are mutually inclined at an angle of 66·3 (3)° while the corresponding value for molecule 2 is 59·4 (3)°. All four independent phenyl rings are planar to within 0·006 Å. Steric interactions are minimized by the adoption of staggered conformations about the C—C single bonds. The crystal packing is determined by a network of hydrogen bonding wherein the hydroxyl groups form hydrogen-bonded chains with two independent O—H···O distances of 2·877 (4) and 2·845 (4) Å.

Fig. 2 shows a perspective view and atom labelling of the structure of (3*RS*,4*RS*)-2-methyl-4-phenyl-5-hexen-3-yl 4-nitrobenzoate (4), which again confirms the structure as the *threo* product. Tables 1 and 2 list atomic coordinates and bonding parameters respectively. Both phenyl rings are planar to within 0·008 Å and are inclined to one another at an angle of 5·9 (3)°; the carbonyl group lies in the plane of the nitrophenyl ring. Although no short intermolecular contacts (< 3·1 Å) exist, the molecules pack in layers with the nitrophenyl groups stacked down the *c* axis.

Fig. 3 shows a perspective view and atom labelling of the structure of (1*RS*,2*SR*)-1-(9-anthryl)-2-phenyl-3-buten-1-ol (5) which again confirms the structure as the *threo* product. Tables 1 and 2 list atomic coordinates and bonding parameters respectively. The anthryl ring is planar to within 0·02 Å. In the solid state the molecules form a hydrogen-bonded cyclic tetramer wherein four hydroxyl groups are hydrogen bonded in a cyclic manner about the four-fold axis with an O—H···O distance of 2·733 (3) Å.

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Acta Cryst. (1991). C**47**, 395–397

Structure of 4-[(1-Amidiniohydrazono)ethyl]-3-methyl-1-pyrazolecarboxamidinium Dichloride Monohydrate

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Abstract. 4-Acetyl-1-amidino-3-methylpyrazole amidinohydrazone dihydrochloride monohydrate, $C_8H_{16}N_8^{2+}.2Cl^-.H_2O$, $M_r = 313{\cdot}19$, triclinic, $P\bar{1}$, $a = 5{\cdot}488$ (2), $b = 9{\cdot}191$ (4), $c = 15{\cdot}013$ (3) Å, $\alpha = 72{\cdot}09$ (3), $\beta = 85{\cdot}51$ (3), $\gamma = 85{\cdot}36$ (4)°, $V = 717$ (6) Å^3, $Z = 2$, $D_x = 1{\cdot}448$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·7107 Å, $\mu = 0{\cdot}45$ mm^{-1}, $F(000) = 328$, $T = 293$ K, $R = 0{\cdot}057$ for 1699 independent reflections. The structural likeness of the title compound and methylglyoxal bis(guanylhydrazone) dihydrochloride (MGBG), which is clearly apparent from this study, should help in interpreting the similarity of some of their biological properties.

Introduction. Among anticancer drugs, mitoguazone or methylglyoxal bis(guanylhydrazone) dihydrochloride (MGBG) (Mihich, 1975), (1), has the striking feature of being structurally related to spermidine (French, Freedlander, Hosking & French, 1960), and is a good inhibitor of the enzyme *S*-adenosylmethioninedecarboxylase (SAM-DC, 4.1.1.50; *Enzyme Nomenclature*, 1978) (Porter, Dave & Mihich, 1981). In our search for new analogs of MGBG, we prepared a homogeneous series of isomeric 1-amidino-4-acylpyrazole amidinohydrazones (Menichi, Naciri, Kokel & Hubert-Habart, 1984; Menichi, Boutar, Kokel, Takagi & Hubert-Habart,

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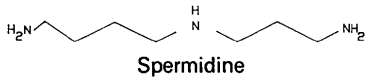
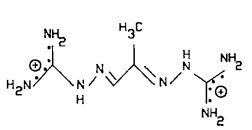
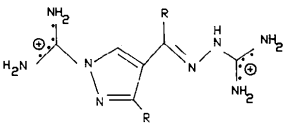
1986; Bajnati, Kokel & Hubert-Habart, 1987) whose structures closely resemble those of spermidine and MGBG. Among these pyrazoles, 4-acetyl-1-amidino-3-methylpyrazole amidinohydrazone dihydrochloride (2) stands out, not only because of its resemblance to MGBG, but also because it shows increased potency and selectivity relative to MGBG for inhibiting SAM-DC (Mamont, 1989).



Spermidine



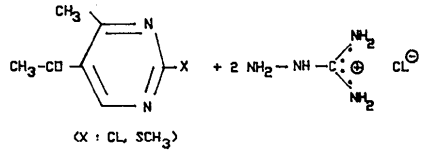
MGBG (1)



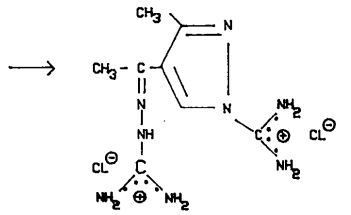
(2) $R = CH_3$

However, in contrast to MGBG, compound (2) does not exhibit as good an activity on experimental leukemia L 1210 and P 388 (screening performed under the auspices of the Developmental Therapeutics Program, Division of Cancer Treatment, National Cancer Institute, Bethesda, MD, USA). This discrepancy between these two biological activities of MGBG and pyrazole derivative (2) prompted us to compare more closely the three-dimensional structure of these molecules, to try and discriminate what could account for their common inhibitory activity on SAM-DC, and what could explain the differences in antitumor activity.

Experimental. After final recrystallization of compound (2) (Menichi, Naciri, Kokel & Hubert-Habart, 1984) in methanol, we let the mother solution stand for 17 days at room temperature.



(X : Cl, SCH_3)



Large crystals could thus be formed and selected. A single crystal, $0.25 \times 0.38 \times 0.42$ mm, giving Weissenberg data of a satisfactory quality, was selected for data collection. The unit-cell dimensions (from 25 reflections, $14 < \theta < 15°$) and reflection

Table 1. *Atomic positional parameters and* U_{eq} *values for non-H atoms*

$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	U_{eq}(Å^2)
N(1)	1·6026 (9)	0·8158 (6)	−0·3255 (4)	0·0533
N(2)	1·399 (1)	0·7224 (6)	−0·1837 (4)	0·0552
N(3)	1·2875 (8)	0·6642 (5)	−0·3123 (3)	0·0449
N(4)	1·1155 (8)	0·5719 (5)	−0·2561 (3)	0·0415
N(5)	0·5659 (8)	0·2815 (5)	−0·1067 (3)	0·0431
N(6)	0·5088 (7)	0·2478 (5)	−0·1846 (3)	0·0381
N(7)	0·218 (1)	0·0920 (6)	−0·0944 (4)	0·0550
N(8)	0·2640 (9)	0·1179 (6)	−0·2501 (3)	0·0473
C(1)	1·428 (1)	0·7350 (6)	−0·2733 (4)	0·0415
C(2)	0·9882 (9)	0·5004 (6)	−0·2941 (4)	0·0391
C(3)	1·010 (1)	0·5090 (8)	−0·3948 (4)	0·0533
C(4)	0·8036 (9)	0·4035 (5)	−0·2343 (3)	0·0367
C(5)	0·744 (1)	0·3752 (6)	−0·1353 (4)	0·0414
C(6)	0·851 (1)	0·4379 (9)	−0·0694 (4)	0·0577
C(7)	0·650 (1)	0·3194 (6)	−0·2607 (4)	0·0387
C(8)	0·3255 (9)	0·1484 (6)	−0·1756 (4)	0·0399
Ow	−1·002 (1)	0·0318 (7)	0·6057 (4)	0·0980
Cl(1)	1·8230 (3)	0·8917 (2)	−0·1302 (1)	0·0527
Cl(2)	0·5036 (3)	0·2266 (2)	0·5316 (1)	0·0663

Table 2. *Intramolecular bond distances* (Å) *and angles* (°)

N(1)—C(1)	1·314 (7)	N(2)—C(1)	1·312 (7)
N(3)—N(4)	1·374 (6)	N(3)—C(1)	1·323 (6)
N(4)—C(2)	1·271 (6)	N(5)—N(6)	1·363 (5)
N(5)—C(5)	1·312 (6)	N(6)—C(7)	1·351 (6)
N(6)—C(8)	1·385 (6)	N(7)—C(8)	1·286 (7)
N(8)—C(8)	1·308 (7)	C(2)—C(3)	1·485 (7)
C(2)—C(4)	1·462 (7)	C(4)—C(5)	1·445 (7)
C(4)—C(7)	1·344 (7)	C(5)—C(6)	1·468 (8)

C(1)—N(3)—N(4)	118·4 (5)	C(2)—N(4)—N(3)	117·6 (5)
C(5)—N(5)—N(6)	105·1 (4)	C(7)—N(6)—N(5)	111·7 (4)
C(8)—N(6)—N(5)	118·3 (4)	C(8)—N(6)—C(7)	130·0 (4)
N(2)—C(1)—N(1)	120·2 (5)	N(3)—C(1)—N(1)	118·7 (5)
N(3)—C(1)—N(2)	121·1 (5)	C(3)—C(2)—N(4)	125·2 (5)
C(4)—C(2)—N(4)	117·5 (5)	C(4)—C(2)—C(3)	117·3 (4)
C(5)—C(4)—C(2)	128·8 (4)	C(7)—C(4)—C(2)	126·8 (5)
C(7)—C(4)—C(5)	104·4 (4)	C(4)—C(5)—N(5)	110·8 (4)
C(6)—C(5)—N(5)	120·4 (5)	C(6)—C(5)—C(4)	128·8 (5)
C(4)—C(7)—N(6)	108·0 (4)	N(7)—C(8)—N(6)	118·5 (5)
N(8)—C(8)—N(6)	119·2 (5)	N(8)—C(8)—N(7)	122·4 (5)

intensities were measured with a four-circle diffractometer (CAD-4), graphite-monochromated radiation [λ(Mo $K\alpha$) = 0·71069 Å], scan type $\theta/2\theta$, scan range $(1·0 + 0·345\tan\theta)°$, $\theta = 1$–$25°$, $-6 \le h \le 6$, $-10 \le k \le 10$, $0 \le l \le 17$, 2634 data collected, 2527 unique, two standard reflections ($\bar{3}15$ and $\bar{1}37$), decomposition less than 0·01, absorption correction by *DIFABS* (Walker & Stuart, 1983), max. and min. transmission 0·99 and 0·85. Structure solved using direct methods [*SHELXS*86 and *CRYSTALS* from Sheldrick (1986) and Watkin, Carruthers & Betteridge (1985) respectively], final $R = 0·057$ and $wR = 0·058$ for 1699 independent reflections such that $I \ge 3\sigma(I)$, $w = 1·0$, form factors were from *International Tables for X-ray Crystallography* (1974, Vol. IV, pp. 99–101), $(\Delta/\theta)_{max} = 0·15$, on the last Fourier difference map $\rho_{max} = 0·4$ and $\rho_{min} = -0·4$ e Å^{-3}. Computer used: MicroVAX Q2.

Discussion. Atomic positional parameters are reported in Table 1. The intramolecular bond distances and angles are reported in Table 2.* A view of the molecule showing its conformation and the numbering system (similar to that of MGBG for comparison) is presented in Fig. 1; Fig. 2 is a stereoscopic view [figures drawn using *ORTEP* (Johnson, 1965) and *AutoCAD* (1987)]. X-ray and neutron diffraction studies on the corresponding crystalline dihydrochloride monohydrate salt of MGBG have been published previously (Hamilton & La Placa, 1968). All intermolecular distances and angles were computed; no evidence was found for hydrogen bonds. Crystalline cohesion seems to be due to van der Waals contacts rather than to hydrogen bonds as for MGBG where parallel planar molecules are linked together by hydrogen bonds through water and Cl^- ions (Hamilton & La Placa, 1968).

Our study points to an obvious partial likeness of type and conformation between the structural sequences (Fig. 1) of molecules (2) and (1). This close similarity could correspond to a common site of binding of the two molecules to the active site of the enzyme SAM-DC, for which they are both good inhibitors of the activity.

The main structural differences between compounds (2) and (1) rest upon the presence of a pyrazole ring in the structure of the former, which might create both steric hindrance and a stiffening from which the latter is free. This might explain why MGBG exhibits good antitumor activity on experimental leukemia, and why molecule (2) does not.

A systematic three-dimensional structure determination of other analogs of MGBG could help in the mapping of the active site of SAM-DC, as well as in designing better anticancer drugs than mitoguazone.

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, and intramolecular bond distances and angles involving H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53249 (13 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

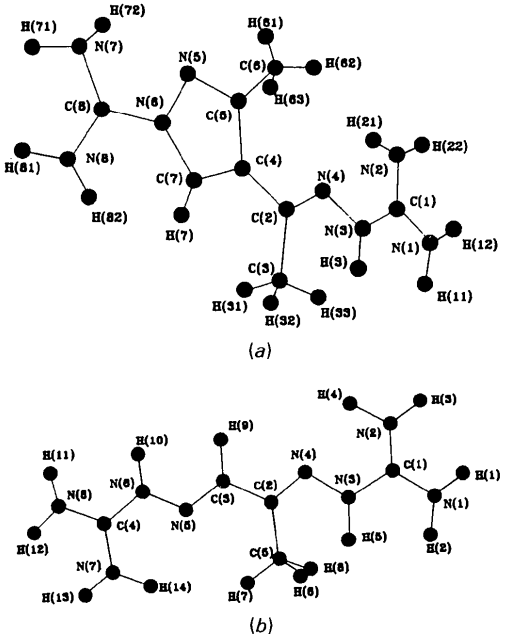


Fig. 1. Molecular structures of (*a*) $C_8H_{16}N_8^{2+}.2Cl^-.H_2O$ and (*b*) MGBG.

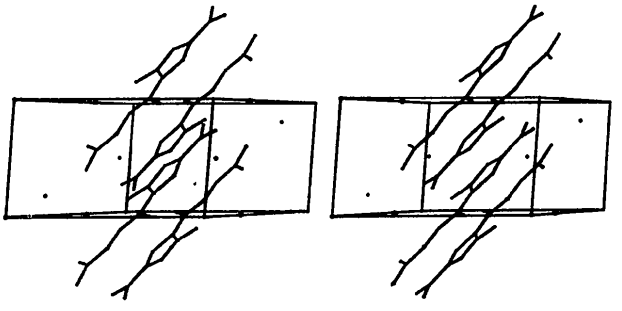


Fig. 2. Stereoscopic view of $C_8H_{16}H_8^{2+}.2Cl^-.H_2O$.

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