TABLE I

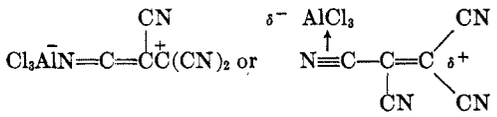
PREPARATION AND PROPERTIES OF TRICYANOVINYL AROMATICS

Ar of ArC=C(CN)$_2$ CN	Yield, %	Mp, °C	Recrystn solvent	Formula	Anal., % Carbon Calcd	Carbon Found	Hydrogen Calcd	Hydrogen Found	Nitrogen Calcd	Nitrogen Found	Other Calcd	Other Found
C_6H_5	35	98.3–99.2[a]	Benzene	$C_{11}H_5N_3$	73.8	73.4	2.81	3.01	...	...		
p-$CH_3C_6H_4$	23[b]	115 5–117	Ether	$C_{12}H_7N_3$	74.6	75.0 74.8	3.66	3.95 3.86	21.8	21.2		
p-FC_6H_4	17[c]	122–123	Benzene–cyclohexane	$C_{11}H_4N_3F$	67.1	67.2	2.05	2.20	21.3	21.0	F, 9.6	F, 9.7
β-$C_{10}H_7$	20[d]	174–178	Acetone–ethanol	$C_{15}H_7N_3$	78.6	78.5	3.08	3.21	18.4	18.5		

[a] Lit.[2] mp 96–97°. [b] *para* substitution shown by 830-cm^{-1} band in infrared (no strong band in 810–750-cm^{-1} region) and proton nmr in d_6-acetone: (CH_3) 2.5 ppm, aromatic typical A_2B_2 centered at −7.75 ppm relative to tetramethylsilane, δ = 0.4 ppm and J = 6 cps. [c] *para* substitution proved by spectral comparison to authentic *p*-fluoro(tricyanovinyl)benzene prepared by literature procedure (ref 2 and 3) of condensing *p*-fluorobenzaldehyde with malononitrile followed by addition of HCN and oxidation. [d] *o*-Dichlorobenzene used as solvent. Reaction run on 8.8 g of naphthalene, 6.0 g of TCNE, and 6 g of $AlCl_3$ in 200 ml of solvent.

by comparison with authentic 1-fluoro-4-(tricyanovinyl)benzene prepared from *p*-fluorobenzaldehyde by a literature procedure.[2] Attack in the β position of naphthalene was indicated by spectral analysis and proved by hydrolysis of the tricyanovinyl derivative[2] to 2-naphthoic acid.[4] In each case, the orientation of substitution is toward minimum steric interactions, suggesting that steric effects are important in the rate-controlling step of substitution. No products could be isolated from reaction of TCNE with durene, probably because steric interference is too great. Chlorobenzene also did not react, but its aromatic ring is more strongly deactivated than that of fluorobenzene.[5]

The interaction of TCNE with aluminum chloride to form a more electrophilic species such as



could explain the enhanced activity of TCNE in attack on a π system, but this species is not electrophilic enough to attack chlorobenzene. When the TCNE solution in benzene is added to aluminum chloride in benzene, the reaction mixture turns from yellow (normal for TCNE–benzene π complex) to red, suggesting formation of a π complex of aluminum chloride–TCNE with benzene. Qualitatively, most of the aluminium chloride remains undissolved, and much of the TCNE can be recovered from the mixture before heating by filtering off the insoluble aluminum chloride and evaporating the red solution. Aluminum chloride is required in molar amounts because it (or some other aluminum salt from reaction with HCN) complexes strongly with the product. Thus the product had to be isolated by chromatography over alumina, and, although tricyanovinylbenzene sublimes quickly at 90° (0.1 mm), only a trace of it was recovered on attempted sublimation of the crude reaction mixture at 150° (0.1 mm). In a control experiment, pure tricyanovinylbenzene was shown to behave similarly when complexed with alumina. Spectral analysis (infrared, ultraviolet, and nmr) on a crude reaction mixture verified that tricyanovinylbenzene was formed in the reaction and not by some rearrangement catalyzed by the alumina in the chromatographic column. Boron trifluoride (anhydrous or as etherate) is not effective as a catalyst. The detailed mechanism proposed for attack of TCNE on N,N-dimethylaniline[3] could accommodate our observations on these catalyzed tricyanovinylations.

Experimental Section

Tricyanovinylation of Benzene.—A mixture of 6.4 g (0.050 mole) of TCNE and 6.6 g (0.050 mole) of $AlCl_3$ in 100 ml of benzene was refluxed for 1 hr. The reaction mixture, which turned from initially deep red to brown, was chromatographed on 200 g of acid-washed alumina in a 90-mm-diameter column using approximately 1.5 l. of 80% ether–20% benzene as eluent. (The chromatography conditions are critical since the product is destroyed by long contact with alumina.) The crude tricyanovinylbenzene, mp 94–95°, was obtained in a yield of 3.2 g (35%) and, after recrystallization from acetonitrile or benzene and sublimation, was identical with an authentic sample prepared previously in this laboratory.[2] A small yield of TCNE was recovered in some reactions.

When 6.4 g (0.050 mole) of TCNE was refluxed with 0.38 g (0.003 mole) of $AlCl_3$ in benzene, 61% of the TCNE was recovered (from chromatography), and only 0.24 g (2.7%) of tricyanovinylbenzene was isolated.

The results for all tricyanovinylations are given in Table I along with analytical data and physical properties on the new tricyanovinylaryl compounds.

Registry No.—$C_{11}H_5N_3$, 4364-80-1; $C_{12}H_7N_3$, 7634-91-5; $C_{11}H_4N_3F$, 7634-92-6; $C_{15}H_7N_3$, 7634-93-7.

(4) (a) The naphthoic acid from hydrolysis, mp 182–184° (lit.[4b] melting points of naphthoic acids: 1 isomer 161°; 2 isomer 184°), had an infrared spectrum identical with that of authentic 2-naphthoic acid. (b) I. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, 1953, p 559.

(5) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, **1**, 35 (1963).

Nucleosides of Thioguanine and Other 2-Amino-6-substituted Purines from 2-Acetamido-5-chloropurine[1]

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The synthesis of 9-substituted nucleosides of guanine, thioguanine, and other 2-amino-6-substituted purines generally has not been accomplished by the direct condensation of guanine or a blocked derivative with a

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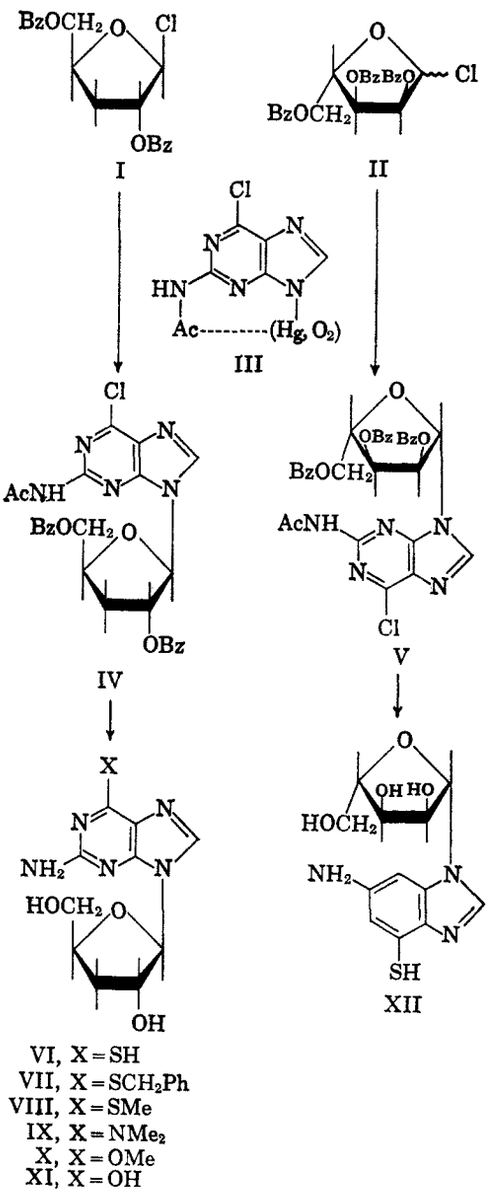
sugar. Recently, however, two such condensations[2,3] were reported, but in both cases a mixture of 7- and 9-substituted guanine nucleosides was formed and separation of the isomers was required. A number of indirect routes to 9-substituted nucleosides of guanine and other 2-amino-6-substituted purines have been reported that utilize 2,6-dichloropurine,[4] 2,6-diaminopurine,[5a] and 2,8-dichloroadenine[5b] as precursors. The last was used in the first synthesis of guanosine.[5b] Clearly, more direct routes are desirable.

Recently, the mercury derivative (III) of 2-acetamido-6-chloropurine was used in the synthesis of 2′-deoxythioguanosine and related nucleosides.[6] Compound III can be easily obtained from commercially available 2-amino-6-chloropurine. In an extension of this work, we find that III can be successfully condensed with the chloro sugars I and II, respectively prepared from methyl 2,5-di-*O*-benzoyl-3-deoxy-D-ribofuranoside[5] and from 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-L-ribofuranose,[7] to afford two series of thioguanine nucleosides and related compounds (see Chart I). These results suggest that III has general utility for the synthesis of nucleosides of thioguanine, guanine, and other 2-amino-6-substituted purines.

Chloro sugars I and II were prepared and converted to the nucleosides in Chart I by modifications of known procedures. For example, treatment of methyl 2,3-anhydro-β-D-ribofuranoside[8] with lithium aluminum hydride[9] instead of Raney nickel afforded methyl 3-deoxy-β-D-ribofuranoside[5a] that contained no detectable amount (by nmr) of isomeric product.[10] In the preparation of chloro sugar I from its methyl glycoside,[5a] the latter did not have to be hydrolyzed first, but could be directly converted to an equilibrium mixture of I and the 1-*O*-acetyl compound (estimated ratio of 3:1) by hydrogen chloride in acetic acid. The conversion to I was completed with hydrogen chloride in ether. Crystalline I was readily isolated in good yield. In our hands, the crystalline chloro sugar I gave better results in the nucleoside condensation than the corresponding bromo sugar.[5a]

The structure of L-thioguanosine (XII) followed from a comparison of its properties with D-thioguanosine. The structures of the 3′-deoxynucleosides are established on this basis. Attachment of the deoxyribosyl group at N-9 is verified by the fact that the ultraviolet spectrum of 3′-deoxy-*S*-benzylthioguanosine (VII) resembles that of 2′-deoxy-*S*-benzylthioguanosine[6] and other 9-substituted 2-amino-6-benzylthiopurines[11a] which are distinct from spectra of 7-alkyl[11b] isomers. The β configuration follows from the *trans* rule.[12] For additional confirmation, a comparison has been made of the properties of 3′-deoxyguanosine (XI) prepared from IV and that prepared by another route.[2]

CHART I



The conversion of IV to XI represents a unique and useful guanine nucleoside synthesis[13] developed from the observation[14] that 6-(2-hydroxyethylmercapto)-purines are easily hydrolyzed. Thus, treatment of IV with sodium 2-hydroxyethylmercaptide caused displacement of the chlorine atom to form the unstable 6-(2-hydroxyethylmercapto)nucleoside. This was rapidly hydrolyzed, and also deacylated, on further contact with the basic reaction medium to afford XI. This one-step preparation was more convenient and afforded higher yields than the conversion of IV to VII followed by hydrogen peroxide oxidation[15] to XI.

(2) S. R. Jenkins, F. W. Holly, and E. Walton, *J. Org. Chem.*, **30**, 2851 (1965).

(3) Z. A. Shabarova, Z. P. Polyakova, and M. A. Prokof'ev, *Zh. Obshch. Khim.*, **29**, 215 (1959); *Chem. Abstr.*, **53**, 21998a (1959).

(4) See E. J. Reist and L. Goodman, *Biochemistry*, **3**, 15 (1964), and references therein.

(5) (a) E. Walton, F. W. Holly, G. E. Boxer, Ruth F. Nutt, and S. R. Jenkins, *J. Med. Chem.*, **8**, 659 (1965); (b) J. Davoll, B. Lythgoe, and A. R. Todd, *J. Chem. Soc.*, 1685 (1948).

(6) R. H. Iwamoto, E. M. Acton, and L. Goodman, *J. Med. Chem.*, **6**, 684 (1963).

(7) E. M. Acton, K. J. Ryan, and L. Goodman, *J. Am. Chem. Soc.*, **86**, 5352 (1964).

(8) C. D. Anderson, L. Goodman, and B. R. Baker, *ibid.*, **80**, 5247 (1958).

(9) M. Dahlgard, B. H. Chastain, and R-J. L. Han, *J. Org. Chem.*, **27**, 929 (1962).

(10) See footnote 18 of ref 5a.

(11) (a) C. W. Noell and R. K. Robins, *J. Med. Pharm. Chem.*, **5**, 558, 1074 (1962); (b) W. A. Bowles, F. H. Schneider, L. R. Lewis, and R. K. Robins, *ibid.*, **6**, 471 (1963).

(12) B. R. Baker, *Ciba Found. Symp., Chem. Biol. Purines*, 120 (1957).

(13) We are synthesizing other guanine nucleosides to test the generality of this method. One example is given by G. L. Tong, W. W. Lee, and L. Goodman, *J. Org. Chem.*, in press.

(14) T. B. Johnston, L. B. Holum, and J. A. Montgomery, *J. Am. Chem. Soc.*, **80**, 6265 (1958).

(15) J. F. Gerster and R. K. Robins, *ibid.*, **87**, 3752 (1965).

Experimental Section[16]

Methyl 3-Deoxy-β-D-ribofuranoside.[5a]—Using a modified procedure of Dahlgard, *et al.*,[9] a mixture of 3.90 g (103 mmoles) of lithium aluminum hydride and 5.00 g (34.2 mmoles) of methyl 2,3-anhydro-β-D-ribofuranoside[8] was allowed to react at ambient temperature for 16 hr (reaction incomplete in 1 hr). After decomposition of the reaction mixture, the suspension was filtered through Celite, the pad was washed well with water and methanol, and the combined filtrates were stirred until neutral with 75 g (wet) of Amberlite IRC 50 ion-exchange resin, filtered, and evaporated *in vacuo*. The residue was redissolved in 75 ml of chloroform, filtered, and again evaporated to afford 4.34 g (85%) of the product as a yellow syrup, which was homogeneous (TC, R_f 0.13), and whose infrared and nmr spectra were compatible with its structure. The nmr spectrum showed no detectable amounts of isomeric product.[10]

2,5-Di-*O*-benzoyl-3-deoxy-β-D-ribofuranosyl Chloride (I).—To a cold (10–15°), stirred solution of 3.25 g (9.1 mmoles) of methyl 2,5-di-*O*-benzoyl-3-deoxy-β-D-ribofuranoside[5a] in 1 ml of acetyl chloride and 10 ml of acetic acid was added slowly 10 ml of cold (10–15°) acetic acid saturated with hydrogen chloride. The solution was stirred, protected from moisture at 10–15° for 1 hr, and then evaporated *in vacuo*. The last traces of acetic acid were removed by the addition and removal *in vacuo* of four 10-ml portions of dry toluene. The residue was dissolved in 100 ml of dry ether, cooled to 0°, and saturated with hydrogen chloride. The solution was stored in a stoppered flask at 0° for 2 days and then evaporated *in vacuo*. The residue was dissolved in 5 ml of dry benzene and evaporated *in vacuo* to dryness. Crystallization of the residue from 40 ml of benzene–Skellysolve C (1:3) gave 2.06 g (62%) of white crystals, mp 90.5–92.5° (softens from 85°). The mother liquors gave a second crop of I: 0.29 g [total 2.35 g (71%)], mp 88.5–92° (softens from 80°). For analysis, a sample was recrystallized from benzene–Skellysolve C (1:3): mp 91.5–93.5° (softens from 85°); nmr peak at τ 3.76 (singlet, C-1 proton); $[\alpha]_{589}^{23}$ −56° (*c* 2.05, $CHCl_3$). It was homogeneous by thin layer chromatography with R_f 0.7 in solvent TA (starting material, R_f 0.9).

Anal. Calcd for $C_{19}H_{17}ClO_5$: C, 63.3; H, 4.75; Cl, 9.83. Found: C, 63.4; H, 4.72; Cl, 9.23.

Examination of the residue from the mother liquor by nmr indicated the presence of more I and some of its anomer (doublet at τ 3.40 and 3.46 for C-1 proton).

In another run, portions of a similar solution of methyl 2,5-di-*O*-benzoyl-3-deoxy-β-D-ribofuranoside in acetic acid containing hydrogen chloride at 10° were removed at intervals, worked up, and examined by nmr, and the 1-substituent composition was estimated (to within ±5%). (See Table I.)

TABLE I

Reacn time, min	1 substituent, % OMe	OAc	Cl
30	5	20+	75−
60	0	30	70
120	0	25	75

2,3,5-Tri-*O*-benzoyl-L-ribofuranosyl Chloride (II).—As described for the D isomer,[17] 11.0 g (0.0218 mole) of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-L-ribofuranose[7] was dissolved in 500 ml of cold, ethereal hydrogen chloride (saturated at 0°), 11 ml of acetyl chloride was added to maintain absence of moisture,[18] and the solution was stored at 0° for 3 days. The solution was evaporated *in vacuo* to form a residual syrup, and benzene was twice added and removed *in vacuo*.[7,18] The syrup (10.5 g, 100%) was used immediately in the next step.

2-Acetamido-6-chloro-9-(2,5-di-*O*-benzoyl-3-deoxy-β-D-ribofuranosyl)-9H-purine (IV).—A mixture of mercury derivative III[6] and Celite (3.23 g of mixture containing 2.21 g, 5.0 mmoles of III) in 200 ml of xylene was dried by azeotropic distillation, treated with 1.81 g (5.0 mmoles) of chloro sugar I in 20 ml of dry xylene and 5.0 g of molecular sieves (Linde Type 4A), and stirred at reflux for 6 hr. The mixture was worked up in the usual way[6] to afford 0.88 g (33%) of IV, mp 197.5–203.5° from benzene. Two recrystallizations from chloroform afforded the analytical sample of IV: mp 206–207°; λ_{max}^{EtOH} 229 mμ (ε 51,200), 259 (11,700), and 284 (10,600); $[\alpha]_{589}^{23}$ +24° (*c* 0.5, $CHCl_3$); homogeneous in solvent TB with R_f 0.39.

Anal. Calcd for $C_{26}H_{22}ClN_5O_6$: C, 58.3; H, 4.14; Cl, 6.62; N, 13.1. Found: C, 58.2; H, 4.43; Cl, 6.91; N, 13.0.

2-Acetamido-6-chloro-9-(2,3,5-tri-*O*-bezoyl-β-L-ribofuranosyl)-9H-purine (V).—In the same way used for IV above, a mixture of III[6] and Celite containing 5.3 g (12 mmoles) of III in 500 ml of xylene and a solution of 5.8 g (12 mmoles, from 12 mmoles of 1-acetate) of the chloro sugar II in 50 ml of anhydrous xylene was heated at reflux temperature for 2 hr and worked up to afford 4.5 g (57%) of a residual glass. The infrared spectrum was dominated by benzoate absorption, with strong bands at 5.78, 7.9, and 14.1, and a medium aryl band at 6.23 μ; a slightly stronger aryl band at 6.32 μ was diagnostic for the purine moiety. Analysis indicated the nucleoside was only 83% pure.

Anal. Calcd for $C_{33}H_{26}ClN_5O_8$: N, 10.7. Found: N, 8.87.

2-Amino-9-β-L-ribofuranosyl-9H-purine-6-thiol (L-Thioguanosine, XII).—According to the procedure for 2′-deoxythioguanosine,[6] 4.50 g (6.85 mmoles) of V was dissolved in 450 ml of anhydrous methanol saturated with hydrogen sulfide (maintained in a continuous stream). To this was added a solution of 1.50 g (27.8 mmoles) of solid sodium methoxide in 20 ml of methanol previously saturated with hydrogen sulfide. The mixture was refluxed for 2 hr with hydrogen sulfide passing through the solution. The hydrogen sulfide source was removed, and refluxing was continued for 15 min. Then 0.75 g of sodium methoxide in 10 ml of methanol was added, and the solution was refluxed for 1 hr, cooled, and clarified by filtration through Celite. The filtrate was evaporated *in vacuo* and the residue was partitioned between 40 ml of water and 60 ml of chloroform. The water layer was washed with 50 ml of chloroform and neutralized (pH 6–7) with acetic acid. The dark solid which formed upon chilling overnight was collected and weighed 0.47 g (23%). Purity of 80–90% was estimated by ultraviolet extinctions.

Since purification could not be completed by recrystallization, the solid was dissolved in 20 ml of 3 *M* ammonium hydroxide solution and this was treated with 5 ml of saturated lead diacetate to precipitate the lead salt. The salt was collected on a filter, washed with water, and dissolved in 50% aqueous acetic acid, and the solution was saturated with a hydrogen sulfide stream for 15 min. Filtration through Celite removed the insoluble sulfides, and the filtrate was evaporated *in vacuo*. The residual solid was crystallized from water to form 0.43 g (20%): mp 231–233° dec; $\lambda_{max}^{pH\ 1}$ 208 mμ (ε 24,600), 264 (7980), and 343 (22,200); $\lambda_{max}^{pH\ 13}$ 222 mμ (ε 13,000), 251 (13,500), 271 (7090), and 319 (20,700); $[\alpha]_{589}^{24}$ +70° (*c* 1, 0.1 *M* sodium hydroxide). The compound was chromatographically homogeneous in solvent A with R_{ad} 1.58, identical with that of a commercial sample of the D enantiomer[19a] which exhibited[19b] $[\alpha]_{589}^{24}$ −72° (*c* 1, 0.1 *M* sodium hydroxide); $\lambda_{max}^{pH\ 1}$ 208 mμ (ε 25,500), 264 (8140), and 343 (22,800); $\lambda_{max}^{pH\ 13}$ 222 mμ (ε 12,000), 251 (13,900), 271 (7180), and 319 (21,300).

Anal. Calcd for $C_{10}H_{13}N_5O_4S \cdot H_2O$: C, 39.7; H, 4.77; N, 22.1. Found: C, 40.0; H, 4.50; N, 22.3.

2-Amino-9-(3-deoxy-β-D-ribofuranosyl)-9H-purine-6-thiol (VI).—Treatment of 3.76 g (7.0 mmoles) of IV with hydrogen sulfide by the procedure used above for XII afforded 1.80 g (86%) of VI·0.8 H_2O as an off-white powder, mp 201–202° dec. For analysis, a similar sample of VI from an earlier run was dissolved

(16) Melting points were determined with the Fisher-Johns apparatus and are corrected. Rotations were determined with a Rudolph photoelectric polarimeter. Nmr spectra were run as solutions in deuteriochloroform using tetramethylsilane as an internal standard on either the Varian A-60 or HA-100 spectrometer. Thin layer chromatograms were run on silica gel HF (E. Merck AG, Darmstadt), in the following solvent systems: TA, benzene–ethyl ether (1:1); TB, chloroform–ethyl acetate (1:1); TC, ether. The spots were detected under ultraviolet light or with sulfuric acid. Paper chromatograms were run by the descending technique on Whatman No. 1 paper. When adenine was used as a standard, the spots were located relative to R_{ad} 1.00. The solvent systems follow: A, 5% aqueous disodium hydrogen phosphate, pH 8.9; B, 1 *N* ammonia; C, *n*-butyl alcohol saturated with water; D, benzene–methanol–water (2:6:1); E, *n*-butyl alcohol–acetic acid–water (5:2:3); F, water. The spots were detected by visual examination under ultraviolet light. Anhydrous magnesium sulfate was used as the drying agent. Skellysolve C is a petroleum solvent fraction, bp 90–100°, essentially *n*-heptane; Skellysolve B, bp 60–80°, is essentially *n*-hexane. Celite is a brand of diatomaceous earth.

(17) H. M. Kissman, C. Pidacks, and B. R. Baker, *J. Am. Chem. Soc.*, **77**, 18 (1955).

(18) E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, **23**, 1753, 1958 (1958).

(19) (a) J. J. Fox, I. Wempen, A. Hampton, and I. L. Doerr, *J. Am. Chem. Soc.*, **80**, 1669 (1958). (b) Ultraviolet extinctions were calculated for the monohydrate.

in 0.1 *N* sodium hydroxide (10 mg/ml), filtered, and precipitated at pH 6–7 by the addition of 1 *M* acetic acid, and this was repeated a second time to afford an 83% recovery of VI: mp 199–200° dec; $\lambda_{max}^{pH\ 1}$ 208 mμ (ε, 25,400), 263 (8400), and 346 (21,000); $\lambda_{max}^{pH\ 7}$ 208 mμ (ε 23,600), 226 (15,300), 257 (8800), 265 shoulder (~8500), and 341 (24,000); $\lambda_{max}^{pH\ 13}$ 220 mμ (ε 15,000), 251 (13,600), 270 (7300), and 319 (19,500); $[\alpha]_{589}^{24}$ −61° (*c* 0.5, 0.1 *N* NaOH). It was homogeneous in solvent A and B with R_{ad} 1.40 and 1.78, respectively (blue fluorescent ring around ultraviolet absorbing spot).

Anal. Calcd for $C_{10}H_{13}N_5O_3S \cdot 0.8H_2O$: C, 40.3; H, 4.94; N, 23.5; S, 10.8. Found: C, 40.6; H, 5.20; N, 23.2; S, 10.8.

An attempt to recrystallize VI from boiling H_2O caused some decomposition; the product crystallized as fine off-white, fibrous needles, mp 197.5–198.5° dec.

A procedure utilizing thiourea[5a] for the preparation of VI from IV was unsuccessful.

2-Amino-6-benzylthio-9-(3-deoxy-β-D-ribofuranosyl)-9H-purine (VII).—To a stirred suspension of 5.36 g (10 mmoles) of IV in 500 ml of methanol was added a solution of 3.67 ml (31 mmoles) of benzyl mercaptan in 30 ml of 1 *M* methanolic sodium methoxide. The mixture was refluxed, under a nitrogen atmosphere, for 1.5 hr. The colorless solution was cooled, neutralized (pH 6–7) with 1 *M* acetic acid, and evaporated *in vacuo* to dryness. The residue was washed well with benzene and water. The solid was dissolved in 75 ml of hot methanol, diluted with 50 ml of water, and cooled to give 1.85 g of VII, mp 155–158.5°. The mother liquors gave a second crop of VII (0.93 g, total 2.78 g, 74%, mp 153–155°. Recrystallization of the combined crops from 55% aqueous methanol gave 2.00 g (54%) of VII, mp 158–159°. Another recrystallization from aqueous methanol gave the analytical sample of VII: mp 158.5–195°; $\lambda_{max}^{pH\ 1}$ 206 mμ (ε 25,500), 249 (10,000), and 322 (12,400); $\lambda_{max}^{pH\ 7}$ 219 mμ (ε 23,800), 246 (13,400), and 313 (13,900); $\lambda_{max}^{pH\ 13}$ 246 mμ (ε 13,300) and 313 mμ (ε 14,000); $[\alpha]_{589}^{24}$ −25° (*c* 0.49, CH_3OH). The product moved as a single spot in solvents C and D with R_{ad} 1.8 and 1.5, respectively.

Anal. Calcd for $C_{17}H_{19}N_5O_3S$: C, 54.7; H, 5.13; N, 18.8; S, 8.59. Found: C, 54.9; H, 5.25; N, 18.6; S, 8.67.

2-Amino-9-(3-deoxy-β-D-ribofuranosyl)-6-methylthio-9H-purine (VIII).—To a stirred suspension of 0.536 g (1.0 mmole) of IV in 50 ml of methanol was added a cold (0°) solution of 1.0 ml (18 mmoles) of methyl mercaptan in 3.0 ml of 1 *N* methanolic sodium methoxide. The mixture was refluxed, under a nitrogen atmosphere, for 3 hr and then evaporated *in vacuo* to dryness. The residue was dissolved in 10 ml of water and washed with three 10-ml portions of ether. The aqueous phase was neutralized (pH 6.5–7) and evaporated *in vacuo*. Two 10-ml portions of absolute ethanol were added and removed *in vacuo*. The residue was extracted with 20 ml of boiling acetonitrile. The extract was evaporated *in vacuo* to give 0.283 g of crude product. Crystallization from 10 ml of acetonitrile gave 0.212 g (71%) of VIII as white crystals, mp 158–159°. The mother liquors gave a second crop of VIII; (0.023 g, total 0.235 g, 79%), mp 157–159°. For analysis a sample was recrystallized from acetonitrile to give VIII: mp 159–159.5°; $\lambda_{max}^{pH\ 1}$ 226 mμ (ε 15,100), 249 (10,100), and 324 (11,000); $\lambda_{max}^{pH\ 7}$ 221 mμ (ε 18,100), 246 (13,600), and 311 (12,200); $\lambda_{max}^{pH\ 13}$ 223 mμ (ε 15,600), 244 (13,600), and 311 (12,400); $[\alpha]_{589}^{21}$ −46° (*c* 0.50, H_2O). The product moved as a single spot with a blue fluorescent ring in solvents E and F with R_{ad} 1.34 and 1.47, respectively.

Anal. Calcd for $C_{11}H_{15}N_5O_3S$: C, 44.4; H, 5.09; N, 23.6; S, 10.8. Found: C, 44.5; H, 5.08; N, 23.7; S, 10.4.

2-Amino-9-(3-deoxy-β-D-ribofuranosyl)-6-dimethylamino-9H-purine (IX).—A stirred suspension of 0.536 g (1.0 mmole) of IV and 5 ml of anhydrous dimethylamine in 50 ml of methanol was heated at 90° for 16 hr in a stainless steel bomb. The solution was evaporated *in vacuo* to dryness and the residue was dissolved in 20 ml of water and washed with three 5-ml portions of chloroform. The aqueous solution was stirred with 0.232 g (1.0 mmole) of silver oxide for 30 min, treated with Norit, and filtered. The filtrate was evaporated *in vacuo* to a gum; the last traces of water were removed by the addition and removal *in vacuo* of two 3-ml portions of absolute ethanol. Crystallization of the residue from 5 ml of absolute ethanol gave 0.100 g (34%) of product, mp 174.5–176°. Recrystallization from absolute ethanol gave white crystals: mp 175–176.5°; $\lambda_{max}^{pH\ 1}$ 206 mμ (ε 19,900), 257 (12,300), and 295 (12,100); $\lambda_{max}^{pH\ 7}$ 229 mμ (ε 18,500), 267 shoulder (10,700), and 285 (15,200); $\lambda_{max}^{pH\ 13}$ 230 mμ (ε 18,200), 267 shoulder (10,700), and 285 (15,300); $[\alpha]_{589}^{21}$ −48° (*c* 0.50, H_2O). The product moved as a single spot with a blue fluorescent ring in solvents A and F with R_{ad} 1.36 and 1.50, respectively.

Anal. Calcd for $C_{12}H_{18}N_6O_3$: C, 49.0; H, 6.16; N, 28.6. Found: C, 48.8; H, 6.05; N, 28.2.

2-Amino-9-(3-deoxy-β-D-ribofuranosyl)-6-methoxy-9H-purine (X).—A stirred suspension of 5.36 g (10 mmoles) of IV in 500 ml of methanol containing 30 ml of 1 *M* methanolic sodium methoxide was refluxed for 2 hr and then evaporated *in vacuo* to dryness. The residue was dissolved in 75 ml of water, adjusted to pH 7–7.5 with 1 *N* hydrochloric acid, and washed with three 25-ml portions of chloroform. Cooling the aqueous solution at 5° gave 1.38 g of crude product, mp 105–120°. The mother liquors gave another 0.95 g (total 2.33 g) of crude X, mp 105–120°. The combined product was crystallized from 85 ml of acetonitrile to give a white, crystalline powder (1.87 g, 66.5%), mp 164–165°. The mother liquors gave a second crop of X (0.24 g, total 2.11 g, 75%), mp 164–165°. Another recrystallization from acetonitrile gave the analytical sample: mp 164.5–165°; $\lambda_{max}^{pH\ 1}$ 210 mμ (ε 23,200), 243 (7200), and 288 (9300); $\lambda_{max}^{pH\ 7}$ 211 mμ (ε 22,800), 248 (9000), and 281 (9100); $\lambda_{max}^{pH\ 13}$ 248 mμ (ε 8950) and 281 mμ (ε 9350); $[\alpha]_{589}^{22}$ −46° (*c* 0.50, H_2O). The product moved as a single spot with a blue fluorescent ring in solvents E and F with R_{ad} 1.32 and 1.68, respectively.

Anal. Calcd for $C_{11}H_{15}N_5O_4$: C, 47.0; H, 5.38; N, 24.9. Found: C, 47.1; H, 5.42; N, 25.0.

9-(3-Deoxy-β-D-ribofuranosyl)guanine (XI).—To a suspension of 0.536 g (1.0 mmole) of IV in 50 ml of methanol was added a solution of 0.3 ml (4.3 mmoles) of 2-mercaptoethanol in 3.0 ml of 1 *M* methanolic sodium methoxide. The stirred suspension was refluxed under a nitrogen atmosphere for 3 hr, during which time IV dissolved and the product precipitated. The mixture was evaporated *in vacuo* to dryness and the residue was dissolved in 15 ml of water and washed with 3–5 ml portions of ether. The aqueous phase was treated with Norit, neutralized (pH 6.5–7) with acetic acid, and cooled to afford 0.158 g of product, mp >300° (browns from 240°). A second crop of product (0.028 g, total 0.186 g, 70%), mp >300° (browns from 240°), was obtained from the mother liquors. Recrystallization of the combined crops from 10 ml of water gave 0.168 g (63%) of white, fibrous needles, mp >300° (browns from 250°). A second recrystallization gave pure 3′-deoxyguanosine (XI): mp >300° unchanged; $\lambda_{max}^{pH\ 1}$ 255 mμ (ε 11,800) and 275 mμ shoulder (~7780); $\lambda_{max}^{pH\ 7}$ 252 mμ (ε 12,900), and 270 mμ shoulder (ε ~9000); $\lambda_{max}^{pH\ 13}$ 260 mμ shoulder (ε ~11,600) and 267 mμ (ε 11,700); $[\alpha]_{589}^{23}$ −41° (*c* 0.3, H_2O). The product moved as a single spot in solvents A, D, and F with R_{ad} 1.62, 1.05, and 1.56, respectively. Literature values for XI[2] are $\lambda_{max}^{pH\ 1}$ 255 mμ (ε 11,300), and 275 mμ inflection (ε 7600); $\lambda_{max}^{pH\ 7}$ 252 mμ (ε 11,800) and 270 mμ inflection (ε 8600); $\lambda_{max}^{pH\ 13}$ 267 mμ (ε 9900), and 260 mμ inflection (ε 9700); $[\alpha]_{589}$ −41.2° (*c* 0.5, H_2O).

Registry No.—2-Acetamido-6-chloropurine, 7602-01-9; I, 7602-02-0; IV, 7602-02-1; V, 7650-63-7; XII, 7602-04-2; VI, 7602-05-3; VII, 7648-31-9; VIII, 7616-78-6; IX, 7602-06-4; X, 7648-32-0; XI, 3608-58-0.

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