6-dimethoxy-6-nitropyrimidine[25] (*XIVc*) with sodium dithionite. 5-Amino-4-dimethylamino-6-methoxypyrimidine (*Ik*) was obtained by reduction of 4-dimethylamino-6-methoxy-5-nitropyrimidine (*XIVd*) with iron in



X = NH_2, R = H

Ia, $R^1 = OCH_3$, $R^2 = SCH_3$
Ib, $R^1 = OCH_3$, $R^2 = SCH_2C_6H_5$
If, $R^1 = Cl$, $R^2 = SCH_3$
Ig, $R^1 = Cl$, $R^2 = SCH_2C_6H_5$
Ii, $R^1 = R^2 = OCH_3$
Il, $R^1 = Cl$, $R^2 = -N$ 
Im, $R^1 = OH$, $R^2 = H$
In, $R^1 = Cl$, $R^2 = OH$
Io, $R^1 = OCH_3$, $R^2 = SH$
Ip, $R^1 = N(CH_3)_2$, $R^2 = SH$
Ic–*Ie*, *Ih*, *Ij*, *Ik*, for substituents see Table I

X = R = NH_2, $R^1 = CH_3$

XIIe, $R^2 = SCH_3$
XIIf, $R^2 = SH$
XIIa–*XIId*, for substituents see Table I

X = NO_2, R = H

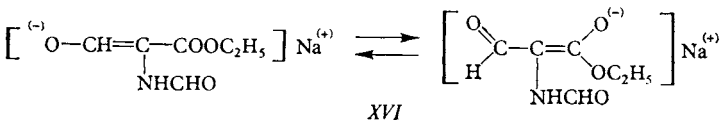
XIVb, $R^1 = N(CH_3)_2$, $R^2 = Cl$
XIVc, $R^1 = R^2 = OCH_3$
XIVa, *XIVd*, for substituents see Table I

X = NHCHO, $R^1 = OH$, $R^2 = H$

XVa–*XVg*, for substituents see Table I

acetic acid; the compound *XIVd* was prepared by reaction of 6-chloropyrimidine[24] *XIVb* with sodium methoxide in methanol. 2,5-Diamino-6-benzylthio-4-methylpyrimidine (*XIIa*) and 2,5-diamino-4-methyl-6-methylthiopyrimidine (*XIIe*) were synthetized from 2,5-diamino-4-methyl-6-thioxo-1,6-dihydropyrimidine (*XIIf*) by the known procedure[26]; the pyrimidines *XIIb*–*XIId* were prepared similarly with

application of the respective substituted benzyl chlorides. The pyrimidine *Im* was prepared both by the known procedure[27] from N-ethoxycarbonylglycine and *via* 5-formylamino-4-hydroxypyrimidine (*XVa*). Action of ethyl formiate on ethyl ester of glycine in the presence of sodium methoxide results in simultaneous formylation of amino group of glycine and the Claisen condensation giving sodium salt of ethyl 3-oxo-2-(formylamino)propionate (*XVI*); condensation of the salt *XVI* with formamidine acetate gave good yields of the formylaminopyrimidine *XVa* which was



XVI

hydrolyzed to 5-amino-4-hydroxypyrimidine (*Im*) in aqueous-ethanolic hydrochloric acid. The reaction given is generally applicable to preparation of 2-substituted 5-formylamino-4-hydroxypyrimidines; the pyrimidines *XVb*–*XVg* were prepared similarly with application of urea, O-methylisourea, thiourea, S-ethylisothiourea, guanidine, and acetamidine, respectively.

EXPERIMENTAL

The melting temperatures were determined with a Kofler apparatus and are not corrected. For elemental analyses the samples were dried at 27 Pa at temperatures proportional to the respective melting points. The UV spectra were measured with a Unicam SP 8000 apparatus at the concentrations of about 0·001% (m/V) in 0·1 M-HCl (A) and 0·1 M-NaOH (B) or in 0·1 M-HCl in 50% (V/V) aqueous methanol (A_1) or in 0·1 M-NaOH in 50% (V/V) aqueous methanol (B_1). The IR spectra were recorded with a UV-457 apparatus in Nujol, if not otherwise stated. The ^{1}H NMR spectra were measured with a C-60 HL and a Tesla BSC 487 (80 MHz) apparatus using tetramethylsilane as the internal standard; the δ values are given in ppm units. The mass spectra were recorded with an MX-1303 apparatus. Purity of the compounds was checked by TLC (silica gel DC-Fertigplatten Kieselgel F_{254} Merck or Silufol UV_{254} Kavalier, eluent systems: chloroform–methanol–conc. ammonia 2 : 2 : 1, n-butanol–acetic acid–water 4 : 1 : 1, ethyl acetate–methanol–conc. ammonia 75 : 20 : 5, chloroform–ethanol–triethylamine 80 : 20 : 5, detection in UV light at 254 nm). Solvents or solvent mixtures used for the crystallizations (Tables I–III): AcOH acetic acid, DMF dimethylformamide, S_1 ethanol–water, S_2 DMF–water, S_3 chloroform–hexane, S_4 benzene–hexane, S_5 ethanol–water–ether, S_6 methanol–acetone–ether.

Substituted 6-(Benzylthio)pyrimidines *Ic*–*Ie*, *Ih*, *XIIa*–*XIId* (Method *A*)

A solution of 12·5 mmol respective 6-thioxo-1,6-dihydropyrimidine (1·97 g *Io*, 2·12 g *Ip*, 1·95 g *XIIf*, resp.) in 85 ml methanol containing 14 ml (12·5 mmol) 5% (m/V) solution of potassium hydroxide in methanol was stirred, and a solution of 12·5 mmol respective benzyl bromide or chloride in 30 ml methanol was added thereto. The mixture was stirred at room temperature 2 h, the precipitated product (sometimes after removing a part of the solvent by distillation under reduced pressure) was collected by filtration and recrystallized (Table I).

TABLE I

Substituted pyrimidines

Compound R	R^1 R^2	Yield, % (method)	M.p., °C (solvent)	Formula (mol. mass)	Calculated/found % C	% H	% N
	$X = NH_2$						
Ic[a]	OCH_3	52	76–78	$C_{15}H_{17}N_3O_3S$	56·51	5·37	13·16
H	$SCH_2C_6H_4COOC_2H_5$ (4-)	(*A*)	(hexane)	(319·4)	56·33	6·05	13·13
Id[b]	OCH_3	44	182–183	$C_{16}H_{20}N_4O_2S$	57·81	6·06	16·85
H	$SCH_2C_6H_4CONHC_3H_7$-i(4-)	(*A*)	(S_1)	(332·4)	57·88	6·10	17·02
Ie[c]	OCH_3	75	138–139	$C_{12}H_{12}N_4O_3S$	49·30	4·14	19·16
H	$SCH_2C_6H_4NO_2$(4-)	(*A*)	(S_2)	(292·3)	49·09	3·99	19·25
Ih[d]	$N(CH_3)_2$	80	65–66	$C_{13}H_{16}N_4S$[m]	59·97	6·20	21·52
H	$SCH_2C_6H_5$	(*A*)	(hexane)	(260·4)	60·29	6·40	21·88
Ij[e]	$N(CH_3)_2$	73	80–81	$C_8H_{15}N_5$	53·01	8·34	38·65
H	$N(CH_3)_2$		(hexane)	(181·2)	52·97	8·23	38·76
Ik[f]	OCH_3	97	69–70	$C_7H_{12}N_4O$	49·98	7·19	33·31
H	$N(CH_3)_2$		(hexane)	(168·2)	50·00	7·21	33·36
XIIa[g]	CH_3	64	157–159	$C_{12}H_{14}N_4S$[n]	58·51	5·73	22·75
NH_2	$SCH_2C_6H_5$	(*A*)	(S_2)	(246·3)	58·60	6·00	22·81
XIIb[h]	CH_3	67	147–153	$C_{12}H_{13}N_5O_2S$	49·47	4·49	24·04
NH_2	$SCH_2C_6H_4NO_2$(4-)	(*A*)	(S_2)	(291·3)	49·36	4·54	24·21
XIIc[i]	CH_3	69	125–127	$C_{15}H_{18}N_4O_2S$	56·60	5·66	17·60
NH_2	$SCH_2C_6H_4COOC_2H_5$(4-)	(*A*)	(S_2)	(318·4)	56·59	5·64	17·86
XIId[j]	CH_3	64	248–251	$C_{16}H_{21}N_5OS$	57·98	6·39	21·13
NH_2	$SCH_2C_6H_4CONHC_3H_7$-i(4-)	(*A*)	(S_2)	(331·4)	57·85	6·30	21·09

TABLE I
(*Continued*)

Compound R	R^1 R^2	Yield, % (method)	M.p., °C (solvent)	Formula (mol. mass)	Calculated/found % C	% H	% N
	X = NO_2						
XIVa[k]	$N(CH_3)_2$	95	159–161	$C_8H_{13}N_5O_2$	45·49	6·20	33·16
H	$N(CH_3)_2$	(*B*)	(ethanol)	(211·4)	45·55	6·31	33·26
XIVd[l]	$N(CH_3)_2$	95	79–80	$C_7H_{10}N_4O_3$	42·42	5·09	28·27
H	OCH_3	(*B*)	(ethanol)	(198·3)	42·57	5·28	28·58
	X = NCHO						
XVa[o]	OH	40	260–264	$C_5H_5N_3O_2$	43·17	3·62	30·21
H	H	(*C*)	(water)	(139·1)	43·10	3·63	30·22
XVb[p]	OH	21	310–313[q]	$C_5H_5N_3O_3$	36·59	3·68	25·60
OH	H	(*C*)	(water)	. 1/2 H_2O (164·1)	36·18	3·64	24·92
XVc[r]	OH	56	185–187	$C_6H_{11}N_3O_5$[s]	35·12	5·40	20·48
OCH_3	H	(*C*)	(water)	(205·2)	35·42	5·16	20·85
XVd[t]	OH	21	>350	$C_5H_5N_3O_2S$[u]	35·08	2·94	24·55
SH	H	(*C*)	(water)	(171·2)	35·67	3·15	24·77
XVe[v]	OH	90	266–268[w]	$C_7H_9N_3O_2S$[x]	42·40	4·55	21·09
SC_2H_5	H	(*C*)	(water)	(199·2)	41·90	4·78	21·49
XVf[y]	OH	26	>300	$C_5H_6N_4O_2$	38·96	3·92	36·35
NH_2	H	(*C*)	(water)	(154·1)	38·16	3·98	36·48
XVg[z]	OH	21	>300	$C_6H_7N_3O_2$	47·10	4·61	27·44
CH_3	H	(*C*)	(water)	(153·1)	47·08	4·59	27·57

TABLE I

(*Continued*)

[a] IR Spectra (ν in Nujol) and mass spectra (M^+): 3 370, 3 480 (NH), 1 710 (C=O) cm^{-1}; [b] 3 468, 3 363, 3 303 (NH), 1 630 (C=N) cm^{-1}; *m/e* 332; [c] 3 410, 3 338 (NH), 1 615, 1 600 (C=O) cm^{-1}; [d] 3 384 (NH), 1 604 (C=O) cm^{-1}; [e] *m/e* 181; [f] 3 383, 3 292 (NH), 1 866, 1 576 (C=N) cm^{-1}; *m/e* 168; [g] 3 376, 3 326, 3 197 (NH), 1 636 (C=N) cm^{-1}; [h] 3 448, 3 352, 3 310, 3 210 (NH), 1 618, 1 597 (C=N) cm^{-1}; [i] 3 440, 3 385, 3 280, 3 145 (NH), 1 702 (C=O), 1 629 (C=N) cm^{-1}; [j] 3 474, 3 418, 3 298, 3 164 (NH), 1 626 (C=N) cm^{-1}; [k] *m/e* 211; [l] 1 580 (C=N) cm^{-1}; *m/e* 198.

Further data: [m] calculated 12·31% S, found 12·12% S; [n] calculated 13·02% S, found 13·33% S; [o] UV spectrum (λ_{max}, log ε): 284 (3·97), 254 (3·91) nm (A); 285 (3·83) 245 (3·95) nm (B). IR spectrum (KBr): 1 695 (CHO), 3 200 (NH), 1 655 (lactam) cm^{-1}; [p] from 5·4 g (0·03 mol) *XVI*, 1·80 g (0·03 mol) urea, and 0·7 g (0·03 mol) sodium in 25 ml methanol, 8 h boiling. UV spectrum (λ_{max}, log ε): 291 (3·84), 235 (4·01) nm (A_1); 282 (3·85), 235 (3·98) nm (B_1). IR spectrum (KBr): 1 710, 1 570 (NHCHO), 3 160 (NH), 1 660, 1 640 (lactam) cm^{-1}; [q] ref.[29] gives m.p. 312°C; [r] by addition of a solution of 9·6 g (55 mmol) *XVI* in 12 ml water to a suspension of 8·61 g (50 mmol) O-methylisouronium hydrogen sulphate in 10 ml (0·1 mol) 10 M-NaOH and stirring at room temperature 24 h. UV spectrum (λ_{max}, log ε): 277 (3·85), 244 (3·96) nm (A_1); 286 (3·88), 246 (3·94) nm (B_1). IR spectrum (KBr): 1 670, 1 550 (NHCHO), 3 340, 3 160 (NH), 1 280, 1 020 (CH_3O) cm^{-1}; [s] dihydrate; [t] from 13·2 g (73 mmol) *XVI* and 5·02 g (66 mmol) thiourea in 30 ml methanol, 3 h boiling; UV spectrum (λ_{max}, log ε): 315 (4·17), 287 (4·14), 222 (4·10) nm (A_1); 310 (4·00), 275 (4·01), 225 (4·14) nm (B_1); IR spectrum (KBr): 1 685 (NHCHO), 1 660 (lactam), 1 120 (C=S), 1 530 (NHCHO), 3 210, 3 120, 3 380 (NH) cm^{-1}; [u] calculated 18·73% S, found 18·34% S; [v] from 5·44 g (30 mmol) *XVI* and 5·55 g (30 mmol) S-ethylisothiouronium bromide in a solution of 1·7 g (30 mmol) KOH in 20 ml water, 24 h at room temperature. UV spectrum (λ_{max}, log ε): 296 (4·04), 235·5 (4·01) nm (A); 296 (3·95), 259 (3·93) nm (B). IR spectrum (KBr): 1 680, 1 540 (NHCHO), 3 200 (NH), 1 650 (lactam) cm^{-1}; [w] ref.[27] gives m.p. 264 to 270°C; [x] calculated 16·09% S, found 16·01% S; [y] from 5·44 g (30 mmol) *XVI*, 2·90 g (30 mmol) guanidinium chloride, and 0·7 g (30 mmol) sodium in 40 ml methanol, 24 h at room temperature. UV spectrum (λ_{max}, log ε): 282 (3·92), 244 (4·03) nm (A); 286 (3·84), 241 (3·91) nm (B). IR spectrum (KBr): 3 300, 3 160, 3 070 (NH_2, NH), 2 700, 2 860, 1 665 (NHCHO), 1 630 (lactam), 1 640 (arom. NH_2) cm^{-1}; [z] from 13·2 g (73 mmol) *XVI* and 3·83 g (66 mmol) acetamidine in 30 ml methanol, 12 h at room temperature. UV spectrum (λ_{max}, log ε): 291 (3·99), 285 (3·99), 256 (3·89) nm (A_1); 292 (3·89), 248·5 (3·98) nm (B_1). IR spectrum (KBr): 1 675, 2 740, 2 820 (NHCHO), 3 210 (NH), 1 655 (lactam) cm^{-1}.

5-Nitropyrimidines *XIVa* and *XIVd* (Method *B*)

A suspension of 5·1 g (25 mmol) 6-chloro-4-dimethylamino-5-nitropyrimidine (*XIVb*) in 150 ml methanol was stirred at 5—10°C and treated with sodium methoxide solution (added drop by drop) prepared by dissolving 0·6 g (26 mmol) sodium in 50 ml methanol (in the case of compound *XIVd*) or with 6·9 ml (50 mmol) 33% (m/V) aqueous solution of dimethylamine (in the case of *XIVa*). The mixture was stirred at room temperature 5 h, the solvent was distilled off, the residue was mixed with water, and the precipitated solid was collected by filtration (Table I).

5-Amino-4,6-bis(dimethylamino)pyrimidine (*Ij*)

A solution of 2·7 g (12·7 mmol) nitropyrimidine *XIVa* in 30 ml methanol was treated with 30 ml water and 10 ml 5% (m/V) methanolic potassium hydroxide solution, and sodium dithionite was added portionwise with stirring. The reaction course was followed by TLC and by colour reaction of samples of the reaction mixture with Methylene Blue. After disappearance of the colour reaction, the mixture was diluted with water (1 : 3), the product was extracted with ethyl acetate, the extract was dried with Na_2SO_4, and the solvent was evaporated to give 1·7 g beige product (Table I).

5-Amino-4,6-dimethoxypyrimidine (*Ii*)

Compound *Ii* was prepared in analogous way as *Ij* from 3·6 g (19 mmol) 4,6-dimethoxy-5-nitropyrimidine *XIVc* dissolved in a mixture of 150 ml methanol, 75 ml water, and 3·5 g potassium hydroxide by reduction with 8 g sodium dithionite. Yield 1·5 g (50%), m.p. 92—94°C (hexane), ref.[28] gives m.p. 95—97°C for the compound prepared by another way.

5-Amino-4-dimethylamino-6-methoxypyrimidine (*Ik*)

A solution of 4·0 g (20 mmol) nitropyrimidine *XIVd* in 150 ml methanol was treated with 11·3 g (200 mmol) activated iron filings, 114 ml glacial acetic acid was added thereto, and the mixture was refluxed 4 h. Inorganic products were removed by filtration and washed on the filter with 50 ml boiling methanol, and the combined filtrates were evaporated. The evaporation residue was dissolved with ethyl acetate and the solution was washed with 70 ml 1 M-KOH and with water (until neutral), dried with Na_2SO_4, and evaporated to give 3·3 g beige residue (Table I).

5-Amino-4-hydroxypyrimidine (*Im*)

A mixture of 150 ml ethanol and 3·5 ml (0·04 mol) conc. hydrochloric acid was stirred, and 5·6 g (0·04 mol) 5-formylamino derivative *XVa* was added thereto. The mixture was refluxed 2 h, cooled (to about 5°C), the precipitated hydrochloride of amino compound *Im* was collected by filtration (yield 5·4 g, 91%), and recrystallized from methanol. M.p. 213—217°C (decomp.). For $C_4H_6ClN_3O$ (147·6) calculated: 32·56% C, 4·10% H, 28·48% N, 24·03% Cl; found: 32·62% C, 4·17% H, 28·59% N, 23·92% Cl. The hydrochloride (4·9 g, 0·033 mol) was dissolved in 25 ml water, and the respective free base was obtained by addition of one equivalent of 10 M-NaOH (3·3 ml) and cooling at 5°C. Yield 2·94 g (80%), m.p. 213—216°C (ref.[27]).

5-Formylamino-4-hydroxypyrimidine (*XVa*) (Method *C*)

Formamidine acetate (40·8 g, 0·39 mol) and sodium salt *XVI* (71·0 g, 0·39 mol) were added to a solution of 9·0 g (0·39 mol) sodium in 170 ml methanol, and the suspension was stirred at room temperature 15 h. The solvent was distilled off under reduced pressure, the residue was

dissolved in hot water (300 ml), filtered with charcoal, and acidified with dilute hydrochloric acid (pH 6). The precipitated *XVa* was cooled and collected by filtration (21·8 g) and recrystallized (Table I). Method *C* was also applied to preparations of compounds *XVb*—*XVg*; the individual reaction conditions are presented in Table I.

Sodium Salt of Ethyl 2-Formylamino-3-oxopropionate (*XVI*)

A mixture of 71·3 g (0·69 mol) ethyl ester of glycine and 127·6 g (1·72 mol) ethyl formiate was stirred at 15—20°C, and 87·2 g (0·69 mol) sodium methoxide was added thereto within 1 h. The mixture was stirred at room temperature 8 h. The suspension was diluted with 500 ml diethyl ether, the precipitated salt *XVI* was collected by filtration and dried in a dessiccator under reduced pressure. Yield 69·7 g (56%) *XVI*, m.p. 149—155°C. For $C_6H_8NNaO_4$ (181·1) calculated: 12·69% Na; found: 12·35% Na. UV spectrum (λ_{max}, log ε): 267 nm (3·61) (in methanol). IR spectrum (KBr): 1 735 (ester), 1 680, 1 570 (NH—CHO), 1 680 (CHO), 3 230 (NH) cm^{-1}.

4-Methoxycarbonyl-5-methylthio-1,2,3-triazole (*IIa*) (Method *D*)

A solution of 0·69 g (10 mmol) sodium nitrite in 5 ml water was added drop by drop to a solution of 0·86 g (5 mmol) *Ia* in 50 ml 10% hydrochloric acid with stirring at —5 to 0°C. The mixture was stirred at the same temperature 1·5 h and left to attain the room temperature, the product was extracted with 5 × 30 ml chloroform, the extract was dried with Na_2SO_4, and the solvent was evaporated under reduced pressure to give 0·62 g needles (Table II). Method *D* was also applied to the preparations of compounds *IIb*—*IId* (from *Ib*—*Id*), *IIh*, *IIi* (from *If*), and *IIj*—*IIr*.

N-Methyl-4-methoxycarbonyl-5-methylthio-1,2,3-triazole (*IIIa*)

A) A solution of 0·4 g (2·7 mmol) acid *III* in 10 ml methanol was added to 30 ml solution of diazomethane in ether (prepared from 5 g nitrosomethylurea and 100 ml ether), the addition being accompanied by evolution of nitrogen. After 30 min the volatile portion was distilled off under reduced pressure, and the oily residue was mixed with hexane. Yield 0·38 g (74%) *IIIa*, m.p. 129—130°C.

B) A solution of 0·2 g (1·1 mmol) *IIa* in 10 ml ether was added to 30 ml ethereal solution of diazomethane prepared as ad *A*). After 30 min, ether was distilled off under reduced pressure to give 0·2 g (93%) *IIIa*, m.p. 128—129°C, identical with the product obtained ad *A*) according to IR and mass spectra and TLC; the mixed melting point of both the products showed no depression. For $C_6H_9N_3O_2S$ (187·2) calculated: 38·49% C, 4·84% H, 22·44% N; found: 38·64% C, 4·81% H, 22·93% N. IR spectrum: 1 725 (C=O) cm^{-1}. Mass spectrum: the molecular ion *m/e* 187.

5-N-Formylcarbamoyl-4-(4-nitrobenzyl)thio-1,2,3-triazole (*IIe*) (Method *E*)

A solution of 0·33 g (4·7 mmol) sodium nitrite in 3 ml water was added drop by drop to a solution of 0·7 g (2·3 mmol) pyrimidine *Ie* in 30 ml glacial acetic acid with stirring at the temperature decreasing from 12 to 0°C. The mixture was stirred 1·5 h, and the precipitated solid was collected by filtration to give 0·4 g crystalline *IIe* (Table II). Method *E* was also applied to the preparation of compounds *IIf* and *IIg* (from *If* and *Ig*).

1,2,3-Triazole-4-carboxylic Acid (*IIt*)

A solution of 1·1 g (10 mmol) amide *IIr* in 5 ml 10 M-NaOH was refluxed 48 h and acidified to pH 2 with dilute hydrochloric acid (1 : 1) to give 0·85 g (75%) acid *IIt*, m.p. 227—230°C (from water), refs[9,15] give m.p. 230—233 and 220°C, resp.

TABLE II

4,5-Disubstituted 1,2,3-triazoles

Compound	$R^2(R^1)$ R^3	Yield, % (method)	M.p., °C (solvent)	Formula (mol. mass)	Calculated/found		
					% C	% H	% N
IIa[a]	SCH_3	71	115–117	$C_5H_7N_3O_2S$[q]	34·94	4·08	24·26
	$COOCH_3$	(*D*)	(S_3)	(173·3)	34·86	4·11	24·43
IIb[b]	$SCH_2C_6H_5$	89	141–143	$C_{12}H_{13}N_3O_2S$[r]	54·74	4·98	15·96
	$COOCH_3$	(*D*)	(benzene)	(249·3)	54·76	4·78	15·96
IIc[c]	$SCH_2C_6H_4COOC_2H_5$(4-)	97	119–120	$C_{14}H_{15}N_3O_4S$[s]	52·32	4·71	13·08
	$COOCH_3$	(*D*)	(S_4)	(321·4)	52·20	4·79	13·26
IId[d]	$SCH_2C_6H_4CONHC_3H_7$-i(4-)	99	176–179	$C_{15}H_{18}N_4O_3S$	53·87	5·42	16·76
	$COOCH_3$	(*D*)	(S_1)	(334·4)	53·72	5·30	16·90
IIe[e]	$SCH_2C_6H_4NO_2$(4-)	54	227–230	$C_{11}H_9N_5O_4S$[t]	42·99	2·93	22·79
	CONHCHO	(*E*)	(S_1)	(307·4)	42·96	2·75	23·00
IIf[f]	SCH_3	57	232–233	$C_5H_6N_4O_2S$	32·26	3·25	30·10
	CONHCHO	(*E*)	(S_1)	(186·2)	32·50	3·26	30·40
IIg[g]	$SCH_2C_6H_5$	48	204–206	$C_{11}H_{10}N_4O_2S$	50·37	3·84	21·36
	CONHCHO	(*E*)	(S_1)	(262·3)	50·40	3·80	21·17
IIh[h]	(Cl)	52	168–172	$C_4H_6Cl_2N_4S$[v]	22·55	2·84	26·30
	$C(=NH)SCH_3$. HCl	(*D*)[u]	(methanol)	(213·1)	22·27	2·84	26·80
IIi[i]	(Cl)	34	104–106	$C_4H_4ClN_3OS$[w]	27·05	2·27	23·66
	$COSCH_3$	(*D*)	(benzene)	(177·6)	27·00	2·10	24·01
IIj[j]	(Cl)	60	110	$C_{10}H_8ClN_3OS$	47·34	3·18	16·56
	$COSCH_2C_6H_5$	(*D*)[x]	(water)	(253·7)	47·21	2·97	16·64

TABLE II
(*Continued*)

Compound	$R^2(R^1)$ R^3	Yield, % (method)	M.p., °C (solvent)	Formula (mol. mass)	Calculated/found		
					% C	% H	% N
IIk[k]	$SCH_2C_6H_5$	61	210–214	$C_{12}H_{16}ClN_5S$[z]	48·40	5·42	23·52
	$C(=NH)N(CH_3)_2$. HCl	(*D*)[y]	(S_5)	(297·8)	48·42	5·37	23·92
III[l]	OCH_3	43	140–143	$C_5H_8N_4O_2$	38·45	5·16	35·88
	$C(=NH)OCH_3$	(*D*)[aa]	(water)	(156·1)	38·56	5·18	35·99
IIm[m]	$N(CH_3)_2$	9	147–149	$C_8H_{14}N_6O$	45·70	6·71	39·97
	$C(=NCHO)N(CH_3)_2$	(*D*)[bb]	(acetone)	(210·2)	46·01	6·60	39·98
IIn[n]	OCH_3	59	202–203	$C_6H_{12}ClN_5O$	35·04	5·88	34·06
	$C(=NH)N(CH_3)_2$. HCl	(*D*)[cc]	(S_6)	(205·6)	35·01	5·92	34·08
IIo[o]	$N(CH_2)_4CH_2$	24	177–179	$C_8H_{11}N_5$	54·22	6·26	39·52
	CN	(*D*)[dd]	(S_1)	(177·3)	54·11	6·39	39·48
IIp[p]	(Cl)	47	236–238	$C_8H_{13}Cl_2N_5$	38·42	5·24	28·00
	$C=NH)N(CH_2)_4CH_2$. HCl	(*D*)	(S_6)	(250·2)	38·36	5·48	28·24
IIr[ee]	H	61	255–259[ff]	$C_3H_4N_4O$	32·14	3·60	49·99
	$CONH_2$	(*D*)[gg]	(AcOH)	(112·1)	32·94	3·67	50·34

[a] IR spectra (ν in Nujol) and mass spectra (M^+): 3 130 (NH as), 1 724 (C=O) cm^{-1}; *m/e* 173; [b] 3 160 (NH), 1 734 (C=O) cm^{-1}; [c] 3 173 (NH), 1 708, 1 675 (C=O) cm^{-1}; [d] 3 494, 3 090 (NH), 1 726, 1 630 (C=O) cm^{-1}; [e] 3 190 (NH as), 1 725, 1 675 (C=O) cm^{-1}; *m/e* 307; [f] 3 250 (NH), 1 724, 1 676 (C=O) cm^{-1}; [g] 3 250 (NH), 1 722, 1 682 (C=O) cm^{-1}; [h] 2 460 (NH), 1 810, 1 690 (C=N) cm^{-1}; *m/e* 176 (the base); [i] 3 160 (NH as), 1 630 (C=O) cm^{-1}; *m/e* 177; [j] 3 190 (NH as), 1 634 (C=O) cm^{-1}; *m/e* 253; [k] 3 270 (NH), 1 660, 1 635 (C=N) cm^{-1}; *m/e* 261; [l] 3 336 (NH), 3 190 (NH as), 1 635 (C=N) cm^{-1}; *m/e* 156; [m] 3 150 (NH as), 1 647 (C=O) cm^{-1}; *m/e* 210; [n] 3 060 (NH), 1 664, 1 630 (C=N) cm^{-1}; *m/e* 169 (the base); [o] *m/e* 177; [p] *m/e* 213.

TABLE II
(*Continued*)

Further data: [q] calculated 18·52% S, found 18·67% S; [r] calculated 12·18% S, found 12·37% S; [s] calculated 9·99% S, found 10·21% S; [t] calculated 10·44% S, found 10·21% S; [u] from 1·2 g (6·7 mmol) *If* in 45 ml 10% aqueous hydrochloric acid and a solution of 0·83 g (13·4 mmol) sodium nitrite in 6 ml water at −5 to 0°C. After 1 h, the separated *IIh* was collected by filtration (0·75 g), the filtrate was evaporated under reduced pressure, and the evaporation residue was extracted with hot benzene; evaporation of the benzene gave 0·4 g *IIi*. With the aim of preparation of the *IIi* itself, the above-mentioned reaction mixture, obtained by action of sodium nitrite, was left to stand at room temperature until all the *IIh* precipitated redissolved; the solution was evaporated under reduced pressure, the residue was extracted with hot benzene, and the solvent was distilled off to give 0·75 g (62%) *IIi*; [v] calculated 33·28% Cl, 15·04% S; found 33·53% Cl, 15·24% S; [w] calculated 19·96% Cl, 18·05% S; found 19·86% Cl, 17·81% S; [x] from 1·0 g (3·9 mmol) *Ig* in 50 ml 10% aqueous hydrochloric acid and solution of 0·55 g (7·9 mmol) $NaNO_2$ in 5 ml water at −5 to 0°C; after 1 h the starting compound was filtered off and the filtrate was left to crystallize; yield 0·06 g *IIj*; [y] similarly as *IIh* from 2·0 g (7·6 mmol) *Ih* in 75 ml 10% aqueous hydrochloric acid by action of 1·06 g (16·8 mmol) $NaNO_2$; yield 1·4 g *IIk*; [z] calculated 11·90% Cl, 10·76% S; found 11·98% Cl, 10·97% S; [aa] from 0·7 g (4·4 mmol) *Ii* in 45 ml 10% aqueous hydrochloric acid and solution of 0·62 g (8·9 mmol) $NaNO_2$ in 4 ml water at −5 to 0°C; after 1·5 h the mixture was neutralized with 2M-NaOH, the product was extracted with ethyl acetate, the solution was dried with Na_2SO_4, and the solvent was distilled off to give 0·3 g *IIl*; [bb] from 1·0 g (5·5 mmol) *Ij* in 10% aqueous hydrochloric acid by action of 0·76 g (11 mmol) $NaNO_2$ in water in similar way as *IIh*; [cc] from 1·4 g (8·3 mmol) *Ik* in 60 ml 10% aqueous hydrochloric acid and solution of 1·0 g (14·5 mmol) $NaNO_2$ in 5 ml water; after 1·5 h water was distilled off under reduced pressure, the residue was extracted with a mixture of methanol and acetone (1 : 2), the inorganic portions were filtered off, and the filtrate was precipitated with ether to give 1·0 g *IIn*; [dd] from 2·0 g (9·4 mmol) *Il* in 70 ml 10% aqueous hydrochloric acid and a solution of 1·28 g (18·5 mmol) $NaNO_2$ in 6 ml water at −5 to 0°C; after 15 min at 0°C the solution separated 0·21 g *IIo*; the precipitate was filtered off, and *IIp* crystallized from the filtrate at room temperature (yield 1·1 g); [ee] UV spectrum (λ_{max}, log ε): 233 (3·98) nm (B); 222 (3·95) nm (water); IR spectrum (KBr): 3 200 (NH), 1 665, 1 610, 1 420 (amide) cm^{-1}; ^1H NMR spectrum (hexadeuteriodimethyl sulphoxide): δ 13·50 (a flat band, NH + H_2O), 8·25 (s, 1H, arom. H), 7·80 (bs, 1H, NH_2), 7·40 (bs, 1H, NH_2); mass spectrum: the molecular ion *m/e* 112; [ff] ref.[9] gives m.p.261−263°C, ref.[14] 256−257°C, ref. [15] 253−254°C; [gg] from 5·5 g (50 mmol) *Im* in 12·7 ml (0·15 mol) concentrated hydrochloric acid and a solution of 3·6 g (52·5 mmol) $NaNO_2$ in 5 ml water at 0 to 5°C; the mixture was stirred at the same temperature 4 h and then it was left to stand at room temperature overnight; the raw product (mass spectrum: molecular ion *m/e* 112 corresponding to *IIr* and *m/e* 140 corresponding to *IIs*) was recrystallized from boiling water to give 3·4 g *IIr*.

TABLE III

$N_{(7)}$-Oxides of 2-amino-4-(4-subst. benzyl)thiopyrimido[5,4-*d*]-1,2,3-triazines

Compound R	Yield, % (method)	M.p., °C (solvent)	Formula (mol. mass)	Calculated/found			
				% C	% H	% N	% S
XIIIa[a]	86	229–231	$C_{12}H_{10}N_6OS$	50·34	3·52	29·36	11·19
C_6H_5	(*F*)	(DMF)	(286·3)	50·49	3·58	29·30	11·28
XIIIb[b]	79 63	215	$C_{12}H_9N_7O_3S$	43·50	2·74	29·60	9·68
$C_6H_4NO_2$(4-)	(*F*) (*G*)	(S_2)	(331·4)	43·47	2·72	29·91	—
XIIIc[c]	89	221–222	$C_{15}H_{14}N_6O_3S$	50·27	3·94	23·45	8·94
$C_6H_4COOC_2H_5$(4-)	(*F*)	(S_2)	(358·4)	50·29	3·89	23·88	8·89
XIIId[d]	89	241–243	$C_{16}H_{17}N_7O_2S$	51·74	4·62	26·40	8·63
$C_6H_4CONHCH(CH_3)_2$(4-)	(*F*)	(S_2)	(371·4)	51·77	4·59	26·70	8·67

[a] IR spectra (ν in Nujol) and mass spectra (M^+): 3 364, 3 320, 3 150, 3 050 (NH), 1 648 (C=N) cm^{-1}; [b] 3 385, 3 342, 3 180, 3 035 (NH), 1 664 (C=N), 1 600 cm^{-1}; *m/e* 331; [c] 3 375, 3 350, 3 150, 3 040 (NH), 1 740 (C=O), 1 642 (C=N) cm^{-1}; [d] 3 368, 3 300, 3 164 (NH), 1 655 (amide), 1 635 cm^{-1}.

2-Diazo-2-cyanoacetamide (*XIa*)

A solution of 0·87 g (12·6 mmol) sodium nitrite in 6 ml water was added drop by drop to a solution of 1·0 g (6·8 mmol) 4-oxo-5-amino-6-chloropyrimidine (*In*) in 55 ml 10% aqueous hydrochloric acid with stirring at −5 to 0°C. The mixture was stirred at the same temperature 1·5 h and left to attain the room temperature. The product was extracted with ethyl acetate, the extract was dried with Na_2SO_4, and the solvent was evaporated to give 0·8 g raw product which was purified by column chromatography (silica gel, chloroform–methanol 10 : 1). Yield 0·3 g (40%) *XIa*, yellow needles unstable in light, m.p. 115–120°C with decomposition (from ethanol), ref.[30] gives identical melting point. IR spectrum: 3 420, 3 330, 3 220 (NH), 2 019 (C≡N), 2 140 (N=N), 1 674 (amide), 1 614 (amide) cm^{-1}; chloroform: 3 520, 3 410 (NH), 2 220 (CN), 2 130 (N=N), 1 690, 1 590 (amide) cm^{-1}. Mass spectrum: the molecular ion *m/e* 110.

2-Diazo-2-cyano-N-methylacetamide (*XIb*)

Compound *XIb* was prepared in analogous way from 1·0 g (6·2 mmol) 3-methyl-4-oxo-5-amino-6-chloropyrimidine (*X*), 55 ml 10% hydrochloric acid, and solution of 0·86 g (12·4 mmol) sodium nitrite. Yield 0·64 g (82%) *XIb*, yellow-green needles, m.p. 111–114°C with decomposition (benzene). For $C_4H_4N_4O$ (124·1) calculated: 38·71% C, 3·24% H, 45·15% N; found: 38·73% C, 3·33% H, 45·26% N. IR spectrum: 3 330 (NH), 2 208 (C≡N), 2 134 (N=N), 1 658, 1 530 (amide) cm^{-1}. Mass spectrum: the molecular ion *m/e* 124.

$N_{(7)}$-Oxide of 2-Amino-4-(4-nitrobenzyl)thiopyrimido[5,4-*d*]-1,2,3-triazine (*XIIIb*)

Method F: A solution of 0·48 g (6·8 mmol) sodium nitrite in 3 ml water was added drop by drop to a suspension of 1·0 g (3·4 mmol) *XIIb* in 60 ml 10% aqueous hydrochloric acid with stirring and cooling at −5°C. After 1 h the mixture was left to attain the room temperature, and the product was collected by filtration. Yield 0·9 g (79%) yellow *XIIIb* (Table III). Method *F* was also applied to the preparations of compounds *XIIIa*, *XIIIc*, *XIIId* (from *XIIa*, *XIIc*, *XIId*).

Method G: A solution of 0·24 g (3·4 mmol) sodium nitrite in 3 ml water was added drop by drop to a solution of 0·5 g (1·7 mmol) *XIIb* in 25 ml glacial acetic acid with stirring at 12°C. Then the mixture was cooled to 0°C, and the precipitated solid was collected by filtration after 1 h. Yield 0·2 g *XIIIb*, and further 0·16 g product was obtained by dilution of the filtrate with water. Overall yield 0·36 g (63%), m.p. 213°C. IR spectrum identical with that of the product of the above Method *F*.

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Translated by J. Panchartek.

Note added in prof. In formula *X* carbon should be replaced by nitrogen in position 3.