NUCLEIC ACID COMPONENTS AND THEIR ANALOGUES. CLVIII.*

PREPARATION OF SOME SUBSTITUTED 2-AMINO- AND 2-MERCAPTOPYRIMIDINES FROM TRIMETHINIUM SALTS**

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Received August 11th, 1972

Condensation of trimethinium salts *I* bearing hydrogen, an alkyl or the dimethylamino group at position 1 and hydrogen, an alkyl, a halo atom, the cyano group, the ethoxycarbonyl group or the benzyloxy group at position 2 with guanidine or thiourea in the presence of sodium methoxide afforded the corresponding substituted 2-amino- (*II*) and 2-mercaptopyrimidines (*III*). 2-Benzyloxytrimethinium perchlorate (*Ig*) was prepared from benzyloxyacetaldehyde diethylacetal by reaction with dimethylchloromethyleneammonium chloride (*VI*), followed by hydrolysis, and reaction with dimethylamine. An analogous process was used in the preparation of 1-dimethylamino-2-ethoxycarbonyltrimethinium perchlorate (*Im*) starting from ethyl N,N-dimethylmalonomonoamide, and of 1-dimethylamino-2-cyanotrimethinium perchlorate (*I*) from N,N-dimethylcyanoacetamide. 5-Methyl-2-pyrimidinone (*IXb*) was obtained from compound *IIIb* by reaction with chloroacetic acid. Reaction of 2-aminopyrimidines *IIg* and *IIi* with nitrous acid afforded the 5-alkoxy-2-pyrimidinones *IXb* and *IXc*, resp.

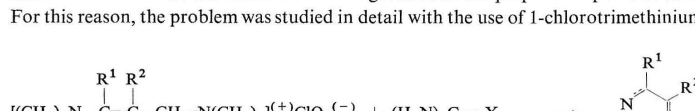
In connection with investigations on biochemical properties of simple pyrimidine derivatives and with a special respect to the recently[1] reported conversion of 2-mercaptopyrimidine and related compounds into L-cysteine derivatives, it was of interest to prepare some substituted derivatives of 2-aminopyrimidine (*II*) and 2-mercaptopyrimidine (*III*). For this purpose, the reaction of substituted trimethinium salts with guanidine or thiourea in alkali was used; this method was developed[2] in our Laboratory and then successfully applied by other authors[3]. In the present paper we wish to describe the preparation of the otherwise less accessible derivatives *II* and *III* by the method mentioned with the use of simple aliphatic compounds as the starting material.

The reaction Scheme 1 shows the principle of the condensation mentioned which is accomplished by heating simply the reaction components (the salts *I* are used as perchlorates) in methanol in the presence of a small excess of sodium methoxide.

* Part CLVII: This Journal *38*, 1173 (1973).

** Part XXVI of the Series: Synthetic Reactions of Dimethylformamide. Part XXV: This Journal *38*, 1168 (1973).

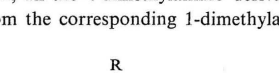
The reaction has a uniform course and affords satisfactory preparative yields of the cyclic products. While the 2-halo substituted trimethinium salts *Id,e* afford readily the appropriate 5-halo derivatives *IIId*, *e*, the situation is more complex with 1-chloro substituted trimethinium salts, since either hydrogen chloride or dimethylamine may be split off by the cyclisation of these salts. The 1-chlorotrimethinium salts are obtained as primary products by formylation of N,N-dimethylamides of substituted acetic acids[4] and their use would be advantageous from the preparative point of view. For this reason, the problem was studied in detail with the use of 1-chlorotrimethinium



In formulae *I*—*III*, *a*, $R^1 = H$; $R^2 = H$ *g*, $R^1 = H$; $R^2 = OCH_2C_6H_5$
b, $R^1 = H$; $R^2 = CH_3$ *h*, $R^1 = H$; $R^2 = OCH_3$
c, $R^1 = H$; $R^2 = C_2H_5$ *i*, $R^1 = H$; $R^2 = OC_2H_5$
d, $R^1 = H$; $R^2 = Cl$ *j*, $R^1 = CH_3$; $R^2 = H$
e, $R^1 = H$; $R^2 = Br$ *k*, $R^1 = N(CH_3)_2$; $R^2 = H$
f, $R^1 = H$; $R^2 = CH$ *l*, $R^1 = N(CH_3)_2$; $R^2 = CN$
m, $R^1 = N(CH_3)_2$; $R^2 = COOC_2H_5$

SCHEME 1

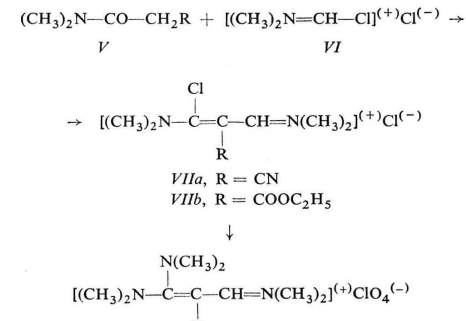
perchlorate[4] *IV* as the model compound. Thus, an exclusive formation of the 2-thiocytosine derivative *IIIk* has been observed in the reaction of compound *IV* with thiourea. We did not find any 4-chloropyrimidine or 4-methoxypyrimidine derivative (the latter compound would be formed by elimination of dimethylamine from the intermediary 1-methoxytrimethinium salt). The cyclisation is therefore accomplished by the preferential elimination of hydrogen chloride (or methanol) under involvement of the substituent at position 1 of the original salt *IV*. The yield of compound *IIIk* from the salt *IV* is however lower than with the use of the 1-dimethylamino salt *Ik*. For this reason, all the 4-dimethylamino derivatives *IIk*—*m* and *IIIk*—*m* have been prepared from the corresponding 1-dimethylaminotrimethinium salts *Ik*—*Im*.



IVa, R = Cl
IVb, R = OCH_3

The parent compound of this series, 1-dimethylaminotrimethinium perchlorate (*Ik*) has been prepared earlier on formylation of N,N-dimethylacetamide with dimethylchloromethyleneammonium chloride (*VI*) and the subsequent treatment of the

resulting 1-chloromethinium salt with dimethylamine[5]. The 1-dimethylaminotrimethinium salts *Il* and *Im* have been prepared by an analogous sequence of reactions from N,N-dimethylmalonomonoamide ethyl ester and N,N-dimethylcyanoacetamide, resp. (Scheme 2); the corresponding 1-chlorotrimethinium salts *VII* have not been isolated but converted directly into the salts *Il* and *Im* by reaction with dimethylamine *in situ*. The 2-benzyloxytrimethinium salt *Ig* is a representative of a group of derivatives that serve as starting compounds in the preparation of 5-alkoxy substituted pyrimidine derivatives. The benzyl group has been used for that reason that its removal might be relatively easy and could lead to 5-hydroxypyrimidine derivatives which are otherwise accessible only with difficulty by multistep syntheses and in low yields. Compound *Ig* has been prepared by formylation of benzyloxyacetaldehyde diethylacetal with the agent *VI* and the subsequent treatment of the intermediary salt *VIII* with aqueous dimethylamine (the formylation of alkoxyacetaldehyde dialkylacetals has been reported in literature[6] without isolation of the primary intermediates of the type *I* and *VIII*). The 2-methoxy- (*Ih*) and 2-ethoxytrimethinium salt (*Ii*) have been prepared by a procedure reported elsewhere[7].



SCHEME 2

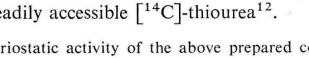
The 2-amino (*II*) and 2-mercapto (*III*) pyrimidine derivatives may be readily converted into the corresponding 2-pyrimidinone derivatives. The latter compounds are of interest as starting compounds for the preparation of nucleosides with a potential biological activity[8]. This conversion has been now accomplished also with the types *II* and *III* by known procedures[9], *i.e.* on treatment of 2-amino-5-alkoxypyrimidines *IIg* and *IIi* with nitrous acid under the formation of 5-alkoxy-2-pyrimidinones *IXb* and *IXc*, or, by reaction of 2-mercapto-5-methylpyrimidine (*IIIb*) with chloro-

TABLE I

Preparation of Pyrimidine Derivatives *II* and *III*

Compound[a]	Method (mmol) yield, %	M.p., °C solvent	Formula (mol. wt.)	Calculated/Found % C	% H	% N	% S
IIf[2]	*B* (8)	250	$C_5H_4N_4$	50·00	3·35	46·65	—
	73	(50% ethanol)	(120·1)	49·73	3·42	46·70	—
IIg[b]	*B* (15)	86—87	$C_{11}H_{11}N_3O$	65·66	5·51	20·89	—
	75	(water)	(201·2)	65·55	5·56	21·18	—
IIh[7]	*B* (18)	70—73	$C_5H_7N_3O$	48·00	5·64	33·59	—
	74	(cyclohexane)	(125·1)	48·18	5·82	33·79	—
IIi[7]	*B* (25)	108—109	$C_6H_9N_3O$	51·77	6·51	30·19	—
	80	(cyclohexane)	(139·2)	51·58	6·49	30·43	—
IIl[b]	*B* (10)	161—162	$C_7H_9N_5$	51·51	5·55	42·94	—
	65	(water)	(163·2)	50·64	5·46	42·57	—
IIm[b]	*B* (15)	106—107	$C_9H_{14}N_4O_2$	51·42	6·71	26·65	—
	83	(water)	(210·2)	50·89	6·70	27·01	—
IIIa[17]	*B* (10)	222—223	$C_4H_4N_2S$	42·81	3·59	24·97	28·58
	60	(75% ethanol)	(112·2)	43·00	3·46	25·31	28·42
IIIb[18]	*A* (50)	217—218	$C_5H_6N_2S$	47·58	4·39	22·20	25·32
	80	(10% ethanol)	(126·2)	47·73	4·85	22·71	25·33
IIIc[e]	*B* (5)	201—202	$C_6H_8N_2S$	51·39	5·74	19·98	22·86
	57	(ethanol)	(140·2)	50·97	5·78	19·41	22·77
IIId[20]	*A* (10)	221—222	$C_4H_3N_2ClS$	32·77	2·06	19·11	21·87
	37		(146·6)[c]	33·00	2·10	19·19	21·92
	B (10)						
	35						
IIIe[2]	*A* (10)	214—215	$C_4H_3N_2BrS$	25·13	1·58	14·66	16·77
	27		(191·1)[d]	25·77	1·66	14·92	17·24
	B (10)						
	28						
IIIf[2]	*B* (8)	175—176[c]	$C_5H_3N_3S$	43·77	2·20	30·63	23·37
	30	(ethanol)	(137·2)	43·32	2·41	30·95	23·72
IIIg[b]	*B* (5)	180—192	$C_{11}H_{10}N_2OS$	60·51	4·61	12·83	14·89
	64	(ethanol)	(218·3)	60·67	4·76	13·10	14·59
IIIh[7]	*B* (2)	174—176	$C_5H_6N_2OS$	42·23	4·24	19·70	22·54
	71	(water)	(142·2)	42·69	4·01	19·69	22·83
IIIi[7]	*B* (5)	203—205	$C_6H_8N_2OS$	46·13	5·16	17·94	20·52
	96	(90% ethanol)	(156·2)	46·25	5·21	18·22	20·23
IIIj[18]	*B* (10)	207—208	$C_5H_6N_2S$	47·58	4·79	22·20	25·32
	63	(ethanol)	(126·2)	47·99	4·77	22·37	24·78
IIIk[6]	*A* (10)	does not melt to 250	$C_6H_9N_3S$	46·43	5·84	27·08	20·62
	57	(ethanol)	(155·2)	46·27	5·89	26·74	21·01
IIIl[b]	*B* (10)	230—231	$C_7H_8N_4S$	46·65	4·47	31·09	17·79
	70	(water)	(180·2)	46·65	4·55	30·87	17·62
IIIm[b]	*B* (10)	186—188	$C_9H_{13}N_3O_2S$	47·55	5·76	18·49	14·10
	73	(ethanol)	(227·3)	47·38	5·70	18·95	14·18

acetic acid and the subsequent acidic hydrolysis of the 2-carboxymethylmercapto derivative *X* under the formation of 5-methyl-2-pyrimidinone (*IXa*). It is of interest that compound *X* is unusually stable in contrast to the unsubstituted derivative; its hydrolysis by refluxing in 1M-HCl requires several hours. The cleavage of 5-benzyloxy-2-pyrimidinone (*IXb*) with concentrated hydrobromic acid afforded a low yield of 2,5-dihydroxypyrimidine[10] (*XI*). The alkaline hydrolysis of esters of pyrimidine-5-carboxylic acids *IIk* and *IIIk* is relatively difficult and affords the acids *XII*. The methyl ester *XIII* is obtained on esterification of the acid *XII* with diazomethane. The attempted ammonolysis of the ester *IIm* failed under usual conditions, *i.e.*, with methanolic ammonia at 100°C. The corresponding amide *XIV* was therefore prepared by hydration of the nitrile[11] *IIl*.



VIII

The present method of preparing substituted pyrimidine derivatives makes readily available numerous compounds hitherto accessible only with difficulty. There are also additional possibilities of synthetic applications. The method is simple and in view of high yields may be also used in the preparation of labelled compounds, *e.g.*, from the readily accessible [^{14}C]-thiourea[12].

The bacteriostatic activity of the above prepared compounds on *E. coli B* was assayed in a synthetic medium with glucose at concentrations from 1 μg to 1 000 μg of the substance per 1 ml of the medium. From all the compounds investigated, only the derivatives *IIk* and *IIIk* exhibited a relatively high bacteriostatic activity (90—95% inhibition) at the concentration of 100 μg/ml in a statical assay. Both these derivatives carry the dimethylamino group at position 4 and the ethoxycarbonyl group at position 5. The substituent at position 2 does not exert any considerable influence on the activity. Hydrolysis of the ester function (*XIIa,b*), its conversion to the amide (*XIV*) or nitrile (*III*) as well as its removal (*IIIk*) results in loss of activity.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block) and are uncorrected. Unless stated otherwise, the solutions were taken down on a rotatory evaporator at 40°C/15 Torr. The substances were dried at 0·1 Torr over P_2O_5.

Preparation of Substituted 2-Aminopyrimidines (*II*) and 2-Mercaptopyrimidines (*III*)

Method A. A suspension of the trimethinium salt *I* (50 mmol) and thiourea (5 g; 66 mmol) in ethanol (100 ml) was treated dropwise under reflux in the course of one hour with 1M methanolic

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[a] Starting compound *I*, reference; [b] described in the present paper; [c] calculated: 24·19% Cl, found: 24·08% Cl; sublimes at 110°C/0·1 Torr; [d] calculated: 41·84% Br, found: 41·24% Br; sublimes at 140°C/0·01 Torr; [e] prepared by the procedure described[2] for the corresponding isopropyl derivative[19]. *Explanations to Table I.*

sodium methoxide (120 ml), the reaction mixture refluxed for 2 hours, neutralised with acetic acid, and evaporated under diminished pressure. The residue was diluted with water (200 ml), the solid collected with suction, washed with water, and the substituted *III* recrystallised from a suitable solvent (Table I).

Method B (*cf.*[3]). A suspension of the trimethinium salt *I* (10 mmol) and guanidine hydrochloride (1,2 g; 12 mmol) or thiourea (0·91 g; 12 mmol) in methanol (25 ml) was treated with 1M methanolic sodium methoxide (22 ml), the mixture kept at room temperature for 30 min, refluxed for 2 h, neutralised with acetic acid, evaporated under diminished pressure, the residue diluted with water (50 ml), the solid collected with suction, and recrystallised from a suitable solvent. For the yields of compounds thus prepared, melting points, and analytical data see Table I.

2-Benzyloxytrimethinium Perchlorate (*Ig*)

A solution of 0·9 mol dimethylchloromethyleneammonium chloride[13] (*VI*) in chloroform (800 ml) was treated dropwise under stirring and ice-cooling over 30 min with benzyloxyacetaldehyde diethylacetal[14] (68·5 g; 0·3 mol). The mixture was refluxed for 3 h, cooled down, poured onto ice (250 g), shaken, the chloroform layer washed with ice-cold water (50 ml), and the combined aqueous layers added to dimethylamine hydrochloride (100 g). Aqueous 20% NaOH was then added dropwise under stirring and ice-cooling until the pH value was 8·5. The resulting mixture was stirred at room temperature for one hour under occasional additions of the above aqueous sodium hydroxide to keep the pH value at 8—8·5. Sodium perchlorate (1 mol) in water (200 ml) was then added, the mixture cooled down, the solid collected with suction, triturated with ice-cold water, washed successively with ethanol and ether, and recrystallised from ethanol. Yield, 44·3 g (44·3%) of compound *Ig*, m.p. 175—176°C. For $C_{14}H_{21}ClN_2O_5$ (332·8) calculated: 50·52% C, 6·36% H, 10·65% Cl, 8·42% N; found: 50·83% C, 6·3% H, 10·74% Cl, 8·57% N.

1-Dimethylamino-2-cyanotrimethinium Perchlorate (*Il*)

A solution of N,N-dimethylcyanoacetamide[15] (*Va*; 11·2 g; 0·1 mol) in chloroform (50 ml) was added dropwise under ice-cooling and stirring to a 2M solution of the agent *VI* (125 ml) (*cf.*[13]). The mixture was kept at room temperature overnight and then extracted with ice-cold water (150 ml). Dimethylamine hydrochloride (0·25 mol) was then added to the aqueous extract and the mixture treated dropwise under stirring and ice-cooling with 20% aqueous sodium hydroxide until the pH value was 8·5. The resulting mixture was stirred at room temperature for 2 h, treated with a solution of sodium perchlorate (0·25 mol) in water (50 ml), the whole stirred under ice-cooling for 30 min, the solid collected with suction, washed successively with ice-cold water, ethanol, and ether, and recrystallised from ethanol. Yield 10·2 g (35%) of compound *Il*, m.p. 145—146°C. For $C_{10}H_{19}ClN_4O_4$ (294·8) calculated: 40·74% C, 6·49% H, 12·02% Cl, 19·02% N; found: 40·52% C, 6·87% H, 12·18% Cl, 19·19% N.

1-Dimethylamino-2-ethoxycarbonyltrimethinium Perchlorate (*Im*)

A solution of 22·5 g (0·14 mol) of ethyl N,N-dimethylmalonomonoamide (*Vb*; b.p. 143—145°C at 12 Torr; *cf.*[16]) in chloroform (50 ml) was added dropwise under ice-cooling and stirring to a solution of the agent *VI* (0·35 mol) in chloroform[13] (220 ml). The mixture was kept at room temperature for 48 h, decomposed with ice (100 g), and the chloroform layer washed with water (25 ml). The aqueous layers were combined, treated with perchloric acid (14 ml), cooled down with ice, and treated under stirring with 25% aqueous dimethylamine (70 ml) and then with saturated aqueous sodium carbonate until the pH value was 7·0—7·5. After 30 min the solid

was collected with suction, washed with a little water, and recrystallised from ethanol (300 ml). Yield, 19·5 g (40·0%) of compound *Im*, m.p. 145—146°C. For $C_{12}H_{24}ClN_3O_6$ (341·8) calculated: 42·16% C, 7·08% H, 10·37% Cl, 12·2% N; found: 42·54% C, 7·57% H, 10·36% Cl, 12·17% N.

5-Benzyloxy-2-pyrimidinone (*IXb*)

A solution of 2-amino-5-benzyloxypyrimidine (*IIg*; 18·1 g; 90 mmol) in 50% aqueous dioxane (500 ml) was treated with a saturated solution of sodium nitrite (20 g) and then dropwise, under stirring and ice-cooling, with 5M-HCl until the pH value was 3. The resulting mixture was kept at 0°C for 2 hours, neutralised under cooling with 10% aqueous sodium hydroxide, concentrated at 30°C/15 Torr to the volume of about 250 ml, the solid collected with suction, washed with water, and dried under diminished pressure. The mother liquor was diluted with water (200 ml), the solid collected with suction, washed with water, and dried as above. The crops of the crude product were combined and recrystallised from ethanol. Yield, 10·0 g (50%) of compound *IXb*, m.p. 196—197°C; additional 3·0 g were obtained by concentration of the mother liquor to a half of the original volume (overall yield, 65%). For $C_{11}H_{10}N_2O_2$ (202·2) calculated: 65·33% C, 4·98% H, 13·85% N; found: 65·00% C, 5·10% H, 13·71% N.

5-Ethoxy-2-pyrimidinone (*IXc*)

A solution of compound *IIi* (1·0 g; 7·2 mmol) in 50% aqueous dioxane (50 ml) was treated with sodium nitrite (1·4 g; 20 mmol) and the mixture was adjusted to pH value 3·5—4·0 by the addition of conc. HCl at 0°C. The whole mixture was stirred at 0°C for 2 h, neutralised under cooling with 1M-NaOH, and evaporated under diminished pressure. The residue was dissolved in water (10 ml) and the solution applied to a column (100 ml) of Dowex 50 X 8 (H^+) ion exchange resin. The column was eluted with water to the loss of conductivity and then with 2·5% aqueous ammonia. The ultraviolet-absorbing fractions of the ammonia eluate containing the chromatographically homogeneous compound *IXc* as shown by thin-layer chromatography on Silufol UV_{235} ready-for-use silica gel plates (Kavalier Glassworks, Czechoslovakia) in 9 : 1 chloroform–ethanol (*IXc*, R_F 0·25; *IIi*, R_F 0·58). The eluate was evaporated and the residue chromatographed on a 40 × 16 × 0·3 cm plate of loose indicator-containing silica gel in 9 : 1 chloroform–ethanol. The band of the product was eluted with methanol, the eluate evaporated, and the residue crystallised from cyclohexane. Yield, 0·42 g (41·5%) of compound *IXc*, m.p. 108—109°C. For $C_6H_8N_2O_2$ (140·1) calculated: 51·47% C, 5·75% H, 20·00% N; found: 51·58% C, 5·49% H, 19·83% N.

2,5-Dihydroxypyrimidine (*XI*)

A mixture of compound *IXb* (4·05 g; 20 mmol) and 35% aqueous HBr (40 ml) was rapidly heated to the boiling point, kept refluxing for 2 min, cooled down with ice, and washed with two 20 ml portions of ether. The aqueous phase was cooled with ice for 1 h, the crystalline hydrobromide collected with suction and transferred into 100 ml of saturated aqueous sodium hydrogen carbonate to deposit the free *XI* which was collected with suction, washed with water, and dried under diminished pressure. Yield, 0·56 g (25%) of compound *XI* which decomposes above 240°C; we could not repeat the yield of 74% reported in the literature[10]. The product is chromatographically homogeneous on paper Whatman No 1 in 7 : 1 : 2 2-propanol–concentrated aqueous ammonia–water (the fluorescent spot, R_F 0·40; uracil, R_F 0·50). The mother liquor remaining after the hydrobromide of compound *XI* contains only a little additional product.

2-Carboxymethylmercapto-5-methylpyrimidine (*X*)

A mixture of 2-mercapto-5-methylpyrimidine (*IIIb*; 1·26 g; 10 mmol) and chloroacetic acid (1·05 g; 11 mmol) in water (5 ml) was refluxed for 2 h, evaporated under diminished pressure, the residue triturated with ether (50 ml), the solid collected with suction, washed with ether (100 ml), and recrystallised from ethanol. Yield, 1·55 g (84%) of compound *X*, m.p. 153—154°C. For $C_7H_8N_2O_2S$ (184·2) calculated: 45·64% C, 4·37% H, 15·21% N; found: 45·85% C, 4·39% H, 15·47% N.

5-Methyl-2-pyrimidinone (*IXa*)

Method A. A solution of compound *X* (0·5 g; 5 mmol) in 2·5M-HCl (5 ml) was refluxed for 5 h, evaporated under diminished pressure, and the residue codistilled with water (25 ml). The final residue was dissolved in water (10 ml), the solution adjusted with concentrated aqueous ammonia to pH 6·5—7·0, and cooled down with ice. The solid was collected with suction, washed with ice-cold water, and recrystallised from water. Yield, 0·44 g (80%), m.p. 217—218°C. For $C_5H_6N_2O$ (110·1) calculated: 54·59% C, 5·50% H, 25·47% N; found: 54·85% C, 5·67% H, 24·92% N.

Method B. A mixture of compound *IIIb* (12·6 g; 0·1 mol) and chloroacetic acid (10·5 g; 0·11 mol) in water (75 ml) was refluxed for 2 hours, treated with concd. HCl (25 ml), and refluxed for additional 5 h. After cooling, the mixture was evaporated under diminished pressure and processed as in the preceding paragraph. Yield, 7·0 g (63·7%), m.p. 217—218°C (water).

2-Amino-4-dimethylaminopyrimidine-5-carboxylic Acid (*XIIa*)

A solution containing compound *IIm* (1·5 g; 7·1 mmol), methanol (10 ml), and 10% aqueous lithium hydroxide was refluxed for one hour, *i.e.*, until the hydrolysis was finished as shown by chromatography on paper Whatman No 1 in 7 : 1 : 2 2-propanol–concentrated aqueous ammonia–water (*IIm*, R_F 0·77; *XIIa*, R_F 0·40). The reaction mixture was applied to a column (100 ml) of pyridinium Dowex 50 X 8 ion exchange resin and the column eluted with 10% aqueous pyridine (500 ml). The eluate was evaporated to dryness under diminished pressure and the residue crystallised from 90% aqueous ethanol. Yield, 1·20 g (92%) of compound *XIIa* which does not melt up to 250°C. For $C_7H_{10}N_4O_2$ (182·2) calculated: 46·14% C, 5·53% H, 30·75% N; found: 46·61% C, 5·81% H, 30·46% N.

4-Dimethylamino-2-mercaptopyrimidine-5-carboxylic Acid (*XIIb*)

The reaction of compound *IIIm* (0·5 g; 2·2 mmol) with aqueous-methanolic lithium hydroxide was performed analogously to compound *XIIa* (paper chromatography: *IIIm*, R_F 0·78; *XIIh*, R_F 0·45). After neutralisation with acetic acid and concentration the product does not crystallise. The mixture was therefore evaporated under diminished pressure, the residue dissolved in water (20 ml), and the solution applied to a column (100 ml) of pyridinium Dowex 50 ion exchange resin. The column was eluted with 10% aqueous pyridine (250 ml), the eluate evaporated under diminished pressure, and the residue coevaporated with four 30 ml portions of water and three 30 ml portions of ethanol. The final residue was dissolved in ethanol (5 ml) and the solution added dropwise into 100 ml of ether. The precipitate was collected by centrifugation, washed with ether, and dried under diminished pressure. Yield, 0·3 g (69%) of compound *XIIb*. For $C_7H_9N_3SO_2$ (199·2) calculated: 42·20% C, 4·55% H, 21·10% N, 16·09% S; found: 42·15% C, 4·53% H, 20·70% N, 16·33% S.

Methyl 2-Amino-4-dimethylaminopyrimidine-5-carboxylate (*XIII*)

A suspension of compound *XIIa* (0·50 g; 2·75 mmol) in 50% aqueous methanol (20 ml) was treated dropwise with ethereal diazomethane until the yellow colour was persistent. The solution was then stirred for additional 15 min, evaporated under diminished pressure, and the residue chromatographed on two 40 × 16 × 0·3 cm loose layers of fluorescent-indicator-containing silica gel (Service Laboratories of our Institute) in 85 : 15 chloroform–ethanol. The bands of the product were eluted with methanol (300 ml), the eluate evaporated under diminished pressure, and the residue crystallised from water (4 ml). Yield, 0·33 g (61·3%) of compound *XIII*, m.p. 136–137°C. For $C_8H_{12}N_2O_2$ (196·2) calculated: 48·97% C, 6·16% H, 28·56% N; found: 48·85% C, 6·22% H, 28·04% N.

2-Amino-4-dimethylaminopyrimidine-5-carboxamide (*XIV*)

A mixture of the nitrile *III* (326 mg; 2 mmol) and 90% sulfuric acid (1·2 ml) was heated on a steam bath for 2 h, cooled down, and decomposed with ice. Excess saturated aqueous potassium carbonate was then added and the product extracted with 1 : 1 benzene–ethanol. The extract was evaporated and the residue crystallised from water. Yield, 318 mg (88%) of compound *XIV*, m.p. 246–248°C. For $C_7H_{11}N_5O$ (181·2) calculated: 46·40% C, 6·12% H, 38·65% N; found: 46·55% C, 6·25% H, 38·39% N.

1-Chloro-1,3-bis-dimethylaminotrimethinium Perchlorate (*IVa*)

A solution of 0·5 mol of the formylating agent[13] *VI* in chloroform (350 ml) was treated dropwise under stirring and ice-cooling with N,N-dimethylacetamide (17·4 g; 0·2 mol). The mixture was kept at room temperature overnight, shaken with crushed ice (150 g), and the chloroform layer extracted with water (25 ml). The aqueous layers were combined, cooled down with ice, treated with concentrated perchloric acid (20 ml), and the mixture kept at −10°C for one hour. The product *IVa* was collected with suction, washed successively with ice-cold water (50 ml) and ethanol (200 ml), and recrystallised from ethanol. Yield, 27·0 g (54%) of compound *IVa*, m.p. 113–115°C (reported[4], m.p. 114–115°C).

Reaction with thiourea. A suspension of the salt *IVa* (2·6 g; 10 mmol) in methanol (40 ml) was treated under stirring with 1M methanolic sodium methoxide (10 ml). A clear solution was formed, neutral to a moistened pH paper, and no dimethylamine escaped from the reaction mixture. The solution was kept at room temperature for 1 hour and then thiourea (1·0 g; 13 mmol) and 1M methanolic sodium methoxide (20 ml) were added. The resulting mixture was refluxed for 3 h, neutralised with acetic acid, evaporated to dryness under diminished pressure, and the residue coevaporated with ethanol. The final residue was refluxed in ethanol (80 ml) for 10 min, the insoluble portion filtered off, the filtrate concentrated under diminished pressure to a half of the original volume, and the crystals collected with suction. The mother liquor was chromatographed on a 40 × 16 × 0·3 cm loose layer of fluorescent-indicator-containing silica gel (produced by Service Laboratories of our Institute) in 4 : 1 chloroform–ethanol. The ultraviolet absorbing band of the product (*IIIk*, R_F 0·60; *IIIi*, R_F 0·60) was eluted with methanol (200 ml), the eluate evaporated, and the residue crystallised from ethanol. Overall yield, 0·5 g (32%) of the product identical with compound *IIIk*. The product sublimes above 200°C and does not melt up to 250°C. For $C_6H_9N_3S$ (155·2) calculated: 46·43% C, 5·84% H, 27·08% N, 20·62% S; found: 46·19% C, 5·99% H, 26·73% N, 21·01% S. In addition to compound *IIIk* and thiourea, the reaction mixture does not contain any other ultraviolet-absorbing material.

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Translated by J. Pliml.