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SYNTHESIS OF (POLYHYDROXYALKYL)HETEROCYCLES: (DIHYDROXYETHYL)PYRIMIDINE DERIVATIVES

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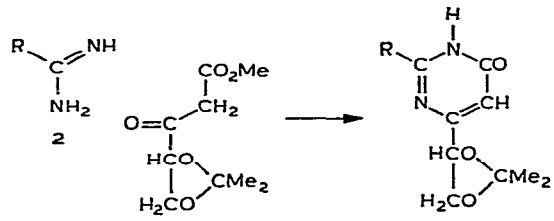
ABSTRACT

The reaction of derivatives of polyhydroxyalkyl-β-ketoesters with urea derivatives allowed the synthesis of pyrimidines having a *C*-polyhydroxyalkyl substituent. Thiourea, *S*-methylthiourea, and guanidine react with methyl (4*R*)-4,5-isopropylidenedioxy-3-oxopentanoate to give 4-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-methylthio-1,6-dihydropyrimidin-6-one (**3a**), 4-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-mercapto-1,6-dihydropyrimidin-6-one (**3b**), and 2-amino-4-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-1,6-dihydropyrimidin-6-one (**3c**), respectively. These structures were proved by physical methods, correlation with well-known reactions, and degradation to orotic acid. Hydrolysis of **3a–c** gave 4-[(*S*)-1,2-dihydroxyethyl]-2-methylthio-1,6-dihydropyrimidin-6-one (**5a**), 4-[(*S*)-1,2-dihydroxyethyl]-2-mercapto-1,6-dihydropyrimidin-6-one (**5b**), and 2-amino-4-[(*S*)-1,2-dihydroxyethyl]-1,6-dihydropyrimidin-6-one (**5c**), respectively. Vigorous hydrolysis of **3a** or **3b** gave 4-[(*S*)-1,2-dihydroxyethyl]-1,2,3,6-tetrahydropyrimidine-2,6-dione (**6**). Desulphuration of **3a** or **3b** gave 4-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-1,6-dihydropyrimidin-6-one. Periodate oxidation of **5a** and **6** gave 4-formyl-2-methylthio-1,6-dihydropyrimidin-6-one and 4-formyl-1,2,3,6-tetrahydropyrimidine-2,6-dione, respectively.

INTRODUCTION

The synthesis of polyhydroxyalkyl-β-ketoester derivatives[1,2] allowed the preparation of *C*-(polyhydroxyalkyl)pyrimidine derivatives by means of the well-known reaction of β-ketoesters with urea derivatives[3]. The recent interest in *C*-nucleosides has prompted us to explore this reaction, and we have reported[1] the synthesis of the β-ketoester **1** *via* reaction of 2,3-*O*-isopropylidene-D-glyceraldehyde with methyl diazoacetate*. We describe now the reaction of **1** with *S*-methylthiourea (**2a**), thiourea (**2b**), and guanidine (**2c**), to give the corresponding 4-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-1,6-dihydropyrimidin-6-one derivatives (**3a–c**).

*By the same method, we have recently prepared[4] methyl 4,7-anhydro-2-deoxy-5,6-*O*-isopropylidene-D-*arabino*-3-heptulosonate, starting from 2,5-anhydro-3,4-*O*-isopropylidene-D-arabinose.



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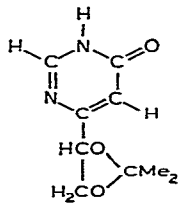
1

3

a series, R = SMe
b series, R = SH
c series, R = NH_2



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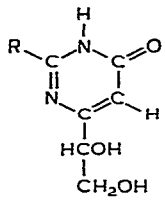
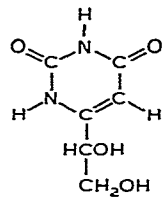


5a, R = SMe
5b, R = SH
5c, R = NH_2



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The *O*-isopropylidene groups in **3a–c** can be easily removed by mild hydrolysis with acid, giving the corresponding glycols (**5a–c**). Correlation of the structures of these compounds was achieved as follows. Desulphuration of **3a** and **3b** with Raney nickel gave the same product, namely, 4-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-1,6-dihydropyrimidin-6-one (**4**). Hydrolysis of **3a** or **3b** with strong acid also gave the same product, namely, 4-[(*S*)-1,2-dihydroxyethyl]-1,2,3,6-tetrahydropyrimidine-2,6-dione (**6**). Oxidation of **5a** and **6** with periodate gave 4-formyl-2-methylthio-1,6-dihydropyrimidin-6-one (**7**) and 4-formyl-1,2,3,6-tetrahydropyrimidine-2,6-dione (**8**), respectively. Further oxidation of **7** or **8** with silver oxide yielded orotic acid monohydrate in yields of 64 and 56%, respectively.

The structures assigned to the foregoing pyrimidine derivatives accorded with the spectroscopic data (see Experimental). The i.r. spectrum of **3a** contained no absorption for hydroxyl. The λ_{max} values were in agreement with those reported for these types of heterocycles[2,3]. Each mass spectrum contained a strong signal for the molecular ion. Two types of fragmentation were generally observed, corresponding to loss from the molecular ion of groups (OH, CHO, SMe) attached to the aromatic nucleus and to the loss of a C–N group of the nucleus, *e.g.*, (M — HOCN), (M — MeSCN). In the compounds containing sulphur, the (M — 2) ion is easily observed.

The p.m.r. data are shown in Table I. The spectra of the aldehydes **7** and **8** and those of their hydrated forms showed signals at δ 9.60 and 9.80, corresponding to the aldehydes, and signals at δ 5.52 and 5.75, corresponding to the proton in deuteriohydrated formyl groups, respectively.

TABLE I

FIRST-ORDER ^{1}H-N.M.R. CHEMICAL SHIFTS (δ) AND COUPLING CONSTANTS (Hz) FOR PYRIMIDINE DERIVATIVES

Compound	*Pyrimidine residue*			*Dioxolane residue*							
	H-5	*HO-4 (NH)*	*R-2 protons*	*H-4'*	*H-5'a*	*H-5'b*	*Me-2*	$J_{5,4'}$	$J_{4',5'a}$	$J_{4',5'b}$	$J_{5'a,5'b}$
3a[a]	6.42d	13.20s	2.51s	4.86dd	4.35dd	3.91dd	1.48s, 1.47s	1	7	6	8
3b[b]	5.78	← 12.40s →		5.00–4.65m	4.50–4.15m	4.05–3.70m	1.46s, 1.38s	small	*f*	*f*	*f*
3c[b]	5.67d	10.70s	6.60s	4.85–4.55m	4.45–4.15m	3.95–3.65m	1.40s, 1.37s	1.2	*f*	*f*	*f*
4[a]	6.72	[c]	8.12s	4.97dd	4.42dd	3.93dd	1.50s, 1.48s	small	6	8	8
				Dihydroxyethyl residue							
				H-1'	*H-2'*	*OH*		$J_{5,1'}$	$J_{1',2'}$		
5a[d,e]	6.60			4.82t	3.87d			small	4		
6[b,c,e]	5.70			4.45t	3.66d			small	5		
5b[b]	5.87	← 11.0–13.0[c,e] →		4.40m	3.60d	5.65; 3.30[c,e]		small	5		
5c[b]	5.90		8.97					small	5.5		
				Hydrate of aldehyde residue							
				H-1'		*OH*					
8[b]	6.60	← 3.32 →		5.52		3.32		small			
7[d]	6.42		2.60s	5.75		3.40		small			

[a]$CDCl_3$. [b]Me_2SO-d_6. [c]Exchangeable with D_2O. [d]In D_2O. [e]CF_3COOD added. [f]Not resolved.

EXPERIMENTAL

General methods. — Melting points are uncorrected. I.r. spectra were recorded for KBr discs with a Beckman Aculab IV spectrometer. U.v. spectra were recorded for aqueous solutions at the stated pH values, using a Beckman DB-GT spectrometer. ^{1}H-N.m.r. spectra were obtained for solutions in $CDCl_3$ or D_2O (internal Me_4Si or DSS) with a Perkin–Elmer–Hitachi R-20B or a Perkin–Elmer R-24B spectrometer. Chemical shifts (first order) are given on the δ scale with first-order coupling in Hz. Mass spectra were recorded with a Hewlett–Packard model 5930A spectrometer. Optical rotations were measured on solutions in ethanol with a Perkin–Elmer 141 polarimeter.

Solvents were evaporated under diminished pressure at $<40°$ by using a rotary evaporator.

Methyl (4R)-4,5-isopropylidenedioxy-3-oxopentanoate[1] (**1**). — To a mixture of methyl diazoacetate[5] (4.25 g, 40 mmol) and 2,3-*O*-isopropylidene-D-glyceraldehyde[6] (5.25 g, 40 mmol) at $-43°$ was slowly added diethyl ether (5 ml) containing a drop of boron trifluoride etherate. Nitrogen evolution started at $-30°$. The solution was stored overnight at room temperature, and, if necessary, heated to 80° for complete decoloration. Ether was removed, and the residue was distilled to yield **1** (5.48 g, 64.5%), b.p. 88°/0.3 mmHg, n_D^{23} 1.4489; ν_{max} 2980, 2940, 2880, 1740, 1715, 1650, 1635, 1460, 1440, 1380, 1370, 1260, 1215, and 1150 cm^{-1}. ^{1}H-N.m.r. data: δ 4.51 (dd, 1 H, *J* 7 Hz), 4.15 (dd, 1 H, *J* 7 and 10.5 Hz), 4.04 (dd, 1 H, *J* 7 and 10.5 Hz), 3.61 (s, 2 H), 3.70 (s, 3 H), 1.45 (s, 3 H), 1.35 (s, 3 H), and [5.45 (s, 1 H) and 11.8 (bs, 1 H) corresponding to the enol].

Anal. Calc. for $C_9H_{14}O_5$: C, 53.42; H, 6.97. Found: C, 53.22; H, 7.01%.

4-[(4S)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2-methylthio-1,6-dihydropyrimidin-6-one (**3a**). — To a solution of *S*-methylthiourea hydrogen iodide (16.3 g, 75 mmol) in water (30 ml), a solution of K_2CO_3 (27.6 g, 0.2 mol) in water (20 ml) was added followed by **1** (10 g, 50 mmol) with stirring at room temperature. After stirring for 48 h, the product (9.6 g, 75%) was precipitated with conc. hydrochloric acid, collected, washed with cold water, dried, and recrystallised from water to yield **3a** (8 g), m.p. 135–137°, $[\alpha]_D^{20}$ +7° (*c* 0.93); ν_{max} 3300, 3200, 3100, 2980, 2920–2800, 1650, 1570, 1540, 1450, 1370, 1360, 1220, 1200, 1160, 1140, 1090, 1070, 1060, and 845 cm^{-1}. U.v. data: pH 1.0, λ_{max} 286 (ε 8.4 × 10^3) and 238 nm (7.9 × 10^3); pH 7.0, 287 (8.5 × 10^3) and 240 nm (7.9 × 10^3); and pH 11.0, 277 (6.0 × 10^3) and 243 nm (9.0 × 10^3). Mass spectrum: *m/e* 244 (M + 2), 243, 242 (M), 227 (M — Me), 195 (M — SMe), 184 (M — Me_2CO), and 74 (M — MeSCN) (100%).

Anal. Calc. for $C_{10}H_{14}N_2O_3S$: C, 49.6; H, 5.8; N, 11.6; S, 13.2. Found: C, 49.3; H, 5.7; N, 11.4; S, 13.1.

Reactions of **3a**. — (*a*) *Strong, acid hydrolysis.* Compound **3a** (7 g) was treated for 4 h with boiling 2M hydrochloric acid (77 ml). Water and hydrochloric acid were then evaporated. Water (2 × 25 ml) was added to, and evaporated (*in vacuo*) from, the residue, to remove acid. The dried, crude product was recrystallised from ethanol,

yielding 4-[(*S*)-1,2-dihydroxyethyl]-1,2,3,6-tetrahydropyrimidine-2,6-dione (**6**; 4.15 g, 85%), m.p. 215–217° $[\alpha]_D^{20}$ +1° (*c* 1.1); ν_{max} 3340, 3160, 3100, 2920, 2860, 1725, 1690, 1670, 1560, 1520, 1120, 1070, 1030, and 1020 cm^{-1}. U.v. data: pH 0.25, λ_{max} 263 (ε 9.2 × 10^3) and 212 nm (8.0 × 10^3); pH 6.0, 263 (9.7 × 10^3) and 208 nm (1.0 × 10^4); and pH 13.0, 269 (6.8 × 10^3) and 226 nm (7.0 × 10^3). Mass spectrum: *m/e* 173 (M + 1), 172 (M), 155 (M — OH), 142 (M — CH_2O), and 43 (HOCN, 100%).

Anal. Calc. for $C_6H_8N_2O_4$: C, 41.86; H, 4.69; N, 16.27; oxidation equiv., 86.06. Found: C, 41.64; H, 4.54; N, 15.96; oxidation equiv., 85.70 (IO_4^-).

(*b*) *Mild, acid hydrolysis.* A solution of **3a** (1.2 g) in ethanol (20 ml) was kept for 1 h at ~100° with a solution of acetic acid (22 ml) in water (60 ml). The solvents were evaporated, and water (3 × 20 ml) was distilled from the residue which was then recrystallised from water to give 4-[(*S*)-1,2-dihydroxyethyl]-2-methylthio-1,6-dihydropyrimidin-6-one (**5a**; 680 mg, 68%), m.p. 149–150°, $[\alpha]_D^{20}$ +7° (*c* 1.1); ν_{max} 3500–3200, 3120, 3020, 2950, 2920, 2850, 1660, 1645, 1570, 1240, 1200, 1160, 1105, 1055, 1035, and 845 cm^{-1}. U.v. data: pH 1.0, λ_{max} 283 (ε 7.8 × 10^3) and 235 nm (8.4 × 10^3); pH 7.0, 287 (8.1 × 10^3) and 236 nm (8.4 × 10^3); and pH 11.0, 275 (6.1 × 10^3) and 242 nm (8.4 × 10^3). Mass spectrum: *m/e* 204 (M + 2), 203, 202 (M), 185 (M — OH), 172 (M — CH_2O), and 171 (M — CH_2OH) (100%).

Anal. Calc. for $C_7H_{10}N_2O_3S \cdot H_2O$: C, 38.17; H, 5.48; N, 12.70; S, 14.55. Found: C, 38.35; H, 5.34; N, 12.99; S, 14.82.

(*c*) *Desulphuration.* To a solution of **3a** (400 mg, 1.65 mmol) in water (10 ml) was added Raney nickel paste (4 g). The mixture was heated for 2 h at 120–130° and then filtered. The catalyst was washed with warm ethanol (4 × 25 ml). The combined filtrate and washings were concentrated to dryness and the residue was recrystallised from ethanol–water (4:1) to give 4-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-1,6-dihydropyrimidin-6-one (**4**; 43 mg, 13%), m.p. 145°, $[\alpha]_D^{20}$ ~0° (*c* 1.2, ethanol); ν_{max} 3200–3000, 2980, 2830–2750, 1670, 1600, 1380, 1370, 1220, 1200, 1150, 1080, and 1060 cm^{-1}. U.v. data: pH 1.0, λ_{max} 263 (ε 3.57 × 10^3) and 222 nm (7.83 × 10^3); pH 7.0, 265 (3.84 × 10^3) and 220 nm (7.36 × 10^3); and pH 11.0, 265 (3.48 × 10^3) and 230 nm (11.4 × 10^3).

4-Formyl-1,2,3,6-tetrahydropyrimidine-2,6-dione (**8**). — A solution of **6** (4.15 g, 24 mmol) in water (90 ml) was treated with a solution of sodium periodate (5.53 g, 24 mmol) in water (50 ml) for 4 h at room temperature in the dark. The solution was concentrated *in vacuo* to 70 ml and then cooled to ~0°. The product was collected, and recrystallised from water to yield **8** (1.35 g). More product (1.4 g) was obtained from the mother liquor by precipitation of iodate with ethanol (200 ml) and concentration of the filtered solution. The product (total yield, 75%) had m.p. 268–270°: ν_{max} 3360, 3360–3100, 3080, 2840, 1700, 1670–1645, 1490, 1250, 1170, 1090, 1060, and 1030 cm^{-1}. U.v. data: pH 1.0, λ_{max} 261 nm (ε 9.31 × 10^3); pH 7.0, 259 nm (9.26 × 10^3); and pH 11.0, 285 (5.2 × 10^3) and 267 nm (5.73 × 10^3). Mass spectrum: *m/e* 141 (M + 1), 140 (M), 139 (M — 1), 123 (M — OH), 111 (M — CHO), 97 (M — HOCN), 85 (M — NCCHO), and 29 (CHO) (100%).

Anal. Calc. for $C_5H_4N_2O_3 \cdot H_2O$: C, 37.98; H, 3.82; N, 17.72%. Found: C, 37.80; H, 4.13; N, 17.96%.

A suspension of silver oxide (3.7 g) in water (50 ml) was stirred with a solution of **8** (1.5 g) in ethanol (50 ml) for 5 h at room temperature and then for 30 min under reflux. The solution was concentrated and a solution of sodium chloride (1 g) in water (10 ml) was added followed by heating for 10 min at ~100°. The filtered solution was acidified with 10% hydrochloric acid to give orotic acid, which was recrystallised from water to give the monohydrate (940 mg, 56%), m.p. 339–340°.

4-Formyl-2-methylthio-1,6-dihydropyrimidin-6-one hydrate (**7**). — By the procedure described for **8**, **5a** (240 mg) was converted into crude **7** (162 mg, 77%). Recrystallisation from water yielded **7**, m.p. 234°; ν_{max} 3400–3200, 3100, 2950, 2920, 2820, 2760, 1645, 1570, 1530, 1235, 1200, 1160, 1090, 1020, and 855 cm^{-1}. U.v. data: pH 1.0, λ_{max} 259 nm (ε 8.95 × 10^3); pH 7.0, 255 nm (9.01 × 10^3); and pH 11.0, 282 (5.22 × 10^3) and 265 nm (5.62 × 10^3). Mass spectrum: *m/e* 172 (M + 2), 171, 170 (M), 169, 153 (M — OH), 142 (M — CO), 141 (M — CHO), 127 (M — HOCN), 123 (M — SMe), 115 (M — NCCHO), 96 (M — MeSCN), and 74 (CH_3SCN).

Anal. Calc. for $C_6H_6N_2O_2S \cdot H_2O$: C, 38.29; H, 4.28; N, 14.88; S, 17.03. Found: C, 38.31; H, 3.99; N, 14.67; S, 16.96.

A suspension of silver oxide (172 mg) in water was stirred with a solution of **7** (34 mg) in ethanol for 6 h at room temperature and then kept overnight. The ethanol was removed *in vacuo*, and the silver was precipitated with 0.1M NaOH to a basic pH. To the filtered mixture was added M hydrochloric acid to pH 4, and the solution was kept at ~100° for 2 h and then cooled to give orotic acid (20 mg) which, after recrystallisation from water, gave the hydrate, m.p. 339–340°.

4-[(4S)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2-mercapto-1,6-dihydropyrimidin-6-one (**3b**). — To a solution of **1** (4 g, 20 mmol) and thiourea (2.28 g, 30 mmol) in methanol (20 ml) was added a solution of sodium methoxide (2.16 g, 40 mmol) in methanol (30 ml). After being heated under reflux for 5 h, the mixture was concentrated to dryness. A solution of the dark residue in water was decolorised with active carbon, filtered, adjusted to pH 7 with conc. hydrochloric acid, and then acidified to pH 4 with acetic acid, to give crude **3b**. Recrystallisation from water gave **3b** (3.5 g, 77%), m.p. 224–225° (a further recrystallisation raised the m.p. to 225–227°), $[\alpha]_D^{20}$ +0.85° (*c* 1); ν_{max} 3300–3100, 2970, 2900, 2600, 1650, 1630, 1570, 1540, 1380, 1370, 1310, 1250, 1220, 1185, 1160, 1083, 1055, and 840 cm^{-1}. U.v. data: pH 1.0, λ_{max} 273 (ε 1.9 × 10^4) and 214 nm (1.6 × 10^4); pH 7.0, 272 (1.7 × 10^4) and 214 nm (1.6 × 10^4); and pH 11.0, 300 (7.5 × 10^3) and 260 nm (1.2 × 10^4). Mass spectrum: *m/e* 230 (M + 2), 229, 228 (M), 213 (M — Me), 198 (M — CH_2O), 170 (M — Me_2CO), 59 (HSCN), and 43 (HOCN) (100%).

Anal. Calc. for $C_9H_{12}N_2O_3S$: C, 47.35; H, 5.29; N, 12.27; S, 14.04; Found: C, 47.59; H, 5.23; N, 11.70; S, 13.80.

Reactions of **3b**. — (*a*) *Mild, acid hydrolysis.* By the procedure described for **3a**, **3b** (500 mg) was converted into 4-[(*S*)-1,2-dihydroxyethyl]-2-mercapto-1,6-dihydropyrimidin-6-one (**5b**; 270 mg, 66%), m.p. 220–221°, $[\alpha]_D^{20}$ +0.7° (*c* 1.1);

ν_{max} 3500–3010, 2920, 2860, 2600, 1660, 1640, 1600, 1550, 1300, 1250, 1230, 1170, 1150, 1050, and 840 cm^{-1}. U.v. data: pH 1.0, λ_{max} 275 (ε 1.75 × 10^4) and 220 nm (1.70 × 10^4); pH 7.0, 270 (1.65 × 10^4) and 217 nm (1.71 × 10^4); and pH 11.0, 300 (7.20 × 10^3) and 257 nm (1.2 × 10^4).

Anal. Calc. for $C_6H_8N_2O_3S$: C, 38.29; H, 4.28. Found: C, 38.59; H, 4.14.

(*b*) *Strong, acid hydrolysis.* The ketal **3b** (350 mg, 1.5 mmol) was heated at 150–170° for 1.5 h with a solution of chloroacetic acid (1.89 g, 20 mmol) in water (5 ml). The solvent was evaporated, and the residue was crystallised from water to yield 4-[(*S*)-1,2-dihydroxyethyl]-1,2,3,6-tetrahydropyrimidine-2,6-dione (**6**, 70 mg), m.p. 215–217°. More product (120 mg; total yield, 45%) was isolated from the mother liquor.

(*c*) *Desulphuration.* Compound **3b** (1 g) was heated for 1.5 h at 120–130° with a mixture of Raney nickel paste (2.8 g), conc. ammonia (1 ml), and water (10 ml). The solution was decanted and the catalyst was washed with boiling water (4 × 10 ml). The combined decantate and washings were concentrated, and the residue was recrystallised from water to yield 4-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-1,6-dihydropyrimidin-6-one (**4**, 127 mg), m.p. 145°. More product (100 mg; total yield, 26%) was obtained by extracting the nickel paste with ethanol (2 × 25 ml).

2-Amino-4-[(4S)-2,2-dimethyl-1,3-dioxolan-4-yl]-1,6-dihydropyrimidin-6-one (**3c**). — A solution of **1** (4 g, 20 mmol) and guanidine carbonate (1.8 g, 10 mmol) in ethanol (5.6 ml) was kept at 100° for 4 h, to give the hydrate of **3c** (2.7 g, 70%), m.p. 232–234° (from water), $[\alpha]_D^{20}$ +1.4° (*c* 0.9); ν_{max} 3480, 3380, 3240, 3100, 2970, 2900, 1680, 1610, 1540, 1380, 1370, 1250, 1220, 1210, 1140, 1080, 1050, and 850 cm^{-1}. U.v. data: pH 1.0, λ_{max} 257 (ε 7.1 × 10^3) and 237 nm (3.9 × 10^3); pH 7.0, 282 (8.3 × 10^3) and 220 nm (9.0 × 10^3); and pH 11.0, 277 (6.0 × 10^3) and 215 nm (2.0 × 10^3). Mass spectrum: *m/e* 211 (M), 196 (M — Me), 153 (M — Me_2CO), 111 (M — $C_2H_2O_2CMe_2$), and 43 (HOCN) (100%).

Anal. Calc. for $C_9H_{13}N_3O_3 \cdot H_2O$: C, 47.57; H, 6.54. Found: C, 47.60; H, 6.75.

The anhydrous product was obtained by heating the hydrate at 130° for 3 h followed by storage over P_2O_5.

Anal. Calc. for $C_9H_{13}N_3O_3$: C, 51.17; H, 6.19; N, 19.8. Found: C, 50.92; H, 5.97; N, 19.0.

Acid hydrolysis of **3c**. — A solution of **3c** (600 mg) in hydrochloric acid at pH 1 was heated under reflux for 1 h and then concentrated, and the solid residue was recrystallised from water to yield 2-amino-4-[(*S*)-1,2-dihydroxyethyl]-1,6-dihydropyrimidin-6-one hydrochloride (**5c**; 500 mg, 85%), m.p. 255°, $[\alpha]_D^{20}$ —2° (*c* 1.7, water); ν_{max} 3400–3200, 3140, 3060, 2900, 2740, 1680, 1640, 1610, 1570, 1270, 1230, 1080, 1050, and 850 cm^{-1}. U.v. data: pH 1.0, λ_{max} 260 nm (ε 7.14 × 10^3); pH 7.0, 280 (6.16 × 10^3) and 218 nm (8.17 × 10^3); and pH 11.0, 272 nm (6.23 × 10^3). Mass spectrum: *m/e* 171 (M), 154 (M — OH), 140 (M — CH_2OH), 84 (M — NCCHOH — CH_2OH), 43 (HOCN), and 36 (HCl) (100%).

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